SYNTHESES OF ALKYLATED ALKANEDIOIC ACIDS[1]

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I. Introduction

The normal-chain aliphatic dicarboxylic acids are well-known substances, many of which occur naturally, and have found considerable technical application. Their branched-chain isomers, however, have received little attention until comparatively recently. This has been mainly due to their relative inaccessibility, for very few of these compounds have been reported to occur naturally and not many are commercially available.

Stimulated by the success of the unbranched dicarboxylic acids in the production of polymers and lubricants, investigations of the potential application of alkylated acids in like products have been reported (57, 168, 484, 583, 584, 736). By affecting the packing of the aliphatic chains (113, 339) the alkyl groups have been observed to modify profoundly the physical and chemical properties of the products. The physiological and potential chemotherapeutic properties of numerous derivatives have also been studied (125, 212, 470, 619). Several alkylated malonic acids are utilized in the production of barbiturates. In the field of structural studies, members of the branched-chain aliphatic dicarboxylic acid series have been encountered among the degradation fragments of natural products, such as camphor, carotenoids, and steroids, and the elucidation of many structures has depended upon the identification of these fragments. Interest in these acids as synthetic intermediates has recently been stimulated by studies of the lipids of the tubercle bacillus and of the macrocyclic components of the ingredients of natural perfumes.

The detailed chemical and physical characteristics of these acids, however, have been the subject of only a few isolated studies. This, together with the technical utilization of the branched-chain acids largely at an exploratory stage, renders a comprehensive review of the properties and applications of these acids premature. The authors, therefore, have limited themselves to a survey and discussion of the methods of synthesis only, hoping to be of assistance to those interested in these promising substances.

Though of simple structure, the branched-chain dicarboxylic acids present problems in synthesis. The classical methods of alkylation, chain extension, and introduction of carboxyl groups, used by earlier workers, have been rivaled by special methods relying on addition or condensation reactions in which these three processes occur simultaneously. Such methods avoid lengthy procedures and permit the utilization of a larger variety of starting materials. Indeed, instances of difficulties using classical methods of synthesis have been reported (202, 592, 678). An additional problem is introduced by the quaternary carbon atom in the synthesis of *gem*-dialkylated acids.

No complete review of the subject has appeared, but selected topics have been discussed previously. Thus, the problem of the quaternary carbon atom has been reviewed (75, 143) in connection with the synthesis of fatty acids. Some problems pertinent to the synthesis of branched-chain alkanedioic acids have been dealt with in reviews of name reactions (41, 120, 300, 509, 629), but these discussions have never been complete and often references to dicarboxylic acids have been omitted altogether. Recent reviews (112, 270, 290) on the chemistry

of fatty acids have included methods suitable for the preparation of certain types of alkanedioic acids. Of the more important procedures for the synthesis of branched-chain dicarboxylic acids, only the anodic synthesis has been recently reviewed (340, 717, 738; references 340 and 738 are to rather inaccessible publications). During the preparation of this manuscript a review (181) covering the literature to 1952 on certain alkylations appeared.

Since the point of branching in these compounds is frequently an asymmetric carbon atom, the task of preparation may not be complete once the synthesis has been achieved. The present article, therefore, includes methods for the separation and resolution of stereoisomers employed in such cases. The appendix contains tables of the known alkylated alkanedioic acids and some of their physical properties, together with references to satisfactory methods for their preparation.

The literature has been reviewed through Beilstein's *Lexikon der Kohlenstoffverbindungen* and *Chemical Abstracts* up to June, 1958; where possible the original articles have been consulted.

The acids of this series are known by a variety of names. The lowest members have derived their names from the natural sources from which their parent compounds were first isolated, the points of alkylation being indicated by numbers or Greek letters. For others, a system based on the longest alkane chain with the carboxyl groups as substituents has been in use for a long time. The authors of this review have used the International Union of Chemistry system of nomenclature throughout the article. Accordingly, the longest chain containing the two carboxyl groups was selected and the positions of the substituents indicated by numbers, designating one of the carboxyl carbon atoms as 1. Occasionally, departures from this style are made for convenience. The correspondence of these systems of nomenclature is indicated in table 1.

TABLE 1

Nomenclature of alkanedioic acids

Formula	Trivial Name	I.U.C. System Name	Name Based on Alkane Substitution System
$HOOCCH_2CH_2COOH$	Succinic acid	Butanedioic acid	1,2-Ethanedicarboxylic acid
$HOOCCH(CH_3)CH_2COOH$	Pyrotartaric acid	2-Methylbutanedioic acid	1,2-Propanedicarboxylic acid
$CH_3(CH_2)_{11}CH(COOH)CH(CH_3)COOH$	Roccellic acid	2-Dodecyl-3-methylbutanedioic acid	2,3-Pentadecanedicarboxylic acid
$HOOCCH_2CH_2CH_2COOH$	Glutaric acid	Pentanedioic acid	1,3-Propanedicarboxylic acid
$CH_3CH_2CH(COOH)CH_2CH(COOH)CH_2CH_3$	α,γ-Diethylglutaric acid	2,3-Diethylpentanedioic acid	3,5-Heptanedicarboxylic acid
$HOOC(CH_2)_4COOH$	Adipic acid	Hexanedioic acid	1,4-Butanedicarboxylic acid
$(CH_3)_2CH(COOH)CH_2CH_2CH(COOH)CH(CH_3)_2$	α,α'-Diisopropyladipic acid	2,5-Diisopropylhexanedioic acid	2,7-Dimethyl-3,6-octanedicarboxylic acid

II. Methods of Synthesis

A. Introduction of branching at points of junction of carbon chains

1. Reformatsky reaction

The Reformatsky reaction depends on interaction between a carbonyl compound, an α-halo ester, and activated zinc in the presence of an anhydrous organic solvent, followed by hydrolysis (629). The reaction is conducted in the same manner as a Grignard reaction except that the carbonyl component is added at the start. A mixture of benzene and ether has some advantages as a solvent for the Reformatsky condensation (148). Magnesium has been used in a few reactions in place of zinc but with poor results, for the more reactive organometallic reagent attacks the ester group. With zinc this side reaction is not appreciable, yet the reactivity is sufficient for addition to the carbonyl group of aldehydes and ketones. The product of the reaction is a β-hydroxy ester; this can be dehydrated to an unsaturated ester, which on catalytic hydrogenation yields the saturated ester.

α-Bromo esters of the types $RCHBrCOOC_2H_5$ and $RR'CBrCOOC_2H_5$ react satisfactorily, but β- and γ-bromo derivatives of saturated esters do not have adequate reactivity. γ-Bromocrotonates and certain substitution products thereof ($BrCH_2CH{=}CHCOOCH_3$, $BrCH_2C(CH_3){=}CHCOOC_2H_5$), however, have a reactive allylic bromine atom and enter into the Reformatsky reaction (5, 42, 259, 350). Such condensations involving methyl γ-bromosenecioate, for example, have been suggested for extending carbon chains by an isoprene unit and thus opening the way for the synthesis of truly carotenoid chains (262). A number of geranic acid derivatives have been prepared using these halo esters and the appropriate aldehydes (137).

Though the bromocrotonates have been condensed with aromatic and aliphatic carbonyl compounds they have not yet been applied directly to the synthesis of dicarboxylic acids; however, they are of potential importance in this field. A type of Reformatsky reaction takes place also between propargyl halides and a variety of carbinol compounds to give β,γ-acetylenic carbinols in fair yields (307). Thus, propargyl bromide (356) has been demonstrated to react with ethyl γ-ketopentanoate under Reformatsky conditions to give ethyl 4-methyl-4-hepten-6-ynoate. The reaction product of this unsaturated acid with ethylmagnesium bromide, after the evolution of ethane had ceased, on treatment with 4-octene-2,7-dione gave 3,7,12,16-tetramethyl-7,12-dihydroxy-3,9,15-octadecatriene-3,13-diyne-1,18-dicarboxylic acid. This substituted polyenedicarboxylic acid was not converted to the saturated derivative. Successful condensations of such halo compounds as bromomalonic ester (701, 702) and bromoacetonitrile (703) with benzaldehyde under Reformatsky conditions have also been reported. These reactions have not yet been extended to the aliphatic aldehydes and ketones. The experimental conditions and the possible reaction mechanisms for the Reformatsky reaction have been indicated earlier (629); hence only the more recent innovations of direct application to the synthesis of alkylated alkanedioic acid esters will be considered here. Among these the 10 to

30 per cent increase in yields with mixtures of copper and zinc (20, 320), the effectiveness of zinc and mercuric halides in the initiation of certain difficult reactions (263), as well as the dependence of the ratio of α to γ addition products on solvent temperatures (205, 350) in the crotonate additions, may be mentioned. It has been claimed that greatly improved yields are obtained if the reaction is carried out in dilute ethereal solution, first adding the aldehyde and the zinc and then gradually introducing the bromo ester (664).

Since in the preparation of dicarboxylic acids the unsaturated esters are desired, the crude Reformatsky product is dehydrated without isolation of the intermediate hydroxy esters. Most of the dehydrating agents described, such as acetic anhydride, acetyl chloride, phosphorus pentoxide, or sulfuric acid in moderate concentration (40, 68), are suitable for the introduction of unsaturation, since the proportion of α,β and β,γ unsaturation products is immaterial in these syntheses. The stereochemical aspects of the Reformatsky reaction have been studied recently (138, 139).

The Reformatsky process can be applied directly to the preparation of branched-chain dicarboxylic acids when dealing with aldehydes or ketones possessing a carboxyl function. Thus an aldehydo ester like $HCO(CH_2)_{11}COOC_2H_5$, obtained along with pelargonaldehyde on ozonization of brassidic ester (from rapeseed oil), in the Reformatsky reaction with ethyl α-bromopropionate (followed by dehydration, saponification, and hydrogenation) yields ethyl 2-methylpentadecanedioate (664).

Ethyl levulinate with halo esters yields substituted butyrolactones, and with ethyl chloroformate gives ethyl α-methyl-α-hydroxysuccinate (20). 6-Ketoheptanoic acid (553) and the appropriate halo esters under similar conditions gave after dehydration and hydrogenation diethyl β-methyl- (517) and α,α,β-trimethyl- (501) suberates, respectively. Likewise, the ethyl ester of 12-keto-1-tridecanecarboxylic acid, on treatment with bromoacetic ester and zinc, gave the hydroxy ester; hydrogenation of this ester gave 2-methyl-1,13-tridecanedicarboxylic acid (602). Additional branching of the carbon chain of the dicarboxylic acid may be introduced by the use of substituted keto esters. For instance, ethyl α,α-dimethyl-β-ketobutyrate with ethyl α-bromopropionate in the presence of zinc gave ethyl β-hydroxy-$\alpha,\alpha,\beta,\gamma$-tetramethylglutarate, which after conversion to the glutaconic acid derivative and catalytic reduction yielded the corresponding tetramethylglutaric acid (48). The use of an α-haloisobutyrate introduces a doubly methylated α-carbon atom (61).

Aliphatic diketones undergo the Reformatsky reaction, although different conditions may be necessary. 2,12-Tridecanedione and ethyl iodoacetate gave a dihydroxydiester which on dehydration, hydrogenation, and hydrolysis gave 2,12-dimethyl-1,13-tridecanedicarboxylic acid. Similarly, 2,11-dimethyl-1,12-dodecanedicarboxylic acid was obtained from 2,11-dodecanedione (480, 481), and ethyl bromoacetate was used to convert the appropriate diketones to 3,6-dimethylsuberic and 3,8-dimethylsebacic acids (124).

Monocarbonyl compounds may be converted to dicarboxylic acids provided they contain a second function for introduction of the second acid group. An

example of such a synthesis is the conversion of 2-pentenal, through a Reformatsky condensation with ethyl α-bromopropionate and oxalation of the unsaturated product, eventually to 2,6-dimethylsuberic acid (401).

It has been shown that formates and oxalates may function as carbonyl components in a Reformatsky synthesis. Ethyl α-bromoisobutyrate reacts with ethyl oxalate (569) and with ethyl formate (82), giving hydroxy esters which could be converted to 2,2-dimethylsuccinic and 2,2,4,4-tetramethylglutaric acids, respectively.

The application of the Reformatsky reaction to nitriles (154) leads to the formation of ketones in a manner comparable with the Grignard reaction and is a convenient method for the synthesis of β-keto esters.

By varying the nature of the carbonyl compounds and the halo esters employed, many alkylated dicarboxylic acids have been prepared with the help of this reaction, yet the possible products may be of only a few types. Branching is confined to the α- and β-positions at one or both ends of the chain, and while the α-position may bear one, two, or no alkyl groups, the β-position cannot bear more than one side chain.

Theoretically, in all of the above cases the ester groups of the final products may be converted into aldehyde or keto groups through the acyl chlorides and dialkyl metals (142).

A repetition of the Reformatsky process would lengthen the chain with or without further branching at the new points of junction of carbon chains (629).

2. Condensations with halo esters

A common side reaction in a Reformatsky condensation is the coupling of halo esters by zinc. This coupling process is an example of the Wurtz reaction and may be commonly effected by treatment of an alkyl halide (747) with one equivalent of sodium metal in dry ether. While the yields with primary halides may be fairly good, secondary and tertiary halides often give very poor yields.

Somewhat better results with halo esters containing secondary or tertiary halogen have been obtained by substituting finely divided silver for the alkali metal and raising the reaction temperature by varying or omitting the solvent. The yield of the coupling product is still low, and the usual by-products of the Wurtz-type condensations are observed. These include the saturated and unsaturated fatty acids and the unsaturated dicarboxylic acids corresponding to the halo ester used. For example, heating the ethyl ester of α-bromopropionic acid with finely powdered silver to 150–160°C. produces 2,3-dimethylsuccinic acid in low yield (306). A similar heating of ethyl α-bromoisobutyrate in the presence of dry silver powder gave trimethylglutaric acid as well as the expected tetramethylsuccinic acid (35). Boiling α-bromo- or α-iodopalmitic acid in heptane with finely divided silver gave ditetradecylsuccinic acid in 8 and 13 per cent yields, respectively (348).

Dialkyl sodium phosphite has also been observed to effect this type of condensation with halo esters in similar yields. Thus α-bromopropionate gave the two stereoisomeric forms of dimethylsuccinic acid. The α-bromocaprylate possibly gave the isomeric dihexylsuccinic acids (160).

The mechanisms of these coupling reactions are in doubt. Two general mechanisms have been proposed and experimental evidence is available in support of both (12, 122).

According to one of them, the Wurtz reaction proceeds through the intermediate formation of an organosodium reagent (416, 487). These reagents may be isolated in high yields on reaction of organic halides with finely divided sodium in inert organic solvents. Such separately prepared compounds undergo subsequent reaction with alkyl halides to produce the coupling product and the usually observed by-products of a normal Wurtz reaction. This coupling process has been described as a nucleophilic displacement on carbon. Thus, such organosodium compounds as the sodium enolates of aliphatic esters prepared from the corresponding esters and triphenylmethylsodium have been demonstrated to condense in fair yields with the α-halo derivatives of these esters. For example, the sodium enolate from ethyl isobutyrate reacted with the ethyl ester of α-bromoisobutyric acid, giving the diethyl ester of tetramethylsuccinic acid in 30 per cent yield (328). Yields as high as 64 and 80 per cent have been obtained by condensing benzylsodium, separately prepared, with 2-bromobutane and 2-bromoöctane, respectively (421). The formation of an intermediate organosodium derivative was also suggested to explain the coupling of halo esters observed in the presence of sodium dialkyl phosphite (160).

An alternative mechanism proposes that the metal reacts with the halide to produce the metal halide and a free radical, which subsequently undergoes coupling, disproportionation, etc. Although this free-radical mechanism has been convincingly demonstrated in the vapor phase (711), the evidence is not nearly so clear-cut for the liquid-phase Wurtz reactions. The reasoning in support of the free-radical mechanism for the Wurtz reaction is simply that the observed products correspond to those which have come to be expected from free-radical processes.

Evidence has now been obtained which indicates that free radicals play only a minor part in the formation of the usual Wurtz coupling and disproportionation products. From a careful study of a variety of Wurtz reactions it has been concluded (122) that these products are formed mainly by heterolytic reactions between metal alkyl and alkyl halide, and that the homolytic reaction with which they compete is appreciable only when lithium is used. The effect of substituting lithium and other metals on the yield of the simple Wurtz reaction has been studied (541).

In addition to these two mechanisms, the formation of the observed reaction products might also be explained as a result of a reductive condensation of the unsaturated fatty acid esters, formed by abstracting hydrogen halide from the halo esters by the active metal. Such an abstraction of hydrogen halide from the halo ester, followed by reduction of the unsaturated ester under the reaction conditions, has already been suggested (348) to account for the formation of the saturated fatty acid.

Reductive condensations of esters of α,β-unsaturated fatty acids have been described before (382, 386, 637, 698) and have resulted in similar low yields of the coupled product. A possible existence of an unsaturated intermediate capable

of reductive condensation involving the α-α, α-β, or β-β carbon atoms would also help to explain the formation of α,α,α'-trimethylglutaric acid (35), in addition to the expected tetramethylsuccinic acid, when the α-halo ester of isobutyric acid is treated with silver powder. This kind of mechanism is supported by the observation that such a coupling also takes place to a significant extent in the presence of agents like sodium dialkyl phosphite, which are better known as reducing agents rather than for their ability to form organometallic reagents (160).

Judging from the yields in the Wurtz-type coupling, the order of reactivity of the halo esters is iodo > bromo > chloro (348). The use of inert solvents, such as heptane, does not appear to exercise any important influence on the reaction process. Surprisingly, it does not matter whether the esters or the free halo acids themselves are used in the condensation (35), and the yields are generally low whether one works with large or with small quantities.

This type of reaction has so far been applied with some success only in the preparation of dialkyl and tetraalkyl derivatives of succinic acid. That it may be capable of further extension to other than α-halo esters is indicated by the success observed with higher alkyl primary halides in the simple Wurtz reaction. Since dicarboxylic acids are usually relatively easy to isolate from the reaction mixture, the by-products should not present the usual difficulties.

A reaction analogous to these condensations with halo esters takes place in the presence of magnesium, and may be considered to proceed through the alkylation of Grignard reagents. For example, esters of α-bromobutyric acid in the presence of esters of butyric acid in contact with magnesium give α,β-diethylsuccinates in two isomeric forms in small yields (479). Somewhat better yields of the succinic acid derivatives have been obtained by adding cupric chloride as soon as a vigorous reaction between the α-bromobutyric ester and magnesium had set in (689). The success or failure of such couplings cannot be predicted with any degree of certainty. Thus, while similar reactions with bromoacetic ester or β-iodopropionic ester failed to give the expected succinic or adipic esters (the iodopropionic acid, for instance, being isolated unchanged), certain other primary (265) and tertiary (731) magnesium bromides could be coupled in 42 and 19 per cent yields, respectively, by using silver bromide. The effect of these halides upon the Grignard reagents is believed to be exercised through an intermediate formation of the organocopper or organosilver compounds, which are relatively stable at low temperatures and may bring about the observed modification of the Grignard reaction (372). The Wurtz type of Grignard reagent coupling is known (325, 519) to become increasingly more important as higher aliphatic halides are involved and may under certain conditions account for 70 to 80 per cent of the halide (424). The yields of the coupling products have also been shown to increase when the halogen occupies an alkyl position, as in isobutenyl bromide (543, 729, 735). Wurtz coupling of Grignard reagents has been claimed to be accentuated by the use of 1,2-dimethoxyethane instead of diethyl ether (64).

The reaction mechanism here again might be interpreted in several ways,

the difference in behavior of Grignard reagents and organoalkali compounds probably being due to the much higher polarity of the carbon–metal linkage, with the organoalkali reagent functioning as a more effective nucleophilic agent (372).

Both types of halo ester condensations give yields which are high enough to be of use in synthesis only when the halogen is in the α-position or otherwise activated. They are of importance in that they open routes to compounds difficult to make by other means and have been employed for many years.

3. Alkylation of active methylene or methinyl positions

A number of methods of some flexibility in the preparation of alkylated dicarboxylic acids involve the alkylation of active methylene or methinyl units of active hydrogen compounds. These procedures have provided the basic classical means for alkylation and are of two main types.

The aldol type of alkylation involves an initial condensation of an aldehyde or ketone and such very active hydrogen compounds as malonic, cyanoacetic, and acetoacetic esters, followed by further chemical modification to convert them into saturated alkylated dicarboxylic acids.

The other type of alkylation is based upon an acylation or alkylation of the active methylene or methinyl unit, using esters or halogen-containing compounds.

Both of these types of alkylation have been extensively used in the preparation of branched-chain dicarboxylic acids, but since only one or two methylene or methinyl units may be introduced at a time into a given carbon chain, the process is not very effective in the preparation of the higher polyalkylated dicarboxylic acids. The large number of steps that may be necessary reduces the overall yield, and the reaction products, differing little among themselves and from the starting materials in their chemical and physical characteristics, are difficult to separate and purify. Therefore, these methods are really effective only when short-chain alkylated dicarboxylic acids are prepared or when the long-chain dicarboxylic acids have to be alkylated only once at one or both ends of the carbon chain. They include the only important methods of making alkylated malonic acid derivatives.

(a) Aldol-type alkylations

Aldehydes condense with malonic acid or malonic esters under the general conditions of the Knoevenagel reaction (199, 380, 536). The experiment may be conducted under a water separator to increase the yield of product in accordance with the law of mass action.

Aliphatic aldehydes do not usually give good yields of alkylidenemalonic esters by this type of condensation because of a marked tendency of their initial product to react further with malonic ester. Acetaldehyde, for instance, reacts with malonic ester in the presence of diethylamine or piperidine to give both ethylidenemalonic ester and ethylene bismalonic ester (379). Other aliphatic aldehydes react similarly with malonic esters (97). By adjusting the experi-

mental conditions, however, the reaction may be made to yield either the initial or the secondary condensation product (the glutarate) in preference (136).

If the formation of the unsaturated esters is desired, the use of acetic anhydride as the condensing agent is recommended and methylenemalonate (135) has been prepared in 40 per cent yield under acid conditions.

While the hydrogenation of alkylidenemalonates gives derivatives of alkylmalonic acids (739), addition of cyanide results in products which may be converted to alkylated succinic acids (410, 571). Cyanoacetic acid and its esters react with aldehydes very much as do malonic acid and the malonates, giving the primary and secondary condensation products (585). Under suitable conditions, one or the other reaction product may be made to predominate. For example, good yields of substituted tricarboxylates could be obtained by reducing the primary condensation products of certain substituted carboxyaldehydes and ethyl cyanoacetate (712, 713, 714). Decarboxylation of the derived polycarboxylic acids gave the corresponding substituted dicarboxylic acids.

The hydrolysis of the hydrogen cyanide addition products of the alkylidenemalonates or alkylidenecyanoacetates has been known as a convenient method for the synthesis of substituted succinic acids (16, 410).

A very useful modification (635) of the Lapworth–McRae procedure is the addition of the potassium cyanide simultaneously with the formation of the alkylidenecyanoacetate, so that the equilibrium condition in the formation of the alkylidenecyanoacetate is displaced in the desired direction through the combination of the alkylidenecyanoacetate with potassium cyanide. It has also been demonstrated recently (622) that there is no need to isolate the intermediate cyano esters, but that the crude reaction products are suitable for direct hydrolysis with hydrochloric acid to the appropriate succinic acids.

Instead of adding the hydrogen cyanide to the alkylidenecyanoacetic esters, the hydrogen cyanide may first be added to the aldehyde or ketone and then the cyanohydrin reacted with the cyanoacetic ester (50, 63, 312, 431, 552). In all of these cases the yields average about 50 per cent.

Ketones do not undergo simple Knoevenagel condensation with malonic acid or its esters; they do, however, condense with the methylene units of cyanoacetic acid, its esters, and its amide. In the presence of ammonia, ketones condense with cyanoacetates to give the Guareschi product (a cyclic dicyano-imide) (216, 287, 288, 574). A similar condensation occurs between ketones and cyanoacetamide in aqueous solution in the presence of a small amount of piperidine or alkali. This procedure has also been adopted in the preparation of β-alkylglutaric acids from aldehydes and cyanoacetamide (366).

The value of the reaction lies in the fact that the condensation product can be hydrolyzed to a β,β-disubstituted glutaric acid. There appears to be a set limit to the general applicability of these methods. They succeed only with dimethyl or methyl alkyl ketones (75). Thus, ethyl *n*-decyl ketone does not undergo the Guareschi reaction, nor can it be condensed with cyanoacetamide in the presence of piperidine.

Ethyl *n*-decyl ketone, as well as many other ketones, does, however, condense

with cyanoacetic acid or its esters under the conditions specified by Cope (178, 180, 565), giving the corresponding alkylidenecyanoacetates, which, on addition of hydrogen cyanide, may be converted to the appropriate succinic acid derivatives. These conditions are also the best for the condensation of methyl ketones with cyanoacetic ester, but the condensation products cannot be hydrolyzed to the substituted glutaric acids. Yields of 60 to 80 per cent are readily obtained, except when cyanoacetic acid is used. The latter products are readily thermally decarboxylated with the formation of unsaturated nitriles (420). Certain alkenylcyanoacetic esters, $RCH{=}C(R')CH(CN)COOC_2H_5$, derived in excellent yields by the condensation of ketones, RCH_2COR', with cyanoacetic esters, are alkylated to produce (dialkylvinyl)alkylcyanoacetic esters, $RCH{=}C(R')C(R'')CNCOOC_2H_5$. The yields are highest when sodium isopropoxide in isopropyl alcohol is employed as the condensing agent (179). The double bond may then be utilized as mentioned above, for the introduction of the second carboxyl group.

Alkylidenecyanoacetic esters may be converted into saturated dicarboxylic acids also by reductive dimerization, giving the difficultly obtainable acids incorporating two adjacent doubly alkylated carbon atoms. In this way, $\beta,\beta,\gamma,\gamma$-tetramethyladipic acid (698) can be prepared by reductive condensation of isopropylidenecyanoacetic ester in the presence of moist aluminum amalgam. Though the yield is only about 8 per cent, it is the highest yielding method yet described for the preparation of acids of this type. Similarly, ethyl propylidenemalonate has been reduced to a mixture of substances from which the ($\pm$) and the meso forms of β,γ-diethyladipic acid could be isolated (386).

Aldehydes undergo condensation also with such active hydrogen compounds as acetoacetic ester and 1,3-diketones. The characteristics of these condensations are very similar to those of the malonic ester condensations discussed above. Thus, aliphatic aldehydes show a great tendency to produce alkylidenebisacetoacetic esters (321, 322). Since with suitable control of the experimental conditions the reaction can be directed to give principally the alkylidenebisacetoacetic esters, this would be a profitable route to the polyalkylated glutaric acid derivatives if the β-keto esters could be reduced (75).

Though ethyl cyanoacetate has been reduced to ethyl butyrate, the *C*-di-*n*-nonyl derivative was found to be highly resistant to reducing agents and was recovered unchanged. It was suggested that the neighboring alkyl chains protect the carbonyl group.

Though the α,β-unsaturated aldehydes usually undergo the Knoevenagel-type condensation with active methylene compounds, the simplest α,β-unsaturated aldehyde, acrolein, undergoes the Michael condensation (712, 713). In addition to acrolein, there are other α,β-unsaturated carbonyl compounds which accept a conjugate addition of an active hydrogen component. Among the acceptors in this type of aldol condensation which are of interest in the synthesis of dicarboxylic acids, the α,β-unsaturated ketones, esters, amides, and nitriles may be mentioned. The condensation of tiglic ester and cyanoacetic ester, followed by methylation, for example, gave α,β,γ-trimethylglutaric acid

(464, 570). The corresponding substituted glutaric acid derivative was also obtained from the condensation of ethyl γ-methyldihydrosorbate and sodiomalonic ester (532).

The ketones are more reactive than esters, which in turn are more reactive than nitriles (173). Substitution on the methylene unit of an addendum molecule, such as malonic ester, generally results in lowered activity towards a given acceptor. This may be overcome by the introduction of the alkyl substituent after the initial condensation. In this way propylidenedimalonic ester was alkylated with ethyl iodide to give the tetraethyl ester of 1,2,3-triethyl-1,1,3,3-tetracarboxypropane, which with hydrogen chloride gave the corresponding α,β,γ-triethylglutaric acid (387). A similar steric effect is also observed with substituents on either the α- or the β-carbon atom in the acceptor (264).

In most cases, both the normal and the abnormal addition products in the Michael condensation may be converted to the corresponding alkylated dicarboxylic acids by standard methods. Thus, the abnormal Michael product, resulting from the condensation of ethyl crotonate and methylmalonic ester in the presence of one equivalent of sodium ethoxide, on saponification and decarboxylation gave α,β-dimethylglutaric acid (463). Methylation of the tricarboxylic acid intermediate resulted finally in the formation of α,β,γ-trimethylglutaric acid. The normal addition product also gives the α,β-dimethylglutaric acid, but the intermediate tricarboxylic acid in this case can not be methylated by sodium and methyl iodide (318, 463). The normal addition products of ketones and active dicarbonyl compounds, instead of condensing with another mole of dicarbonyl compound, may condense with some other active hydrogen compound. For example, ethyl isopropylidenecyanoacetate may add a mole of nitromethane (118). The condensation product may then be hydrolyzed to α,α-dimethylsuccinic acid in low yield.

Longer conjugated systems have been observed to undergo 1,6-addition of the Michael type (214, 215). The effect of solvents on the ability of a carbonyl compound to undergo the Michael condensation and *C*-alkylation has been studied (506).

A special case of the Michael condensation involving an α,β-unsaturated carbonyl compound is the cyanoethylation reaction (450). It has been utilized in the preparation of α-substituted glutaric acid derivatives from monoalkyl malonates or cyanoacetates and acrylonitrile (17), methyl, ethyl, propyl, and butyl derivatives being prepared in good yields. 2-Alkylaldehydes have been successfully condensed with acrylonitrile in the presence of potassium hydroxide or sodium cyanide (121, 242). Oxidation by potassium permanganate and acid hydrolysis of the product gave the corresponding α,α-dialkylglutaric acids. Condensation of acrylonitrile with monosubstituted β-keto esters gives α-alkyl-α-(2-cyanoethyl)acetoacetates, which on acid hydrolysis with concentrated alkali give the α-substituted glutaric acid derivatives (467, 473).

The keto dinitriles resulting from an alkaline condensation of ketones with acrylonitrile have apparently not been reduced and hydrolyzed to the appropriate γ,γ-dialkylpimelic acids.

Since cyanoethylation usually proceeds until all available active hydrogen is used up, these reactions often give better yields with substituted starting materials having a more limited number of available hydrogen atoms. Under suitable conditions, substituted and unsubstituted acrylates may condense with themselves or with other alkylated or unalkylated unsaturated fatty acids. For example, at 245–300°C. and preferably in the presence of some polymerization inhibitor, alkyl-substituted or unsubstituted 5-hexenoic acids or esters condense with acrylic or methacrylic acid or their esters to give unsaturated substituted dicarboxylic acids, which on hydrogenation give the saturated derivatives. In this way 5-methylnonanedioic and 2,5,8-trimethylnonanedioic acids were prepared in good yields (7). Under reductive conditions (186), self-condensation of methyl 2-*tert*-butylacrylate gave a head-to-head dimer which could be hydrolyzed to 2,5-di-*tert*-butyladipic acid.

A special extension of the Michael condensation occurs when butyraldehyde reacts with its self-aldolization product (302). The glutaraldehyde derivative initially formed appears to undergo an unexpected intramolecular Cannizzaro reaction, and the product isolated was the corresponding lactone. Upon hydrolysis and oxidation α,γ-diethyl-β-propylglutaric acid resulted.

Aldehydes and ketones in the presence of alkoxides undergo an aldol-type condensation also with succinic esters (531, 739). This reaction, known as the Stobbe condensation (342), has been successfully applied to the preparation of alkylated succinic acid derivatives. The alkylidene derivatives prepared from the required ketones and diethyl succinate on saponification followed by hydrogenation give the α-alkylsuccinates in good yields. A great variety of alkenyl-, alkylidene-, and dialkylidenesuccinic acids has been prepared (346), only a few of which have been actually reduced to the corresponding succinic acid derivatives. But since no difficulties in reduction have been reported, these intermediates may be considered as potential sources of alkylated succinic acids. The proportion of mono- to disubstituted products depends to a considerable extent upon the experimental conditions and the ratios of reactants, low temperatures favoring the disubstituted products. Use of sodium *tert*-butoxide and sodium hydride has given higher yields than the conventional sodium ethoxide (346). As potential sources of substituted dicarboxylic acids one may also consider the substituted glutaraldehydes, obtained in good yields by condensing alcohols with α-methylenealdehydes in 1:2 to 1:10 molar ratios under anhydrous conditions (633).

An aldol-type condensation also occurs between aldehydes or ketones and α-halo esters, producing glycidic esters (509). Though the esters of diketones and α-halo esters might be considered as potential sources of alkylated dicarboxylic acids, the use of this rather difficult reaction appears to offer no particular advantage over the simpler and better known condensations.

(b) Acylations and alkylations

A number of alkylation reactions depend upon an initial replacement of an active hydrogen by an acyl group, followed by reduction to the alkyl derivative.

This type of acylation may be brought about by an ester, an anhydride, or an acyl chloride (301).

Among the base-catalyzed acylations of active hydrogen compounds, through the agency of esters as acylating agents, there are several special cases of interest for the synthesis of substituted dicarboxylic acids. Diethyl oxalate has been condensed with a number of aliphatic esters to afford the mixed condensation products in high yield (300). The basis of this ready applicability to the synthesis of dicarboxylic acids is the easy thermal elimination of carbon monoxide which these keto acids undergo (185). This reaction has been used to prepare monosubstituted malonic esters which are not available by direct alkylation of the malonic ester. The high yields observed and the absence of contamination with the dialkylation product have made it the method of choice in a large number of preparations (31, 185, 233). The acylation products of diethyl oxalate may be further alkylated by alkyl halides. Thus diethyl sodioethoxalylsuccinate has been condensed with ethyl bromide and the product hydrolyzed to ethylsuccinic acid in 90 per cent yield (432).

The higher aliphatic esters do not give good yields of ethoxalyl derivatives on reaction with diethyl oxalate under equilibrium conditions, but by forcing the reactions, yields of 80 to 90 per cent of the ethoxalyl compounds may be obtained (234).

Diethyl carbonate also condenses with other esters possessing α-hydrogen atoms. Monosubstituted malonic esters result from the condensations, in yields of 25 to 60 per cent (708). The reaction is performed with equimolar proportions of the ester and sodium ethoxide with excess diethyl carbonate, while the ethyl alcohol formed in the reaction is continuously removed by distillation. The principal side reaction with aliphatic esters, also of interest to the synthesis of branched-chain dicarboxylic acids, is a further alkylation of the monoalkylmalonic ester by diethyl carbonate, giving the dialkylmalonate.

Alkyl isobutyrates and isovalerates also do not undergo self-condensation in the presence of sodium alkoxides, despite the fact that they possess α-hydrogen atoms, and may be used successfully as acylating agents for other aliphatic esters (589). The products are branched keto esters, and the applicability of such condensations in synthesis is limited by the absence of satisfactory procedures for reducing the β-keto group.

The Claisen condensation of aliphatic esters with nitriles, giving good yields with aromatic esters, has often resulted in polymeric products when carried out in the presence of the usual base catalysts (399). The use of sodium amide (425), however, has given satisfactory yields with aliphatic esters and at least acetonitrile. The resulting β-keto nitriles may then be further alkylated by other means to give the substituted ketones, the cyanohydrins of which, isolated as the acetates, can be pyrolyzed to the corresponding alkylated unsaturated dinitriles (63). Hydrolysis and reduction give the appropriate succinic acids. The necessary substituted β-keto nitriles for this synthesis may also be prepared by the dimerization of aliphatic nitriles in the presence of sodium followed by subsequent alkylation and careful partial hydrolysis (475).

Condensation of nitriles with an excess of diethyl carbonate in the presence of sodium ethoxide produces α-cyano esters (707). The alcohol formed during the reaction is distilled out with the excess diethyl carbonate. While acetonitrile affords only a 10 per cent yield of ethyl cyanoacetate, the higher aliphatic nitriles have been observed to give good to excellent yields.

Acylation of the metal salts of 1,3-dicarbonyl compounds with acyl chlorides (437) is also of potential interest in the preparation of alkylated dicarboxylic acids, if satisfactory procedures can be developed for the reduction of β-keto esters. The acylation of diazoalkanes by acyl chlorides (41), however, has found some application in the preparation of alkylated dicarboxylic acids. While the simplest diazoalkane, diazomethane (155, 482, 483, 678), effects only an extension of the carbon chain, the use of diazoethane (49) introduces also a methyl branch. Should this reaction prove to be capable of extension to other higher diazoalkanes, it would provide an effective general method for the synthesis of α-alkylated dicarboxylic acids.

In the preparation of branched-chain dicarboxylic acids the alkylation of the metal salts of active methylene or methinyl compounds by alkyl monohalides (151, 411, 518, 572, 582, 690), alkyl dihalides (58, 59, 163, 219, 241, 293, 510, 522, 657), and halo esters (25, 27, 164, 254, 433, 447, 459, 609, 686) has been most often used. These have been the classical procedures with the help of which most of the now known alkylated dicarboxylic acids have been prepared. Though simple and relatively high yielding, these procedures are capable of producing only certain types of alkylated dicarboxylic acids.

The alkylation of 1,3-dicarbonyl or equivalent systems, such as (181) malonic, cyanoacetic, and β-keto esters or their monoalkylation products, is usually accomplished by first converting these compounds into the corresponding anions and adding the alkyl halide. Good yields of monoalkylated products are usually obtained, but dialkylation using sodium alkoxides gives only 35 to 40 per cent yields. Superior yields of the dialkylated derivatives, however, may be obtained by alkylating the monoalkyl derivatives in *tert*-amyl alcohol with potassium *tert*-amyl oxide (576). The di-*n*-butylacetoacetic ester, for example, was prepared by this procedure in 70 per cent yield. This method gives also better yields with the monoalkyl derivatives, particularly with secondary alkyl halides. Isopropylacetoacetic ester, for instance, could be prepared in 50 per cent yield by this method. Sodium *tert*-butoxide is also claimed (695) to improve the yields in difficult alkylations of malonates.

When the methylene or methinyl unit comes from acetoacetic ester the alkylation product should be subjected to hydrolysis by concentrated alkali to effect the acid cleavage, with removal of the keto function. Actually it is best to avoid the use of acetoacetic ester in these alkylations, because even with concentrated alkali the acid and the ketone types of cleavage are competing reactions and may cause low yields of the desired products (577). It is better to use malonic or cyanoacetic esters, since only one mode of cleavage of an alkyl- or dialkylmalonic ester is possible.

As the alkylation of the active hydrogen compounds with an alkyl halide

involves a nucleophilic displacement at a saturated carbon atom, the usual limitations are placed upon the alkyl halide that can be successfully used (329, 588). In general, only the primary halides of the type RCH_2CH_2X may be used with good results. Secondary halides give poorer results, especially when branching occurs in the 2-position. Vinyl and tertiary halides are unsuitable.

Since some dialkylation unavoidably occurs during attempted monoalkylation of malonic or cyanoacetic esters, it is advisable in the preparation of dialkylmalonic acid derivatives containing two different alkyl groups to introduce the larger group first (411). The lower alkyl and dialkyl derivatives boil rather close together, so that it is difficult to purify the monoalkylation product. However, since alkyl groups diminish acid strength and since a large alkyl substituent may sterically hinder further alkylation, the second substitution step does not proceed as readily as does the first, and it has often been found that better yields, though of products with lower purity, are obtained when the smaller alkyl group is introduced first and the second alkylation performed on the monoalkyl-1,3-dicarbonyl compound (151, 219, 293, 657). If one-step dialkylation is desired, sodium hydride (611) is the preferred reagent.

A special case of a secondary halide alkylation is the use of α-halo esters (other than esters of haloacetic acid) (447, 459, 609) in the alkylation of active hydrogen positions in 1,3-dicarbonyl compounds. No unusual difficulties comparable to those encountered with secondary alkyl halides have been observed when alkylating esters of cyanoacetic acid with α-bromo fatty acids (189, 459, 722). About 70 per cent yields have been realized in a number of cases, and this method of synthesis has been used extensively in the preparation of higher monoalkylsuccinic acids from the readily available α-bromo fatty acids and 1,3-dicarbonyl compounds. The condensation of these halo esters with the alkylated dicarbonyl compounds (25, 27) has been observed to be somewhat more difficult, but this problem may be solved by first reacting the halo ester with the unsubstituted dicarbonyl compound and then introducing the second alkyl group by alkylation of the sodium salt of the initial alkylation product (447). Besides the α-halo esters, the β- (607) and δ- (141) halo esters have been used in the alkylation of malonic ester derivatives. The alkylation of 1,3-dicarbonyl compounds by ω-halo esters differs little from the alkylation of these substances by primary alkyl halides. Thus, the alkylation of acetoacetic ester with ethyl chloroacetate affords ethyl acetosuccinate (3), which on methylation followed by hydrolysis with concentrated alkali gives methylsuccinic acid (398).

The use of cyanoacetic esters in these alkylations of halo esters is preferred. With malonic esters extensive dehydrohalogenation of the α-bromo esters has been occasionally observed (94, 609), giving a derivative of glutaric acid as the main product. This phenomenon is particularly pronounced when tertiary halides in the form of α-bromo esters react with monoalkyl sodiomalonates of low molecular weight (609). Depending on the starting materials and the reaction conditions either the glutarate or the more obvious product, the succinate, may predominate, and reactions of this description have been used for the preparation of compounds of both types (331, 726). The yield of the succinic acid de-

rivative may be increased by using the cyanoacetic ester and introducing the second alkyl group after the alkylation of the halo ester has already been effected (447, 609). Some experimental results (412) indicate that the use of hydrocarbon solvents might decrease the extent of dehydrohalogenation and consequently produce less of the glutarate isomer.

Certain simple ketones may be alkylated by means of alkyl halides in the presence of sufficiently powerful basic catalysts. The scope of this reaction has been investigated, and it has been found to be one of the most useful methods for the preparation of $\alpha,\alpha,\alpha',\alpha'$-tetraalkylalkanedioic acids (1, 132, 295). Thus, isobutyrophenone in the presence of sodium amide reacts with alkyl dihalides to give the dibenzoyldimethylalkanes, which may be decomposed to the diamides of the corresponding tetramethyldicarboxylic acids. In this way all the $\alpha,\alpha,\alpha',\alpha'$-tetramethyl dibasic acids from adipic acid to the tetradecanedioic acids have been prepared (1). It appears that this method should be capable of extension to other alkyl isobutyrophenones to give the corresponding tetraalkylalkanedioic acids.

A somewhat simpler method, but one of wider potential application in the synthesis of alkylated dicarboxylic acids, is the alkylation of aliphatic nitriles by alkyl halides in the presence of sufficiently powerful bases (618, 645). For example, acetonitrile has been alkylated to triethylacetonitrile by an excess of ethyl bromide and sodium amide. The reaction does not need to be carried out under pressure, as even at the boiling point of ethyl bromide the yield of triethylacetonitrile is good. Other aliphatic nitriles behave similarly. Certain unsaturated nitriles are prepared by alkylation at the allyl position of β,γ-olefinic nitriles like vinylacetonitrile and 3-ethyl-3-pentenonitrile (732). Other olefinic nitriles may be obtained by the alkylation of malononitrile with unsaturated halides (182).

The points of unsaturation can then be utilized for the introduction of the second carboxyl group with or without additional branching. A variety of cases of the direct alkylation of aliphatic nitriles has been recently summarized (704).

A satisfactory method for the hydrolysis of these highly hindered nitriles or amides has been developed by their reaction with alkyl nitrites in organic solvents in the presence of gaseous hydrogen chloride (645). The excellent yields observed with a number of aliphatic nitriles recommend this method as a potentially useful tool for the preparation of polyalkylated dicarboxylic acids.

Besides the tertiary alkyl aryl ketones and aliphatic nitriles, the esters of certain aliphatic acids have also been successfully alkylated under the above conditions. Thus, trialkylacetic esters have been prepared in good yields by the alkylation of triethylcarbinyl esters of dialkylacetic acids by means of sodium amide and an alkyl halide. The success of this method is thought to depend on hindering the usual attack of the amide ion at the carbonyl carbon of the dialkylacetic acid by the tertiary alkoxy group, thus permitting the preferential ionization of its α-hydrogen as required for alkylation. The hydrolysis of the hindered esters was observed to be readily effected by refluxing with hydrochloric acid in dioxane.

Potassium hydroxide in acetal solvents may also serve as an effective basic reagent in the alkylation of certain esters by reactive halides, and these conditions have also been used in Michael additions (724). Liquid ammonia (24) is recommended as a solvent for alkylations catalyzed by alkali hydroxide.

An interesting preparation of tetramethylsuccinic acid involves the alkylation of ethyl isobutyrate with ethyl α-bromoisobutyrate. The yield was 30 per cent (328). A number of succinic acid derivatives have been prepared (9, 10, 317, 452) by the reaction of monoalkynes with maleic anhydride and fumaric esters. This, an extension of the pseudo Diels–Alder reaction (317), takes place under conditions much more vigorous than those employed for typical Diels–Alder reactions. The reaction in this case is one of substitution rather than addition. The intermediate alkenyl derivatives prepared by heating the starting materials at 180–250°C. for several hours are converted to the corresponding saturated derivatives by hydrogenation and opening of the anhydride ring. Acetoacetic ester, malonic ester, and similar compounds containing active hydrogen may also be alkylated by means of ethylene oxide (275) and by quaternary ammonium salts (39, 114, 638).

4. Syntheses using organometallic reagents

Certain syntheses utilizing organometallic reagents directly (halo ester condensations) and as intermediates (Reformatsky reaction) in the reaction process have been already mentioned.

(a) Reactions with carbon dioxide

Treatment of a Grignard reagent with carbon dioxide gives the magnesium salt of a carboxylic acid. In order to inhibit secondary reactions leading to the formation of ketones and tertiary alcohols, it is desirable to have carbon dioxide present in excess and to effect the addition at a low temperature (90, 337). Both requirements are met quite simply by pouring the solution of the Grignard reagent on to dry ice (227, 273). Carbon dioxide under pressure is sometimes required for the preparation of tertiary Grignard reagents (419). By using one or the other of the above techniques 50 to 85 per cent yields of the carboxylic acids have been obtained. When dealing with labeled carbon dioxide even such yields may be found unsatisfactory. The high-vacuum technique developed for the conservation of isotopic carbon dioxide during the carbonation of a Grignard reagent is capable of giving 85 to 95 per cent yields (417, 590).

It should be pointed out that this method has advantages over nitrile synthesis, which is applicable only to the primary halides if reasonable yields are to be expected (493). Sodium cyanide, being a strongly basic reagent, on reaction with secondary and particularly the tertiary halides gives mostly olefins rather than cyanides. Of the other organometallic reagents the lithium derivatives have been the most popular and have also given carboxylic acids on carbonation under suitable conditions (274).

Adaptation of the carbonation of an organometallic reagent to the preparation of branched-chain dicarboxylic acids would require the use of either di-

Grignard reagents prepared from branched-chain alkyl dihalides or mono-Grignard reagents already possessing an actual or potential carboxyl group. Normal-chain alkyldimagnesium halides have been shown to give good yields of dicarboxylic acids on reaction with carbon dioxide. Complications, however, may arise, and instead of the corresponding dicarboxylic acid, coupling and/or cyclization products may be formed (507). Thus, trimethylene dibromide has given suberic acid (755), while sebacic acid and an acid with fourteen carbon atoms were obtained from 1,4-dibromobutane in a similar manner (109), the principal product being the cycloalkanone. Dicarboxylic acids have also been obtained from 1,5-dibromopentane, 1,7-dibromoheptane, and 1,10-diiododecane (282). When the Grignard reagents from β-acetylenic bromides were carbonated, allenic acids were found in the reaction product (195).

Selection of suitable reaction conditions usually results in improved yields of the desired product. The carbonation of a bifunctional bromomagnesium enolate of 1,4-dimesitoylbutane gave 2,5-dimesitoyladipic acid in good yield (260). Under similar conditions the dimagnesium derivatives of 1,4-dibromobutane, 1,5-dibromopentane, and 1,6-dibromohexane were also shown (261) to give mainly the normal addition products.

The preparation of certain difunctional Grignard reagents capable of carbonation to alkylated dicarboxylic acids has been recently disclosed in the patent literature (512). The formation of these reagents is based on unsaturated compounds. In this way butadiene gave a mixture of bis(chloromagnesium)octadienes which on carbonation yielded 28 parts of sebacic acid, 42 parts of α-ethylsuberic acid, and 40 parts of α,α-diethyladipic acid. Recent patent literature also reports the preparation of other olefinic Grignard reagents such as the vinylmagnesium chloride complexes and similar complexes from dichloropropene (462). These compounds also undergo most of the characteristic reactions of Grignard reagents and may be of potential use in the synthesis of carboxylic acids.

There are some results, however, to indicate that the Grignard method may not be as general as formerly supposed. Thus, for tertiary acids above dimethylethylacetic acid, carbonation of the appropriate Grignard compounds is not generally utilizable, since such reagents prepared from higher halides usually react abnormally, yielding mixtures of alkanes and alkenes (618). Also, the Wurtz type of Grignard reagent coupling is known to become increasingly more important as higher aliphatic halides are involved.

The carbonation of Grignard reagents possessing a carboxyl function cannot be realized, because experimental conditions suitable for the preparation of such reagents, as from the halo esters, have not been developed. Under ordinary conditions the Grignard function interacts with the ester group. Protection of such ester or other active groups from the Grignard function by the introduction of shielding structures has met with some success. For instance, several sterically hindered keto Grignard reagents have been prepared (64, 512, 623) and shown to react without attacking the keto group.

The extent to which 1,2-addition (to the carbonyl group) takes place is also

determined by the nature of the alkoxy group. Large groups at the carbonyl carbon atom, such as the *sec*-butyl group, reduce the yield of the 1,2-addition product (389, 498). The relative absence of interference of the Grignard reagent with the ester or cyano groups during the addition of Grignard reagents to 2-cyano-3-methyl-3-pentenoate has also been attributed to steric shielding (555).

Although the Reformatsky reaction is often pictured to proceed through an organometallic intermediate similar to that of the Grignard reagent, such organozinc halides have not yet been reported to undergo carbonation.

(b) Reactions with ketones

The reaction of Grignard reagents with keto esters has been used extensively in the preparation of branched-chain fatty acids (446). The tertiary alcohols obtained may be dehydrated by boiling with iodine. The unsaturated esters produced are then hydrogenated catalytically. Streamlining of the Grignard reaction by an extraction method has been reported (742).

The addition of Grignard reagents to the levulinates (146, 429) produces the γ-alkanolactones, which may be decomposed to the 4-alkyl esters with thionyl chloride and ethanol saturated with hydrogen chloride. In most experiments the yields have been of the order of 30 per cent or less. However, yields as high as 70 to 80 per cent may be obtained by carrying out the reaction at 0°C. and adding sufficient benzene to dissolve the ether-insoluble reaction product.

The above γ- and δ-lactones, prepared similarly from suitable keto esters, may be converted to the appropriate dicarboxylic acids by reaction with an alkali cyanide and subsequent hydrolysis of the γ- or δ-cyanocarboxylic acids.

Grignard reagents have also been demonstrated to give tertiary alcohols with keto dicarboxylic acids. For example, isobutylmagnesium bromide has been shown to yield the corresponding hydroxy dicarboxylic acid ester with α-acetyl-α-methylsuccinic acid ester (683). Several esters of hydroxyaryl dicarboxylic acids have also been obtained by reacting the arylmagnesium bromides with diethylmesoxalic acid. The yields in these cases varied from 25 to 40 per cent. Although such reaction products should yield alkylated dicarboxylic acids on dehydration and hydrogenation, no reports of such reactions have yet been made.

No reports were found in the literature regarding the alkylation of keto esters by double Grignard reagents with a simultaneous formation of an alkylated dihydroxydicarboxylic acid. The high yields obtained with the double Grignard reagents from acetylene dibromide and a variety of ketones (750, 751) and aldehydes (193, 750, 751) suggest such an approach as a possible means for the preparation of certain higher symmetrically alkylated dicarboxylic acids.

(c) Reactions with acid chlorides

Grignard reagents react with cadmium chloride to form dialkylcadmium compounds which combine readily with carbethoxy-substituted acyl chlorides to give keto esters. The keto esters are easily reduced to the free acid, usually by the Wolff-Kishner reaction. This process has found much application in the

synthesis of branched-chain acids. The branching may be in the dibasic acid (145, 150, 152) or in the organocadmium (153, 229) moiety.

Should it be possible to extend this method to the alkyldicadmiums from di-Grignard reagents or to carbethoxy-substituted dialkylcadmiums, this technique would be useful for the introduction of branching into dicarboxylic acids at points other than the junction of the carbon chains. In order to introduce the branching at the point of junction of carbon chains, the secondary or tertiary cadmium reagents would be required. Since such organocadmium compounds are not readily available (142), the organomagnesium reagents would have to be used. Such a reaction sequence, however, may be difficult to realize, since reduction of highly branched acid halides by means of branched Grignard reagents appears to be a general phenomenon (281, 728), although normal reactions have been observed (177) in the presence of cuprous chloride.

It has been suggested (508) that acid chlorides might be successfully condensed with Grignard reagents at $-70°C$. This reaction has already been profitably utilized in the preparation of methyl ketones from secondary and tertiary Grignard reagents and acetic anhydride. At this temperature the intermediate reaction product is stable, so that no ketone is produced in the reaction mixture to react further with the Grignard reagent. It may also be possible to utilize double Grignard reagents, giving the corresponding diketone esters. Double secondary or tertiary Grignard reagents would then effect the introduction of branching at the points of junction of the carbon chains. In the absence of actual experimental data the usefulness of such schemes, however, may only be guessed.

(d) Reactions with unsaturated compounds

The addition of Grignard reagents to α,β-unsaturated carboxylic esters has also been utilized in the preparation of substituted dicarboxylic acids. The addition takes place either in the 1,2- or the 1,4-position, depending on the character of the Grignard reagent and on the substituents in the unsaturated ester. By substituting a cyano or another carboxylic ester group on the α-carbon atom, the addition of the Grignard reagent takes place exclusively 1,4. It has been found (326), for example, that both aryl- and alkylmagnesium bromides add to ethyl ethylenetetracarboxylate.

With alkylmagnesium halides some reduction of the ethyl ethylenetetracarboxylate takes place, but the yields are generally good, varying from 25 to 80 per cent. The saponification of the tetraester and the decarboxylation of the poly acid are carried out by the usual methods.

Although a number of methods for the preparation of monosubstituted succinic acids are available, the above approach has the advantage of starting with readily prepared material. Also, certain monosubstituted succinic acids may be prepared by this method that can be prepared only with great difficulty by any other method. Besides the reduction of unsaturated esters by *tert*-butylmagnesium halide and the usual coupling of the Grignard reagent radicals themselves, another important side reaction takes place under these reaction conditions. The unsaturated compounds may undergo a Michael condensation, followed by

a 1,4-addition of the Grignard reagent to the dimerization product. Such dimerization, followed by addition of a Grignard reagent, has been observed with crotonic acid esters. The final products on saponification give the corresponding α,β-dialkylglutaric acids (498). The yields of these products depend on the reaction conditions, the nature of the alkylmagnesium halide, and the proportions of reactants and catalyst; they have been observed to be in the range from 25 to 50 per cent.

This initial condensation of the crotonic ester with itself is suppressed by increasing the excess of the Grignard reagent. For example, in the case of *n*-butyl- and *n*-octylmagnesium bromides, an increase in the amount of Grignard reagent from 1.2 to 1.5 equivalents resulted in an increase in the yield of the simple 1,4-addition product from 60 to 85 per cent, while the yield of the Michael–Grignard product dropped to practically zero. In the case of *n*-tetradecylmagnesium bromide an increase from 1.2 to 2.0 equivalents of the Grignard reagent similarly resulted in an increase in the yield of 1,4-addition product from 10 to 86 per cent. On the other hand, it was also found that the ratio of the condensation product to the addition product was increased if a more concentrated solution of the crotonic ester and a shorter time of ester addition were used.

Consequently, the Michael condensation products, when prepared in advance from suitable starting materials, can be effectively alkylated to the corresponding α,β-dialkyldioic acids.

In addition to the substituents present in the unsaturated ester, the nature of the addition product obtained is also determined by inorganic chlorides, which favor the 1,4-addition. Thus, the presence of one mole per cent of cuprous chloride resulted in an increase in the yield of 1,4-addition product from 25 to 60 per cent (in the reaction of *n*-butylmagnesium bromide with *sec*-butyl crotonate) (498), a yield which could be further improved to 85 per cent by increasing the ratio of Grignard reagent. Ferric chloride, however, behaved differently, giving a mixture of compounds from which only a dimerization product of the crotonic ester was isolated.

The introduction of a methyl group in the α-position of an α,β-unsaturated ester, such as methacrylic and tiglic esters, results in the exclusive formation of the condensation addition product, even in the presence of a large excess of the Grignard reagent and copper chloride. The yields are only fair (498). Thus, *sec*-butyl tiglate with *n*-butylmagnesium bromide gave a 25 per cent yield of di-*sec*-butyl α-(2-hexyl)-α,β,γ-trimethylglutarate, while *sec*-butyl methacrylate with *n*-butylmagnesium bromide in the presence of copper chloride gave 30 to 50 per cent yields of di-*sec*-butyl α-*n*-amyl-α,γ-dimethylglutarate, depending on the reactant ratios.

Similar observations have also been made with other acrylate and methacrylate esters and alkylmagnesium halides (413, 414, 415). Dialkyl esters of substituted glutaric acids were isolated from the reaction mixtures in yields up to 50 per cent. The formation of the substituted glutarates in this case was explained (414) by 1,4-addition of the alkylmagnesium halide to the acrylate, followed by reaction of the enolate with another mole of the acrylate.

The addition of Grignard reagents to alkylidenemalonic esters has been de-

veloped into an important practical method for the preparation of malonates with tertiary alkyl substituted groups (127, 128, 326, 733, 734). The direct alkylation of sodiomalonates with tertiary alkyl halides is impractical because of the easy dehydrohalogenation of the tertiary halides to unsaturated hydrocarbons. On the other hand, secondary and tertiary Grignard reagents have been reported to give poor yields with alkylidenecyanoacetic esters (13, 555).

The 1,4-addition to alkylidenemalonates is also favored by using the cadmium compounds (581). The 1,2-addition of a diorganocadmium compound to a carbonyl double bond takes place either to a negligible extent or not at all. The 1,4-addition product from isopropylmagnesium chloride and diethyl fumarate or maleate was obtained in about the same yield (30 per cent) as from diisopropylcadmium and ethyl maleate (448). *sec*-Butyl crotonate with di-*n*-butylcadmium, however, was reported to give very little (498), if any, 1,4-addition product; even after heating under reflux in ether–benzene solution, the crotonic ester was recovered.

Appreciable quantities of alkylmalonic acids have also been obtained as a result of α-metalation and carbonation of monobasic acids or alkyl chlorides (486). In this way phenylmalonic acid (485) and *tert*-butylmalonic acid (127) have been prepared. Branched-chain dialkylmalonic acid derivatives are also accessible through the addition of Grignard reagents to butylbutadienoic acid followed by carbonation of the adduct (743).

5. Introduction of carboxyl groups into suitable unsaturated compounds

Some methods for the formation of alkylated dicarboxylic acids by the introduction of carboxyl groups into unsaturated compounds have already been considered. Among others, the addition of hydrogen halides to singly unsaturated fatty acids followed by nitrilation or malonation of the halide may be mentioned.

When hydrogen bromide is used, the addition may take place in two ways (453, 634), nitrilation or malonation, and hydrolysis then gives two isomers which are difficult to separate. It is possible, however, to control the addition of the bromide in such a way that either the terminal or the proximal addition product is predominantly obtained. Thus, a terminal bromo acid is obtained when hydrogen bromide is passed into a solution of a terminally unsaturated acid in a hydrocarbon in the presence of oxygen or a peroxide (266, 453). Nonterminal addition predominates when the acid is undiluted and the reaction is carried out in hydrogen or in the presence of an antioxidant (96, 164, 266).

Peroxides supposedly initiate a free-radical mechanism, and this fast reaction supplants the normal ionic process when the free radicals are stable enough (453).

Acrylic acid gives only the normal Markownikoff product, α-bromopropionic acid. The nonterminal addition of hydrogen halides produces a secondary or a tertiary halide, which generally does not give a satisfactory yield on nitrilation. The reaction with substituted or unsubstituted malonic esters has been used in such cases to introduce further additional branching and the carboxyl group (164, 601).

In this way, for example, β-methylsuberic and β-methylsebacic acids were

prepared from the nonterminal addition products of hydrogen bromide and the terminally unsaturated heptenoic and nonenoic acids, respectively (266). In view of the previous discussion, it may be possible that the alkyl halides or suitably protected halo esters, derived from these additions of hydrogen halide, would lend themselves also to Grignard carbonation. Nitrilation may be performed in 90–95 per cent yield in anhydrous ethylene glycol to suppress hydrolysis (102).

The direct addition of hydrogen cyanide to dienes in the presence of dicobalt octacarbonyl at 130°C. in sealed vessels (22, 23) appears to be unsatisfactory for the unambiguous synthesis of branched-chain dicarboxylic acids. A number of mono- and dihydrocyanation products are obtained. For example, butadiene gave an 8 per cent yield of 2-methyl-3-butenenitrile, a 60 per cent yield of 3-pentenenitrile, a 2 per cent yield of 4-pentenenitrile, a 5 per cent yield of 2,3-dimethylsuccinonitrile, and a 20 per cent yield of 2-methylglutaronitrile. Similar mixtures of nitriles were obtained with isoprene and hydrogen cyanide. Addition of hydrogen cyanide to isolated double bonds in nitriles and esters in the presence of dicobalt octacarbonyl (22) is somewhat more profitable for the preparation of dicarboxylic acids because fewer isomers are possible.

Compounds in which a negative group is attached to an unsaturated carbon atom show considerable reactivity towards hydrogen cyanide, which reacts with α,β-unsaturated acids, their esters, and α,β-unsaturated nitriles forming saturated β-cyano derivatives (408, 409). For example, hydrocyanic acid adds at the double bond in isocrotonic acid to give β-cyanobutyric acid (381). The reaction is accelerated by primary or secondary amines.

Hydrocyanation takes place particularly readily when activated double bonds are present. Alkylidenecyanoacetic acids (409) or esters (635, 698), alkylidenemalononitriles (184), and alkylidenemalonic esters (15, 386, 465), where two activating groups are attached to the α-carbon atom, add hydrogen cyanide in excellent yields. The products are easily converted by hydrolysis and decarboxylation to the corresponding substituted succinic acids. The additions are catalyzed by bases and are carried out by treating the unsaturated compound with an alkali cyanide in aqueous or aqueous-alcoholic solutions.

Because both the carbonyl and the unsaturated bonds in mesityl oxide react with hydrogen cyanide, it gives a saturated cyanocyanohydrin, $(CH_3)_2C(CN)$-$CH_2C(OH)CNCH_3$ (408). Phorone (407) and vinyl ethyl ketone (441) similarly give cyanocyanohydrins.

The addition of hydrogen cyanide to acetylene has been disclosed in numerous patents (493). Acetylene itself adds hydrogen cyanide under catalytic conditions to give acrylonitrile or succinonitrile. Propiolic acid esters react with hydrocyanic acid to form β-cyanoacrylic ester (406). Potassium cyanide reacts also with methyl fumarate and methyl citraconate, but cyclic products are formed. Allyl cyanide reacts with potassium cyanide to form the dinitrile of pyrotartaric acid (465).

All these compounds may be converted to the appropriate saturated alkylated dicarboxylic acids by standard methods. The addition of hydrogen cyanide to

unsaturated esters and nitriles and other unsaturated compounds has been discussed, and the literature has been surveyed in two review articles (405, 493) and a monograph (466).

Olefins may also be made to react with carbon monoxide and water at temperatures in the neighborhood of 300°C. and under 700 atm. pressure in the presence of acid catalysts and certain solids offering a large contact surface, to yield saturated acids (691). When nickel carbonyl is used as catalyst, the reaction takes place under more moderate conditions.

A simple route to the half-esters of α-methylenedicarboxylic acids has been found in the reaction of fatty acids possessing a terminal triple bond with nickel carbonyl. In this way the itaconic, mesaconic, α-methyleneglutaric, adipic, and pimelic acids have been prepared in 28 to 46 per cent yields (351). Unsaturated acids of this type have been readily hydrogenated to the corresponding saturated derivatives.

The simultaneous reaction of carbon monoxide and hydrogen with olefins (323), the so-called oxo process, takes place under pressure and high temperatures in the presence of suitable catalysts. The primary products are aldehydes, but suitable starting materials may also give dicarboxylic acids or other products which may easily be converted into such acids (443).

Various conditions for the carbonylation of acetylenic substances with carbon monoxide have been discussed in a special monograph on this subject (578).

A simultaneous interaction of acetylene with carbon monoxide and compounds having a reactive hydrogen atom has been demonstrated to yield α,β-unsaturated carboxylic acids and their derivatives (579).

The carbonation of certain dialkali derivatives of conjugated diolefins by carbon dioxide to give branched-chain unsaturated dicarboxylic acids has also been recently described (500). An aliphatic diolefin, such as butadiene, is dimerized by finely divided sodium in an aliphatic ether in the presence of minor amounts of polycyclic aromatic hydrocarbons. Pouring the slurry on to dry ice yields, in addition to a small amount of a rubbery polymer, as much as 67 per cent of the sodium salts of unsaturated ten-carbon-atom acids. On hydrogenation 2,5-diethyladipic, 2-ethylsuberic, and sebacic acids were obtained in 8, 36, and 23 per cent yields, respectively. Isoprene gave mixed C_{12} acids, and a mixture of 2-methyl- and 4-methyl-1,3-pentadienes similarly gave a 56 per cent yield of mixed C_{14} dicarboxylic acids.

Most of these processes, though capable of economical yields industrially, are of little use for the preparation of individual branched-chain dicarboxylic acids in the laboratory.

B. INTRODUCTION OF BRANCHING AT POINTS OTHER THAN THOSE OF JUNCTION OF CARBON CHAINS

1. Utilization of suitably substituted cyclic compounds

Though the fission of complex natural products by a variety of chemical reagents to produce substituted dicarboxylic acids had been known for a long time, the low yields encountered and the poor availability of these substances

prohibited their utilization in the preparation of dicarboxylic acids. The yields improved as more suitable cleaving agents were discovered, but it was not until the chemical and structural factors governing such fissions were determined that this method could be satisfactorily utilized for preparative purposes.

At the present time, in addition to the modified natural products, various wholly synthetic substituted cyclic structures are prepared and cleaved to the desired substances. Among them the reductive desulfurization of the thiophene substitution products may prove to be of the widest applicability in the synthesis of branched-chain dicarboxylic acids. While at times the preparation of suitably substituted cyclic compounds may still be difficult or impossible, in those cases where the substituted cyclic compounds are readily available, cleavage of the ring is the most direct and efficient way to the corresponding alkylated acids.

(a) Cleavage of cyclic oxygenated compounds

Monoesters (292) of dicarboxylic acids, of the general formula $ROOC(CH_2)_n$-$CHRCR_2COOH$, where R is H or a hydrocarbon radical and n is zero or a whole number, may be prepared by catalytic hydrogenation of ester lactones of the formula $ROOC(CH_2)_nCRCR_2CO$ or preferably small polymers thereof. The
└─O─┘
lactones themselves are suitably prepared from a ketene and an ester of a keto acid with an acidic catalyst. Ethyl acetoacetate thus gave monoethyl β-methylglutarate. Similarly, the lactone from ethyl levulinate gave monoethyl β-methyladipate, and methyl pyruvate so condensed and reduced gave monomethyl methylsuccinate.

Alkylated dicarboxylic acids are also formed on oxidation of substituted lactones. For example, α,γ,γ-trimethyl-β-ethyl-δ-valerolactone, prepared from the condensation of $C_2H_5CH{=}C(CH_3)CHO$ and isobutyraldehyde in the presence of potassium, has been subsequently oxidized to α,α,γ-trimethyl-β-ethylglutaric acid with potassium permanganate (457). Potassium permanganate has also been shown to convert α-isopropyl-γ-hydroxyglutarolactonic acid, obtained from allylisopropylacetic acid by the action of alkaline permanganate, to *dl*-isopropylsuccinic acid (668).

On oxidation with bromine, γ-lactones in the presence of magnesium hydroxide are converted into γ-keto acids in good yields. Monomeric β-lactones of monocarboxylic acids having at least one unsubstituted hydrogen atom on the α-carbon atom and containing only unreactive hydrocarbon substituents may be polymerized and then pyrolyzed to give α-unsaturated monocarboxylic acids, which can be reduced to the appropriate saturated acids (400). The lactone rings may also be opened by treatment with phosphorus halides. The organic halides resulting may then react further with cyanide, with ethyl sodiomalonate or ethyl cyanoacetate (85) or, as in cases when the lactone already possesses a carboxy substituent, they may be reduced to the halogen-free derivative (559). Another method for the removal of such halogens is thermal dehydrohalogena-

tion of the chloro ester (144). Thus, the chloro ester obtained on chlorination with hydrogen chloride and ethanol of the thionyl chloride scission product of δ-carbethoxy-β,β,γ-trimethyl-γ-valerolactone was thermally dehydrohalogenated to the unsaturated ester corresponding to β,β,γ-trimethyladipic acid (60).

A more direct route to the unsaturated ester, at least with some chloro esters, has been found in simple alkaline hydrolysis (60).

Ketones in general are quite resistant to oxidation, as indicated by the successful utilization of acetone as solvent in oxidations by alkaline permanganate. Oxidation with more vigorous oxidizing agents, such as acid permanganate or dichromate, however, leads to chain cleavage with formation of carboxylic acids and/or ketones. The utilization of cyclic ketones or alcohols in such oxidations has resulted in efficient methods for the preparation of substituted dicarboxylic acids of the corresponding chain length.

The following general equations represent the course of vigorous oxidations of cyclic ketones of various structural types:

$$R_3CCOCH_2R' \xrightarrow{2(O)} R_3CCOOH + R'COOH \quad (1)$$

$$RCH_2COCH_2R' \xrightarrow{2(O)} \begin{cases} RCOOH + R'CH_2COOH \\ RCH_2COOH + R'COOH \end{cases} \quad (2)$$

$$R_2CHCOCH_2R' \xrightarrow{2(O)} R_2CO + R'CH_2COOH \quad (3)$$

Equation 1 represents the case of a ketone having only a single methylene unit capable of oxidative attack. In the more general case, equation 2, oxidation occurs at two different methylene units, with production of a mixture of carboxylic acids. Oxidative attack by such reagents as dichromate appears to occur preferentially at a methinyl carbon rather than a methylene carbon, as in equation 3. This tendency is illustrated by the permanganate oxidation of menthone. The major oxidation product is β-methyladipic acid, together with smaller amounts of the ketonic acid. This general behavior has been shown by cyclic ketones of various ring sizes and with a variety of substituents.

For example, 1,2,2-triethyl-4-cyclobutanone and 1,1-dimethyl-2,2-diethyl-4-cyclobutanone gave on strong oxidation triethylsuccinic acid and α,α-dimethyl-β,β-diethylsuccinic acid, respectively (171, 172). When both the 1- and the 3-carbon atoms carried methyl groups, one of the methyl groups was also oxidized, giving the α-ketoglutaric acids, which again could be converted to the alkylated succinic acids. Thus, 1,3-dimethyl-2,2-dipropyl-4-cyclobutanone was converted to β,β-dipropyl-γ-methyl-α-ketoglutaric acid. The cyclobutanones were obtained by addition of hydrogen bromide to the required α- or β-unsaturated ketones, followed by cyclization of the β-bromo ketones upon refluxing with alcoholic potassium hydroxide (172).

Oxidation by alkaline permanganate of 4-isopropyl- and 4-*tert*-butylcyclohexanols (526) gave the corresponding substituted dicarboxylic acids in about 85 per cent yield.

In the five-carbon-ring series, 2,2-diisopropylcyclopentanol has been cleaved to α,α-diisopropylglutaric acid by a potassium dichromate–sulfuric acid mixture

(218). In a study of the auxins, another alcohol, 2,5-di(*sec*-butyl)-1,3,4-cyclopentanetriol on treatment with lead tetraacetate and alkaline potassium permanganate gave a mixture of α,α'-di(*sec*-butyl)-β-hydroxyglutaric acids (383). These could be reduced to the corresponding saturated glutaric acids by hydrogen iodide and phosphorus. Similarly, treatment of 3,3-dimethylcycloheptanone (492) and 1,4,4-trimethyl-2-cycloheptanone (170) with alkaline permanganate resulted in the formation of the correspondingly substituted dicarboxylic acids. 1-Methyl-2,3-cyclopentanediol, obtained on oxidation with performic acid of a methylcyclopentene resulting from the isomerization of cyclohexene with hot alumina, gave a good yield of α-methylglutaric acid on oxidation with chromic acid–sulfuric acid. Similarly, β-methyladipic acid was obtained from a methylcyclohexene (4).

The oxidation of 4,5-dipropyl-1,2-cyclohexanediol with chromic anhydride–acetic acid gave β,β'-dipropyladipic acid (385). The diol itself was obtained on hydrogenation of the 4,5-dipropylpyrocatechol. Potassium persulfate has also been shown to be able to effect similar transformations. Thus, 1-methyl-2,3-cyclopentanedione was converted to α-methylglutaric acid in good yield (309).

Alkaline peroxide has also been shown to attack cyclic keto compounds. Thus, 1,1,2,2-tetramethyl-4-cyclopentanone has been converted into $\alpha,\alpha,\beta,\beta$-tetramethylglutaric acid in fair yield. The sulfuric acid cyclization product of dibromophorone gave a similar product (236).

The most effective means for the oxidation of cyclic ketones or alcohols to the dicarboxylic acids with the same number of carbon atoms is oxidation by nitric acid. The use of vanadate as catalyst improves the yields from some 60 to 70 per cent, with nitric acid alone, to 80 to 90 per cent in the presence of the catalyst (276, 545). For example, a number of mono- (175, 211, 315, 360, 503, 639), di- (361, 720), and poly- (77, 561) alkyladipic acids have been prepared in 60 to 80 per cent yields by the oxidation of alkylated cyclohexanols. α,β-Dimethyladipic acid was obtained in 60 per cent yield from 1,3-dimethyl-5-cyclohexanol, while a similar oxidation of 4-isopropylcyclohexanol gave β-isopropyladipic acid in 80 per cent yield (720). Similar procedures were used to prepare other alkylated dicarboxylic acids. The alkylcyclohexanols were obtained from *p*-alkylphenols on reduction, or from the alkylbenzenes on oxidation and reduction. Another method for the preparation of substituted cyclic compounds suitable for oxidation by nitric acid to substituted dicarboxylic acids is based upon the condensation of acetone by powerful basic condensing agents, such as sodium amide, to give isophorone, which on subsequent reduction gives the corresponding substituted cyclohexanol (539). Other cyclic oxygenated compounds have also given high yields. For example, 4,4-dimethylcycloheptanol on oxidation by nitric acid gave β,β-dimethylpimelic acid in 80 per cent yield (284).

It is important to add the hydroxy compound dropwise to the hot (60–90°C.) acid, since the reaction may become violent if the ketone is not instantaneously oxidized. A molar ratio of one part of hydroxy compound to 3 parts of 67 per cent nitric acid has been found to give the highest yields of adipic acid from

cyclohexanol (90 per cent) (276). The mechanism of the oxidation of cyclohexanol to adipic acid by nitric acid has been studied and several intermediates isolated (276).

In the same manner, hot nitric acid has been observed to convert 2,6,6-trimethylcycloheptanone to 2,2,6-trimethylpimelic acid. On an industrial scale, the oxidation of alkyl-substituted cyclic keto compounds may give better yields and be carried out more readily when performed at elevated temperatures and pressures, in the presence of nitric acid, nitrous gases, oxygen, air, and water (384).

The presence of centers of unsaturation in the ring itself or adjacent to it (see below) provides other points of attack to these oxidizing agents. For example, 2,5,5-trimethyl-3-methylenecyclohexanone with potassium permanganate yields 3,3-dimethylglutaric acid (358). Reduction of the unsaturated ketone to 2,3,5,5-tetramethylcyclohexanone, followed by oxidation with nitric acid, gives 2,2,4,5-tetramethyladipic acid (358).

The substituted cyclic ketones are also cleaved by hypochlorites. A rather special case is the formation of β,β-dimethylglutaric acid in 81 to 91 per cent yield from menthone (636). The acid is presumably formed by the oxidation of the intermediate Wagner–Meerwein rearrangement product.

The cleavage of alkyl-substituted cyclic ketones possessing an α-cyano or carboxyl group by alkali has been shown (278, 338, 368, 491, 719) to produce high yields (50 to 80 per cent) of alkyl-substituted dicarboxylic acids. For instance, 2-cyanomenthone on hydrolysis with 30 per cent potassium hydroxide gave a 74 per cent yield of 2-isopropyl-5-methylpimelic acid (347). In addition to aqueous alkali, such cleavages have also been accomplished with sodium methoxides and ethoxides (64, 338). A variety of dialkylpimelates, for example, were prepared by boiling the corresponding alkyl-substituted 2-cyclohexanonecarboxylic acids with sodium ethoxide (388). The presence of an additional alkyl substituent on the carbon carrying the carboxyl group appears not to affect the course of such cleavages (228, 538).

The products of the Michael addition of 1,3-cyclohexanedione or its derivatives to α,β-unsaturated carbonyl compounds, esters, and nitriles, followed by reduction and saponification carried out simultaneously under the Wolff–Kishner conditions, have also been shown to produce substituted long-chain dicarboxylic acids. In this way, γ-ethylazelaic acid has been prepared from the condensation product of ethyl acrylate and 1-ethyl-2,6-cyclohexanedione (660). This reaction has also been extended to the dimedones (663) and dihydroresorcinols (662); besides the Michael addition products, the compounds formed from a bromo ester or an α,ω-dihaloalkane and the cyclic dione condensation may be similarly cleaved and reduced to the corresponding alkylated dicarboxylic acids. For example, methylenebisdimedone (663) has been converted in this manner to 2,2,10,10-tetramethyl-1,11-undecanedicarboxylic acid. 4,4-Dimethyl-2,6-dioxocyclohexanepropionic acid gave 2,2-dimethyl-1,7-heptanedicarboxylic acid by the reductive acid cleavage. 2,2-Dimethyl-1,6-hexanedicarboxylic acid has also been prepared in this way.

Among the other alkylated cyclic oxygen-containing compounds that on acid hydrolysis yield substituted dicarboxylic acids are 2-alkoxy-3,4-dihydropyran derivatives (435). For example, 2-methoxy-4-methyl-3,4-dihydro-1,2-pyran, obtained by condensing crotonaldehyde and methyl vinyl ether, on acid hydrolysis followed by oxidation with potassium permanganate gave a 61 per cent yield of β-methylglutaric acid. A 70 per cent yield of α-methylglutaric acid was obtained on hydrolysis and oxidation of the 2-methoxy-5-methyl derivative, previously prepared by condensing methacrolein with methyl vinyl ether.

α-Tetrahydrofurfuryl alcohols have been shown to be split in sodium and potassium hydroxide melts at 220–270°C. to produce substituted dicarboxylic acids. The products are usually accompanied by olefins and dicarboxylic acids with fewer carbon atoms than the starting material. For instance, the 3-(α-tetrahydrofuryl) derivatives of 2-methyl- and 2-ethyl-1-propanol gave 34 and 21 per cent yields of α-methyl- and α-ethylpimelic acids, respectively (593).

The mixtures of cyclic ethers (oxido alkanes) obtained on cyclization of α,ω-alkanediols by sulfuric acid have been shown to give on transformation into dibromides and then dicyanides mixtures of alkyl-substituted dicarboxylic acids (239, 240). Though the yields were occasionally fair, the separation of the isomers presented difficulties. Thus, the cyclic ethers from 1,6-hexanediol on ring opening with bromine in chloroform solution, followed by nitrilation of the dibromides, gave a 10 per cent yield of suberic acid, a 25 per cent yield of α-methylpimelic acid, and a 65 per cent yield of α-ethyladipic acid (240).

(b) Cleavage of cyclic nitrogen-containing compounds

Besides thc cyclic oxygenated compounds, suitably substituted nitrogen-containing cyclic structures may be cleaved to yield alkylated dicarboxylic acids. For example, thermal decomposition of a diethyl *N*-methyltetrahydrocollidine-dicarboxylate (497) gives the diester of 1,3-dimethyl-2,4-butadienedicarboxylic acid, which on catalytic reduction gives α-ethyl-β-methylglutaric acid.

Similarly, heating *N*-benzoyl-γ,γ-dimethylpiperidine (391) with phosphorus pentachloride yielded benzonitrile and γ,γ-dimethylpentamethylene dichloride. From this was obtained the dicyanide, which could be hydrolyzed to γ,γ-dimethylpimelic acid in good yield.

Numerous alkyl derivatives of maleic and citraconic acids have been obtained from oxidative degradation of the pyrrole fragments of blood and plant pigments. Thus, oxidation of 2,4-dimethylpyrrole with chromic acid gave a good yield of citraconic acid (548). These unsaturated dicarboxylic acids may be converted to the corresponding alkylated succinic acid derivatives on catalytic hydrogenation (297).

Cyanoacetamide condenses with 1,2-diketones, giving first a dialkyl cyanohydroxypyrrolinone. A second molecule of cyanoacetamide adds to the double bond, and the resulting pyrrolidone may be hydrolyzed to a β-alkyl-β-acylglutaric acid (345).

The oxidation of 3-nitro-4-hydroxytoluene (537) to β-methylmuconic acid by sulfuric acid may be mentioned as another example. The yield of the product is

low but of interest, since though the animal organism is capable of splitting the benzene ring to the muconic acid, chemical reagents have failed to do it. This acid also may be catalytically hydrogenated to β-methyladipic acid.

(c) Reductive desulfurization of thiophene derivatives

Raney nickel not only desulfurizes thiophenes but also reduces the ring unsaturation. If two actual or potential carboxylic acid functions are present, either on the thiophene nucleus or on a substituent group, the desulfurization product is a dicarboxylic acid. Since alkyl groups, with or without a carboxylic acid group (740), can be readily attached to the thiophene nucleus, this method offers an excellent possibility of preparing a large variety of branched-chain dicarboxylic acids. The possibility of acylation of the thiophene nuclei by half-acid chlorides of dicarboxylic acids followed by Wolff–Kishner reduction of the ketones is particularly fortunate, because this permits the utilization of the rather readily available alkylated short-chain dicarboxylic acids in the preparation of the more difficultly available long-chain acids. The overall yields are reasonable, and in only a few cases (674) was resistance noted to the desulfurization step.

Thus, 6,6-dimethylundecanedioic acid (43) was prepared in 93 per cent yield by the reductive desulfurization of 2,2-di(5-carboxy-2-thienyl)propane, which had been previously obtained on acetylation and hypobromite oxidation of the acetone–thiophene condensation product.

Though at the present time this method, mainly because of its rather recent description (88), has not been extensively applied to the preparation of branched-chain aliphatic dicarboxylic acids, its generality may be judged from the success in the synthesis of a number of unsubstituted (133) and aryl-substituted (673) fatty acids.

(d) Cleavage of unsaturated carbocyclic compounds

Oxidation of an unsaturated compound with alkaline potassium permanganate under mild conditions generally results in the formation of a glycol. Under more vigorous reaction conditions, with higher reagent concentration, and at a higher temperature, carbon–carbon cleavage occurs. The reaction products depend upon the structure of the starting material. A monosubstituted ethylenic carbon is ultimately oxidized to carboxyl, an unsubstituted ethylenic carbon is oxidized to carbon dioxide, and a disubstituted ethylenic carbon is oxidized to the stage of a ketone.

These observations are utilized in the preparation of substituted dicarboxylic acids by the cleavage of suitably alkylated cyclic olefins by alkaline permanganate. Thus, 1-methyl-3-cyclohexene has been oxidized by potassium permanganate to β-methyladipic acid (489). Similarly, 3-propylcyclohexene in acetone was oxidized with alkaline permanganate at room temperature to yield 2-propyladipic acid, while 3-ethylcyclohexene gave 2-ethyladipic acid (46). Comparable results have also been obtained with the substituted cyclopentenes

(438). Occasionally the yields are only moderate. For example, β,β-dimethyladipic acid (546) was obtained in 34 per cent yield from 4,4-dimethylcyclohexene on oxidation with this reagent.

As in the case of the oxidation of cyclic oxo compounds, the action of the permanganate is rather slow and, when complete, may have gone further than desired. In some cases a two-stage process involving the use of a stronger oxidizing agent upon the intermediate glycol has given the expected results. For example, the oxidation of β-dihydrohumulene with potassium permanganate gave α,α-dimethylsuccinic acid and β,β-dimethyladipic acid. Partial oxidation by permanganate of this same substance followed by oxidation with nitric acid, on the other hand, gave β,β-dimethylpimelic acid (299).

Occasionally better yields of dicarboxylic acids may be obtained by subjecting the cycloölefins first to oxidation with a per acid, followed by further oxidation with the common oxidizing agents of either the epoxides or glycols themselves or the dialdehydes after a glycol cleavage. Particularly high yields of glycols have been obtained with osmium tetroxide (187), but this reagent is uneconomical and poisonous.

There is, however, always a degree of uncertainty in obtaining the dicarboxylic acid corresponding to the position of the double bond in the starting material when acid or basic oxidizing agents are used, since these reagents frequently cause migration of a double bond. An example of such a migration occurs when the Diels–Alder adduct from butadiene and methyl crotonate is treated with alkali, giving β-methylpimelic acid as the chief product (547). Therefore in cases where the activities of the acidic or alkaline oxidizing agents may be suspect, a superior procedure is a two-step oxidation with ozonization the first step. For example, from 2,4,4,5,5-pentamethyl-1-acetylcyclopentene was obtained a keto acid and then α,α,β,β-tetramethylglutaric acid (390). The ozonization of 3,3,4-trimethyl-1-cycloheptene-1-carboxylic acid, followed by oxidation with chromic anhydride, yielded 2,2,3-trimethylheptanedioic acid (598), and ozonization of 4,4-dimethyl-1-cycloheptene-1-carboxylic acid gave β,β-dimethyladipic acid (285). γ-Irone on similar treatment gave 3,3,4-trimethylheptanedioic acid (599). A large number of other terpene derivatives have been cleaved to the corresponding substituted dicarboxylic acid derivatives under similar conditions (631, 632). The corresponding types of succinic, glutaric, adipic, and pimelic acids have occasionally been obtained in fair yields. The methyl ketone intermediates often encountered yield the appropriate dicarboxylic acids readily on oxidation with hypohalite.

Ozonization has also been used for a successful and reliable cleavage of such substituted unsaturated cyclic ketones (612) as

$$\underline{C(CH_3)_2CH(CH_3)CH_2CH_2CH_2C{=}CHOHCO}$$

obtained on cyclization of suberic acid followed by treatment with sodium ethoxide and isoamyl formate in ether. This compound on ozonization gave α,α,β-trimethylpimelic acid. Cyclization of this trimethylpimelic acid, followed by formylation, ozonization, and oxidation, gave α,α,β-trimethyladipic acid, which

on repetition of the above sequence of reactions once more resulted in the formation of α,α,β-trimethylglutaric acid.

Ozonization of 4,5,5-trimethyl-2-cyclopenten-1-one followed by oxidation with nitric acid gave trimethylsuccinic acid (238). Similarly, the corresponding succinic acid derivatives were obtained in good yields from other substituted cyclopentenones (308), and isophorone, a cyclohexenone, may be cleaved to α,α-dimethylsuccinic acid (231).

The alkaline hydrolysis of cycloölefin carboxylates to dicarboxylic acids with one more carbon atom is now recognized as fundamentally similar to the alkaline cleavage of α-carboxycycloalkanones (725). The hydrolysis proceeds by an alkaline isomerization to the intermediate 1-carboxylic acid, which undergoes attack by a hydroxyl ion to give cyclohexanone-α-carboxylic acid as a further intermediate. The latter is then cleaved to pimelic acid or decarboxylated to cyclohexanone in relative amounts depending on the reaction conditions.

Since this reaction depends upon an initial isomerization of the double bond to give the vulnerable 1-carboxylic acid, low yields are to be expected when alkyl groups also present on the ring give steric protection (547). An extreme case of such blocking of double-bond migration appears to be 3,6-endomethylenecyclohexene-4-carboxylic acid (725), which gives only tars. If the proposed mechanism is true, good yields, however, could be expected from substituted cycloölefins in which the carboxyl group is already in the α-position and no isomerization is necessary. The most satisfactory method for the preparation of the unsubstituted pimelic acid (494), the reduction of salicylic acid by sodium and amyl alcohol, has apparently not yet been extended to the preparation of the substituted pimelic acids by utilizing alkylated salicylic acids. Among the other aromatic compounds which have been converted to substituted dicarboxylic acids with some success are *p*-xylene and some homocatechols (211) and 4-methyl-1,2-benzoquinone (210), which on oxidation with peracetic or monoperphthalic acid gave the corresponding substituted muconic acids in about 15 per cent yield. On hydrogenation using the Adams catalyst the corresponding adipic acid derivatives were obtained.

A cyclic structure that can be readily opened because of its high strain is the cyclopropane ring. For example, the trans-anhydride of 1,2-dimethyl-1,2-cyclopropanedicarboxylic acid forms (38) a polymeric product on boiling for 1 hr. with acetyl chloride. Heating this polymer gives the anhydride of α-methylene-γ-methylglutaric acid, which on reduction forms α,γ-dimethylglutaric acid. A method recently described (371) for the preparation of long-chain unsaturated α,ω-dicarboxylic acids from cyclohexanone or cyclopentanone and butadiene in the presence of hydrogen peroxide has apparently not yet been extended to the substituted cyclanones.

2. Utilization of suitably substituted acyclic compounds

There are numerous acyclic compounds either of natural or synthetic origin which may or may not already possess actual or potential carboxyl functions, but which have the common characteristic of being convertible into alkylated

alkanedioic acids by relatively simple treatments with only minor modification of their hydrocarbon skeletons.

(a) Unsaturated alkylated dicarboxylic acids

Though the alkylated saturated dicarboxylic acids have only rarely been isolated from natural sources, the unsaturated alkylated dicarboxylic acids have been encountered more often. Thus, mesaconic acid, an isomer of citraconic and itaconic acids, is found in cabbage (129) and may be reduced to methylsuccinic acid on hydrogenation (297). Seeds of annatto (*Bixa orella*) contain a yellow pigment, bixin, which is a monomethyl ester of an unsaturated methyl-substituted dicarboxylic acid. This has been reduced and hydrolyzed to perhydronorbixin or 4,8,13,17-tetramethyleicosanedioic acid (354).

Another pigment, crocin, contains the unsaturated methyl-substituted dicarboxylic acid crocetin, in the form of its digentobiose ester. Catalytic hydrogenation and hydrolysis give perhydrocrocetin or 2,6,11,15-tetramethylhexadecanedioic acid (332, 333, 354). Bixin and crocetin esters have recently been elegantly synthesized by using the Wittig reaction (335, 336).

1-Ethylmalic acid, isolated from the milky juice of *Euphorbia highlandulosa Desf. III*, has been converted into ethylsuccinic acid on reduction with red phosphorus and hydrogen iodide (404). A degradation product obtained on dry distillation of the dimethyl ester of crocetin *in vacuo* has also been converted to the corresponding saturated alkylated dicarboxylic acid by catalytic hydrogenation (375). Several α-substituted alkyl derivatives of citric acid found in various other plant sources have been thermally decomposed and reduced to the appropriate alkylsuccinic acids (352). Thus, norcaperatic acid on thermal decomposition and reduction with hydrogen iodide gave α-methyl-β-tetradecylsuccinic acid. α-Methyl-β-cetylsuccinic acid was obtained similarly from agaricinic acid. Methyl malonate has been reported (53) as a product of the metabolism of valine, and 2,2-dimethylsuccinic acid (54) appears in the urine of rats fed on a diet producing liver necrosis.

The naturally occurring acids and their derivatives reported above are obviously not available in quantities sufficient for extensive synthetic work.

(b) Ketones, aldehydes, and alcohols

The familiar iodoform test for the presence of the grouping $RCOCH_3$, or a structure which may be oxidized to this group, may be applied to the preparation of carboxylic acids. For preparational purposes, sodium or potassium hypochlorite is a cheaper and more suitable reagent than either hypobromite or hypoiodite, and chloroform is more easily removed from the product than bromoform or iodoform. In this way the geronic acids (594), for instance, gave the *gem*-dimethylated acids. The diketone resulting from the condensation of *tert*-butylmagnesium bromide and 2-methyl-3-oxo-1-butene on oxidation with hypochlorite gave 2,4-dimethyl-2-neopentylglutaric acid (206).

Alkyl-substituted α-keto dicarboxylic acids have been oxidized with alkaline

hydrogen peroxide to the corresponding dicarboxylic acids containing one carbon atom less. For example, α-keto-ζ-methyl-γ-isopropylsuberic acid, obtained from *l*-tetrahydrocarvone on acylation with diethyl oxalate and subsequent hydrolysis, gave *d*-α-methyl-δ-isopropylpimelic acid (100).

Saturated aliphatic aldehydes are smoothly converted to the corresponding carboxylic acids by a variety of oxidizing agents, including alkaline permanganate, hydrogen peroxide, per acids, silver oxide, hypohalites, and molecular oxygen. Freshly precipitated silver oxide has found considerable success in the conversion of a variety of aliphatic aldehydes to the corresponding carboxylic acids (194). The yields for such oxidations are usually high. On an industrial scale the oxidation of aldehydes in air has been satisfactory (617). The oxidation of alicyclic aldehydes to alicyclic acids and aliphatic dicarboxylic acids by bringing the aldehydes into contact with anhydrous fused alkali hydroxides has also been reported (230).

The practical drawback to this reaction as a preparative method for branched-chain dicarboxylic acids is the general unavailability of the necessary aldehydes. The Darzens glycidic ester synthesis (509) is capable of producing such branched aldehydes (606), but the careful control of experimental conditions necessary for good yields may render it unattractive to many workers. However, with increased commercial production of various aldehydic synthetic intermediates (617), this method may become increasingly more important for the laboratory preparation of branched-chain dicarboxylic acids. A number of methods for the preparation of aldehydes of importance in fatty acid synthesis have been recently summarized (270).

Carboxylic acids may also be prepared by the oxidation of primary alcohols. The formation of ester on the oxidation of alcohols with acid oxidizing agents may be avoided by the use of an alkaline oxidant, like alkaline permanganate, or by adding the alcohol slowly to the hot acid oxidant over a period of time, thus avoiding esterification by excess of alcohol. In recent years, hexavalent chromium has become somewhat more popular than permanganate as an alcohol-oxidizing agent. The difficulty here again is the unavailability of branched-chain diols. In fact, when such diols were needed, it has been found expedient to prepare the branched-chain dicarboxylic acids first and then reduce them to the desired diols.

(c) Alkanes, alkenes, and alkynes

The alkanes are generally inert to the common laboratory oxidizing agents. Alkanes containing tertiary hydrogen, however, are attacked rather readily, but this defeats the purpose in attempts to prepare branched-chain dicarboxylic acids. A few exceptions are known. Thus, among the products of the oxidation of isoöctane by nitric acid is α,α-dimethylsuccinic acid (499).

Oxidation by air or molecular oxygen under controlled conditions has resulted in satisfactory yields of carboxylic acids when dealing with high-boiling petroleum cuts and paraffin waxes, and has attracted considerable commercial interest. This process has yielded carboxylic acids as well as aldehydes, ketones, lactones, and other oxygenated products (237). Though some branched-chain

dicarboxylic acids have also been obtained, the general vulnerability of the tertiary hydrogen, despite the difference between the course of the reaction in the gas-phase and the liquid-phase oxidations (461), results in a rapid annihilation of the points of branching even before the carboxyl groups have been formed.

The autoxidation (oxidation with molecular oxygen) of alkenes (237) follows a course analogous to that for the autoxidation of alkanes. The initial product is a hydroperoxide, which subsequently decomposes to the various products finally isolated from the reaction. The point of attack in this case is at a carbon atom adjacent to the double bond (an allyl position) rather than at the double bond itself (217).

In any case such oxidations are only used industrially for producing mixtures of carboxylic acids and are seldom applied to the preparation of individual acids.

Certain chemical reagents resemble molecular oxygen in that oxidative attack on an alkene occurs at an allyl position rather than at the double bond itself. Selenium dioxide effects oxidation of alkenes at an allyl position to produce α,β-unsaturated ketones. Thus, a methylene group is attacked in preference to methyl; methinyl groups do not appear to be attacked; a methylene group adjacent to the most alkylated ethylenic carbon atom is preferentially attacked (564). Oxidation of olefins with such vigorous reagents as dichromate or permanganate generally leads to production of carboxylic acids. However, a considerable amount of degradation also takes place, and the oxidation products can not be predicted with certainty. For example, the oxidation of olefins with alkaline permanganate frequently leads to carboxylic acids of shorter chain lengths than anticipated from the position of the double bond in the original compound. It has been shown (314) that such oxidation of oleic acid or its derived isomeric glycols gives suberic and octanoic acids instead of the expected azelaic and nonanoic acids. An oxidative degradation beyond expectation during oxidation with permanganate has been observed also with citronellonitrile. The (−)-citronellonitrile, for instance, obtained by dehydration of citronellal oxime, with excess potassium permanganate in acetone gave in addition to the expected (+)-4-methyl-5-cyanopentanoic acid, also large amounts of β-methylglutarimide and smaller quantities of (−)- and (±)-methylsuccinic acids and other products (460). The cleavage of olefins by ozonization, as already discussed, is again more reliable and the expected products are obtained exclusively. For example, citronellylacetic and ϵ-citronellylcaproic acids on ozonization gave pure γ-methylsuberic and 3-methyl-1,10-decanedicarboxylic acids, respectively (601). Alkynes are much less reactive than alkenes to per acids. Acetylene itself is attacked at an immeasurably slow rate; dialkylacetylenes, however, are somewhat more reactive and give a variety of products. During the oxidation of certain acetylenic hydrocarbons with peracetic acid a molecular rearrangement takes place, resulting in the formation of α-branched carboxylic acids. For example, 2,8-decadiyne on oxidation with peracetic acid gave α,α'-dimethyloctanedioic acid (244). The triple bond also shows less reactivity than the double bond in chromic acid oxidation (568). Consequently, the introduction of carboxyl groups through the oxidation of points of acetylenic unsaturation is limited to special cases only.

C. FREE-RADICAL REACTIONS

Though all of the reactions about to be discussed are based upon a coupling of carbon fragments with the introduction of branching at either the point of junction of the carbon chains or elsewhere, and consequently could have been discussed in the appropriate previous sections, other considerations have led to their separate treatment in this review.

These reactions are characteristic free-radical combinations and may result in symmetrically or asymmetrically substituted products, according to the choice of starting materials.

In general, the free radicals are generated either under suitable oxidizing conditions, under the influence of a reagent carrying an unpaired electron, or by decomposing certain labile organic compounds which yield the desired radicals capable of combination.

1. Anodic oxidation

Since recent general reviews on anodic syntheses are available (340, 671, 717, 738), only those aspects directly concerned with the preparation of substituted dicarboxylic acids will be considered here.

Anodic oxidation of the free dibasic acids from malonic acid to sebacic acid has been demonstrated to give instead of the expected long-chain dicarboxylic acids or cycloalkanes ill-defined degradation products, including olefins and alcohols, containing two carbon atoms less than the starting material, and both saturated and unsaturated acids by loss of only one carbon atom (692). Thus, β,β-dimethylglutaric acid gave 2-methylbutene, with rearrangement of the carbon chain (705).

In contrast to the free acids themselves, the corresponding half-esters readily undergo the Kolbe reaction, giving high yields of the diesters (115). The only severe restriction upon the utilization of this method in the preparation of branched-chain dicarboxylic acids is the observation that substitution in the α-position lowers the yield (672). Only a few such combinations have been reported (26, 29, 225). For example, an anodic oxidation of the half-ester of α,α-dimethylsuccinic acid gave only a 5 to 8 per cent yield of $\beta,\beta,\gamma,\gamma$-tetramethyladipic acid (213). Monosubstitution at the α-position appears to be less obstructive and gives higher yields. The half-ester of α-methylsuccinic acid, for instance, has been reported to give a 40 per cent yield of crude β,γ-dimethyladipic acid (116). Alkyl substituents located farther from the interacting centers, however, create no special problems. Numerous examples have been reported of anodic couplings in high yield with β-monoalkyl- (330, 426, 428, 429, 648) and dialkyl (213, 291, 418) dicarboxylic acid half-esters, and the coupling of γ-methyl (354, 355) acids was very successful in the preparation of synthetic perhydrobixin and perhydrocrocetin. Thus, the half-ester of β,β-dimethylglutaric acid gave a 75 per cent yield of $\beta,\beta,\delta,\delta$-tetramethylsuberic acid (76), which could be further partially esterified and electrolyzed to dimethyl 2,2,5,5,8,8,11,11-octamethyl-1,12-dodecanedicarboxylate in a similar yield. Occasionally, however, lower yields are encountered; for instance, the half-ester of α,α-dimethylsuccinic acid

has been reported to give only a 32 to 35 per cent yield of the corresponding $\alpha,\alpha,\alpha',\alpha'$-tetramethyladipic acid (213). Unsaturation no closer than the γ-position causes no difficulty (224, 428).

Since asymmetry at positions other than α, as well as ethylenic geometry, is preserved, anodic oxidations are useful for stereospecific syntheses and for establishing both optical and geometrical relationships between high-molecular-weight products and low-molecular-weight starting materials. Electrolysis of (+)-L- and (−)-D-methyl hydrogen β-methylglutarate gives (+)- and (−)-methyl β,β'-dimethylsuberates in 63 and 75 per cent yields, respectively, no racemization being detected (426). Similarly, electrolysis of (+)-methyl hydrogen β-methylglutarate yielded a mixture of meso and (+)-diesters, from the mixture of which all the four forms, (+), (−), meso, and racemic, could be obtained. In this way branched long-chain dicarboxylic acids of the desired steric configuration may be synthesized by utilizing the product of one such optically controlled coupling in another coupling.

The present system for naming these compounds, however, may introduce confusion, because coupling of two optically identical residues yields a molecule which is named in such a way as to imply a difference between the two centers, as has already been pointed out (426). For example, the product of anodic coupling of two (−)-D-methyl hydrogen β-methylglutarate residues is termed methyl 2(L),5(D)-dimethylhexane-1,6-dicarboxylate (427).

An anodic oxidation of a mixture of two different dicarboxylic acid half-esters gives diesters of three kinds: the two symmetrical diesters and the diester of the cross-product. Depending on the starting materials more or less difficulty may be encountered in isolating the desired product. Generally the sodium or potassium salt of the methyl or ethyl half-ester is used, although certain advantages have been claimed for the benzyl half-ester (200, 430). The technique of the reaction has been discussed (671).

The free-radical mechanism recently proposed (310, 716) accounts not only for the normal products of the Kolbe synthesis, but also for its accompanying side reactions.

2. Oxidations by persulfate

It has been demonstrated that the anodic syntheses with the acid esters of dicarboxylic acids may be simulated by persulfate oxidation of the corresponding half-esters. Thus, the potassium salt of the monoethyl ester of dimethylmalonic acid is oxidized by alkaline potassium persulfate with loss of carbon dioxide to the diethyl ester of tetramethylsuccinic acid (222). A similar oxidation of the monoethyl ester of methylmalonic acid gave only an 8.6 per cent yield of the corresponding diethyl α,α'-dimethylsuccinate.

While the yields with the α-substituted dicarboxylic acid half-esters in these oxidations are of the same order as those with similar compounds in anodic oxidations, the monoesters of unsubstituted dicarboxylic acids give considerably lower yields of the coupled product. The yields from such persulfate oxidations also decrease with increasing molecular weight of the starting material. Persulfate

oxidation of the acid ester from sebacic acid, for instance, gave hardly any yield of the corresponding 1,16-hexadecanedicarboxylic acid.

The lower yields obtained in persulfate oxidations in comparison with anodic oxidations may probably be explained as a result of the lower specificity of the oxidizing agent. For example, potassium persulfate also attacks the α-hydrogen atoms of carboxylic acids, giving the corresponding succinic acid derivatives. Isobutyric acid or its ester have given the tetramethylsuccinic acid or its ester, respectively, in 3 to 4 per cent yield (223). Though these hydrogens are attacked much less readily than the carboxyl groups, there is possibility of destruction of the starting material or even the end product.

In all of these persulfate oxidations the products are accompanied by large quantities of the unreacted starting materials, and their decarboxylated saturated and unsaturated derivatives, which are also characteristic of the anodic oxidations.

Though it may be possible to improve the yields from these persulfate oxidations, particularly with the α-substituted dicarboxylic acid half-esters, where anodic oxidations give low yields, at the present time persulfate oxidation appears to offer no advantage over the anodic oxidations.

3. Utilization of aliphatic azo compounds

Thermal decomposition of azobisnitriles has been shown to give among other products large quantities of alkane dinitriles. For example, the 2,2′-azobisisobutyronitrile, obtained by oxidation of the 1,2-diisobutyronitrilehydrazine by bromine, gave tetramethylsuccinonitrile when a suspension of the solid in water or a solution of the azo compound in phenol or amyl alcohol was heated (679). Hydrolysis of the dinitrile gave tetramethylsuccinic acid. The substituted hydrazine itself was obtained by the reaction of hydrazine sulfate and potassium cyanide with acetone under reflux.

Besides acetone, other monofunctional ketones (202, 530) react with cyanide ion and hydrazine to give symmetrically 1,2-disubstituted hydrazines, which upon oxidation, decomposition, and hydrolysis yield the corresponding tetraalkylsuccinic acids. Since the azo compounds may contain asymmetric carbon atoms, their decomposition may yield a mixture of stereoisomeric substituted succinic acids, unless all the alkyl substituents are similar.

The yields of the substituted hydrazines may be improved by a simultaneous addition of anhydrous hydrazine and liquid hydrogen cyanide to these ketones (523). With hindered ketones, such as pinacolone and methyl isobutyl ketone, however, even this treatment is unsatisfactory. Moderate yields in such cases have been secured by preparing the azines first (11, 523) and then treating them with liquid hydrogen cyanide, at either ordinary or elevated temperatures and pressures. The conversion of the substituted hydrazines to the azo compounds by oxidation with bromine has been generally satisfactory, although other oxidizing agents such as permanganate and nitrous acid have been tried. Studies on the mechanism of the decomposition of these azonitriles have indicated that on heating the azobisnitriles in toluene solution, for example, free radicals are

formed, which are sufficiently long-lived to participate in cross-coupling with the decomposition products of other azobisnitriles (524). For example, the decomposition of a solution of two azonitriles of approximately the same decomposition rates, 2,2′-azoisobutyronitrile and 1,1′-azobis-1-cyclopentanenitrile, gave the three possible coupled products.

A mechanism for this decomposition has been proposed (530), and the rate of decomposition of at least the 2,2′-azobisisobutyronitrile has been shown to be essentially independent of the solvent type. Evidence has been presented that this decomposition proceeds through the intermediate formation of dimethylketene cyanoisopropylimine (677).

It has been also shown that the structure of these substituted hydrazine compounds can be varied to include the products from diketones (527). Several such compounds have already been made, at least one of which on decomposition and hydrolysis gave a substituted dicarboxylic acid. For example, 3,7-dicyano-3,7-dimethylhomopiperidazine (528) [subsequently shown to be actually 1-amino-2,6-dicyano-2,6-dimethylpiperidine (529), obtained from 2,6-heptanedione, hydrazine sulfate, and sodium cyanide] gave on oxidation with bromine and loss of nitrogen the two substituted cyclopentanes and also a 28 to 38 per cent yield of an α,β-unsaturated nitrile, which on hydrogenation and hydrolysis could be converted into α,α'-dimethylpimelic acid.

Oxidation with neutral potassium permanganate of 3,6-dimethyl-3,6-dicyano-1,2,4,5-tetrahydropyridazine, the product from the condensation of acetonylacetone, hydrazine, and hydrogen cyanide, resulted in loss of nitrogen from the unstable azo compound and a 43 per cent yield of 1,2-dimethyl-1,2-dicyanocyclobutane (525). No open-chain dinitriles were isolated, indicating little disproportionation of the intermediate biradicals.

These examples indicate that because of the nature of the biradicals formed, in the absence of a ready source of hydrogen atoms, the formation of the cyclic structures is bound to predominate, consequently rendering this method of little use in the preparation of branched long-chain dicarboxylic acids. The killing of the intermediate radicals by hydrogen atoms would also be of value only in such cases where the cyanohydrins of the corresponding diketones present difficulties either in their preparation or in conversion to the appropriate substituted dicarboxylic acids. The cross-coupling of these biradicals, should they be capable of it, with single radicals, resulting in the formation of $\alpha,\alpha,\alpha',\alpha'$-tetraheteroalkyl dicarboxylic acids, might be of greater interest. The difficulties experienced with simple cross-coupling, however, discourage one from entertaining high hopes of such accomplishments.

4. Utilization of peroxide-generated free radicals

It has been shown that a free methyl radical, generated in solution by the thermal decomposition of diacetyl peroxide, abstracts an α-hydrogen atom from carboxylic acids, esters, nitriles, ketones, and certain other compounds, forming new free radicals capable of coupling. When carboxylic acids are used, the products of the reaction are methane and a free carboxylic acid radical, which may

dimerize to the corresponding succinic or substituted succinic acid. Thus, when acetyl peroxide is decomposed in isobutyric acid, as much as 80 per cent of tetramethylsuccinic acid has been isolated (370). Though the yields are not always as high (554), such reactions are of preparative value (343, 369).

In special cases, in the absence of α-hydrogen atoms, such active methyl or other free radicals may abstract a β-hydrogen atom and give the corresponding adipic acid. For example, tetramethyladipic acid has been obtained in 75 per cent yield from trimethylacetic acid (373). A similar dimerization of the trimethylacetic acid free radical to the corresponding tetramethyladipic acid has also been effected with diisopropyl peroxydicarbonate but in much lower yield (454).

A simultaneous peroxide-catalyzed generation of free radicals from two different fatty acids of about the same hydrogen-surrendering ability might result in simple and crossed dimerization. Such crossed dimerizations might proceed similarly to the mixed-ester anodic oxidations, giving good yields when suitable starting materials are used and effective methods for the isolation of the crossed product are available.

The types of free radicals that can be effectively combined in these reactions are limited. The more reactive free radicals (the more electronegative free radicals, in the sense of Kharasch) do not survive long enough to attain sufficient concentrations for mutual encounter. The less reactive free radicals, depending on their structures, either undergo dimerization or disproportionation or both (373). The ratio of dimerization to disproportionation depends upon the experimental conditions.

These reactions are usually carried out by keeping the fatty acid, its ester, its anhydride, or the acid chloride or nitrile at a temperature of 85–90°C. and introducing the peroxide, dissolved in the appropriate reactant, gradually into the hot solution. A peroxide:reactant ratio of 1:3–5 moles has been found to be optimum (370).

A general synthesis of carboxylic acids recently developed (167) uses a free radical, generated by Fenton's reagent, to alkylate carbon monoxide.

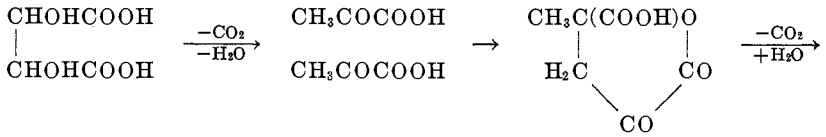
D. MISCELLANEOUS METHODS

A number of methods for the preparation of branched-chain dicarboxylic acids have either not been satisfactorily investigated to enable their integration even with the loose scheme of classification used above, or are of a very special nature and extremely limited application. Hence they have been selected here for special treatment.

Among these are the pyrolytic methods for the preparation of α-methylsuccinic acid. It has been obtained by the distillation of glyceric acid (477), by heating pyruvic acid with hydrochloric acid at 100°C. in a closed vessel (166), by the dry distillation of tartaric acid (62), and by heating tartaric acid with acetic acid (610).

It has been proposed that all these processes are basically similar and proceed through the intermediate formation of pyruvic acid, and then of a ketovalero-

lactone which on loss of carbon dioxide and addition of water yields methylsuccinic acid (741).



$HOOCCH(CH_3)CH_2COOH$

Another special method for the preparation of methylsuccinic acid in good yield calls for the action of hydrogen under pressure on solutions of sodium lactate (334).

Recently, alkyl-substituted dicarboxylic acids have been prepared by alkali-induced rearrangement of the dibromination products of 2-alkylacetoacetates (693). Initially, 2-alkylfumaric acids or the corresponding substituted maleic anhydrides are formed, which on reduction give the appropriate succinic acid derivatives.

A simple example of the pinacol rearrangement of an aliphatic tetraol is reported (19) to give a diketone which yielded 2,2,7,7-tetramethyloctanedioic acid on oxidation.

E. SIMPLE MODIFICATION OF THE CHAIN LENGTH OF ALKYLATED ALKANEDIOIC ACIDS

When attempting to prepare a certain substituted dicarboxylic acid, a complete synthesis may be impractical. It may be found much more convenient to obtain the desired compound by chain extension from some other suitably substituted dicarboxylic acid which may be available commercially or prepared more easily in the laboratory. Occasionally degradation by standard methods may be used for the preparation of an alkylated dicarboxylic acid. Such processes can take place at one end or both ends of the chain.

In this way several substituted dicarboxylic acids of known configuration have been converted to either their higher or their lower homologs.

1. Extension

The extension of carboxylic acid chains by one, two, or more carbon atoms without a simultaneous introduction of branching has been adequately dealt with in recent reviews on fatty acid synthesis (112, 270, 290). With minor modifications these methods may also be adapted to the extension of the carbon chains in alkylated dicarboxylic acids either at only one end of the chain or at both. Thus, for example, the nitrile synthesis has been used to prepare 4-methylsuberic acid from 3-methyladipic acid (560). 3,5,5-Trimethyl-1,6-hexanedicarboxylic acid was similarly prepared from 2,4,4-trimethyl-1,6-hexanediol by bromination, formation of the dinitrile, and saponification (600).

By going through the diols, dibromides, and a malonic ester synthesis twice, it was possible to obtain 7-methyl-1,14-tetradecanedicarboxylic acid from diethyl 3-methylsuberate (603).

2. Degradation

Degradation of silver carboxylates with halogens to alkyl halides is well known (243, 737). It has also been utilized for the shortening of carbon chains in alkyl-substituted dicarboxylic acids. The substituted dihalides obtained are converted into the corresponding diols, which may then be oxidized to the dicarboxylic acids by permanganate. Such a bis-degradation, for example, was used in the preparation of (−)-2D,5L- and (+)-2L,5D-dimethyladipic acids from (+)-3D,6L- and (−)-3L,6D-dimethylsuberic acids, respectively (304). This particular method is quite laborious and the yields may not be high enough to justify its use for ordinary preparative purposes, yet it is important in correlating the structures of the low-molecular-weight end products with those of the high-molecular-weight starting materials.

The decomposition of the silver salts is best effected by bromine; iodine forms undesirable side products, while chlorine gives smaller yields than bromine. The silver salts themselves may be replaced by lead, mercury, or alkali metal salts. The reaction is supposed to involve free radicals (243).

In addition to this, also known as the Hunsdiecker degradation, there are other degradative processes peculiar to the dicarboxylic acids. Thus the dicarboxylic acids may be cyclized to the ketones, then formylated in the α-position, and on ozonization and oxidation with chromic acid degraded to the dicarboxylic acid having one carbon atom less. In this manner, 2,2,3-trimethylsuberic acid was converted in high yield into 2,2,3-trimethyladipic acid, and the latter subsequently into 2,2,3-trimethylglutaric acid (612).

Since in these cases one of the carbon atoms adjacent to the keto group was always doubly alkylated, the formylation could take place only in one position, and the α-carbon atom was always the next carboxyl carbon. Whether this method is capable of extension to the bis-degradation of suitably substituted α,α-unsubstituted dicarboxylic acids remains to be seen.

Another method suitable for the degradation of dicarboxylic acids consists of an initial formation of the anhydride, reaction with methylmagnesium iodide, and oxidation of the resulting keto acid with chromic anhydride in sulfuric acid. In this way racemic isopropylglutaric acid gave racemic isopropylsuccinic acid, and the (+)-isopropylglutaric acid gave mainly (−)-isopropylsuccinic acid (252).

III. Separation of Stereoisomers

A. Separation of DL and Meso Compounds

Many of the most accessible compounds of this series are low-molecular-weight symmetrically disubstituted acids and therefore exist in D, L, DL, and meso forms. Separation of the racemic and meso isomers has been easily achieved in such cases because of the relatively large differences in melting point and solubility. For example, the meso and DL forms of 2,3-dimethylsuccinic acid may be separated by fractional crystallization from water (81, 753) or from benzene or chloroform (232), in which the meso form is much less soluble. Also, the formation of an anhydride (94) may be a basis for separation, since the DL compound gives it readily with acetyl chloride, while the meso compound does not.

Besides the anhydride, other derivatives of such diastereoisomers, like the inorganic and organic salts (92), may be used in the separation of the meso and DL derivatives of 2,3-dimethylsuccinic acid. Diastereoisomeric pairs of other similarly substituted dicarboxylic acids have been separated by like means (37, 70, 311, 476, 515, 573, 650, 754). It has been repeatedly shown that the higher-melting isomer is the meso form, while the lower-melting isomer may be resolved into its optical antipodes (71, 104, 126, 253, 304, 575, 745). However, in cases where the substituents are relatively far removed from both carboxyl groups and suitably spaced, the chemical and physical differences between the meso and the DL forms may not be so pronounced, and separation may become a problem. Thus γ-methyl-β-isoamylpimelic acid (595), supposedly a mixture of isomers, behaved as a single compound. Similarly, 4,15-dimethyloctadecanedioic (163) and α-methyl-β-isopropylpimelic (605) acids failed to show the characteristic differences in the chemical and physical properties of their isomers supposedly present.

B. SEPARATION OF MIXTURES OF RACEMATES

Asymmetrically substituted succinic acids such as 2-methyl-3-ethylsuccinic acid exist as two pairs of racemates, sometimes loosely termed "fumaroid" and "malenoid." Such mixtures from the simpler dicarboxylic acids also differ significantly in their physical and chemical properties and may be separated with little effort. Thus the racemates from 2-methyl-3-ethylsuccinic acid, for example, have been separated by crystallizing the mixture from hot water (34); on cooling most of the fumaroid type of acid crystallizes. The acids left behind in the mother liquors may be separated in the form of their neutral calcium salts, since the fumaroid acid salt is difficultly soluble in hot water and easily soluble in cold, while the malenoid acid salt is difficultly soluble in both hot and cold water.

Fractional crystallization has proven satisfactory also for the separation of the racemic pairs of 2-methyl-4-ethylglutaric acid (78, 79), 2-methyl-3-isopropylsuccinic acid (67), and other (80, 221) similarly substituted dialkyl dicarboxylic acids. The naming of the substituted succinic acids as either the fumaroid or malenoid type is based on the mode of preparation as well as on the observation that when the fumaroid form is prepared with certainty, these acids are usually higher melting. In the case of acids higher than succinic, the corresponding dialkyl forms are referred to as the para and the anti forms, respectively (374), though the symmetrical dialkyl dicarboxylic acid derivatives have also been occasionally referred to as of the malenoid or fumaroid type (36).

Another type of mixture of racemates is obtained from an asymmetrical substitution of the dicarboxylic acid chain by similar alkyl substituents. For example, a liquid form of 2,3-dimethylglutaric acid is obtained on hydrolysis and decarboxylation of 2,3-dimethyl-2-cyanoglutaric acid by hot concentrated hydrochloric acid (682). A by-product of this reaction, 2,3-dimethylglutarimide, on hydrolysis gives a solid form of 2,3-dimethylglutaric acid. Again, on the basis of the mode of preparation the solid or higher-melting form is thought to be the meso or cis pair of enantiomorphs, while the liquid form would be the trans

racemate. Such assignment of structure is in agreement with the observations on other similarly substituted dicarboxylic acids (95). These two racemic pairs have not been further characterized or resolved. It has been suggested that purification of the solid form might be achieved through distillation of the ethyl ester (83).

An asymmetric substitution of the carbon chain by two dissimilar alkyl substituents differs little from the previous case. The two racemic pairs appear to possess again enough difference in their physical and chemical properties to permit their separation when the molecular weight is low. Thus, 2-methyl-3-isopropylglutaric acid gives the so-called cis and trans pairs on fractional crystallization from suitable solvents (324, 514).

As the number of asymmetric carbon atoms in the branched-chain dicarboxylic acid increases, the separation of racemic pairs becomes difficult. This may be due to the lack of difference in their physical and chemical properties or because of the formation of quasi-racemates. Accordingly, the dicarboxylic acids with more than two asymmetric carbon atoms prepared by ordinary stepwise syntheses appear to be mixtures. These acids are either oils or waxy solids and they melt over a range of temperature. For example, 2,3,6-trimethylpimelic acid has been obtained as an oil (756).

When a particular isomer of a substituted dicarboxylic acid with asymmetric carbon atoms is to be made, the number of isomers obtained has to be limited. This may be done by employing asymmetric starting materials (140, 245), using reagents of stereospecific activity (252), or performing the reaction under controlled stereospecific conditions (648). The discovery that anodic syntheses are optically controlled has been particularly rewarding, and the availability of polysubstituted dicarboxylic acids of known configuration has been one of the results.

The stereochemical problems discussed here have been limited to the simpler cases, because with very few exceptions only the simpler alkyl substitution products of dicarboxylic acids have been thus far prepared. New problems of synthesis and separation are encountered as more complicated tasks are attempted. The presence of asymmetric carbon atoms in the side chains is a complication not yet investigated.

C. RESOLUTION OF ENANTIOMORPHS

Satisfactory discussions of proven and potential means for the resolution of racemic modifications are to be found in several rather recent publications (56, 66, 377, 630). Therefore only a short review of these as they concern the resolution of enantiomorphic pairs of alkyl-substituted dicarboxylic acids will be presented here.

Resolution of an inactive substance into its optically active components can be accomplished only in rare instances by crystallization and mechanical separation, as in the classical experiment by Pasteur (534), or by subsequently introduced modifications. A special case arising from the original observations of Pasteur and of great importance in the resolution of enantiomorphic alkylated

dicarboxylic acids is the formation of salts with optically active natural or synthetic bases (535), such as quinine, strychnine, brucine, or their quaternary ammonium hydroxides (442). Thus, if a DL acid is neutralized with a dextrorotatory base, the two salts are diastereoisomers and possess different rotatory values, different solubilities, and different melting points, and are separable by fractional crystallization, the course of separation being followed by the determination of the appropriate physical constants.

Once the salt has been secured pure, it can be treated with alkali hydroxide, the resolving base recovered, and the optically active acid liberated by acidification of the alkaline solution. The resolving agents that have been particularly useful in these separations are the naturally occurring tertiary amines. With the help of these practically all of the resolutions of racemic alkyl-substituted dicarboxylic acids have been performed (70, 248). These means have proven satisfactory also for the resolution of the racemic half-esters of alkyl-substituted dicarboxylic acids (33).

The methohydroxides of quinine, quinidine, and cinchonine are much stronger bases than the tertiary amines themselves and are also excellent resolving agents for certain racemates.

High rotatory power of the resolving agent facilitates following the separation by polarimetric examination of the crystallizates. Availability and cost of the reagent are considerations, particularly when preparing large quantities of the optically active material; however, a reasonably stable substance may be recovered without undue loss.

When a pair of diastereoisomeric salts is fractionated, the less soluble isomer can be often obtained relatively easily, but isolation of the more soluble salt in pure form may present difficulties. Change to another resolving agent has sometimes been advantageous (251), for with another pair of salts the solubility relationships were found to be reversed. For a number of partially resolved, optically active, substituted dicarboxylic acids, it has been found that the preparation and recrystallization of the anhydrides (248) effected the final purification most effectively. In such a procedure, however, there is a danger of racemization. Sometimes it also pays just to recrystallize the alkali salts of the partly resolved acids (271).

A modification in the resolution of DL bases consists in treating the base with half the amount of a resolving organic acid required for neutralization, together with a further equivalent of hydrochloric acid (551). Equilibrium is set up among the two pairs of salts, but those derived from the organic acid are distinctly less soluble than the hydrochlorides. Thus the less soluble of the two diastereoisomeric organic salts tends to crystallize, and the solution contains chiefly the hydrochloric acid salt of the enantiomeric base. A utilization of this phenomenon but in the reverse to the resolution of DL acids, however, met with somewhat less success (254).

A still further modification of the phenomenon of the diastereoisomeric salt formation is the use of asymmetric chromatography media for the resolution of DL mixtures. Though no attempts with aliphatic dicarboxylic acid derivatives have been recorded, certain other carboxylic acids have been separated. Thus

DL-mandelic acid has been resolved on a column of Amberlite XE-64 combined with quinine (286).

The separation of racemates by first converting them into the diastereoisomers by combination with a D or an L compound, followed by passing the mixture through a column of optically inactive adsorbent, has also been attempted. A partial separation of *l*-menthyl-*d*-mandelate from *l*-menthyl-*l*-mandelate has been obtained on alumina (341). L(+)-*N*-Methylvaline was similarly prepared from the (±) isomer by condensation with (−)-α-bromoisovaleryl chloride and decomposition of the product on alumina.

Diastereoisomers are usually easily separated by various chromatographic methods. Thus partition chromatography on paper with certain solvents effected a complete separation of D,D-, L,L-, and the meso forms of 2,6-diaminopimelic acid (580). A review on the subject of stereochemistry and chromatography has been published (752).

Fractional distillation of diastereoisomeric salts or esters of substituted alcohols or carboxylic acids through a packed column has also met with some success (47).

D. DETERMINATION OF CONFIGURATION

The resolution of an enantiomorphic pair of substituted dicarboxylic acids into the dextrorotatory and levorotatory components, by asymmetric bases, for example, leaves the structure of these components still unsettled. Knowledge of the extent and direction of rotation does not supply any information about the absolute or relative configuration of the substance. Since potential methods for the determination of the configuration of organic substances have been adequately discussed elsewhere, only those that have actually been used for the determination of configuration in dicarboxylic acids will be mentioned here.

One such method for the determination of configuration of substituted dicarboxylic acids, which has found considerable success in recent years, is based on the determination of melting-point curves of quasi-racemates. The principle underlying this phenomenon has been recognized for a considerable time (684, 685), but results of outstanding importance have been obtained only recently (249, 250, 422). In this method molecular compounds in a 1:1 ratio are formed between compounds which are of different configuration yet of closely similar structures. While compounds of similar configuration show in the melting-point diagram only a eutectic, there is a melting-point maximum in the case of opposite configuration (258, 451).

In such a way it has been possible to correlate a number of substituted dicarboxylic acids with one another and through the lactic and thiolactic acids with D-glyceraldehyde (245, 247, 252, 544, 552, 653). These results have now been confirmed by direct chemical correlations (257, 513).

An interesting additional observation made in these studies was that in all the cases investigated, those acids which had the same direction of rotation had also the same configuration. Thus all the monosubstituted (+)-alkylsuccinic acids examined had the D configuration.

Correlations of absolute configurations deduced solely from optical rotation

data, however, can not in many cases be accepted as decisive; yet the optical method often provides an easy, and sometimes the only way of achieving a correlation (256, 378, 471, 727).

The steric configuration of alkyl-substituted dicarboxylic acids has also been the subject of infrared absorption studies (614, 615).

IV. References

(1) Adams, R., and Anderson, J. L.: J. Am. Chem. Soc. **73,** 136 (1951).
(2) Adams, R., and Duuren, B. L. van: J. Am. Chem. Soc. **75,** 4638 (1953).
(3) Adkins, H., Isbell, N., and Wojcik, B.: In *Organic Syntheses,* Collective Vol. II, p. 262. John Wiley and Sons, Inc., New York (1943).
(4) Adkins, H., and Roebuck, A. K.: J. Am. Chem. Soc. **70,** 4041 (1948).
(5) Akiyoshi, S., Okuno, K., and Nagahama, S.: J. Am. Chem. Soc. **76,** 902 (1954).
(6) Albisetti, C. J., Jr., England, D. C., Hogsed, M. J., and Joyce, R. M.: J. Am. Chem. Soc. **78,** 472 (1956).
(7) Albisetti, C. J., and Fisher, N. G. (to E. I. du Pont de Nemours and Co.): U. S. patent 2,584,527 (February 5, 1952); Chem. Abstracts **46,** 8674*a* (1952).
(8) Alder, K., Pascher, F., and Schmitz, A.: Ber. **76B,** 27 (1943).
(9) Alder, K., Schumacher, M., Boehne, H., and Mueller, G.: Chem. Ber. **87,** 447 (1954).
(10) Alder, K., and Soell, H.: Ann. **565,** 57 (1949).
(11) Alderson, W. L., and Robertson, J. A.: U. S. patent 2,469,358 (May 10, 1949); Chem. Abstracts **43,** 6652*e* (1949).
(12) Alexander, E. R.: *Ionic Organic Reactions,* p. 203. John Wiley and Sons, Inc., New York (1950).
(13) Alexander, E. R., McCollum, J. D., and Paul, D. E.: J. Am. Chem. Soc. **72,** 4791 (1950).
(14) Allan, G. G., MacLean, D., and Newbold, G. T.: J. Chem. Soc. **1952,** 5053.
(15) Allen, C. F. H., and Johnson, H. B.: Org. Syntheses **30,** 83 (1950).
(16) Alles, B. J. P., Kandiah, A., and Sultanbawa, M. U. S.: J. Chem. Soc. **1956,** 797.
(17) Ansell, M. F., and Hey, D. H.: J. Chem. Soc. **1950,** 1683.
(18) Ansell, M. F., Hickinbottom, W. J., and Holton, P. G.: J. Chem. Soc. **1955,** 349.
(19) Ansell, M. F., Hickinbottom, W. J., and Hyatt, A. A.: J. Chem. Soc. **1955,** 1781.
(20) Antia, M. B., and Kaushal, R.: Agra Univ. J. Research, Science **3,** 197 (1954); Chem. Abstracts **49,** 6121*h* (1955).
(21) Armendt, B. F., and Adams, R.: J. Am. Chem. Soc. **52,** 1289 (1930).
(22) Arthur, P., Jr., England, D. C., Pratt, B. C., and Whitman, G. M.: J. Am. Chem. Soc. **76,** 5364 (1954).
(23) Arthur, P., Jr., and Pratt, B. C.: U. S. patent 2,666,748 (January 19, 1954); Chem. Abstracts **49,** 1774*f* (1955).
(24) Asami, R., and Shimo, K.: Sci. Repts. Research Insts., Tôhoku Univ. **9A,** 341 (1957); Chem. Abstracts **52,** 3677*h* (1958).
(25) Asano, M., and Azumi, T.: J. Pharm. Soc. Japan **59,** 605, 214 (1939).
(26) Asano, M., Kamdta, Y., and Wada, T.: J. Pharm. Soc. Japan **65,** No. 7/8A, 5 (1945); Chem. Abstracts **45,** 5617*c* (1951).
(27) Asano, M., and Kameda, Y.: J. Pharm. Soc. Japan **61,** 405 (1941).
(28) Asano, M., and Ohta, J.: Ber. **67B,** 1842 (1934).
(29) Asano, M., and Ohta, J.: J. Pharm. Soc. Japan **65,** No. 5/6A, 10 (1945); Chem. Abstracts **45,** 4302*i* (1951).
(30) Asano, M., and Yamakawa, T.: J. Pharm. Soc. Japan **69,** 388 (1949).
(31) Asano, M., and Yamakawa, T.: J. Pharm. Soc. Japan **70,** 474 (1950).
(32) Aschan, O.: Ann. **387,** 1 (1912).
(33) Asselineau, C., Asselineau, J., and Stallberg-Stenhagen, S.: Acta Chem. Scand. **10,** 478 (1956).

(34) AUWERS, K. VON, AND FRITZWEILER, R.: Ann. **298,** 154 (1897).
(35) AUWERS, K. VON, AND MEYER, V.: Ber. **22,** 2013 (1889); **23,** 293 (1890).
(36) AUWERS, K. VON, AND OTTENS, B.: Ber. **57B,** 437 (1924).
(37) AUWERS, K. VON, AND THORPE, J. F.: Ann. **285,** 310, 315, 332, 335 (1895).
(38) AUWERS, K. VON, AND UNGEMACH, O.: Ann. **511,** 152 (1934).
(39) BABAYAN, A. T.: Trudy Inst. Khim. in P. G. Melikishvili, Akad. Nauk Gruzin. S.S.R. **12,** 149 (1956); Chem. Abstracts **52,** 4467*i* (1958).
(40) BACHMANN, W. E.: J. Org. Chem. **3,** 434 (1938).
(41) BACHMANN, W. E., AND STRUVE, W. S.: In *Organic Reactions,* Vol. I, Chap. 2. John Wiley and Sons, Inc., New York (1942).
(42) BACHMANN, W. E., AND WENDLER, N. L.: J. Am. Chem. Soc. **68,** 2580 (1946).
(43) BADGER, G. M., RODDA, H. J., AND SASSE, W. H. F.: J. Chem. Soc. **1954,** 4162.
(44) BAILEY, A. S., POLGAR, N., AND ROBINSON, R.: J. Chem. Soc. **1953,** 3031.
(45) BAILEY, A. S., POLGAR, N., TATE, F. E. G., AND WILKINSON, A.: J. Chem. Soc. **1955,** 1547.
(46) BAILEY, B., HAWORTH, R. D., AND MCKENNA, J.: J. Chem. Soc. **1954,** 967.
(47) BAILEY, M. E., AND HAAS, H. B.: J. Am. Chem. Soc. **63,** 1969 (1941).
(48) BAKER, J. W.: J. Chem. Soc. **1931,** 1546.
(49) BALENOVIC, K., AND JAMBRESIC, I.: Chemistry & Industry **1955,** 1673.
(50) BARDHAN, J. C.: J. Chem. Soc. **1928,** 2611.
(51) BARDHAN, J. C., DE, N. C., AND DATTA, B. B.: J. Chem. Soc. **1951,** 3195.
(52) BARDHAN, J. C., AND SENGUPTA, S. C.: J. Chem. Soc. **1932,** 2798.
(53) BARNABEI, O., VALYASEVE, A., BARNESS, L. A., AND GYORGY, P.: Arch. Biochem. Biophys. **69,** 259 (1957).
(54) BARNESS, L. A., MOESKI, H., AND GYORGY, P.: J. Biol. Chem. **221,** 93 (1956).
(55) BARRY, V. C., AND TWOMEY, D.: Proc. Roy. Irish Acad. **51B,** 137 (1947).
(56) BASALO, F.: In *The Chemistry of the Coordination Compounds,* edited by J. C. Bailar Jr., and D. H. Bush, Chap. 8, p. 274. Reinhold Publishing Corporation, New York (1956).
(57) BATZER, H.: Makromol. Chem. **10,** 13 (1953).
(58) BATZER, H., AND WILOTH, F.: Chem. Ber. **83,** 340 (1950).
(59) BATZER, H., AND WILOTH, F.: Chem. Ber. **84,** 680 (1951).
(60) BAUMGARTEN, H. E., AND GLEASON, D. C.: J. Org. Chem. **16,** 1658 (1951).
(61) BAYLISS, P. L., AND HAUSER, C. R.: J. Am. Chem. Soc. **76,** 2306 (1954).
(62) BECHAMP, F.: Z. Chemie **1870,** 371.
(63) BEECH, W. F., AND PIGGOTT, H. A.: J. Chem. Soc. **1955,** 423.
(64) BELL, A., STRICKLAND, T. H., AND WRIGHT, G. F.: J. Org. Chem. **16,** 1742 (1951).
(65) BENDZ, G.: Acta Chem. Scand. **9,** 1729 (1955).
(66) BENT, R. L.: J. Chem. Educ. **30,** 220, 284, 328 (1953).
(67) BENTLEY, W. H., PERKIN, W. H., JR., AND THORPE, J. F.: J. Chem. Soc. **69,** 270 (1896).
(68) BERGMANN, E., AND BOGRACHOV, E.: J. Am. Chem. Soc. **62,** 3017 (1940).
(69) BERGSTROM, S., BORGSTROM, B., TRYDING, N., AND WESTOO, G.: Biochem. J. **58,** 604 (1954).
(70) BERNER, E., AND LANDMARK, L. H.: Acta Chem. Scand. **7,** 1347 (1953).
(71) BERNER, E., LEONARDSEN, R., GRONTOFT, A. T., AND DAHL, K.: Ann. **538,** 1 (1939).
(72) BHATTACHARYYA, K. C.: Current Sci. (India) **21,** 312 (1952).
(73) BICKEL, A. F., AND WATERS, W. A.: Rec. trav. chim. **69,** 312 (1950).
(74) BIER, G.: Experientia **2,** 82 (1946).
(75) BIRCH, A. J., AND ROBINSON, R.: J. Chem. Soc. **1942,** 488.
(76) BIRCH, S. F., GRIPP, V. E., MCALLAN, D. T., AND NATHAN, W. S.: J. Chem. Soc. **1952,** 1363.
(77) BIRCH, S. F., AND JOHNSON, E. A.: J. Chem. Soc. **1951,** 1493.
(78) BISCHOFF, C. A.: Ber. **24,** 1050 (1891).
(79) BISCHOFF, C. A., AND MINTZ, N.: Ber. **23,** 3410 (1890).

(80) BISCHOFF, C. A., AND TIGERSTEDT, A.: Ber. **23,** 1940 (1890).
(81) BISCHOFF, C. A., AND VOIT, E.: Ber. **22,** 389 (1889).
(82) BLAISE, E. E.: Compt. rend. **126,** 1808 (1898).
(83) BLAISE, E. E.: Compt. rend. **136,** 243 (1903).
(84) BLAISE, E. E., AND GAULT, H.: Bull. soc. chim. [4] **1,** 75 (1907).
(85) BLANC, G.: Bull. soc. chim. [4] **3,** 286, 292 (1908).
(86) BLANC, G.: Compt. rend. **145,** 681 (1908).
(87) BLEYBERG, W., AND ULRICH, H.: Ber. **64B,** 2504 (1931).
(88) BLICKE, F. F., AND SHEETS, D. G.: J. Am. Chem. Soc. **71,** 4010 (1949).
(89) BLOMQUIST, A. T., WHEELER, E. S., AND CHU, Y.: J. Am. Chem. Soc. **77,** 5423 (1955).
(90) BODROUX, F.: Compt. rend. **137,** 710 (1903).
(91) BOEDECKER, F., AND GRUBER, H.: U. S. patent 2,220,638 (November 5, 1941); Chem. Abstracts **35,** 1806[3] (1941).
(92) BONE, W. A., AND PERKIN, W. H. JR.: J. Chem. Soc. **69,** 262 (1896).
(93) BONE, W. A., AND SPRANKLING, C. H. G.: J. Chem. Soc. **75,** 839 (1899).
(94) BONE, W. A., AND SPRANKLING, C. H. G.: J. Chem. Soc. **75,** 857 (1899).
(95) BONE, W. A., AND SPRANKLING, C. H. G.: J. Chem. Soc. **77,** 660 (1900).
(96) BOORMAN, E. J., LINSTEAD, R. P., AND RYDON, H. N.: J. Chem. Soc. **1933,** 568.
(97) BOTTOMLEY, J. F., AND PERKIN, W. H.: J. Chem. Soc. **77,** 294 (1900).
(98) BOUVEAULT, L., AND LOCQUIN, R.: Bull. soc. chim. [4] **3,** 449 (1908).
(99) BOUVEAULT, L., AND LOCQUIN, R.: Compt. rend. **146,** 138 (1908).
(100) BRADFIELD, A. E., JONES, E. R., AND SIMONSEN, J. L.: J. Chem. Soc. **1935,** 315.
(101) BRADSHER, C. K., BROWN, F. C., AND GRANTHAM, R. J.: J. Am. Chem. Soc. **73,** 5377 (1951).
(102) BRANDSTROM, A.: Acta Chem. Scand. **10,** 1197 (1956).
(103) BRAUN, J. VON, ANTON, E., AND MAY, W.: Ber. **70B,** 1250 (1937).
(104) BRAUN, J. VON, AND HAENSEL, W.: Ber. **59B,** 1999 (1926).
(105) BRAUN, J. VON, KELLER, W., AND WEISSBACH, K.: Ann. **490,** 179 (1931).
(106) BRAUN, J. VON, KRAPER, H., AND WIENHAUS, H.: Ber. **62B,** 2880 (1929).
(107) BRAUN, J. VON, MANNES, L., AND REUTER, M.: Ber. **66B,** 1499 (1933).
(108) BRAUN, J. VON, AND SCHATTNER, O.: Ber. **74B,** 22 (1941).
(109) BRAUN, J. VON, AND SOBECKI, W.: Ber. **44,** 1921 (1911).
(110) BRAUN, J. VON, TEUFFERT, W., AND MANZ, G.: Ber. **62B,** 235 (1929).
(111) BRAUN, J. VON, AND WERNER, G.: Ber. **62B,** 1050 (1929).
(112) BREUSCH, F. L.: *Fortschritte chemischen Forschung,* Vol. I, p. 567. Springer Verlag, Berlin (1949–1950).
(113) BREWSTER, J. H.: J. Am. Chem. Soc. **73,** 366 (1951).
(114) BREWSTER, J. H., AND ELIEL, E. L.: In *Organic Reactions,* Vol. VII, p. 99. John Wiley and Sons, Inc., New York (1953).
(115) BROWN, A. C., AND WALKER, J.: Ann. **261,** 107 (1891).
(116) BROWN, A. C., AND WALKER, J.: Ann. **274,** 42 (1893).
(117) BROWN, J. G. T., ROSE, J. D., AND SIMONSEN, J. L.: J. Chem. Soc. **1944,** 101.
(118) BROWN, R. F., AND VAN GULICH, N. M.: J. Am. Chem. Soc. **77,** 1079 (1955).
(119) BRUNNER, O., AND WIEDMANN, G.: Monatsh. **66,** 438 (1935).
(120) BRUSON, H. A.: In *Organic Reactions,* edited by R. Adams, Vol. V, Chap. 2. John Wiley and Sons, Inc., New York (1949).
(121) BRUSON, H. A., AND RIENER, T. W.: J. Am. Chem. Soc. **66,** 56 (1944).
(122) BRYCE-SMITH, D.: J. Chem. Soc. **1956,** 1603.
(123) BUCHI, J., ENEZIAN, G., EICHENBERGER, H., AND LIEBERHERR, R.: Helv. Chim. Acta **35,** 75 (1952).
(124) BUCHTA, E., AND BURGER, K.: Ann. **580,** 125 (1953).
(125) BUECHI, J., ENEZIAN, G., EICHENBERGER, H., AND LIEBERHERR, R.: Helv. Chim. Acta **35,** 75 (1952).
(126) BURGER, G., AND KILLEN MCBETH, A.: J. Chem. Soc. **1946,** 145.

(127) BUSH, M. T.: J. Am. Chem. Soc. **61,** 637 (1939).
(128) BUSH, M. T., AND BEAUCHAMP, W. D.: J. Am. Chem. Soc. **75,** 2949 (1953).
(129) BUSTON, H. W.: Biochem. J. **22,** 1523 (1928).
(130) BUU-HOÏ, NG. PH., AND CAGNIANT, P.: Bull. soc. chim. **10,** 477 (1943).
(131) BUU-HOÏ, NG. PH., AND CAGNIANT, P.: Ber. **76B,** 689 (1943).
(132) BUU-HOÏ, NG. PH., AND CAGNIANT, P.: Z. physik. Chem. **279,** 76 (1943).
(133) BUU-HOÏ, NG. PH., SY, M., AND XUONG, N. DAT: Bull. soc. chim. France **1955,** 1583.
(134) CALDWELL, J. R.: U. S. patent 2,744,092 (May 1, 1956); Chem. Abstracts **50,** 16182*b* (1956).
(135) CANNON, J. G.: J. Am. Pharm. Assoc. **45,** 430 (1956).
(136) CANONICA, L., AND BACCHETTI, T.: Gazz. chim. ital. **83,** 1043 (1953).
(137) CANONICA, L., AND MARTINOLLI, M.: Gazz. chim. ital. **83,** 431 (1953); Chem. Abstracts **49,** 3800*f* (1955).
(138) CANONICA, L., AND PELIZZONI, F.: Gazz. chim. ital. **84,** 553 (1954); Chem. Abstracts **50,** 879*g* (1956).
(139) CANONICA, L., PELIZZONI, F., AND FEDELI, E.: Gazz. chim. ital. **85,** 130 (1955); Chem. Abstracts **50,** 9290*d* (1956).
(140) CARNMALM, B.: Acta Chem. Scand. **10,** 477 (1956).
(141) CARTER, A. S.: J. Am. Chem. Soc. **50,** 1967 (1928).
(142) CASON, J.: Chem. Revs. **40,** 15 (1947).
(143) CASON, J.: J. Org. Chem. **13,** 227 (1948).
(144) CASON, J., ADAMS, C. E., BENNETT, L. L., JR., AND REGISTER, U. D.: J. Am. Chem. Soc. **66,** 1764 (1944).
(145) CASON, J., ALLINGER, N. L., AND SUMRELL, G.: J. Org. Chem. **18,** 850 (1953).
(146) CASON, J., ALLINGER, N. L., SUMRELL, G., AND WILLIAMS, D. E.: J. Org. Chem. **16,** 1170 (1951).
(147) CASON, J., ALLINGER, N. L., AND WILLIAMS, D. E.: J. Org. Chem. **18,** 842 (1953).
(148) CASON, J., AND FESSENDEN, R. J.: J. Org. Chem. **22,** 1326 (1957).
(149) CASON, J., AND FRIEMAN, C.: J. Biol. Chem. **205,** 449 (1953).
(150) CASON, J., GASTALDO, C., GLUSKER, D. L., ALLINGER, J., AND ASH, L. B.: J. Org. Chem. **18,** 1129 (1953).
(151) CASON, J., AND KALM, M. J.: J. Org. Chem. **19,** 1836 (1954).
(152) CASON, J., PIPPEN, E. L., TAYLOR, P. B., AND WINANS, W. R.: J. Org. Chem. **15,** 135 (1950).
(153) CASON, J., AND PROUT, F. S.: *Organic Syntheses,* Collective Vol. III, p. 601. John Wiley and Sons, Inc., New York (1955).
(154) CASON, J., RINEHART, K. L., JR., AND THORNTON, S. D., JR.: J. Org. Chem. **18,** 1594 (1953).
(155) CASON, J., AND SMITH, R. D.: J. Org. Chem. **18,** 1201 (1953).
(156) CAVANNA, R., AND STALLBERG-STENHAGEN, S.: Atti accad. nazl. Lincei, Mem. classe sci. fís. mat. e nat. [8] **3,** No. 2, 31 (1950); Chem. Abstracts **45,** 9470*d* (1951).
(157) CHARGAFF, E.: Ber. **65B,** 745 (1932).
(158) CHARGAFF, E., AND ABEL, G.: Biochem. J. **28,** 1901 (1934).
(159) CHAVANE, V.: Ann. chim. [12] **4,** 352 (1949).
(160) CHAVANE, V., AND RUMPF, P.: Compt. rend. **225,** 1322 (1947).
(161) CHICHIBABIN, A. E., AND KATZNELSON, M. M.: Bull. acad. sci. U.R.S.S., Classe sci. math. nat. **1933,** 267; Chem. Abstracts **27,** 3698 (1933).
(162) CHRISTIE, S. M. H., KROPMAN, M., NOVELLIE, L., AND WARREN, F. L.: J. Chem. Soc. **1949,** 1703.
(163) CHUIT, P., BOELSING, F., AND MALET, G.: Helv. Chim. Acta **12,** 1096 (1929).
(164) CHUIT, P., BOELSING, F., HAUSSER, J., AND MALET, G.: Helv. Chim. Acta **10,** 167 (1927).
(165) CLEMO, G. R., AND MCQUILLIN, F. J.: J. Chem. Soc. **1952,** 3835.
(166) CLERMONT, P. DE: Ber. **6,** 72 (1873).

(167) COFFMAN, D. D., CRAMER, R., AND MOCHEL, W. E.: J. Am. Chem. Soc. **80,** 2882 (1958).
(168) COHEN, G., MURPHY, C. M., O'REAR, J. G., RAVNER, H., AND ZISMAN, W. A.: Ind. Eng. Chem. **45,** 1766 (1953).
(169) COLONGE, J., AND DUMONT, P.: Bull. soc. chim. France **1947,** 38.
(170) COLONGE, J., AND DUMONT, P.: Compt. rend. **220,** 500 (1945).
(171) COLONGE, J., AND JOLY, D.: Ann. chim. **18,** 286, 321 (1943).
(172) COLONGE, J., AND JOLY, D.: Compt. rend. **217,** 249 (1943).
(173) CONNOR, R., AND MCCLELLAN, U. R.: J. Org. Chem. **3,** 570 (1939); **6,** 690 (1941).
(174) COOK, A. H., COX, S. F., AND FARMER, T. H.: Nature **162,** 61 (1948).
(175) COOK, J. W., PHILIP, R., AND SOMERVILLE, A. R.: J. Chem. Soc. **1948,** 164.
(176) COOK, J. W., AND ROBINSON, A. M.: J. Chem. Soc. **1938,** 505.
(177) COOK, N. C., AND PERCIVAL, W. C.: J. Am. Chem. Soc. **71,** 4141 (1949).
(178) COPE, A. C.: J. Am. Chem. Soc. **59,** 2327 (1937).
(179) COPE, A. C., AND HANCOCK, E. M.: J. Am. Chem. Soc. **60,** 2903 (1938).
(180) COPE, A. C., HOFMANN, C. M., WYCKOFF, C., AND HARDENBERGH, E.: J. Am. Chem. Soc. **63,** 3452 (1941).
(181) COPE, A. C., HOLMES, H. L., AND HOUSE, H. O.: In *Organic Reactions,* Vol. IX, p. 107. John Wiley and Sons, Inc., New York (1957).
(182) COPE, A. C., HOYLE, K. E., AND HEYL, D.: J. Am. Chem. Soc. **63,** 1843 (1941).
(183) CORNUBERT, R., AND BORRELL, C.: Bull. soc. chim. [4] **47,** 301 (1930).
(184) CORSON, B. B., AND STOUGHTON, R. W.: J. Am. Chem. Soc. **50,** 2825 (1928).
(185) COX, F. B., AND MCELVAIN, S. M.: In *Organic Syntheses,* Collective Vol. II, p. 279. John Wiley and Sons, Inc., New York (1943).
(186) CRAWFORD, J. W. C.: J. Chem. Soc. **1953,** 2658.
(187) CRIEGEE, R.: Ann. **522,** 75 (1936).
(188) CURTIS, R. H., DAY, J. N. E., AND KIMMINS, L. G.: J. Chem. Soc. **123,** 3131 (1923).
(189) CURTIUS, T., AND SANDHAAS, W.: J. prakt. Chem. **125,** 95 (1930).
(190) CURTIUS, T., SIEBER, W., NADENHEIM, F., HAMBSCH, O., AND RITTER, W.: J. prakt. Chem. **125,** 152 (1930).
(191) DAVID, I. S., AND IMER, C.: Bull. soc. chim. France **1951,** 634.
(192) DAY, J. N. E., AND THORPE, J. F.: J. Chem. Soc. **117,** 1465 (1920).
(193) DEEMER, L. F., LUTWAK, L., AND STRONG, F. M.: J. Am. Chem. Soc. **70,** 154 (1948).
(194) DELÉPINE, M., AND BONNET, P.: Compt. rend. **149,** 39 (1909).
(195) DESSEY, R. E., WOTIZ, J. H., AND HOLLINGSWORTH, C. A.: J. Am. Chem. Soc. **79,** 358 (1957).
(196) DIAPER, D. G. M.: D. Phil. Thesis, Oxford University, 1949.
(197) DICKENS, F., KON, G. A. R., AND THORPE, J. F.: J. Chem. Soc. **121,** 1496 (1922).
(198) DIKMAN, E.: Rev. fac. sci. univ. Istanbul **15A,** 108 (1950); Chem. Abstracts **45,** 6155*a* (1951).
(199) DOEBNER, O.: Ber. **33,** 2140 (1900); **35,** 1136 (1902).
(200) DOLEJS, L., AND NOVOTNY, L.: Chem. Listy **48,** 401 (1954); Collection Czechoslov. Chem. Communs. **19,** 716 (1954); Chem. Abstracts **49,** 3881*e* (1955).
(201) DOX, A. W.: J. Am. Chem. Soc. **46,** 1708 (1924).
(202) DOX, A. W.: J. Am. Chem. Soc. **47,** 1473 (1925).
(203) DOX, A. W., AND BYWATER, W. G.: J. Am. Chem. Soc. **58,** 731 (1936).
(204) DOX, A. W., AND JONES, E. G.: J. Am. Chem. Soc. **50,** 2033 (1928).
(205) DREIDING, A. S., AND PRATT, R. J.: J. Am. Chem. Soc. **75,** 3717 (1953).
(206) DREUX, J.: Bull. soc. chim. France **1954,** 1309.
(207) DUPONT, G., DULOU, R., AND DEFAY, N.: Bull. soc. chim. France **6,** 310 (1939).
(208) DUTTA, P. C.: J. Indian Chem. Soc. **19,** 79 (1942).
(209) EASTMAN, R. H., AND OKEN, A.: J. Am. Chem. Soc. **75,** 1029 (1953).
(210) ELVIDGE, J. A., LINSTEAD, R. P., AND SIMMS, P.: J. Chem. Soc. **1951,** 3386, 3398.
(211) ELVIDGE, J. A., LINSTEAD, R. P., AND SMITH, J. F.: J. Chem. Soc. **1952,** 1026.

(212) EVANS, D. W. S., AND ROBERTS, J. C.: J. Chem. Soc. **1957,** 2104.
(213) FARMER, E. H., AND KRACOVKSI, J.: J. Chem. Soc. **1926,** 2318.
(214) FARMER, E. H., AND MARTIN, S. R. W.: J. Chem. Soc. **1933,** 960.
(215) FARMER, E. H., AND MEHTA, T. N.: J. Chem. Soc. **1930,** 1610.
(216) FARMER, E. H., AND ROSS, J.: J. Chem. Soc. **127,** 2358 (1925).
(217) FARMER, E. H., AND SUNDRALINGAM, A.: J. Chem. Soc. **1942,** 121.
(218) FAVORSKAYA, T. A., AND YAKOVLEV, J. P.: Zhur. Obshcheĭ Khim. **22,** 113 (1952).
(219) FAWCETT, R. W., AND HARRIS, J. O.: Chem. & Ind. (London) **1953,** 18; J. Chem. Soc. **1954,** 2669.
(220) FERNHOLZ, E., AND FINKELSTEIN, J.: J. Am. Chem. Soc. **60,** 2402 (1838).
(221) FICHTER, F.: Ann. **361,** 363 (1908).
(222) FICHTER, F., AND HEER, J.: Helv. Chim. Acta **18,** 1276 (1935).
(223) FICHTER, F., AND HEER, J.: Helv. Chim. Acta **19,** 149 (1936).
(224) FICHTER, F., AND HOLBRO, T.: Helv. Chim. Acta **20,** 333 (1937).
(225) FICHTER, F., AND RUDIN, M.: Helv. Chim. Acta **24,** 398E (1941).
(226) FIESER, L. F., *et al.*: J. Am. Chem. Soc. **70,** 3174 (1948).
(227) FIESER, L. F.: *Experiments in Organic Chemistry,* p. 73. D. C. Heath and Company, Boston, Massachusetts (1935).
(228) FIESER, L. F., LEFFLER, M. T., AND COWORKERS: J. Am. Chem. Soc. **70,** 3206 (1948).
(229) FIESER, L. F., AND SCHNEIDER, W. P.: J. Am. Chem. Soc. **74,** 2254 (1952).
(230) FINCH, H. DE V., BALLARD, S. A., AND EVANS, T. W.: U. S. patent 2,454,047 (November 16, 1948); Chem. Abstracts **43,** 5416*d* (1949).
(231) FINCH, H. DE V., FURMAN, K. E., AND BALLARD, S. A.: J. Am. Chem. Soc. **73,** 4299 (1951).
(232) FITTIG, R.: Ann. **304,** 178 (1899).
(233) FLOYD, D. E. (to General Mills, Inc.): U. S. patent 2,523,692 (September 26, 1950).
(234) FLOYD, D. E., AND MILLER, S. E.: J. Am. Chem. Soc. **69,** 2354 (1947).
(235) FOURNEAU, E., AND MATTI, J.: J. pharm. chim. **14,** 513 (1931); Chem. Abstracts **26,** 3073^4 (1932).
(236) FRANCIS, F., AND WILSON, F. G.: J. Chem. Soc. **103,** 2238 (1913).
(237) FRANK, C. E.: Chem. Revs. **46,** 155 (1950).
(238) FRANK, R. L., ARMSTRONG, R., KWIATEK, J., AND PRICE, H.: J. Am. Chem. Soc. **70,** 1379 (1948).
(239) FRANKE, A., AND KROUPA, A.: Monatsh. **56,** 347 (1930).
(240) FRANKE, A., KROUPA, A., AND COWORKERS: Monatsh. **69,** 167 (1936).
(241) FRANKE, A., KROUPA, A., AND HADZIDIMITRIU, S.: Monatsh. **62,** 119 (1930).
(242) FRANKE, W., AND BUERLEN, J.: Z. Naturforsch. **5b,** 122 (1950).
(243) FRANZEN, V.: Chem.-Ztg. **81,** 138 (1957).
(244) FRANZEN, V.: Chem. Ber. **87,** 1219 (1954).
(245) FREDGA, A.: Acta Chem. Scand. **3,** 208 (1949).
(246) FREDGA, A.: Arkiv Kemi **6,** 277 (1953).
(247) FREDGA, A.: Arkiv Kemi, Mineral. Geol. **14B,** No. 27 (1941), **15B,** No. 23 (1942), **24A,** No. 32 (1947).
(248) FREDGA, A.: Arkiv Kemi, Mineral. Geol. **23B,** No. 2 (1946).
(249) FREDGA, A.: The Svedberg Anniversary Volume, p. 261. Almquist and Wiksells, Stockholm (1944).
(250) FREDGA, A.: Svensk Kem. Tidskr. **67,** 343 (1955).
(251) FREDGA, A., AND LERKINEN, E.: Arkiv Kemi, Mineral. Geol. **19B,** No. 1 (1945).
(252) FREDGA, A., AND MIETTINEN, J. K.: Acta Chem. Scand. **1,** 371 (1947).
(253) FREDGA, A., AND OSTMAN, B.: Acta Chem. Scand. **10,** 703 (1956).
(254) FREDGA, A., AND SAHLBERG, U.: Arkiv Kemi, Mineral. Geol. **18A,** No. 16 (1944).
(255) FRENCH, C. M., AND TREW, V. C.: Trans. Faraday Soc. **47,** 365 (1951).
(256) FREUDENBERG, K.: Monatsh. **85,** 537 (1954).

(257) FREUDENBERG, K., AND HOHMANN, W.: Ann. **584,** 54 (1953).
(258) FREUDENBERG, K., AND LWOWSKI, W.: Ann. **587,** 213 (1954).
(259) FUSON, R. C., ARNOLD, R. T., AND COOKE, H. G., JR.: J. Am. Chem. Soc. **60,** 2272 (1938).
(260) FUSON, R. C., AND HILL, R. W.: J. Org. Chem. **19,** 1575 (1954).
(261) FUSON, R. C., AND SHACHAT, N.: J. Org. Chem. **22,** 1394 (1957).
(262) FUSON, R. C., AND SOUTHWICK, P. L.: J. Am. Chem. Soc. **66,** 679 (1944).
(263) FUSON, R. C., AND THOMAS, N.: J. Org. Chem. **18,** 1762 (1953).
(264) GARDNER, J. A., AND RYDON, H. N.: J. Chem. Soc. **1938,** 48.
(265) GARDNER, J. H., AND BORGSTROM, P.: J. Am. Chem. Soc. **51,** 3375 (1929).
(266) GAUBERT, P., LINSTEAD, R. P., AND RYDON, H. N.: J. Chem. Soc. **1937,** 1971.
(267) GAUBERT, P., LINSTEAD, R. P., AND RYDON, H. N.: J. Chem. Soc. **1937,** 1974.
(268) GAUTHIER, B.: Compt. rend. **218,** 650 (1944).
(269) GAY, R., AND HOREAU, H.: Bull. soc. chim. France **1955,** 962; Chem. Abstracts **50,** 10065*e* (1956).
(270) GENSLER, W. J.: Chem. Revs. **57,** 191 (1957).
(271) GERO, A.: U. S. patent 2,650,938 (September 1, 1953); Chem. Abstracts **49,** 1785*a* (1955).
(272) GIBBS, E. M., AND HENRY, T. A.: J. Chem. Soc. **1939,** 1284.
(273) GILMAN, H., AND KIRBY, R. H.: In *Organic Syntheses*, Collective Vol. I, 2nd edition, p. 361. John Wiley and Sons, Inc., New York (1941).
(274) GILMAN, H., AND VAN ESS, P. R.: J. Am. Chem. Soc. **55,** 1258 (1933).
(275) GLICKMAN, S. A., AND COPE, A. C.: J. Am. Chem. Soc. **67,** 1012 (1945).
(276) GODT, H. C., JR., AND QUINN, J. F.: J. Am. Chem. Soc. **78,** 1461 (1956).
(277) GOLDEN, J. H., AND LINSTEAD, R. P.: J. Chem. Soc. **1958,** 1732.
(278) GOUIN, L.: Compt. rend. **238,** 1235 (1954).
(279) GRAER, C. M., AND ADAMS, R.: J. Am. Chem. Soc. **52,** 2540 (1930).
(280) GREAVES, W. S., LINSTEAD, R. P., SHEPHARD, B. R., THOMAS, S. L. S., AND WEEDON, B. C. L.: J. Chem. Soc. **1950,** 3333.
(281) GREENWOOD, F. L., WHITMORE, F. C., AND CROOKS, H. M.: J. Am. Chem. Soc. **60,** 2028 (1938).
(282) GRIGNARD, V., AND VIGNON, G.: Compt. rend. **144,** 1358 (1907).
(283) GRIMSHAW, D. C., GUY, J. B., AND SMITH, J. C.: J. Chem. Soc. **1940,** 68.
(284) GRIPENBERG, J.: Acta Chem. Scand. **3,** 1137 (1949).
(285) GRIPENBERG, J.: Acta Chem. Scand. **5,** 995 (1951).
(286) GRUBHOFER, N., AND SCHLEIFER, L.: Naturwissenschaften **40,** 508 (1953).
(287) GUARESCHI, I.: Atti reale accad. sci. Torino **36,** 443 (1901).
(288) GUARESCHI, I.: Atti reale accad. sci. Torino **53,** 831 (1918).
(289) GUHA, P. C., AND KRISHNAMURTHY, S.: Ber. **70B,** 2112 (1937).
(290) GUNSTONE, F. D.: Quart. Revs. (London) **7,** 175 (1953).
(291) GUSTBEE, G., AND STENHAGEN, E.: Svensk Kem. Tidskr. **54,** 243 (1942); Chem. Zentr. **1943,** I, 1769; Chem. Abstracts **38,** 3611[9] (1944).
(292) HAGEMEYER, H. J., JR.: U. S. patent 2,444,735 (July 6, 1948); Chem. Abstracts **42,** 7326*hi* (1948).
(293) HALL, D. M., MAHBOOB, S., AND TURNER, E. E.: J. Chem. Soc. **1950,** 1842.
(294) HALL, D. M., MAHBOOB, S., AND TURNER, E. E.: J. Chem. Soc. **1952,** 1956.
(295) HALLER, A., AND BAUER, E.: Compt. rend. **152,** 1638–42 (1911).
(296) HAMLIN, K. E., AND WESTON, A. W.: In *Organic Reactions*, Vol. IX, p. 1. John Wiley and Sons, Inc., New York (1957).
(297) HANCOCK, J. E. H., AND LINSTEAD, R. P.: J. Chem. Soc. **1953,** 3490.
(298) HANSCHKE, E.: Chem. Ber. **88,** 1043 (1955).
(299) HARRIS, J. O.: J. Chem. Soc. **1953,** 184.
(300) HAUSER, C. R., AND HUDSON, B. E.: In *Organic Reactions*, Vol. I, Chap. 9. John Wiley and Sons, Inc., New York (1942).

(301) HAUSER, C. R., SWAMER, F. W., AND ADAMS, J. T.: In *Organic Reactions*, Vol. VIII, Chap. 3. John Wiley and Sons, Inc., New York (1954).
(302) HAUSERMANN, M.: Helv. Chim. Acta **34,** 1482 (1951).
(303) HAWKINS, E. G. E.: J. Chem. Soc. **1955,** 3463.
(304) HEDLUND, I.: Arkiv Kemi **8,** 89 (1955).
(305) HELL, C., AND LUMP, H.: Ber. **17,** 2218 (1884).
(306) HELL, C., AND ROTHBERG, M.: Ber. **22,** 60 (1889).
(307) HENBEST, H. B., JONES, E. R. H., AND WALLS, I. M. S.: J. Chem. Soc. **1949,** 2696.
(308) HENNION, G. F., AND DAVIS, R. B.: J. Org. Chem. **16,** 1289 (1951).
(309) HESSE, G., AND BREIG, K.: Ann. **592,** 120 (1955).
(310) HEY, D. H., AND WATERS, W. A.: In *Chemistry of Carbon Compounds*, edited by E. H. Rodd, Vol. IA, pp. 195–217. Elsevier Publishing Company, New York (1951).
(311) HIGGINBOTHAM, L., AND LAPWORTH, A.: J. Chem. Soc. **123,** 1624 (1923).
(312) HIGSON, A., AND THORPE, J. F.: J. Chem. Soc. **89,** 1462 (1906).
(313) HILDEBRANDT, G., AND LEUBE, E.: German patent 494,320 (December 8, 1928); Chem. Abstracts **24,** 2756[4] (1930).
(314) HILDITCH, T. P.: *The Chemical Constitution of Natural Fats*, p. 322. John Wiley and Sons, Inc., New York (1944).
(315) HIRSJARVI, V. P.: Ann. Acad. Sci. Fennicae, Ser. A. II, Chem. No. 23, 108 pp. (1946).
(316) HOCH, D., AND KARRER, P.: Helv. Chim. Acta **37,** 397 (1954).
(317) HOGSED, M. J., AND LINDSEY, R. V.: J. Am. Chem. Soc. **75,** 4846 (1953).
(318) HOLDEN, N. E., AND LAPWORTH, A.: J. Chem. Soc. **1931,** 2368.
(319) HOLMES, H. L., OPENSHAW, H. T., AND ROBINSON, R.: J. Chem. Soc. **1946,** 910.
(320) HORII, Z., KUGITA, H., AND TAKEUCHI, T.: J. Pharm. Soc. Japan **73,** 895 (1953); Chem. Abstracts **48,** 11329*g* (1954).
(321) HORNING, E. C., DENEKAS, M. O., AND FIELD, R. E.: J. Org. Chem. **9,** 548 (1944).
(322) HORNING, E. C., DENEKAS, M. O., AND FIELD, R. E.: *Organic Syntheses*, Collective Vol. III, p. 317. John Wiley and Sons, Inc., New York (1955).
(323) HOUBEN-WEYL: *Methoden der organischen Chemie*, 4th edition, edited by E. Mueller, Band VII, Teil I, 55 (1954); Band IV, Teil II, 376 (1955), George Thieme Verlag, Stuttgart.
(324) HOWLES, F. H., THORPE, J. F., AND UDALL, W.: J. Chem. Soc. **77,** 946 (1905).
(325) HOWTON, D. R., DAVIS, R. H., AND NEVENZEL, J. C.: J. Am. Chem. Soc. **76,** 4970 (1954).
(326) HSING, C., AND LI, L.: J. Am. Chem. Soc. **71,** 774 (1949).
(327) HSUEN, C. M., AND MARVEL, C. S.: J. Am. Chem. Soc. **50,** 855 (1928).
(328) HUDSON, B. E., JR., AND HAUSER, C. R.: J. Am. Chem. Soc. **63,** 3156 (1941).
(329) HUGHES, E. D.: Trans. Faraday Soc. **37,** 603 (1941).
(330) HUNSDIECKER, H.: Ber. **75B,** 1197 (1942).
(331) ING, H. R.: J. Chem. Soc. **1933,** 504.
(332) INHOFFEN, H. H., BORK, S., AND SCHWIETER, U.: Ann. **580,** 1 (1953).
(333) INHOFFEN, H. H., ISLER, O., BEY, G. VON DER, RASPE, G., ZELLER, P., AND AHRENS, R.: Ann. **580,** 7 (1953).
(334) IPATIEV, W., AND RASUWAJEW, G.: Ber. **60,** 1971, 1973 (1927).
(335) ISLER, O., GUTMANN, H., LINDLAR, H., MONTAVON, M., RUEGG, R., RYSER, G., AND ZELLER, P.: Helv. Chim. Acta **39,** 463 (1956).
(336) ISLER, O., GUTMANN, H., MONTAVON, M., RUEGG, R., RYSER, G., AND ZELLER, P.: Helv. Chim. Acta **40,** 1242 (1957).
(337) IVANOFF, D.: Bull. soc. chim. **37,** 287 (1925); Chem. Abstracts **19,** 1694[9] (1925).
(338) IVANOFF, N.: Bull. soc. chim. France **1948,** 660.
(339) IZARD, E. F.: J. Polymer Sci. **8,** 503 (1952).
(340) IZGARYSHEV, N. A., AND FIOSHIN, M. YA.: Uspekhi Khim. **25,** 486 (1956); Chem. Abstracts **50,** 14500*i* (1956).
(341) JAMISON, M. M., AND TURNER, E. E.: J. Chem. Soc. **1942,** 611.

(342) JEFFREY, D., AND FRY, A.: J. Org. Chem. **22,** 735 (1957).
(343) JENNER, E. L.: U. S. patent 2,700,051 (January 18, 1955); Chem. Abstracts **49,** 15953*e* (1955).
(344) JOCELYN, P. C., AND POLGAR, N.: J. Chem. Soc. **1953,** 132.
(345) JOCELYN, P. C., AND QUEEN, A.: J. Chem. Soc. **1957,** 4437.
(346) JOHNSON, W. S., AND DAUB, G. H.: In *Organic Reactions*, Vol. VI, Chap. 1. John Wiley and Sons, Inc., New York (1951).
(347) JOHNSON, W. S., AND SHELBERG, W. E.: J. Am. Chem. Soc. **67,** 1754 (1945).
(348) JONES, D. B.: J. Am. Chem. Soc. **37,** 586 (1915).
(349) JONES, D. M.: U. S. patent 2,363,003 (November 21, 1944); Chem. Abstracts **39,** P3792[1] (1945).
(350) JONES, E. R. H., O'SULLIVAN, D. G., AND WHITING, M. C.: J. Chem. Soc. **1949,** 1415.
(351) JONES, E. R. H., WHITHAM, G. H., AND WHITING, M. C.: J. Chem. Soc. **1954,** 1865.
(352) KAMEDA, Y.: J. Pharm. Soc. Japan **61,** 266 (1941); Complete Abstracts Japan. Chem. Lit. **15,** 1025 (1941); Chem. Abstracts **44,** 9356*d* (1950).
(353) KAMEDA, Y.: J. Pharm. Soc. Japan **61,** 261 (1941); Complete Abstracts Japan. Chem. Lit. **15,** 1024 (1941); Chem. Abstracts **45,** 2870*h* (1951).
(354) KARRER, P., BENZ, F., MORF, R., RAUDNITZ, H., STOLL, M., AND TAKAHASHI, T.: Helv. Chim. Acta **15,** 1399 (1932).
(355) KARRER, P., BENZ, F., AND STOLL, M.: Helv. Chim. Acta **16,** 297 (1933).
(356) KARRER, P., EUGSTER, C. H., AND RECORDATI, M.: Chem. Ber. **89,** 366 (1956).
(357) KARRER, P., FARINGER, M., MERZ, A., AND MILHAND, G.: Helv. Chim. Acta **31,** 1505 (1948).
(358) KASMAN, S., AND WRIGHT, G. F.: J. Org. Chem. **17,** 505 (1952).
(359) KATZNELSON, M. M., AND KONDAKOVA, M. S.: Compt. rend. acad. sci. (U.R.S.S.) [N.S.] **2,** 21 (1934); Chem. Abstracts **28,** 5042[6] (1934).
(360) KAZANSKIĬ, B. A., KOPERINA, A. V., AND ZEMSKAYA, O. A.: Zhur. Obscheĭ Khim. **26,** 1212 (1950); Chem. Abstracts **45,** 1525*c* (1951).
(361) KAZANSKIĬ, B. A., RUMYANTSEVA, Z. A., AND BATNEV, M. I.: Bull. acad. sci. U.R.S.S., Classe sci. chim. **1947,** 483; Chem. Abstracts **42,** 4536*f* (1948).
(362) KEIL, W.: Z. physiol. Chem. **274,** 175 (1942).
(363) KEIL, W., AND SCHILLER, G.: Z. physiol. Chem. **282,** 135 (1947).
(364) KELSO, R. G., GREENLEE, K. W., DERFER, J. M., AND BOORD, C. E.: J. Am. Chem. Soc. **77,** 1751 (1955).
(365) KENNEDY, G., BREEN, J., KEANE, J., AND NOLAN, T. J.: Sci. Proc. Roy. Dublin Soc. **21,** 557 (1937).
(366) KENT, R. E., AND MCELVAIN, S. M.: *Organic Syntheses*, Collective Vol. III, p. 591. John Wiley and Sons, Inc., New York (1955).
(367) KENYON, J., AND ROSS, W. A.: J. Chem. Soc. **1952,** 2307.
(368) KESKAR, A. Y., AND BOKIL, K. V.: J. Univ. Bombay **19,** Sect. A, Pt. 3, Sci. No. 28, 23 (1950); Chem. Abstracts **46,** 11123*i* (1952).
(369) KHARASCH, M. S.: U. S. patent 2,426,224 (August 26, 1947); Chem. Abstracts **42,** 213*b* (1948).
(370) KHARASCH, M. S., AND GLADSTONE, M. T.: J. Am. Chem. Soc. **65,** 15 (1943).
(371) KHARASCH, M. S., AND NUDENBERG, W.: J. Org. Chem. **19,** 1921 (1954).
(372) KHARASCH, M. S., AND REINMUTH, O.: *Grignard Reactions of Nonmetallic Substances*, pp. 63, 64, 118–24, 131–2. Prentice-Hall, Inc., New York (1954).
(373) KHARASCH, M. S., ZIMMERMANN, M., ZIMMT, W., AND NUDENBERG, W.: J. Org. Chem. **18,** 1045 (1953).
(374) KIPPING, F. S.: J. Chem. Soc. **67,** 139 (1895).
(375) KIRYALOV, N. P.: J. Gen. Chem. (U.S.S.R.) **10,** 65 (1940); Chem. Abstracts **34,** 4727[8] (1940).
(376) KIZHNER, H.: J. Russ. Phys. Chem. Soc. **43,** 1149; Chem. Abstracts **6,** 596[8] (1912).
(377) KLYNE, W.: *Progress in Stereochemistry*, Vol. I. Academic Press, Inc., New York (1954).

(378) KLYNE, W.: In *The Structures of Organic Compounds*, edited by E. A. Braude and F. C. Nachod. Academic Press, Inc., New York (1954).
(379) KNOEVENAGEL, E.: Ber. **31,** 2585 (1898).
(380) KNOEVENAGEL, E.: Ber. **31,** 2596 (1898); German patents 97,734, 156,560, and 161,171.
(381) KNOEVENAGEL, E.: Ber. **37,** 4065 (1904).
(382) KNUNYANTS, I. L., AND VYAZANKIN, N. S.: Doklady Akad. Nauk S.S.S.R. **113,** 112 (1957); Chem. Abstracts **51,** 14637*h* (1957).
(383) KOEGL, F., ERXLEBEN, H., MICHAELIS, R., AND VISSER, H. S.: Z. physiol. Chem. **235,** 181 (1935).
(384) KOEGLER, F.: German patent 854,507 (November 4, 1952); Chem. Abstracts **50,** 16841*g* (1956).
(385) KOELSCH, C. F.: J. Am. Chem. Soc. **68,** 148 (1946).
(386) KOELSCH, C. F., AND STRATTON, C. H.: J. Am. Chem. Soc. **66,** 1881 (1944).
(387) KOETZ, A.: J. prakt. Chem. **75,** 433 (1907).
(388) KOETZ, A., BIEBER, A., AND SCHWARTZ, A.: Ann. **357,** 192 (1908).
(389) KOHLER, E. P., AND HERITAGE, G.: Am. Chem. J. **33,** 21 (1905).
(390) KOLOBIELSKI, M., AND WIEMANN, J.: Compt. rend. **233,** 691 (1951).
(391) KOMPPA, G.: Ber. **62B,** 1371 (1929).
(392) KON, G. A. R., AND THORPE, J.: J. Chem. Soc. **115,** 686 (1919).
(393) KON, G. A. R., AND THORPE, J. F.: J. Chem. Soc. **121,** 1800 (1922).
(394) KONDAKOVA, M. S., AND KATZNELSON, M. M.: Compt. rend. acad. sci. U.R.S.S. **18,** 271 (1938); Chem. Abstracts **32,** 4523[5] (1938).
(395) KONDO, H., AND SUZUKI, H.: Ber. **69B,** 2459 (1936).
(396) KOTZ, A., NUSSBAUM, E., AND TAKENS, E.: J. prakt. Chem. **90,** 357 (1914).
(397) KOPP, M., AND TCHOUBAR, B.: Bull. soc. chim. France **1951,** 30.
(398) KRESSNER, L.: Ann. **192,** 135 (1878).
(399) KROEKER, E. H., AND MCELVAIN, S. M.: J. Am. Chem. Soc. **56,** 1171 (1934).
(400) KUENG, F. E.: Canadian patent 422,362 (August 29, 1944); Chem. Abstracts **38,** 6301[5] (1944).
(401) KUHN, R., AND GRUNDMANN, C.: Ber. **70B,** 1894 (1937).
(402) KUHN, R., KOHLER, F., AND KOHLER, C.: Z. physiol. Chem. **242,** 171 (1936).
(403) KUHN, R., AND SUGINOME, H.: Helv. Chim. Acta **12,** 915 (1929).
(404) KUHN, R., AND WINTERSTEIN, A.: Ber. **66,** 1737 (1933).
(405) KURTZ, P.: Ann. **572,** 23 (1951).
(406) KURTZ, P.: U. S. patent 2,224,022 (December 3, 1940); Chem. Abstracts **35,** 1807[1] (1941).
(407) LAPWORTH, A.: J. Chem. Soc. **83,** 995 (1903).
(408) LAPWORTH, A.: J. Chem. Soc. **85,** 1214 (1904).
(409) LAPWORTH, A., AND MCRAE, J. A.: J. Chem. Soc. **121,** 1699 (1922).
(410) LAPWORTH, A., AND MCRAE, J. A.: J. Chem. Soc. **121,** 2741 (1922).
(411) LARSSON, E., AND VAN DER PALS, E. VAN GILSE: Trans. Chalmers Univ. Technol., Gothenburg No. 121, 3–7 (1951).
(412) LAWRENCE, W. T.: Proc. Chem. Soc. **16,** 154 (1901).
(413) LEBEDEVA, A. I.: Vestnik Leningrad Univ. **9,** No. 11, Ser. Mat., Fiz. i Khim. No. **4,** 175 (1954); Chem. Abstracts **49,** 15753*b* (1954).
(414) LEBEDEVA, A. I., AND VAINRUB, E. D.: Zhur. Obshcheĭ Khim. **22,** 1974 (1952); Chem. Abstracts **47,** 8640*d* (1953).
(415) LEBEDEVA, A. I., AND VAINRUB, E. D.: Zhur. Obshcheĭ Khim. **24,** 1207 (1954); Chem. Abstracts **49,** 12300*i* (1955).
(416) LEGOFF, E., ULRICH, S. E., AND DENNEY, D. B.: J. Am. Chem. Soc. **80,** 622 (1958).
(417) LEMMON, R. M.: Unpublished work; cited in *Isotopic Carbon* by M. Calvin, C. Heidelberger, J. C. Reid, B. M. Talbert, and P. E. Yankwich, p. 178. John Wiley and Sons, Inc., New York (1949).
(418) LEONARD, N. J., AND MADER, P. M.: J. Am. Chem. Soc. **72,** 5388 (1950).
(419) LESTER, C. T., AND PROFFITT, J. R., JR.: J. Am. Chem. Soc. **71,** 1877 (1949).

(420) LETCH, R. A., AND LINSTEAD, R. P.: J. Chem. Soc. **1932,** 443.
(421) LETSINGER, R. L.: J. Am. Chem. Soc. **70,** 406 (1948).
(422) LETTRE, H.: Ergeb. Enzymforsch. **9,** 1 (1943).
(423) LEVENE, P. A., AND KUNA, M.: J. Biol. Chem. **140,** 255 (1941).
(424) LEVENE, P. A., WEST, C. J., AND VAN DER SCHEER, J.: J. Biol. Chem. **20,** 521 (1915).
(425) LEVINE, R., AND HAUSER, C. R.: J. Am. Chem. Soc. **68,** 760 (1946).
(426) LINSTEAD, R. P., LUNT, J. C., AND WEEDON, B. C. L.: J. Chem. Soc. **1950,** 3333.
(427) LINSTEAD, R. P., LUNT, J. C., AND WEEDON, B. C. L.: J. Chem. Soc. **1951,** 1130.
(428) LINSTEAD, R. P., LUNT, J. C., WEEDON, B. C. L., AND SHEPHARD, B. R.: J. Chem. Soc. **1952,** 3621.
(429) LINSTEAD, R. P., SHEPHARD, B. R., WEEDON, B. C. L., AND LUNT, J. C.: J. Chem. Soc. **1953,** 1538.
(430) LINSTEAD, R. P., WEEDON, B. C. L., AND WLADISLAW, B.: J. Chem. Soc. **1955,** 1097.
(431) LINSTEAD, R. P., AND WHALLEY, M.: J. Chem. Soc. **1954,** 3722.
(432) LITTLE, J. S., SMITH, A. G., TAYLOR, W. I., AND THOMAS, B. R.: J. Chem. Soc. **1954,** 2636.
(433) LIVSHITS, R. S., PREOBRAZHENSKIĬ, S., AND BARDINSKAYA, M. S.: J. Gen. Chem. (U.S.S.R.) **15,** 836 (1945); Chem. Abstracts **41,** 709*i* (1947).
(434) LONGINOV, V.: J. Russ. Phys. Chem. Soc. **47,** 1132 (1915); Chem. Abstracts **9,** 3053[6] (1915).
(435) LONGLEY, R. I., JR., AND EMERSON, W. S.: J. Am. Chem. Soc. **72,** 3079 (1950).
(436) LUKES, R., AND PESEK, J.: Collection Czechoslovak. Chem. Communs. **20,** 1253 (1955); Chem. Abstracts **50,** 4023*h* (1956).
(437) LUND, H.: Ber. **67,** 935 (1934); *Organic Syntheses*, Collective Vol. II, p. 594, John Wiley and Sons, Inc., New York (1943).
(438) LUTZ, G. A., BEARSE, A. E., LEONARD, J. E., AND CROXTON, F. C.: J. Am. Chem. Soc. **70,** 4135, 4139 (1948).
(439) MAEKAWA, E.: Bull. Nagoya Inst. Technol. **6,** 271 (1954): Chem. Abstracts **50,** 11943*g* (1956).
(440) MAILLARD, A., DELUZARCHE, A., AND RUDLOFF, A.: Compt. rend. **240,** 317 (1955).
(441) MAIR, L.: Bull. soc. chim. [4] **3,** 284 (1908).
(442) MAJOR, R. T., AND FINKELSTEIN, J.: J. Am. Chem. Soc. **63,** 1368 (1941).
(443) MANNES, L., AND PACK, W.: German patent 745,265 (December 2, 1943); Chem. Abstracts **40,** 3131[5] (1946).
(444) MARSHALL, F. C. B.: J. Chem. Soc. **1930,** 2754.
(445) MARSHALL, F. C. B.: Rec. trav. chim. **51,** 233 (1932).
(446) MARVEL, C. S., AND BROOKS, L. A.: J. Am. Chem. Soc. **63,** 2853 (1941).
(447) MARVEL, C. S., AND FULLER, J. A.: J. Am. Chem. Soc. **74,** 1506 (1952).
(448) MARVEL, C. S., MYERS, R. L., AND SAUNDERS, J. H.: J. Am. Chem. Soc. **70,** 1694 (1948).
(449) MARVEL, C S., AND WILLIAMS, W. W.: J. Am. Chem. Soc. **61,** 2714 (1939).
(450) MASTAGLI, P., LAMBERT, P., AND FRANCOIS, G.: Bull. soc. chim. France **1957,** 1108; Chem. Abstracts **52,** 4547*a* (1958).
(451) MATELL, M.: Arkiv Kemi **5,** 17 (1952).
(452) MATSUDA, S., YAMAUCHI, T., AND YAMANOUE, K.: J. Chem. Soc. Japan, Ind. Chem. Sect. **58,** 296 (1955).
(453) MAYO, F. R., AND WALLING, C.: Chem. Revs. **27,** 351 (1940).
(454) MCBAY, H. C., AND TUCKER, O.: J. Org. Chem. **19,** 869 (1954).
(455) MCELVAIN, S. M., AND ALDRIDGE, C. L.: J. Am. Chem. Soc. **75,** 3987 (1953).
(456) MEERWEIN, H.: Ann. **396,** 200 (1913).
(457) MEERWEIN, H.: Ber. **53B,** 1829 (1920).
(458) MEHTA, S. U., AND NARGUND, K. S.: J. Univ. Bombay **10,** Pt. 5, 141 (1942); Chem. Abstracts **37,** 611[1] (1943).
(459) MEHTA, S. U., AND NARGUND, K. S.: J. Univ. Bombay **11,** Part 3, 134 (1942); Chem. Abstracts **37,** 2349[3] (1943).

(460) MELUCH, W. C., AND MISLOW, K.: J. Org. Chem. **20,** 1311 (1955).
(461) MELVILLE, H. W.: Trans. Faraday Soc. **42,** 317 (1946).
(462) METAL AND THERMIT Co.: British patent 777,158 (June 19, 1957); Chem. Abstracts **51,** 17981*e* (1957).
(463) MICHAEL, A., AND ROSS, J.: J. Am. Chem. Soc. **52,** 4598 (1930); **55,** 1632 (1933).
(464) MICHAEL, A., AND ROSS, J.: J. Am. Chem. Soc. **53,** 1150 (1931).
(465) MICHAEL, A., AND WEINER, N.: J. Am. Chem. Soc. **59,** 744 (1937).
(466) MIGRDICHIAN, V.: *The Chemistry of Organic Cyanogen Compounds.* Reinhold Publishing Corporation, New York (1947).
(467) MIKESKA, L. A. (to Standard Oil Development Co.): U. S. patent 2,461,336 (February 8, 1949); Chem. Abstracts **43,** 4689*h* (1949).
(468) MILAS, N. A.: U. S. patent 2,407,672 (September 17, 1946); Chem. Abstracts **41,** 996*f* (1947).
(469) MILLER, R. F., AND ADAMS, R.: J. Am. Chem. Soc. **58,** 787 (1936).
(470) MILLER, C. A., AND LONG, L. M.: J. Am. Chem. Soc. **75,** 373 (1953).
(471) MILLS, J. H., AND KLYNE, W.: In *Progress in Stereochemistry,* edited by W. Klyne, Chap. 5. Butterworths Scientific Publications Ltd., London (1954).
(472) MISLOW, K., AND STEINBERG, I. V.: J. Am. Chem. Soc. **77,** 3807 (1955).
(473) MISRA, G. S., AND SHUKLA, J. S.: J. Ind. Chem. Soc. **29,** 455 (1952).
(474) MITTER, M. C., AND DUTTA, P. C.: J. Indian Chem. Soc. **25,** 306 (1948).
(475) MOHR, E.: J. prakt. Chem. **90,** 189 (1914).
(476) MOHR, O.: Ber. **34,** 807 (1901).
(477) MOLDENHAUER, J.: Ann. **131,** 340 (1865).
(478) MOLLER, E.: Ber. **43,** 3250 (1910).
(479) MONTAGNE, M., AND ROCH, M.: Bull. soc. chim. **10,** 193 (1943).
(480) MOROE, T.: J. Pharm. Soc. Japan **70,** 416 (1950); Chem. Abstracts **45,** 2396*c* (1951).
(481) MOROE, T.: J. Pharm. Soc. Japan **71,** 116 (1951); Chem. Abstracts **45,** 8455*h* (1951).
(482) MOROE, T., MUKAI, T., AND MATSUMOTO, S.: Proc. Japan Acad. **27,** 110 (1951).
(483) MOROE, T., SETO, S., KIKUCHI, K., MUKAI, T., MATSUMOTO, S., AND MURASE, M.: Proc. Japan Acad. **26,** No. 7, 43 (1950); Chem. Abstracts **45,** 7099*b* (1951).
(484) MORRIS, R. C., DANENBERG, H., AND FINCH, H. DE V.: U. S. patent 2,442,958; Chem. Abstracts **42,** 6583*f* (1948).
(485) MORTON, A. A., FALLWELL, F., JR., AND PALMER, L.: J. Am. Chem. Soc. **60,** 1426 (1938).
(486) MORTON, A. A., LEFEVRE, W. J., AND HECHENBLEIKNER, I.: J. Am. Chem. Soc. **58,** 754 (1936).
(487) MORTON, A. A.: Chem. Revs. **35,** 1 (1944).
(488) MOTTI, J.: Anesthésie et analgésie **2,** 52 (1936); Chem. Abstracts **31,** 3010[6] (1937).
(489) MOUSSERON, M., FROGER, P., GRANGER, R., AND WINTERNITZ, F.: Bull. soc. chim. France **1947,** 843.
(490) MOUSSERON, M., GRANGER, R., BOURRELL, H., CELLIER, M., JULLIEN, J., CANALS, E., AND CABANES, J.: Bull. soc. chim. France **1947,** 605.
(491) MOUSSERON, M., AND JULLIEN, J.: Compt. rend. **231,** 410 (1950).
(492) MOUSSERON, M., AND MANON, G.: Bull. soc. chim. France **1949,** 392.
(493) MOWRY, D. T.: Chem. Revs. **42,** 189 (1948).
(494) MUELLER, A.: Monatsh. **65,** 18 (1934).
(495) MUKHERJEE, S. M.: J. Indian Chem. Soc. **24,** 425 (1947).
(496) MUKHERJEE, S. M.: J. Indian Chem. Soc. **24,** 449 (1947).
(497) MUMM, O., BUTTENSCHOEN, W., FRIEDRICHSEN, W., AND GRASSMANN, W.: Ann. **529,** 115 (1937).
(498) MUNCH-PETERSEN, J.: J. Org. Chem. **22,** 170 (1957).
(499) NAMETKIN, S. S., AND ZABRODINA, K. S.: Doklady Akad. Nauk S.S.S.R. **75,** 543 (1951); Chem. Abstracts **45,** 7519*f* (1951).
(500) NATIONAL DISTILLERS AND CHEMICAL Co.: British patent 756,385 (September 5, 1956); Chem. Abstracts **51,** 15557*g* (1957).

(501) NAVES, Y. R.: Helv. Chim. Acta **31,** 151 (1948).
(502) NAZAROV, I. N., AND BAKHMUTSKAYA, S. S.: Zhur Obshcheĭ Khim. **20,** 1837 (1950); Chem. Abstracts **45,** 2866*g* (1951).
(503) NAZAROV, I. N., BERGELSON, L. D., TORGOV, I. V., AND ANANCHENKO, S. N.: Izvest. Akad. Nauk S.S.S.R., Otdel Khim. Nauk **1953,** 889; Chem. Abstracts **49,** 1083*a* (1955).
(504) NAZAROV, I. N., AND KOTLYAREVSKIĬ, I. L.: Zhur. Obshcheĭ Khim. **20,** 1449 (1950); Chem. Abstracts **45,** 1965*g* (1951).
(505) NAZAROV, I. N., AND PINKINA, L. N.: Zhur. Obshcheĭ Khim. **19,** 1870 (1949); Chem. Abstracts **44,** 8908*c* (1950).
(506) NAZAROV, I. N., AND ZAVY'ALOV, S. I.: Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk **1957,** 325; Chem. Abstracts **51,** 14597*b* (1957).
(507) NENITZESCU, C. D., AND NECSOIU, I.: J. Am. Chem. Soc. **72,** 3483 (1950).
(508) NEWMAN, M. S., AND BOOTH, W. T., JR.: J. Am. Chem. Soc. **67,** 154 (1945).
(509) NEWMAN, M. S., AND MAGERLEIN, B. J.: In *Organic Reactions,* Vol. V, Chap. 10. John Wiley and Sons, Inc., New York (1949).
(510) NEWMAN, M. S., WALTCHER, I., AND GINSBERG, H. F.: J. Org. Chem. **17,** 962 (1952).
(511) NIEDERL, J. B., AND SMITH, R. A.: J. Am. Chem. Soc. **59,** 715 (1937).
(512) NOBIS, J. F., AND ROBINSON, R. E.: U. S. patent 2,795,625 (June 11, 1957); Chem. Abstracts **51,** 15581*d* (1957).
(513) NOYCE, D. S., AND DENNY, D. B.: J. Am. Chem. Soc. **72,** 5743 (1950); **76,** 768 (1954).
(514) NOYES, W. A., AND DOUGHTY, H. W.: Ber. **38,** 947 (1905); Am. Chem. J. **27,** 237 (1905).
(515) NOYES, W. A., AND KYRIAKIDES, L. P.: Am. Chem. J. **32,** 1060 (1910).
(516) NOZOE, T., MUKAI, T., AND MATSUMOTO, S.: Proc. Japan Acad. **27,** 110 (1951); Chem. Abstracts **46,** 5035*a* (1952).
(517) OKAZAKI, K.: J. Pharm. Soc. Japan **63,** 629 (1943); Chem. Abstracts **45,** 2884*c*.
(518) OLDHAM, J. W. H.: J. Chem. Soc. **1950,** 100.
(519) OLDHAM, J. W. H., AND UBBELOHDE, A. R.: J. Chem. Soc. **1938,** 201.
(520) OLIVIER, S. C. J.. : Rec. trav. chim. **55,** 1027 (1936).
(521) OSBOND, J. M., FULTON, J. D., AND SPOONER, D. F.: J. Chem. Soc. **1952,** 4785.
(522) OUCHI, S.: J. Pharm. Soc. Japan **74,** 980 (1954).
(523) OVERBERGER, C. G., AND BERENBAUM, M. B.: J. Am. Chem. Soc. **73,** 2618 (1951).
(524) OVERBERGER, C. G., AND BERENBAUM, M. B.: J. Am. Chem. Soc. **73,** 4883 (1951).
(525) OVERBERGER, C. G., BYRD, W. R., AND MESROBIAN, R. B.: J. Am. Chem. Soc. **78,** 1961 (1956).
(526) OVERBERGER, C. G., FISCHMAN, A., ROBERTS, C. W., AROND, L. H., AND LAL, J.: J. Am. Chem. Soc. **73,** 2540 (1951).
(527) OVERBERGER, C. G., GIBB, T. B., JR., CHIBNIK, S., HUANG, P., AND MONAGLE, J. J.: J. Am. Chem. Soc. **74,** 3290 (1952).
(528) OVERBERGER, C. G., HUANG, P., AND GIBB, T. B., JR.: J. Am. Chem. Soc. **75,** 2082 (1953).
(529) OVERBERGER, C. G., AND MARKS, B. S.: J. Am. Chem. Soc. **77,** 4097 (1955).
(530) OVERBERGER, C. G., O'SHAUGHNESSY, M. T., AND SHALIT, H.: J. Am. Chem. Soc. **71,** 2661 (1949).
(531) OVERBERGER, C. G., AND ROBERTS, C. W.: J. Am. Chem. Soc. **71,** 3618 (1949).
(532) PAILER, M.: Monatsh. **79,** 331 (1948).
(533) PARKE, DAVIS & Co.: British patent 725,812 (March 8, 1955); Chem. Abstracts **50,** 5023*f* (1956).
(534) PASTEUR, L.: Ann. chim. phys. [37] **24,** 442 (1848).
(535) PASTEUR, L.: *Researches on Molecular Asymmetry,* Alembic Club Reprints, No. 14 (1905).
(536) PATAI, S., ISRAELI, Y., AND ZABICKY, J.: Chem. & Ind. (London) **1957,** 1671; Chem. Abstracts **52,** 9011*g* (1958).
(537) PAULY, H., AND WILL, G.: Ann. **416,** 14 (1918).

(538) PENNINGTON, F. C., CELMER, W. D., MCLAMORE, W. M., BOGERT, V. V., AND SOLOMONS, I. A.: J. Am. Chem. Soc. **75,** 109 (1953).
(539) PEPPIATT, E. G., AND WICKER, R. J.: U. S. patent 2,790,835 (April 30, 1957); Chem. Abstracts **51,** 15560*g* (1957).
(540) PETROV, A. C.: Rev. inst. franc. pétrole et Ann. combustibles liquides **11,** No. 11, 1471 (1956); Chem. Abstracts **52,** 1046*c* (1958).
(541) PETROV, A. D., NEFEDOV, O. M., AND GRIGOR'EV, F. I.: Zhur. Obshcheĭ Khim. **27,** 1876 (1957); Chem. Abstracts **52,** 4465*d* (1958).
(542) PETROV, A. D., SUSHCHINSKIĬ, V. L., AND SHEBANOVA, M. P.: Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk **1956,** 510; Chem. Abstracts **50,** 16657*i* (1956).
(543) PETROV, A. D., SUSHCHINSKIĬ, V. L., ZAKHAROV, E. P., AND ROGOZHNIKOVA, T. I.: Zhur. Obshcheĭ Khim. **27,** 467 (1957); Chem. Abstracts **51,** 15392*e* (1957).
(544) PETTERSEN, K.: Arkiv Kemi **7,** 39 (1954).
(545) PINES, H., AND IPATIEFF, V. N.: J. Am. Chem. Soc. **61,** 2728 (1939).
(546) PINES, H., PAVLIK, F. J., AND IPATIEFF, V. N.: J. Am. Chem. Soc. **73,** 5738 (1951).
(547) PISTOR, H. J., AND PLIENINGER, H.: Ann. **562,** 239 (1949).
(548) PLANCHER, G., AND CATTADORI, F.: Gazz. chim. ital. **33,** I, 405 (1903).
(549) POLGAR, N., AND ROBINSON, R.: J. Chem. Soc. **1945,** 389.
(550) POLGAR, N., AND ROBINSON, R.: J. Chem. Soc. **1943,** 615.
(551) POPE, W. J., AND PEACHEY, F.: J. Chem. Soc. **75,** 1066 (1899).
(552) PORATH, J.: Arkiv Kemi **1,** 385, 525 (1949); **3,** 163 (1951).
(553) PRICE, C. C.: J. Am. Chem. Soc. **61,** 1847 (1939).
(554) PRICE, C. C., AND MORITA, H.: J. Am. Chem. Soc. **75,** 3686 (1953).
(555) PROUT, F. S.: J. Am. Chem. Soc. **74,** 5915 (1952).
(556) PROUT, F. S., CASON, J., AND INGERSOLL, A. W.: J. Am. Chem. Soc. **70,** 298 (1948).
(557) PUMMERER, R., AND GRASER, F.: Ann. **583,** 207 (1953).
(558) QUDRAT-I-KHUDA, M.: J. Indian Chem. Soc. **8,** 215 (1931).
(559) QUDRAT-I-KHUDA, M., AND GHOSH, S. K.: J. Indian Chem. Soc. **16,** 287 (1939).
(560) QUDRAT-I-KHUDA, M., AND GHOSH, S. K.: J. Indian Chem. Soc. **17,** 19 (1940); Chem. Abstracts **34,** 6233[5] (1940).
(561) QUDRAT-I-KHUDA, M., AND MUKHERJI, A.: J. Indian Chem. Soc. **23,** 435 (1946).
(562) QUILICO, A., CARDANI, C., AND D'ALCONTRES, G. S.: Gazz. chim. ital. **83,** 754 (1953); Chem. Abstracts **49,** 3057*d* (1955).
(563) QUILICO, A.: Gazz. chim. ital. **78,** 111 (1948); Chem. Abstracts **42,** 6834*h* (1948).
(564) RABJOHN, N.: In *Organic Reactions*, Vol. V, Chap. 8. John Wiley and Sons, Inc., New York (1949).
(565) RAHA, C. R.: J. Indian Chem. Soc. **30,** 205 (1953); **34,** 537 (1957).
(566) RAKSHIT, U., BHATTACHARYYA, K. C., AND BARDHAN, J. C.: J. Chem. Soc. **1956,** 790.
(567) RAO, V. S., AND SHESHADRI, T. R.: Proc. Indian Acad. Sci. **12A,** 466 (1940).
(568) RAPHAEL, R. A.: *Acetylenic Compounds in Organic Synthesis*. Butterworths Scientific Publications Ltd., London (1955).
(569) RASSOW, B., AND BAUER, R.: Ber. **41,** 963 (1908).
(570) RAY, F. E.: J. Am. Chem. Soc. **50,** 558 (1928); **51,** 930 (1929).
(571) RAY, R. K., AND BHATTACHARYYA, K. B.: J. Indian Chem. Soc. **23,** 469 (1946).
(572) REED, R. I., AND THORNLEY, M. B.: J. Chem. Soc. **1954,** 2148.
(573) REFORMATSKY, S.: Chem. Zentr. **1902,** II, 107.
(574) REID, E. B., AND GOMPF, T. E.: J. Org. Chem. **18,** 661 (1953).
(575) REID, J., AND REID, W. G.: J. Soc. Chem. Ind. **47,** 115 (1928).
(576) RENFROW, W. B.: J. Am. Chem. Soc. **66,** 144 (1944).
(577) RENFROW, W. B., AND WALKER, G. B.: J. Am. Chem. Soc. **70,** 3957 (1948).
(578) REPPE, W.: *Chemie und Technik der Acetylen-Druck Reaction*, 2nd edition, Riv. combustibili **9,** 501–58 (1955).
(579) REPPE, W., *et al.*: Ann. **582,** 1 (1953).

(580) RHULAND, L. E., WORK, E., DENMAN, R. F., AND HOARE, D. S.: J. Am. Chem. Soc. **77,** 4844 (1955).
(581) RIEGEL, B., SIEGEL, S., AND LILIENFELD, W. M.: J. Am. Chem. Soc. **68,** 984 (1946).
(582) ROBERTS, J. C., AND SHAW, B.: J. Chem. Soc. **1950,** 2842.
(583) ROBEY, R. F.: U. S. patent 2,548,493; Chem. Abstracts **45,** 6833*c* (1951).
(584) ROBINSON, M. I., AND AUTEN, R. W.: U. S. patent 2,585,409; Chem. Abstracts **46,** 4276*c* (1952).
(585) ROBINSON, R.: J. Chem. Soc. **125,** 226 (1924).
(586) ROBINSON, R.: J. Chem. Soc. **125,** 228 (1924).
(587) ROTHSTEIN, B.: Bull. soc. chim. [5] **2,** 80 (1935).
(588) ROYALS, E. E.: *Advanced Organic Chemistry,* Chap. 4. Prentice-Hall, Inc., Englewood Cliffs, New Jersey (1954).
(589) ROYALS, E. E., HOPPE, J. C., JORDAN, A. D., JR., AND ROBINSON, A. G., III: J. Am. Chem. Soc. **73,** 5857 (1951).
(590) RUBEN, S., ALLEN, M. B., AND NAHINSKY, P.: J. Am. Chem. Soc. **64,** 3050 (1942).
(591) RUEGG, R., AND JEGER, O.: Helv. Chim. Acta **31,** 1753 (1948).
(592) RUHL, K.: Z. Naturforsch. **4b,** 199 (1949).
(593) RUNGE, F., HUETER, R., AND WULF, H. D.: Chem. Ber. **87,** 1430 (1954).
(594) RUPE, H., AND LIECHTENHAN, C.: Ber. **41,** 1284 (1908).
(595) RUZICKA, L., AND PFEIFFER, M.: Helv. Chim. Acta **9,** 858 (1926).
(596) RUZICKA, L., AND SEIDEL, C. F.: Helv. Chim. Acta **31,** 160 (1948).
(597) RUZICKA, L., SEIDEL, C. F., SCHINZ, H., AND PFEIFFER, M.: Helv. Chim. Acta **25,** 188 (1942).
(598) RUZICKA, L., SEIDEL, C. F., SCHINZ, H., AND PFEIFFER, M.: Helv. Chim. Acta **31,** 422 (1948).
(599) RUZICKA, L., SEIDEL, C. F., SCHINZ, H., AND TAVEL, C.: Helv. Chim. Acta **31,** 257 (1948).
(600) RUZICKA, L., SCHINZ, H., AND SEIDEL, C. F.: Helv. Chim. Acta **23,** 935 (1940).
(601) RUZICKA, L., AND STEIGER, R.: Helv. Chim. Acta **10,** 680 (1927).
(602) RUZICKA, L., AND STOLL, M.: Helv. Chim. Acta **10,** 691 (1927).
(603) RUZICKA, L., AND STOLL, M.: Helv. Chim. Acta **17,** 1308 (1934).
(604) RUZICKA, L., AND TREBLER, H.: Helv. Chim. Acta **3,** 762 (1920).
(605) RUZICKA, L., AND TREBLER, H.: Helv. Chim. Acta **3,** 779 (1920).
(606) RUZICKA, L., AND TREBLER, H.: Helv. Chim. Acta **4,** 666 (1921).
(607) RYDON, H. N.: J. Am. Chem. Soc. **68,** 376 (1946).
(608) RYDON, H. N.: J. Chem. Soc. **1936,** 593.
(609) RYDON, H. N.: J. Chem. Soc. **1936,** 1444.
(610) SACC, M.: Z. Chemie **1870,** 432; Compt. rend. **70,** 1191 (1870).
(611) SANDBERG, R.: Acta Chem. Scand. **11,** 748 (1957); Chem. Abstracts **52,** 8966*h* (1958).
(612) SCHAPPI, G., AND SEIDEL, C. F.: Helv. Chim. Acta **30,** 2199 (1947).
(613) SCHMID, H., AND BENCZE, W.: Helv. Chim. Acta **36,** 1468 (1953).
(614) SCHOTTE, L.: Arkiv Kemi **9,** 397 (1956); Chem. Abstracts **50,** 12654*h* (1956).
(615) SCHOTTE, L., AND ROSENBERG, A.: Arkiv Kemi **7,** 479 (1954).
(616) SCHRAUTH, W.: U. S. patent 1,921,101 (August 8, 1933); Chem. Abstracts **27,** 5085[1] (1933).
(617) SCHREYER, R. C.: U. S. patent 2,564,131 (August 14, 1951); Chem. Abstracts **46,** 9583*g* (1952).
(618) SCHUERCH, C., JR., AND HUNTRESS, E. H.: J. Am. Chem. Soc. **70,** 2824 (1948).
(619) SCHULMAN, J. H., AND ARMSTRONG, W. M.: Research (London) Suppl., Surface Chemistry **1949,** 263, 273.
(620) SCHULTE, K. E., WEISSKOPF, W., AND KIRSCHNER, J.: Hoppe-Seyler's Z. physiol. Chem. **288,** 69 (1951).
(621) SEBE, Y., AND NAITO, T.: J. Taiwan Pharm. Assoc. **2,** No. 1, 23 (1950); Chem. Abstracts **45,** 6164*a* (1951).

(622) SEN, K., AND BAGCHI, P.: J. Org. Chem. **20,** 845 (1955).
(623) SHACHAT, N.: Univ. Microfilms (Ann Arbor, Michigan) Publ. No. 23386; Dissertation Abstracts **17,** 2427 (1957).
(624) SHIRLEY, D. A., AND ZIETZ, J. R., JR.: J. Org. Chem. **18,** 1591 (1953).
(625) SHONLE, H. A., AND DORAN, W. J.: J. Am. Chem. Soc. **58,** 1358 (1936).
(626) SHONLE, H. A., KELTCH, A. K., AND SWANSON, E. E.: J. Am. Chem. Soc. **52,** 2440 (1930).
(627) SHONLE, H. A., AND WALDO, J. H.: J. Am. Chem. Soc. **55,** 4649 (1933).
(628) SHONLE, H. A., WALDO, J. H., KELTCH, A. K., AND COLES, H. W.: J. Am. Chem. Soc. **58,** 585 (1936).
(629) SHRINER, R. L.: In *Organic Reactions*, edited by R. Adams, Vol. I, Chap. 1. John Wiley and Sons, Inc., New York (1942).
(630) SHRINER, R. L., ADAMS, R., AND MARVEL, C. S.: In *Organic Chemistry*, edited by H. Gilman, 2nd edition, Vol. I, Chap. 4, p. 214. John Wiley and Sons, Inc., New York (1943).
(631) SIMONSEN, J. L.: *The Terpenes*, 2nd edition, Vol. 1, Chap. IV. Cambridge University Press, London (1947).
(632) SIMONSEN, J. L.: *The Terpenes*, 2nd edition, Vol. 2, Chap. V. Cambridge University Press, London (1949).
(633) SMITH, C. W., AND NORTON, D. G. (to Shell Development Co.): U. S. patent 2,718,235 (March 5, 1957).
(634) SMITH, J. C.: Ann. Repts. Progr. Chem. (Chem. Soc. London) 219 (1939).
(635) SMITH, P. A. S., AND HORWITZ, J. P.: J. Am. Chem. Soc. **71,** 3418 (1949).
(636) SMITH, W. T., JR., AND MCLEOD, G. L.: Org. Syntheses **31,** 40 (1951).
(637) SNYDER, H. R., AND PUTNAM, R. E.: J. Am. Chem. Soc. **76,** 1893 (1954).
(638) SNYDER, H. R., SMITH, C. W., AND STEWART, J. M.: J. Am. Chem. Soc. **66,** 200 (1944).
(639) SOGOMONYANTS, Z. S., AND VOLKENSHTEIN, M. V.: Izvest. Akad. Nauk S.S.S.R., Otdel Khim. Nauk **1957,** 611.
(640) SOMMAIRE, C.: Bull. soc. chim. **33,** 189 (1923).
(641) SORM, F., STREIBL, M., JAROLIM, V., NOVOTNY, L., DOLEJS, L., AND HEROUT, V.: Chemistry & Industry **1954,** 252.
(642) SORM, F., STREIBL, M., JAROLIM, V., NOVOTNY, L., DOLEJS, L., AND HEROUT, V.: Chem. Listy **48,** 575 (1954).
(643) SORM, F., STREIBL, M., JAROLIM, V., NOVOTNY, L., DOLEJS, L., AND HEROUT, V.: Collection Czechoslov. Chem. Communs. **19,** 570 (1954).
(644) SPECK, S. B.: J. Am. Chem. Soc. **74,** 2876 (1952).
(645) SPERBER, N., PAPA, D., AND SCHWENK, E.: J. Am. Chem. Soc. **70,** 3091 (1948).
(646) SPIERS, C. H., AND THORPE, J. F.: J. Chem. Soc. **127,** 538 (1925).
(647) STACEY, G. W.: J. Am. Chem. Soc. **74,** 2936 (1952).
(648) STALLBERG-STENHAGEN, S.: Arkiv Kemi **2,** 95 (1950).
(649) STALLBERG-STENHAGEN, S.: Arkiv Kemi **2,** 431 (1950).
(650) STALLBERG-STENHAGEN, S.: Arkiv Kemi **3,** 249 (1951).
(651) STALLBERG-STENHAGEN, S.: Arkiv Kemi **3,** 267 (1951).
(652) STALLBERG-STENHAGEN, S.: Arkiv Kemi **3,** 517 (1951).
(653) STALLBERG-STENHAGEN, S.: Arkiv Kemi, Mineral. Geol. **25A,** No. 10 (1947).
(654) STALLBERG-STENHAGEN, S.: Arkiv Kemi, Mineral. Geol. **26A,** No. 1, No. 12 (1948).
(655) STANLEY, W. M., JAY, M. S., AND ADAMS, R.: J. Am. Chem. Soc. **51,** 1261 (1929).
(656) STAUDINGER, H., BIER, G., AND LORENTZ, G.: Makromol. Chem. **3,** 251 (1949).
(657) STEELE, C. C.: J. Am. Chem. Soc. **53,** 283 (1931).
(658) STENHAGEN, S.: Arkiv Kemi, Mineral. Geol. **19A,** No. 28 (1945).
(659) STENHAGEN, E., AND TAGSTROM, B.: Svensk Kem. Tidskr. **54,** 145 (1942); Chem. Zentr. **1942,** II, 2782.
(660) STETTER, H., BUENTGEN, C., AND COENEN, M.: Chem. Ber. **88,** 77 (1955).
(661) STETTER, H., AND COENEN, M.: Chem. Ber. **87,** 990 (1954).

(662) STETTER, H., AND DIERICHS, W.: Chem. Ber. **85,** 290 (1952).
(663) STETTER, H., KESSELER, H., AND MEISEL, H.: Chem. Ber. **87,** 1617 (1954).
(664) STOLL, M.: Helv. Chim. Acta **34,** 678 (1951).
(665) STOLL, M., AND COMMARMONT, A., Helv. Chim. Acta **31,** 1435 (1948).
(666) STRUBE, R. E.: Org. Syntheses **37,** 34 (1957).
(667) SUNKO, P. E., AND PROSTENIK, M.: Arhiv kem. **26,** 7 (1954); Chem. Abstracts **49,** 7563 (1955).
(668) SUTTER, M.: Helv. Chim. Acta **29,** 1488 (1946).
(669) SUTTER, M., AND SCHLITTLER, E.: Helv. Chim. Acta **30,** 403 (1947).
(670) SUZUKI, H.: J. Pharm. Soc. Japan **56,** 860 (1936); Chem. Abstracts **33,** 130^{9} (1939).
(671) SWANN, S., JR.: In *Technique of Organic Chemistry,* edited by A. Weissberger, 2nd edition, Vol. II, p. 385. Interscience Publishers, Inc., New York (1956).
(672) SWANN, S., JR.: Trans. Electrochem. Soc. **56,** 457 (1929).
(673) SY, M.: Bull. soc. chim. France **1955,** 1175.
(674) SY, M., BUU-HOÏ, NG. PH., AND XUONG, N. DAT: Compt. rend. **239,** 1813 (1954).
(675) TABERN, D. L., AND VOLWILER, E. H.: J. Am. Chem. Soc. **56,** 1139 (1934).
(676) TAKATA, Y., YAMAMOTO, K., AND TAKATA, Y.: J. Pharm. Soc. Japan **74,** 148 (1954); Chem. Abstracts **48,** 6598*e* (1954).
(677) TALAT-ERBEN, M., AND BYWATER, S.: J. Am. Chem. Soc. **77,** 3710 (1955).
(678) TEWARI, L. D., AND TEWARI, J. D.: Current Sci. (India) **17,** 149 (1948).
(679) THIELE, J., AND HEUSER, K.: Ann. **290,** 1 (1896).
(680) THOLE, F. B., AND THORPE, J. F.: J. Chem. Soc. **99,** 422 (1911).
(681) THOLE, F. B., AND THORPE, J. F.: J. Chem. Soc. **99,** 538 (1911).
(682) THORPE, J. F., AND YOUNG, W. J.: J. Chem. Soc. **83,** 357 (1903).
(683) TIFFENEAU, M., AND TCHOUBAR, B.: Compt. rend. **198,** 941 (1934).
(684) TIMMERMANS, J.: Bull. soc. chim. Belg. **40,** 105 (1931).
(685) TIMMERMANS, J., AND HAEGEN, J. VAN DER: Bull. soc. chim. Belg. **42,** 448 (1933).
(686) TREIBS, W., AND HOLBE, O.: Chem. Ber. **85,** 608 (1952).
(687) TREIBS, W., MAYER, R., AND MADEJSKI, M.: Chem. Ber. **87,** 356 (1954).
(688) TSCHUDI, G., AND SCHINZ, H.: Helv. Chim. Acta **33,** 1865 (1950).
(689) TURNER, E. E.: J. Proc. Royal Soc. N. S. Wales **54,** 37 (1920).
(690) ULUSOY, E.: Rec. fac. sci. univ. Istanbul **19C,** 46 (1954); Chem. Abstracts **49,** 12283*c* (1955).
(691) VAIL, W. E.: U. S. patent 1,979,717 (November 6, 1934); Chem. Abstracts **29,** 181^{8} (1935).
(692) VANZETTI, B. L.: Atti reale accad. Lincei **16,** 79, 139 (1907). See Weedon, B. C. L.: Quart. Revs. (London) **6,** 380 (1952).
(693) VAUGHAN, W. R., AND ANDERSON, K. S.: J. Am. Chem. Soc. **77,** 6702 (1955).
(694) VERKADE, P. E., AND COOPS, J.: Proc. Acad. Sci. Amsterdam **36,** 76 (1933).
(695) VERRIER, M.: Bull. soc. chim. France **1957,** 905.
(696) DU VIGNEAUD, V., STACEY, G. W., AND TODD, D.: J. Biol. Chem. **176,** 907 (1948).
(697) VOGEL, A. I.: J. Chem. Soc. **1934,** 1758.
(698) VOGEL, I.: J. Chem. Soc. **1928,** 2010.
(699) VOGEL, I.: J. Chem. Soc. **1934,** 333.
(700) VOLWILER, E. H., AND TABERN, D. L.: J. Am. Chem. Soc. **52,** 1676 (1930).
(701) VUL'FSON, N. S.: Sbornik Statei Obshcheĭ Khim., Akad. Nauk S.S.S.R. **1,** 523 (1953); Chem. Abstracts **49,** 850*e* (1955).
(702) VUL'FSON, N. S.: Zhur. Obshcheĭ Khim. **24,** 1853 (1954); Chem. Abstracts **49,** 13168*c* (1955).
(703) VUL'FSON, N. S., AND VINOGRAD, L. KH.: Doklady Akad. Nauk S.S.S.R. **106,** 669 (1956); Chem. Abstracts **50,** 13811*h* (1956).
(704) WAGNER, R. B., AND ZOOK, H. D.: *Synthetic Organic Chemistry,* 1st edition, p. 599. John Wiley and Sons, Inc., New York (1953).
(705) WALKER, J., AND WOOD, J. K.: J. Chem. Soc. **89,** 598 (1906).

(706) WALLINGFORD, W. H., AND JONES, D. M.: J. Am. Chem. Soc. **64,** 576 (1942).
(707) WALLINGFORD, V. H., JONES, D. M., AND HOMEYER, A. H.: J. Am. Chem. Soc. **64,** 576 (1942).
(708) WALLINGFORD, V. H., HOMEYER, A. H., AND JONES, D. M.: J. Am. Chem. Soc. **63,** 2056 (1941).
(709) WALTHER, H., TREIBS, W., AND MICHAELIS, K.: Chem. Ber. **89,** 60 (1956); Chem. Abstracts **50,** 15426*a* (1956).
(710) WANDER, A., A.-G.: Swiss patent 261,218 (August 16, 1949); Chem. Abstracts **44,** 4027*a* (1950).
(711) WARHURST, E.: Quart. Revs. (London) **5,** 44 (1951).
(712) WARNER, D. T., AND MOE, O. A.: J. Am. Chem. Soc. **70,** 2763, 3470 (1948).
(713) WARNER, D. T., AND MOE, O. A.: J. Am. Chem. Soc. **74,** 371 (1952).
(714) WARNER, D. T., AND MOE, O. A. (to General Mills, Inc.): U. S. patent 2,506,050 (May 2, 1950); Chem. Abstracts **44,** 8946*d* (1950).
(715) WARNER, D. T., AND MOE, O. A.: U. S. patent 2,468,352 (April 26, 1949); Chem. Abstracts **43,** 7505*i* (1949).
(716) WATERS, W. A.: *The Chemistry of Free Radicals,* 2nd edition. Clarendon Press, Oxford (1948).
(717) WEEDON, B. C. L.: Quart. Revs. (London) **6,** 380 (1952).
(718) WEITZEL, G.: Z. physiol. Chem. **282,** 208 (1947).
(719) WEITZEL, G.: Z. physiol. Chem. **287,** 254 (1951).
(720) WEITZEL, G., QUECKENSTEDT, H., GRELLMANN, W., AND LAUTNER, H.: Z. physiol. Chem. **285,** 58 (1950).
(721) WEITZEL, G., AND WOJAHN, J.: Z. physiol. Chem. **285,** 220 (1950).
(722) WEIZMANN, C.: J. Org. Chem. **8,** 287 (1943).
(723) WEIZMANN, C., BERGMANN, E., AND HASKELBERG, L.: Chemistry & Industry **1937,** 587.
(724) WEIZMANN, C., BERGMANN, E., AND SULZBACHER, M.: J. Org. Chem. **15,** 918 (1950).
(725) WERBER, F. X., JR., JANSEN, J. E., AND GRESHAM, T. L.: J. Am. Chem. Soc. **74,** 532 (1952).
(726) WHEELER, H. L., AND MCFARLAND, D. F.: Am. Chem. J. **43,** 22 (1910).
(727) WHIFFEN, D. H.: Chem. & Ind. (London) **1956,** 964.
(728) WHITMORE, F. C., *et al.*: J. Am. Chem. Soc. **63,** 643 (1941).
(729) WHITMORE, F. C., AND HOMEYER, A. H.: J. Am. Chem. Soc. **55,** 4555 (1933).
(730) WHITMORE, F. C., JONES, D. M., AND NOLL, C. I.: U. S. patent 2,161,213 (June 6, 1939); Chem. Abstracts **33,** P7313*g* (1939).
(731) WHITMORE, F. C., STEHMAN, C. J., AND HERNDEN, J. M.: J. Am. Chem. Soc. **55,** 3807 (1933).
(732) WHYTE, D. E., AND COPE, A. C.: J. Am. Chem. Soc. **65,** 1999 (1943).
(733) WIDEQVIST, S.: Arkiv Kemi **2,** 321 (1950).
(734) WIDEQVIST, S.: Arkiv Kemi, Mineral Geol. **B23,** No. 4, 6 pp. (1946).
(735) WILKINSON, R.: J. Chem. Soc. **1931,** 3057.
(736) WILOTH, F.: Makromol. Chem. **8,** 111 (1952).
(737) WILSON, C. V.: In *Organic Reactions,* edited by R. Adams, Vol. IX, Chap. 5. John Wiley and Sons, Inc., New York (1957).
(738) WLADISLAW, B.: Selecta chim. No. **14,** 77 (1955); Chem. Abstracts **50,** 6305*c* (1956).
(739) WOJCIK, B., AND ADKINS, H.: J. Am. Chem. Soc. **56,** 2424 (1934).
(740) WOLF, D. E., AND FOLKERS, K.: In *Organic Reactions,* Vol. VI, Chap. 9. John Wiley and Sons, Inc., New York (1951).
(741) WOLFF, L.: Ann. **317,** 22 (1901).
(742) WOLFHARDT, E.: German patent 856,597 (November 24, 1952); Chem. Abstracts **52,** 9205*h* (1958).
(743) WOTIZ, J. H., AND MERRILL, H. E.: J. Am. Chem. Soc. **80,** 866 (1958).
(744) WREN, H., AND BURNS, H.: J. Chem. Soc. **117,** 266 (1920).

(745) WREN, H., AND CRAWFORD, J.: J. Chem. Soc. **1937,** 230.
(746) WREN, H., AND HALLER, J. W. E.: J. Chem. Soc. **1937,** 230.
(747) WURTZ, A.: Ann. chim. [3] **44,** 275 (1855).
(748) YAMAKAWA, T.: J. Pharm. Soc. Japan **70,** 633 (1950); Chem. Abstracts **45,** 4324*a* (1951).
(749) YUREV, Y. K., KONDRATEVA, G. Y., AND SADOVAYA, N. K.: Zhur. Obshcheĭ Khim. **23,** 844 (1953); Chem. Abstracts **48,** 3956*a* (1954).
(750) ZAL'KIND, YU. S., AND LABUZOV, S. M.: J. Gen. Chem. (U.S.S.R.) **9,** 1525 (1939); Chem. Abstracts **34,** 2788[3] (1940).
(751) ZAL'KIND, Yu. S., AND NAGOIDELI, A. I.: J. Gen. Chem. (U.S.S.R.) **8,** 1382 (1938); Chem. Abstracts **33,** 4195[3] (1939).
(752) ZECHMEISTER, L.: Ann. N. Y. Acad. Sci. **49,** 220 (1948).
(753) ZELINSKY, N.: Ber. **21,** 3160 (1888).
(754) ZELINSKY, N.: Ber. **24,** 3997 (1891).
(755) ZELINSKY, N., AND GUTT, J.: Ber. **40,** 3049 (1907).
(756) ZELINSKY, N., AND REFORMATZKY, A.: Ber. **28,** 2943 (1895).

V. Appendix: Tables of Known Alkylated Alkanedioic Acids

TABLE 2

Derivatives of malonic (propanedioic) acid

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
	°C.	°C.				
$C_4H_6O_4$:						
Methyl-	117, 135					(445, 699)
dimethyl ester		176-177/735 mm.	1.4136 (20°)	1.0952 (20°)		(699)
$C_5H_8O_4$:						
Ethyl-						
dimethyl ester		189/760 mm.	1.41845 (20°)	1.0637 (20°)		(699)
Dimethyl-	190-192					(563)
dimethyl ester		78.5/20 mm.	1.41505 (20°)	1.0624 (20°)		(364, 699)
$C_6H_{10}O_4$:						
Propyl-	102					(445)
dimethyl ester		203/756 mm.	1.42155 (20°)	1.0398 (20°)		(699)
Isopropyl-	108					(445)
diethyl ester		211-215/760 mm.	1.4180			(700)
Methylethyl-	116-118					(367)
dimethyl ester		90/21 mm.	1.42175 (20°)	1.0497 (20°)		(699)
$C_7H_{12}O_4$:						
Butyl-	102					(305)
diethyl ester		127/23 mm.	1.42291 (20°)	0.97639 (20°)		(255)
sec-Butyl-						
diethyl ester		105/9 mm.				(658)
di-*sec*-butyl ester		115/3 mm.	1.4282 (20.2°)			(706)
Isobutyl-	107.5-108					(520)
tert-Butyl-	155-157					(128)
diethyl ester		98-101/10 mm.	1.4180 (25°)	1.0144 (25°)		(203)
Methylpropyl-	96					(699)
dimethyl ester		101/20 mm.	1.42445 (20°)	1.0250 (20°)		(699)
Diethyl-						
dimethyl ester		97/17 mm.	1.42765 (20°)	0.98762 (20°)		(699)
$C_8H_{14}O_4$:						
Amyl-						
diethyl ester		121-123/6 mm.	1.4253 (20°)			(626)
1-Methylbutyl-						
diethyl ester						(91, 626)
Isoamyl-						
diethyl ester		102/3 mm.	1.4255 (20°)			(626)
2-Methylbutyl-						
diethyl ester		150-152/45 mm.	1.4235			(700)
1-Ethylpropyl-						
diethyl ester						(91, 696)
Methyl-*sec*-butyl-	118-119					(161)
diethyl ester		230-240				(161)
Methyl-*tert*-butyl-						
diethyl ester		100/5 mm.	1.4291 (30°)			(128)
Ethylpropyl-						
dimethyl ester		121/22 mm.	1.42435 (20°)	0.97846 (20°)		(255, 699)
Ethylisopropyl-						
dimethyl ester		112-115/18 mm.				(397)
$C_9H_{16}O_4$:						
Hexyl-	105					(201)
diethyl ester		143/15 mm.	1.4278 (21°)	0.9577 (21°)		(587)
dihydrazide	151					(676)
Isohexyl-						
diethyl ester		136-139/11 mm.				(395)
1-Methylamyl-	91.5-93.5					(429)
diethyl ester		86-87/0.5 mm.	1.4307 (17°)			(429)
2-Methylamyl-						
diethyl ester		146-147/24 mm.	1.4263 (25°)	0.9566 (25°)		(182)

TABLE 2—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
	°C.	°C.				
1-Ethylbutyl-						
diethyl ester						(235)
2-Ethylbutyl-						
diethyl ester		143/15 mm.	1.4278 (21°)	0.9577 (21°)		(587)
3,3-Dimethylbutyl-						
diethyl ester		77-78.5/1-2 mm.				(730)
Methylamyl-						
diethyl ester		99/8 mm.	1.4254 (25°)			(625)
Methylisoamyl-						
diethyl ester		103-104/3 mm.	1.4248 (25°)			(625, 640)
Methyl-1-methylbutyl-	139-140					(394)
diethyl ester		124/10 mm.	1.4288 (25°)			(394, 625)
Ethylbutyl-						
diethyl ester		113/20 mm.	1.42834 (20°)	0.97287 (20°)		(255)
dibutyl ester		117-119/1 mm.	1.4329 (26.5°)			(706)
Ethyl-*sec*-butyl-	108					(359)
diethyl ester		240-247/760 mm.		0.9786 (25°)		(359)
Ethylisobutyl-	97-98					(190)
diethyl ester		121-124/13 mm.				(190)
diisobutyl ester		175/30 mm.	1.4320 (26.5°)			(706)
Ethyl-*tert*-butyl-						
diethyl ester		90/3 mm.	1.4335 (20°)	0.9829 (25°)		(128, 203)
Dipropyl-	143					(445)
ethyl diethylaminoethyl ester		115/0.5 mm.				(710)
Propylisopropyl-						
monoethyl ester		107/0.45 mm.				(125)
Diisopropyl-	182					(445)
dimethyl ester	32	228/744 mm.	1.4417 (20°)			(445)
diethyl ester		246.2/751 mm.	1.4356 (20°)	0.9774 (20°)		(445)
$C_{10}H_{18}O_4$:						
Heptyl-						
diethyl ester		157/18 mm.	1.4294 (22.5°)	0.9495 (22.5°)		(587)
dihydrazide	147					(676)
Isoheptyl-						
diethyl ester						(670)
tert-Heptyl-	78-79					(734)
diethyl ester		129.5/8 mm.				(734)
1-Methylisohexyl-						
diethyl ester		130-135/4 mm.		0.9590 (20°)		(395)
2-Ethylamyl-						
diethyl ester		94-95/0.5 mm.	1.4298 (25°)	0.9549 (25°)		(182)
4,4-Dimethylamyl-						
diethyl ester		77-78/1-2 mm.				(730)
Methylhexyl-						
diethyl ester		125/3.5 mm.	1.4280 (25°)			(625)
Methyl-1-methylamyl-						
diethyl ester		126/6 mm.	1.4323 (25°)			(625)
Methylisohexyl-						
diethyl ester		122-125/7 mm.				(474)
Methyl-1-ethylbutyl-						
diethyl ester		130-131/11 mm.				(397)
Methyl-2-ethylbutyl-						
diethyl ester		153/28 mm.				(488)
Ethylamyl-						
diethyl ester		139-141/14 mm.	1.4295 (20°)			(204, 626)
Ethylisoamyl-						
diethyl ester		135/16 mm.	1.4290-5 (20°)			(349)

TABLE 2—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
	°C.	°C.				
diisoamyl ester		126-129/1 mm.	1.4351-9 (26°)			(349)
Ethyl-*tert*-amyl-						
diethyl ester		93-96/1.5 mm.	1.4435 (20°)			(203)
Ethyl-1-methylbutyl-						
diethyl ester		133-140/14 mm.	1.4343 (20°)			(626, 700)
Ethyl-2-methylbutyl-						
diethyl ester		141-143/15 mm.	1.4316 (20°)			(626)
Ethyl-1-ethylpropyl-						
diethyl ester		110-112/4 mm.	1.4329 (20°)			(626)
Ethyl-1,2-dimethylpropyl-						
diethyl ester		110-116/7 mm.	1.4400 (25°)			(626)
Isopropylbutyl-						
diethyl ester		254-256/760 mm.				(313)
ethyldiethylaminoethyl						
ester		160/11 mm.				(710)
Propyl-*sec*-butyl-						
diethyl ester		122-124/6 mm.	1.4331-1.4342			(627)
potassium salt	134-136					(394)
Isopropyl-*sec*-butyl-						
diethyl ester		120-123/10 mm.	1.4363-89 (21°)			(707)
Isopropylisobutyl-						
diethyl ester		119-121/10 mm.	1.4352 (18°)			(707)
$C_{11}H_{20}O_4$:						
Octyl-	116					(586)
diethyl ester		167/16 mm.	1.4322 (20°)	0.9444 (20°)		(587)
methyl ethyl ester		185-190/1 mm.				(220)
dihydrazide	158					(676)
1-Methylheptyl-	96					(620)
diethyl ester		141-142/2 mm.	1.4310			(620, 700)
2-Methylheptyl-						
diethyl ester		88-98/1 mm.				(423)
1,5-Dimethylhexyl-						
diethyl ester		128/4 mm.				(208)
5,5-Dimethylhexyl-						
diethyl ester		125/2-3 mm.				(730)
2-Ethylhexyl-						
diethyl ester		189/20 mm.				(723)
1-Ethylisohexyl-						
diethyl ester		119-124/4 mm.		0.95825 (20°)		(395)
1-Ethyl-4-methylamyl-						
diethyl ester		119-120/3 mm.				(395)
Methylisoheptyl-	126					(395)
diethyl ester		140-145/4 mm.		0.95129 (20°)		(395)
Methyl-1,4-dimethylamyl-						
diethyl ester						(730)
Methyl-4,4-dimethylamyl-						
diethyl ester						(730)
Ethylisohexyl-	102					(395)
diethyl ester		119-120/3 mm.		0.96044 (20°)		(395)
Ethyl-1-methylamyl-						
diethyl ester		126-134/9 mm.	1.4331			(626)
Ethyl-2-methylamyl-						
diethyl ester		103-105/2 mm.	1.4392 (28°)			(628)
Ethyl-4-methylamyl-						
diethyl ester		108/2 mm.	1.4347 (28°)			(628)
Ethyl-1,3-dimethylbutyl-						
diethyl ester		97.5-99/3 mm.	1.4353 (25°)			(628)
Ethyl-3,3-dimethylbutyl-						
diethyl ester		148-151/4-5 mm.				(730)
Ethyl-1-ethylbutyl-						
diethyl ester		144-145/18 mm.	1.4363-1.4369			(397, 627)

TABLE 2—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
	°C.	°C.				
Ethyl-2-ethylbutyl-						
diethyl ester		148/18 mm.	1.4360 (25°)			(488, 628)
Propylamyl-						
diethyl ester		99-101/2.6 mm.	1.4323 (19°)			(707)
Isopropylamyl-						
diethyl ester		186-190/50 mm.	1.4320			(700)
Propylisoamyl-	150					(395)
diethyl ester		137-138/4 mm.		0.95215 (20°)		(395)
Propyl-1-methylbutyl-						
diethyl ester		140-144/45 mm.				(675)
Propyl-2-methylbutyl-						
diethyl ester		100/1 mm.	1.4319 (25°)			(625)
Propyl-1-ethylpropyl-						
diethyl ester		165-170/40 mm.				(675)
Isopropyl-1,3-dimethyl-isopropyl-						
diethyl ester		258-289/760 mm.	1.4380 (20°)	0.9594 (20°)		(445)
monoethyl ester		152-158/20 mm.	1.455 (18°)	1.015 (18°)		(445)
Dibutyl	160					(644)
diphenyl ester	49	191-192/1-2 mm.				(644)
Butyl-*sec*-butyl						
diethyl ester		114-116/4.5 mm.	1.4339 (24.5°)			(707)
Di-*sec*-butyl-						
diethyl ester		94-98/2 mm.	1.4366-433 (21°)			(707)
di-*sec*-butyl ester		112-114/1.5 mm.	1.4433 (26°)			(707)
Diisobutyl-	140					(445)
diethyl ester						(445)
$C_{12}H_{22}O_4$:						
Nonyl-						
diethyl ester		176/15 mm.	1.4336 (21°)	0.9379 (21°)		(587)
dihydrazide	153					(676)
1-Methyloctyl-						
diethyl ester						(362)
3-Methyloctyl-						
diethyl ester		176-177/19 mm.				(549)
1-Methylisoöctyl-						
diethyl ester		117-118/0.5 mm.	1.4358 (23°)			(226)
2,6-Dimethylheptyl- (−)- diethyl ester		175-180/18 mm.			−2.6 (18°)	(344)
6,6-Dimethylheptyl-						
diethyl ester						(730)
2-Ethyl-3-methylhexyl-						
diethyl ester		128-129/3 mm.	1.4367 (24°)			(227)
Methyloctyl-						
diethyl ester		134/1.5 mm.				(156)
Methyl-2-ethylhexyl-						
diethyl ester		126/1.5 mm.	1.4353 (25°)			(625)
Ethylheptyl-						
diethyl ester		143.5/3.5 mm.	1.4343 (20°)			(626)
Ethyl-1,3-dimethylamyl-						
diethyl ester		126-127/4 mm.	1.4366 (25°)			(628)
Ethyl-1,4-dimethylamyl-						
diethyl ester		133-134/7.5 mm.	1.4351 (25°)			(628)
Ethyl-2,4-dimethylamyl-						
diethyl ester		140-141/10 mm.	1.4343 (25°)			(628)
Ethyl-4,4-dimethylamyl-						
diethyl ester		126-128/4-5 mm.				(730)
Ethyl-1-propylbutyl-						
diethyl ester		110-111/3 mm.	1.4376 (25°)			(628)
Propyl-2-ethylbutyl-						
diethyl ester		158/23 mm.				(488)
Isopropyl-2-ethylbutyl-						
diethyl ester		150/15 mm.				(488)

TABLE 2—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
	°C.	°C.				
Butylamyl-						
diethyl ester		185–193/55 mm.	1.4312			(700)
sec-Butylamyl						
diethyl ester		89.5–92.5/1–1.5 mm.	1.4380 (20°)			(707)
Isobutylamyl-						
diethyl ester		184–192/47 mm.	1.4327			(700)
Butylisoamyl-						
diethyl ester		91–93/1.5 mm.	1.4316 (23°)			(707)
sec-Butylisoamyl-						
diethyl ester		95–99/2–2.5 mm.	1.4370 (20°)			(707)
Isobutylisoamyl-	122–124					(190)
diethyl ester		170–176/35 mm.	1.4316			(700)
Butyl-1-methylbutyl-						
diethyl ester		170–180/40 mm.	1.4310			(675, 700)
Butyl-2-methylbutyl-						
diethyl ester		165–170/22 mm.	1.4330			(700)
Butyl-1-ethylpropyl-						
diethyl ester		155–170/40–50 mm.	1.4353			(700)
$C_{13}H_{24}O_4$:						
Decyl-	120					(708)
diethyl ester		182/13 mm.	1.4344 (23.5°)	0.9314 (23.5°)		(157, 587)
dihydrazide	148					(676)
1-Methylnonyl- (±)	73.6–75.5					(556)
dibutyl ester		178/1 mm.	1.4403 (25°)	0.9186 (20°)		(556)
(+)	99.5–100.5				7.07 (25°)	(556)
dibutyl ester		165–176/0.5 mm.		0.914 (27°)	0.31 (27°)	(556)
(−)	99.3–100.6				−7.17 (25°)	(556)
dibutyl ester		178–182/2 mm.			−0.36 (25°)	(556)
3,7-Dimethyloctyl-						
diethyl ester		183–187/13 mm.				(103)
4-Ethyloctyl-	107–108					(620)
diethyl ester		159–161/1 mm.				(620)
Methylnonyl-	94–95					(158)
diethyl ester		147–148/5 mm.				(158)
Methyl-2-methyloctyl-						
diethyl ester		162.5–163.5/7.5 mm.	1.4358 (25°)			(149)
Ethyloctyl	72					(110)
diethyl ester		171–180/13 mm.				(110, 349)
Ethyl-*sec*-octyl						
diethyl ester (±)		135–140/3 mm.	1.4365 (25°)	0.9434 (25°)		(327)
diethyl ester (+)		137–138/3 mm.	1.4370 (25°)	0.9323 (25°)	8.22 (25°)	(327)
diethyl ester (−)					−8.07 (25°)	(327)
Ethyl-4-methylheptyl-						
diethyl ester		115–116/1 mm.	1.4398 (20°)			(628)
Ethyl-2-ethylhexyl-						
diethyl ester		127–130/4 mm.	1.4393 (24°)			(628)
Ethyl-2,4-dimethylhexyl-						
diethyl ester		107–109/1 mm.	1.4412 (20°)			(628)
Ethyl-4,4-dimethylhexyl-						
diethyl ester		127–128/2–3 mm.				(730)
Ethyl-5,5-dimethylhexyl-						
diethyl ester		129–130/3–5 mm.				(730)
Propylheptyl-	110–111					(106)
diethyl ester		165/10 mm.				(106)
Isopropylheptyl-						
diethyl ester		137–140/4 mm.	1.4375 (25°)	0.9249 (25°)		(21)
Propyl-4,4-dimethylamyl-						
diethyl ester						(730)

TABLE 2—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
	°C.	°C.				
Butylhexyl-	134					(106)
diethyl ester		143-147/4 mm.	1.4347 (25°)	0.9233 (25°)		(21)
Butyl-2-ethylbutyl-						
diethyl ester		172/28 mm.				(488)
Isobutyl-2-ethylbutyl-						
diethyl ester		163/22 mm.				(488)
Diamyl-						
diethyl ester		158-161/11 mm.	1.4343 (25°)	0.9334 (25°)		(21, 204)
Diisoamyl-						
ethyl diethylaminoethyl ester		135/0.5 mm.				(710)
$C_{14}H_{26}O_4$:						
Hendecyl-						
diethyl ester		192/13 mm.	1.4376 (20°)	0.9302 (20°)		(587)
dihydrazide	152					(676)
1-Methyldecyl-						
diethyl ester		163-168/5 mm.				(226)
4-Ethyl-1-methyloctyl-						
diethyl ester		136-141/2.5 mm.	1.4385 (24°)			(226)
Methyldecyl-						
diethyl ester		152-153/2 mm.				(147)
Methyl-3,7-dimethyloctyl- (−)						
diethyl ester		189-190/15 mm.			−1.16 (20°)	(344)
Ethyl-6,6-dimethylheptyl-						
diethyl ester		138-140/3-4 mm.				(730)
Ethyl-2-ethyl-3-methylhexyl-						
diethyl ester		120-123/2.5 mm.	1.4451 (20°)			(628)
Ethyl-2-ethyl-5-methylhexyl-						
diethyl ester		125-128/1 mm.	1.4412 (20°)			(628)
Butylheptyl-						
diethyl ester		138-140/3.5 mm.	1.4365 (25°)	0.9288 (25°)		(21)
Butyl-4,4-dimethylamyl-						
diethyl ester						(730)
Amylhexyl-						
diethyl ester		146-149/4 mm.	1.4361 (25°)	0.9300 (25°)		(21)
$C_{15}H_{28}O_4$:						
Dodecyl-	119					(587)
diethyl ester		170-173/2.5 mm.	1.4388 (25°)	0.9257 (21°)		(587, 676)
dihydrazide	146					(676)
3-Methylhendecyl- (+)						
diethyl ester		172-173.5/4 mm.	1.4378 (25°)		2.04 (20°)	(147)
2-Ethyl-3-methylnonyl-						
diethyl ester		152-155/4 mm.	1.4401 (25°)			(226)
Methyl-2-methyldecyl-(L+)	44.6-45.8					
diethyl ester		173.5-175/6.5 mm.	1.4389 (25°)	0.9244 (25°)		(149)
Ethyldecyl-						(439)
diethyl ester						(131)
Ethyl-6,6-dimethyloctyl-						
diethyl ester						(730)
Ethyl-7,7-dimethyloctyl-						
diethyl ester						(730)
Butyloctyl-						
diethyl ester		156-159/4 mm.	1.4360 (25°)	0.9263 (25°)		(21)
Butyl-1-methylheptyl-						
diethyl ester		185-190/16 mm.	1.4410			(700)
Amylheptyl-						
diethyl ester		163.5-165/5 mm.	1.4371 (25°)	0.9239 (25°)		(21)

TABLE 2—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
	°C.	°C.				
Dihexyl-						
diethyl ester		155-158/4 mm.	1.4374 (25°)	0.9249 (25°)		(21)
Di(2-ethylbutyl)-						
diethyl ester		178/23 mm.				(488)
$C_{16}H_{30}O_4$:						
Tridecyl-						(694)
1-Hexylheptyl-						
diethyl ester		151-152/0.2 mm.	1.4420 (20°)			(647)
Methyldodecyl-						
diethyl ester		161-164/1.5-2.5 mm.	1.4412 (20°)	0.9217 (20°)		(279)
Methyl-3-methylundecyl- (+)						
diethyl ester		186-187/4.5 mm.	1.4398 (21°)		1.36 (21°)	(147)
Ethylundecyl-						
diethyl ester		150-154/0.2-1.0 mm.	1.4420 (20°)	0.9262 (20°)		(279)
Propyldecyl-						
diethyl ester		143-148/0.1-1.0 mm.	1.4416 (20°)	0.9256 (20°)		(279)
Butylnonyl-						
diethyl ester		143-147/0.1-1.0 mm.	1.4420 (20°)	0.9241 (20°)		(279)
Amyloctyl-						
diethyl ester		142-146/0.1-1.0 mm.				(279)
Hexylheptyl-						
diethyl ester		146-152/0.1-1.0 mm.	1.4412 (20°)	0.9231 (20°)		(279)
$C_{17}H_{32}O_4$:						
Tetradecyl-	123-124					(157)
diethyl ester		182-185/2 mm.	1.4413 (25°)			(157)
4-Ethyl-1-isobutyloctyl-						
diethyl ester		135-140/1 mm.	1.4438 (24°)			(226)
Methyltridecyl-						
diethyl ester		167-170/3 mm.	1.4418 (25°)	0.9181 (25°)		(655)
Ethyldodecyl-	78					(131)
diethyl ester		214-218/15 mm.				(131)
Propylhendecyl-						
diethyl ester		178-179/4 mm.	1.4422 (25°)	0.9186 (25°)		(655)
Butyldecyl-						
diethyl ester		181-183/4 mm.	1.4424 (25°)	0.9229 (25°)		(655)
sec-Butyldecyl-						
diethyl ester		196-198/10 mm.	1.4454 (25°)	0.9523 (25°)		(655)
Isobutyldecyl-						
diethyl ester		160-162/2 mm.	1.4428 (25°)	0.9207 (25°)		(655)
Amylnonyl-						
diethyl ester		185-186/5 mm.	1.4462 (25°)	0.9282 (25°)		(655)
Hexyloctyl-						
diethyl ester		170-174/0.5-1.5 mm.	1.4441 (20°)	0.9178 (20°)		(279)
Diheptyl-						
diethyl ester		178-180/3 mm.	1.4459 (25°)	0.9169 (25°)		(655)
Di(4,4-dimethylamyl)-						
diethyl ester						(730)
$C_{18}H_{34}O_4$:						
Pentadecyl-	114-115					(667)
diethyl ester						(558)
3,7,11-Trimethyldodecyl-						
diethyl ester						(357)
Methyltetradecyl-						
diethyl ester		172-176/0.5-1.0 mm.	1.4436 (20°)	0.9164 (20°)		(279)

TABLE 2—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
	°C.	°C.				
Ethyltridecyl-diethyl ester		178-181/0.8-2.0 mm.	1.4435 (20°)	0.9207 (20°)		(279)
Propyldodecyl-diethyl ester		173-177/0.5-1.0 mm.	1.4438 (20°)	0.9191 (20°)		(279)
Butylhendecyl-diethyl ester		171-176/0.5-1.0 mm.	1.4439 (20°)	0.9173 (20°)		(279)
Amyldecyl-diethyl ester		148-154/0.1-0.8 mm.				(279)
Heptyloctyl-diethyl ester		157-161/0.2-1.0 mm.	1.4436 (20°)	0.9171 (20°)		(279)
Heptyl-1-methylheptyl-diethyl ester						(198)
$C_{18}H_{34}O_4$:						
Hexadecyl-diethyl ester	24-25	238-240/14 mm.				(130)
Methylpentadecyl-diethyl ester		179-183/5 mm.	1.4453 (25°)	0.9119 (25°)		(655)
Ethyltetradecyl-diethyl ester		183-186/2 mm.				(157)
Propyltridecyl-diethyl ester		183-187/5 mm.	1.4475 (25°)	0.9048 (25°)		(655)
Isopropyltridecyl-diethyl ester		179-183/5 mm.	1.4491 (25°)	0.9144 (25°)		(655)
Butyldodecyl-diethyl ester		175-180/3.5 mm.	1.4473 (25°)	0.9104 (25°)		(119, 655)
sec-Butyldodecyl-diethyl ester		180-184/5 mm.	1.4501 (25°)	0.9163 (25°)		(655)
Isobutyldodecyl-diethyl ester		180-185/5 mm.	1.4481 (25°)	0.9115 (25°)		(655)
Amylhendecyl-diethyl ester		180-185/5 mm.	1.4509 (25°)	0.9124 (25°)		(655)
sec-Amylhendecyl-diethyl ester		175-178/4 mm.	1.4509 (25°)	0.9155 (25°)		(655)
Hexyldecyl-diethyl ester		185-188/2.5 mm.	1.4476 (25°)	0.9118 (25°)		(655)
Heptylnonyl-diethyl ester		193-197/5 mm.	1.4471 (25°)	0.9118 (25°)		(655)
Dioctyl-	92					(656)
diethyl ester		192-195/3 mm.	1.4471 (25°)	0.9135 (25°)		(119, 655)
ditetradecyl ester	22.0-22.5					(656)
dihexadecyl ester	30-30.5					(656)
distearyl ester	38.5-39					(656)
$C_{20}H_{38}O_4$:						
1-Methylhexadecyl-diethyl ester		180-182/0.3 mm.	1.4492 (19°)			(402)
2-Methylhexadecyl-diethyl ester						(721)
3-Methylhexadecyl-diethyl ester		193/0.5 mm.				(721)
4-Methylhexadecyl-diethyl ester		194/0.5 mm.				(721)
5-Methylhexadecyl-diethyl ester		190/0.4 mm.				(721)
6-Methylhexadecyl-diethyl ester		188/0.3 mm.				(721)
7-Methylhexadecyl-diethyl ester		192/0.4 mm.				(721)
8-Methylhexadecyl-diethyl ester		200/0.6 mm.				(721)

TABLE 2—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
	°C.	°C.				
9-Methylhexadecyl-diethyl ester		192/0.4 mm.				(721)
10-Methylhexadecyl-diethyl ester		196/0.5 mm.				(721)
11-Methylhexadecyl-diethyl ester						(721)
12-Methylhexadecyl-diethyl ester						(721)
13-Methylhexadecyl-diethyl ester		190/0.4 mm.				(721)
14-Methylhexadecyl-diethyl ester						(721)
15-Methylhexadecyl-diethyl ester		194/0.5 mm.				(721)
Methylhexadecyl-	97.0-97.5					(721)
diethyl ester		202/0.5 mm.				(721)
Propyltetradecyl-diethyl ester		180-184/0.2-1.0 mm.	1.4459 (20°)	0.9141 (20°)		(279)
Amyldodecyl-diethyl ester		178-181/0.2-1.0 mm.	1.4460 (20°)	0.9112 (20°)		(279)
Heptyldecyl-diethyl ester		182-186/0.2-1.0 mm.	1.4459 (20°)	0.9116 (20°)		(279)
$C_{21}H_{40}O_4$:						
Octadecyl-diethyl ester						(87, 624)
Methylheptadecyl-	100-101					(283)
diethyl ester	11	195-197/0.5 mm.				(283)
Ethylhexadecyl-	80-81, 76-77					(656, 721)
diethyl ester		208/0.5 mm.				(721)
$C_{22}H_{42}O_4$:						
Methyloctadecyl-	98-100					(659)
Propylhexadecyl-	87-88					
diethyl ester		213/0.5 mm.				(721)
$C_{28}H_{44}O_4$:						
3,7,11,15-Tetramethylhexadecyl-diethyl ester		191-192/0.34 mm.				(403)
Methyl-2-methyloctadecyl-						(45)
Butylhexadecyl-	94-95					(721)
dibutyl ester		265-268/4 mm.	1.4500 (20°)			(706)
diethyl ester		219/0.5 mm.				(721)
Didecyl-diethyl ester		196-198/0.2 mm.				(108)
$C_{24}H_{46}O_4$:						
Amylhexadecyl-	78-79					(721)
diethyl ester		225/0.5 mm.				(721)
$C_{26}H_{48}O_4$:						
Methyl-2-methyleicosyl-	66-68					(44)
Hexylhexadecyl-	72-73					(721)
diethyl ester		231/0.5 mm.				(721)
Dihendecyl-diethyl ester		242-247/1 mm.	1.4453 (20°)			(690)
$C_{26}H_{50}O_4$:						
1,9,12-Trimethyleicosyl-diethyl ester		212-216/0.15 mm.				(647)
3-Decyltridecyl-diethyl ester		221-224/0.45 mm.				(550)
1-Methyldecyldodecyl-diethyl ester		210-212/0.16 mm.				(550)

TABLE 2—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
	°C.	°C.				
Heptylhexadecyl-	73.5-74.0					(721)
diethyl ester		240/0.5 mm.				(721)
$C_{27}H_{52}O_4$:						
Ethyldocosyl-	55					(157)
diethyl ester	49-49.5					(157)
Butyleicosyl-	92-93					(157)
diethyl ester						(157)
Octylhexadecyl-	69.5-70					(721)
diethyl ester		250/0.5 mm.				(721)
Decyltetradecyl-	62-63					(157)
diethyl ester						(157)
Didodecyl-	80					(157)
diethyl ester		251-253/3 mm.				(690)
$C_{28}H_{54}O_4$:						
Nonylhexadecyl-	68-69					(721)
diethyl ester		260/0.5 mm.				(721)
$C_{28}H_{56}O_4$:						
Decylhexadecyl-	68.5-69.5					(721)
diethyl ester		271/0.5 mm.				(721)
Ditridecyl-						
diethyl ester		260-265/10.5 mm.	1.4500 (27°)			(690)
$C_{30}H_{58}O_4$:						
Hendecylhexadecyl-	68.5-69					(721)
diethyl ester		233/0.1 mm.				(721)
$C_{31}H_{60}O_4$:						
Dodecylhexadecyl-	72-72.5					(721)
diethyl ester		243/0.1 mm.				(721)
Ditetradecyl-						
dipropyl ester						(74)
$C_{36}H_{68}O_4$:						
Dihexadecyl-						
diethyl ester	34.5-35	305-310/2-2.5 mm.				(130, 656)
dimethyl ester	38					(656)

TABLE 3

Derivatives of succinic (butanedioic) acid

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
	°C.	°C.				
$C_5H_8O_4$:						
Methyl-	114–115	102–106/12 mm.				(718, 720)
$C_6H_{10}O_4$:						
Ethyl-	98					(432)
(+)	83.5–85				+20.65 (16.8°)	(745)
(−)	83.5–85				−20.80 (23.8°)	(745)
2,2-Dimethyl-	138–140					(308)
diethyl ester		101/15 mm.	1.4233 (20°)	0.9936 (20°)		(749)
2,3-Dimethyl-						(615)
meso	197–199					
(±)	128–129					
(+)	134					
(−)	134					
$C_7H_{12}O_4$:						
Propyl-	100.5					(718, 720)
(+)	93.9				9.6 (25°)	(685)
Isopropyl-	115–116					(635)
(+)	86–87				23.7 (20°)	(258)
2-Methyl-2-ethyl-	81–83, 104					(552, 557, 681)
2-Methyl-3-ethyl-	145–160					(447)
2,2,3-Trimethyl-	144					(502)
mono-*p*-toluidide	125–126					(238)
$C_8H_{14}O_4$:						
Butyl-						
(±)	82.5–83.5					(254)
(+)	82.5–83.5				22.6 (25°)	(254)
(−)	82.5–83.5				−22.6 (25°)	(254)
Isobutyl-						
(±)	109–110					(8)
(+)	95–96				26.8 (25°)	(254)
(−)	95–96				−27 (25°)	(254)
tert-Butyl-	132					(733)
2-Methyl-2-isopropyl-						
(±) (a)	131.5–133					(209)
(±) (b)	148–149, 152–153					(209, 552)
(+)					12.5 (25°)	(552)
(−)					−12.6 (25°)	(552)
2-Methyl-3-isopropyl-	105–120					(447)
2,2-Diethyl-	110–111					(308)
monomethyl ester	46–47					(72)
2,3-Diethyl-						
meso	190–192, 207					(159, 746)
(±)	127–128, 130					(159, 746)
(+)	125				34.5 (24°)	(746)
(−)	125				−34.3 (24°)	(746)
2,2,3,3,-Tetramethyl	188–189, 191–192					(370, 554)
$C_9H_{16}O_4$:						
Amyl-						
(±)	85–87					(246)
anhydride		140/13 mm.				(459)
(+)	84–86				26.7 (25°)	(246)
(−)	83–85				−26.3 (25°)	(246)
Isoamyl-	77–78					(562)
anilide	135					(562)
1-Methylbutyl-	138					(10)
2-Methyl-2-butyl-	91–93					(470)
2-Methyl-3-butyl-	85–105					(447)

TABLE 3—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
	°C.	°C.				
2-Ethyl-3-propyl-						
(a)	178–179					(221)
diethyl ester		134–135/16 mm.				(221)
(b)	97–98					(221)
2-Ethyl-3-isopropyl-						
(a)	210					(221)
(b)	96					(221)
2,2-Dimethyl-3-iso-propyl-	135					(505)
2-Methyl-3,3-diethyl-	99–102					(470)
$C_{10}H_{18}O_4$:						
Hexyl-						
(±)	87.3, 88–89					(55, 685, 744)
p-toluidide	79–80					(720)
(+)	83.2				14.3 (25°)	(685)
(−)	82–83				−2.66 (15.8°)	(55)
Isohexyl-	73–74					(434)
2-Butyl-2-ethyl-						
anhydride		153–155/21 mm.				(533)
2,2-Dimethyl-3-butyl-						(609)
2,2-Dimethyl-3-*tert*-butyl-	138					(504)
2,3-Dipropyl-	115–117					(449)
diethyl ester (mixture)		86–87/1 mm.	1.4302 (20°)			(449)
2,2,3-Triethyl-	117					(172)
2,2-Dimethyl-3,3-di-ethyl-	145					(172)
$C_{11}H_{20}O_4$:						
Heptyl-	90–91					(55, 718)
(4,4-Dimethylamyl)-	132					(10)
2-Methyl-2-hexyl-						
imide	115					(75)
2,2-Dimethyl-3-amyl-	119					(609)
2-Isopropyl-3-isobutyl-	124, 185–186					(221)
$C_{12}H_{22}O_4$:						
Octyl-	90					(55)
$C_{13}H_{24}O_4$:						
Nonyl-	94.5–95.5					(55, 718)
$C_{14}H_{26}O_4$:						
Decyl-	91–93, 94–95					(55)
anhydride	70–71					(459)
diethyl ester		175–180/13 mm.	1.4342 (33.6°)			(459)
2-Butyl-2-hexyl-	70.5–72, 141–142					(55)
2,3-Dimethyl-2,3-di-*tert*-butyl-		124–126/5 mm.	1.4602 (20°)			(18)
$C_{15}H_{28}O_4$:						
Hendecyl-	96.5–98					(55, 718)
2-Methyl-2-decyl-						
imide	98					(75)
anhydride	37	187/8 mm.				(75)
diethyl ester		189–192/8 mm.				(75)
2-Amyl-3-hexyl-	68–70, 148–149					(55)
$C_{16}H_{30}O_4$:						
Dodecyl-	98–99					(55, 718)
2-Ethyl-2-decyl-	84–86					(571)
diethyl ester		170/4 mm.				(571)
2-Ethyl-3-decyl-	59–63, 132–134					(353)

TABLE 3—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
	°C.	°C.				
2,3-Dihexyl-	95-96, 144-144.5					(55)
$C_{17}H_{32}O_4$:						
Tridecyl-	101.5-103					(55)
2-Methyl-2-dodecyl-	132-133					(365, 567)
2-Methyl-3-dodecyl-	80-81, 131-132					(55)
2-Propyl-3-decyl-	73-74, 131-132.5					(55)
$C_{18}H_{34}O_4$:						
Tetradecyl-	110, 100-101					(55, 458, 718)
dimethyl ester		220/20 mm.	1.4440 (27.5°)			(458)
diethyl ester		230/20 mm.	1.4430 (27.5°)			(458)
anhydride	74					(458)
imide	98-99					(458)
2-Ethyl-3-dodecyl-	77.5-79, 131-132					(55)
2,3-Diheptyl-	87-88, 140-141					(55)
$C_{19}H_{36}O_4$:						
Pentadecyl-	100-104.5					(55)
2-Methyl-3-tetradecyl-						
(a)	134-136					(28)
anil	63.5-64.5					(28)
(b)	98-101					(25)
$C_{20}H_{38}O_4$:						
Hexadecyl-	89-90, 105-106					(55, 75)
dimethyl ester		205-210/10 mm.	1.4460 (28.5°)			(75)
diethyl ester		215-220/10 mm.	1.4435 (28.5°)			(75)
anhydride	63					(75)
imide	94-95					(75)
2,3-Dioctyl-	86-87, 145					(55)
$C_{21}H_{40}O_4$:						
2-Methyl-3-hexadecyl-						
(a)	134-136					(55)
anil	67.5-69.5					(28)
(b)	86-88					(55)
$C_{22}H_{42}O_4$:						
Octadecyl-	103.5-104.5					(55)
$C_{32}H_{62}O_4$:						
2,3-Ditetradecyl-						
meso	135-136					(348)
(±)	95-96					(348)
anhydride	45-45.5					(348)

TABLE 4

Derivatives of glutaric (pentanedioic) acid

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
	°C.	°C.				
$C_6H_{10}O_4$:						
2-Methyl- (±)	76, 77					(309, 473)
ethyl ester		125/15 mm.				(309)
(+)						(247)
(−)						(247)
3-Methyl- (±)	84-84.5					(101, 592)
dianilide	213.5-214					(101)
di-*p*-toluidide	221-221.5					(101)
(+) (L)					0.58 (22°)	(654)
(−) (D)					−0.58 (22°)	(654)
$C_7H_{12}O_4$:						
2-Ethyl-	59-60					(473)
monoanilide	153-154					(298)
(+)					3.20 (30°)	(472)
3-Ethyl-						(134)
2,2-Dimethyl-	82-84					(242)
imide	146-147					(316)
2,3-Dimethyl-	64-66					(592)
2,4-Dimethyl-						
meso	105-108, 128					(36, 615)
(±)	141					(592)
imide	173-174					(316)
(+)					41.9 (20°)	(247, 478)
(−)					−24.3 (20°)	(247, 478)
3,3-Dimethyl-	97-100					(636)
diethyl ester		90-91/3 mm.				(574)
imide	146-147					(316)
$C_8H_{14}O_4$:						
2-Propyl-	69.5-70.5	165/0.5 mm.	1.4493 (24.5°)			(17, 413, 473, 748)
2-Isopropyl-						
(±)						(248)
anhydride	60-62	148-152/8 mm.				(621)
(+)	93.5-94.2				18.2	(248)
(−)	94-95				−14.6, −18.2	(248, 621)
3-Propyl-	52					(192)
diethyl ester		110-115/2 mm.				(521)
diamide	195					(272)
dianilide	219					(272)
3-Isopropyl-	101					(207)
dimethyl ester		117.5-118/12 mm.				(669)
2-Ethyl-3-methyl-	67, 88, 100-101					(162, 464, 497)
imide	92, 102, 113-114					(162, 464)
2-Methyl-4-ethyl-	67-74, 70-71, 83.5-84.5, 105.5					(2, 65)
3-Methyl-3-ethyl-	86					(680)
mono-*p*-toluidide	111.5-113.5					(557)
anhydride		185/20 mm.				(680)
2,2,3-Trimethyl-	113-114					(597)
imide	137-138					(316)
2,2,4-Trimethyl-	98.5-99.5					(455)
dimethyl ester		112.5-113.5/24 mm.	1.4272 (25°)			(455)
monoanilide	164.5-165.5					(455)
bis(*p*-nitrobenzyl) ester	91-92					(73)
imide	138-140					(316)
2,3,3-Trimethyl-						(570)
2,3,4-Trimethyl-	134, 190					(570)
$C_9H_{16}O_4$:						
2-Butyl-	40, 41	170-180/3 mm.				(17, 473, 467, 613)

TABLE 4—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
	°C.	°C..				
anhydride		170-172/12 mm.				(582)
2-Isobutyl-	68					(608)
dimethyl ester		98-99/2 mm.	1.4338 (20°)			(415)
3-Isobutyl-	47					(188)
3-*sec*-Butyl-	68-70					(532)
anhydride	140-150					(532)
3-Methyl-3-propyl-	92-93					(697)
methyl ester		142/20 mm.				(697)
3-Methyl-3-isopropyl-	100					(392)
anhydride	41-42					(392)
2,2-Diethyl-	84					(121)
anhydride	10-11					(376)
2,4-Diethyl-						
meso	119-120					(70)
(±)	93.5-94.5					(70)
(+)					30.3/20	(70)
(−)					−30.3/20	(70)
3,3-Diethyl-	106					(646, 697)
2-Ethyl-3,3-dimethyl-	112-113					(646)
semianilide	136					(393, 646)
2-Ethyl-3,4-dimethyl-	123					(264)
2,2-Dimethyl-3-ethyl-	47.5					(269)
2,2,3,3-Tetramethyl-	144					(390)
2,2,3,4-Tetramethyl-	121					(48)
2,2,4,4-Tetramethyl-	192					(32)
$C_{10}H_{18}O_4$:						
2-Amyl-	27-28	193-197/3 mm.				(467, 473)
2-Isoamyl-						(473)
3-Amyl-						
anhydride		138/2 mm.				(214)
anilic acid	81					(214)
2-Methyl-4-butyl-						(609)
3-Methyl-3-isobutyl-	63-65					(288)
2,4-Dimethyl-2-propyl-	65-66					(413)
3-Ethyl-3-propyl-	69, 71-72					(288, 697)
3-Ethyl-2,2,4-trimethyl-	135-136					(457)
$C_{11}H_{20}O_4$:						
2-Hexyl-	38-39					(473)
anhydride		195-197/14 mm.				(582)
3-Hexyl-	38					(136)
anhydride		194/12 mm.				(84)
imide	115					(188)
2-Methyl-4-amyl-	76	180-200/4 mm.				(331, 609)
imide	52-54, 71-72					(331, 609)
2-Ethyl-2-butyl-	81-82					(121)
anhydride		153.5/5.5 mm.				(143)
dimethyl ester		122-124/4 mm.	1.4418 (28°)			(143)
2,2-Dimethyl-4-butyl-						(609)
2,4-Dimethyl-2-isobutyl-	124-125					(413, 414)
anhydride	73-74					(414)
dimethyl ester		108-109/4 mm.	1.4405 (20°)			(414)
2,2-Diisopropyl-	168-170					(218)
3,3-Dipropyl-	112-113, 117					(288, 646, 697)
2,3,4-Triethyl-						(387)
$C_{12}H_{22}O_4$:						
2-Heptyl-	47					(582)
anhydride	36					(582)
3-Methyl-3-hexyl-	52-53, 61					(75, 288)
anhydride		196/9 mm.				(75)
dimethyl ester		163-168/9 mm.				(75)
3-Methyl-3-isohexyl-	62-63					(288)
2,2-Dimethyl-4-amyl-	119					(609)
2,4-Dimethyl-2-neopentyl-	98					(206)
2,4-Diethyl-3-propyl-	149-150					(302)
$C_{18}H_{24}O_4$:						
2-Octyl- (±)	50.5					(582)

TABLE 4—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
	°C.	°C.				
anhydride	42.5					(582)
(−)					−9 (20°)	(383)
2,4-Dibutyl- (meso)	95–96					(383)
anhydride		187–189/11 mm.				(383)
(±)	53–56					(383)
2,4-Di-*sec*-butyl-						
(a)	104.5				−4.7 (20°)	(383)
(b)	106–108				9.35 (20°)	(383)
(c)	129				−11.3 (20°)	(383)
$C_{14}H_{28}O_4$:						
3-Methyl-3-octyl-	58					(75)
anhydride		210–212/13 mm.				(75)
imide	91					(75)
diethyl ester		195/18 mm.				(75)
dimethyl ester		128/19 mm.				(197)
$C_{15}H_{28}O_4$:						
2-Decyl-	57.5					(582)
anhydride	51					(582)
3-Methyl-3-nonyl-	46.5–47.5					(288)
$C_{18}H_{30}O_4$:						
3-Methyl-3-decyl-	63–64					(75)
anhydride	31	235–237/18 mm.				(75)
imide	71					(75)
$C_{17}H_{32}O_4$:						
2-Dodecyl-	71.5					(582)
anhydride	58.5					(582)
$C_{19}H_{36}O_4$:						
2-Tetradecyl-	77.5					(582)
anhydride	62.5					(582)
$C_{21}H_{40}O_4$:						
2-Hexadecyl-	78					(582)
anhydride	69					(582)

TABLE 5

Derivatives of adipic (hexanedioic) acid

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
	°C.	°C.				
$C_7H_{12}O_4$:						
2-Methyl-						
(+)	89					(165)
(±)	63, 78					(98, 278, 572)
diethyl ester		127-129/13 mm.				(572)
dimethyl ester		112-114/10 mm.				(98)
diamide	185-186					(98)
3-Methyl-						
(±)	95-97					(14)
(+)	84.6-85.6					(460)
$C_8H_{14}O_4$:						
2-Ethyl-	48, 52.5-53					(572, 719)
diamide	179-179.5					(719)
diethyl ester		131-134/10 mm.				(719)
3-Ethyl-	61-62					(363)
diamide	176-179					(720)
di(*p*-phenyl)phenacyl ester	100-101					(117)
2,2-Dimethyl-	81					(69)
2,3-Dimethyl-						(616)
2,4-Dimethyl-	65-66	210-212/14 mm.				(104, 720)
diethyl ester		131-132/14 mm.				(104)
diamide	153-159					(104)
2,5-Dimethyl- (meso)	143.5-144					(6, 113)
dimethyl ester		112-116/13 mm.	1.4295 (22.5°)			(297)
(±)	71-75, 75-76					(6, 113)
(+)	104.5-105.5				30.75 (27°)	(113)
(2L, 5D-)	103.2-103.8				0.99 (24.5°)	(304)
(2D, 5L-)	103.5-103.8				−0.70 (24°)	(304)
3,3-Dimethyl-	80, 87					(546, 678)
3,4-Dimethyl- (meso)	133-134					(650)
dimethyl ester		72/0.5 mm.				(650)
(±)	115.5-116.5					(650)
(−)	100.0-100.4				−3.2 (25°)	(650)
dimethyl ester		76/0.6 mm.			7.81 (22°)	(650)
$C_9H_{16}O_4$:						
2-Propyl-	56	182-183/1 mm.				(46, 240)
diamide	181-182					(240)
3-Propyl-	50-51	189-190/4 mm.				(268, 720)
diamide	149-151					(720)
2-Isopropyl-	40-42, 66-67	222/12 mm.				(98, 572)
diethyl ester		141-143/10 mm.				(591)
3-Isopropyl- (±)	85, 75, 81.7-82.3	215-218/12 mm.				(85, 111, 526)
(+)	66, 71-73				5.2 (25°)	(111, 126, 245)
diamide	169.5					(111)
diethyl ester		145-150/13 mm.				(111)
(−)	60, 73-73.5				−1.534 (20°)	(111, 126)
2-Ethyl-5-methyl- ethyl ester		136-137/15 mm.	1.4290 (17°)			(183)
3-Ethyl-4-methyl-	58-70	176-178/0.7 mm.				(105)
2,2,3-Trimethyl-	105-107					(598)
2,2,4-Trimethyl-	79-80, 100.1-100.5					(77, 559, 561)
dianilide	169.4-169.8					(77)
2,2,5-Trimethyl-	113-114					(86)
2,4,4-Trimethyl-	68.6-69.2					(77)
dianilide	162.8-163.3					(77)
3,3,4-Trimethyl	126.5-127.5					(60)
$C_{10}H_{18}O_4$:						
2-Butyl-	63	176/0.25 mm.				(240)
diamide	180.9, 182.5-183					(240, 719)

TABLE 5—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
	°C.	°C.				
diethyl ester		157–159/12 mm.				(719)
3-Butyl-	61–63					(720)
monoamide	146–148					(720)
3-*tert*-Butyl-	117, 115–115.5					(526, 545)
2-Isopropyl-5-methyl-	110					(99, 289)
dianilide	230					(289)
diethyl ester		144–146/14 mm.				(99)
2,2-Diethyl-	90–92					(456)
3,3-Diethyl-	133–134					(678)
3,4-Diethyl-						
meso	101–102					(386)
(+)	114–114.5				10.4 (37°)	(386)
2,2,4,5-Tetramethyl-	121					(358)
anhydride	90					(358)
2,2,5,5-Tetramethyl-	191					(213, 454)
3,3,4,4-Tetramethyl-	175–176, 207–208					(213, 642, 698)
diethyl ester		145–150/16 mm.				(213)
$C_{11}H_{20}O_4$:						
2-Amyl-	48–49					(436)
anilide	171–173					(436)
3-Isoamyl-	66					(191)
3-*tert*-Amyl-	77–78					(545)
4-Isoamyl-	66–68					(518)
2-Isobutyl-5-methyl-		230/25 mm.				(183)
$C_{12}H_{22}O_4$:						
2-Hexyl-	65.4	175/0.2 mm.				(241)
diamide	187.5–188					(241)
3-Hexyl-	68–69					(720)
diamide	170–171					(720)
3,4-Dipropyl-	94–95					(385)
2,5-Diethyl-2,5-dimethyl- (−)	130–131				−6.5 (25°)	(651)
dimethyl ester		85–87/0.6 mm.				(651)
3,4-Dimethyl-3,4-diethyl-						(542)
$C_{13}H_{24}O_4$:						
2-Heptyl-	58					(440)
2-Butyl-3,3,4-trimethyl-	93–95					(596)
dimethyl ester		94–95/0.07 mm.				(596)
$C_{14}H_{26}O_4$:						
2-Octyl-	72, 75	191/0.5 mm.				(241, 440)
diamide	186.7					(241)
2-(1,5-Dimethyl)hexyl-						(468)
diethyl ester		155–158/5 mm.				(474)
3-(1,5-Dimethyl)hexyl-						(496)
diethyl ester		159–160/4 mm.				(496)
3-(2,2,4,4-Tetramethyl)butyl-	133–134					(511)
2,5-Di-*tert*-butyl-						
dimethyl ester						(186)
$C_{15}H_{28}O_4$:						
2-Nonyl-	74					(440)
2-Methyl-3-*sec*-isoöctyl-						
diethyl ester		175/6 mm.				(495)
$C_{16}H_{30}O_4$:						
2-Decyl-	83					(687)
3-Decyl-	82–84					(720)
$C_{17}H_{32}O_4$:						
2-Undecyl-	86					(440)
$C_{18}H_{34}O_4$:						
2-Dodecyl-	84					(440)
2,5-Bis(2-methylamyl)-						
methyl ester		140–149/0.3 mm.	1.4635 (19°)	0.9931 (20°)		(709)
$C_{24}H_{46}O_4$:						
2,5-Dinonyl-						
dimethyl ester		200–205/0.5 mm.	1.4609 (12°)	0.8596 (20°)		(709)

TABLE 6

Derivatives of heptanedioic and higher dicarboxylic acids

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
		Heptanedioic acids				
	°C.	°C.				
$C_8H_{14}O_4$:						
2-Methyl-	56–57					(338)
diethyl ester		136.5–137.5/10 mm.				(226)
3-Methyl- (+)		195–205/2 mm.	1.4309 (25°)		7.65	(547)
diethyl ester		152/25 mm.			3.13	(490)
dimethyl ester		135/25 mm.			4.63	(490)
diamide	135–136, 144–145					(490, 491)
$C_9H_{16}O_4$:						
2-Ethyl-	41–42	153–157/0.2 mm.				(713)
dianilide	160–161					(714, 715)
diethyl ester		148–149/20 mm.	1.4682 (20°)			(319, 338)
3-Ethyl-		205/0.4 mm.				(107)
2,5-Dimethyl-						
diethyl ester		152–153/12 mm.				(388)
2,6-Dimethyl-	76.8–78	208/12 mm.	1.4539 (25°)			(354, 528)
3,3-Dimethyl-	100–101, 104					(285, 299, 492)
4,4-Dimethyl-	83, 95–96					(89, 391, 574)
diethyl ester		155/7 mm.	1.4399 (20°)	0.9732 (20°)		(469)
dimethyl ester		130/11 mm.	1.4458 (20°)			(688)
diamide	176					(391)
dianilide	165					(391)
dinitrile	123					(391)
$C_{10}H_{18}O_4$:						
2-Propyl-	62–63	187–188/0.15 mm.				(338, 748)
2-Isopropyl-						
diamide	165–166					(411)
4-Isopropyl-						
diethyl ester		170/27 mm.				(52)
2-Ethyl-5-methyl-						
diethyl ester		142–144/19 mm.				(388)
4-Ethyl-4-methyl-						(584)
2,2,3-Trimethyl-	67–68					(598)
2,2,6-Trimethyl-	125					(169, 358)
3,3,4-Trimethyl-						(599)
3,3,6-Trimethyl-	55–56					(85)
$C_{11}H_{20}O_4$:						
2-Butyl-	49–50					(338)
diethyl ester		168–170/20 mm.				(338)
2-Propyl-5-methyl-						
diethyl ester		163–164/12 mm.				(396)
2-Isopropyl-5-methyl-	66–67, 87–88					(51, 347)
diethyl ester		128–129/4 mm.				(347)
diamide	211.5–213					(347)
2-Methyl-5-isopropyl- (+)		186–188/1.5 mm.			12	(100)
diethyl ester		110/0.5 mm.				(176, 604)
diamide	181–182					(100)
di-*p*-toluidide	156–157					(100)
dimethyl ester		108/0.3 mm.				(604)
2,2,6,6-Tetramethyl-	168–169					(1)
diamide	191–193					(1)
$C_{12}H_{22}O_4$:						
2-Amyl-		232–234/11 mm.				(240)
diamide	164.2					(240)
$C_{13}H_{24}O_4$:						
2-Hexyl-	38					(411)
2-Butyl-2-ethyl-						
dimethyl ester		136–136.5/3 mm.	1.4442 (25°)			(155)

TABLE 6—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
		Heptanedioic acids—*Continued*				
	°C.	°C.				
$C_{14}H_{26}O_4$:						
2-Heptyl-	60, 75	190–193/1 mm.				(239, 240)
diamide	166.4, 186					(239, 240)
3-Methyl-3-isohexyl-						
diethyl ester		147–148/6 mm.				(566)
$C_{15}H_{28}O_4$:						
2,6-Dibutyl-	107–108					(293)
2,6-Diisobutyl-	107–109					(293)
$C_{17}H_{32}O_4$:						
2,6-Diamyl-	109–112.5					(293)
2,6-Diisoamyl-	140					(293)
2,6-Dibutyl-4,4-di-						
methyl-						(293)
$C_{19}H_{36}O_4$:						
2,6-Dihexyl-	112–114					(293)
$C_{23}H_{44}O_4$:						
2,6-Di(2-ethylhexyl)-						(293)
		Octanedioic acids				
$C_9H_{16}O_4$:						
2-Methyl-		143–146/1 mm.				(226)
3-Methyl-	83					(267, 516)
diethyl ester		120–125/5 mm.				(267)
diamide	161–162					(516)
4-Methyl-	81, 146					(560, 601)
$C_{10}H_{18}O_4$:						
2-Ethyl-	68–70					(363)
3-Ethyl-	44.0–45.3					(516)
diamide	142.0–143.5					(516)
4-Ethyl-						(362)
2,6-Dimethyl-		168–174/0.07 mm.	1.4635 (26°)			(401)
bis(*p*-bromophenacyl)						
ester	110–111					(401)
2,7-Dimethyl-	91–92, 132–133					(657)
dimethyl ester		216–219/30 mm.				(657)
diethyl ester		178–183/25 mm.				(657)
diamide	214–215					(193)
3,3-Dimethyl-	97					(663)
3,6-Dimethyl-	96–98					(124, 429)
meso	107.5–108.5					(648)
(±)	78, 82					(280, 648)
(3D,6D)	83.5				13.1 (19.4°)	(280)
(3D,6L)	84.0–84.3				16.68 (21°)	(648)
dimethyl ester		94.6/0.8 mm.			10.67 (22°)	(648)
(3L,6D)	84.2–84.5				16.63 (21°)	(648)
dimethyl ester		94.6/0.8 mm.			−10.68 (22°)	(648, 649)
(3L,6L)	83.5				−13.2 (19.6°)	(280)
4,4-Dimethyl-		140–160/0.001 mm.				(219)
bis(*p*-phenylphenacyl)						
ester	36					(219)
bis(*p*-bromobenzyl-						
thiouronium) salt	155					(219)
$C_{11}H_{20}O_4$:						
3-Isopropyl-						
diamide	154–156					(516)
4-Isopropyl-	69.5–71					(175)
2,2,3-Trimethyl-	69.5–70					(501, 598)
diethyl ester		128–129/1.8 mm.	1.4419 (20°)			(598)
2,5,5-Trimethyl-	45	168–170/0.36 mm.				(643)
dimethyl ester		97/0.45 mm.	1.4419 (23°)			(643)

TABLE 6—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
Octanedioic acids—*Continued*						
	°C.	°C.				
2,6,6-Trimethyl monomethyl ester		150-153/1.2 mm.	1.4508 (20°)			(643)
3,5,5-Trimethyl-						(600)
$C_{12}H_{22}O_4$:						
2,2,7,7-Tetramethyl-	179-181					(1)
diamide	196-197.5					(1)
3,3,6,6-Tetramethyl- dimethyl ester		292/760 mm.	1.4435 (20°)			(76, 291)
3,6-Diethyl-3,6-dimethyl-	100-103					(26)
$C_{16}H_{30}O_4$:						
2,7-Dibutyl-						
meso	71-73					(59)
(±)	109-110					(59)
$C_{18}H_{34}O_4$:						
2,7-Diamyl-	99					(293)
2,7-Diisoamyl-	119-121					(293)
$C_{20}H_{38}O_4$:						
2,7-Dihexyl-	97					(293)
$C_{24}H_{46}O_4$:						
2,7-Di(2-ethylhexyl)-						(293)
Nonanedioic acids						
$C_{10}H_{18}O_4$:						
3-Methyl-	101-102					(30)
4-Methyl- dimethyl ester		158/16 mm.				(661)
5-Methyl-	69-71	180/0.5 mm.				(7)
dimethyl ester		127.5-128.5/3 mm.	1.4370 (25°)			(7)
$C_{11}H_{20}O_4$:						
4-Ethyl- dimethyl ester		125/2 mm.				(660)
3,3-Dimethyl- diethyl ester		143-144/4 mm.				(663)
5,5-Dimethyl-	68-69.5					(89)
diethyl ester		102/0.05 mm.	1.4412 (20°)			(89)
$C_{12}H_{22}O_4$:						
2,5,8-Trimethyl-		180-181/0.5 mm.				(7)
dimethyl ester		116-118/1.5 mm.	1.4372 (25°)			(7)
$C_{13}H_{24}O_4$:						
2,2,8,8-Tetramethyl-	139.5-141					(1)
diamide	156-159					(1)
$C_{17}H_{32}O_4$:						
2,8-Dibutyl-	90-94					(293)
2,8-Diisobutyl-	111-112					(293)
$C_{21}H_{40}O_4$:						
2,8-Dihexyl-	72.5-75.5					(293)
Decanedioic acids						
$C_{11}H_{20}O_4$:						
3-Methyl-	75-76					(267)
$C_{12}H_{22}O_4$:						
3,8-Dimethyl-	74-82					(124)
diethyl ester		127-128/0.5 mm.	1.4360 (25°)			(428)
$C_{18}H_{24}O_4$:						
4,6,6-Trimethyl-						(600)
$C_{14}H_{26}O_4$:						
2,2,9,9-Tetramethyl-	117-118					(1)
diamide	210-213					(1)
2,5,5,9-Tetramethyl-	88-92					(219)
dimethyl ester		113-116/0.5 mm.				(219)

TABLE 6—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
Decanedioic acids—*Continued*						
	°C.	°C.				
p-bromobenzylthiouronium salt	140					(219)
3,4,7,8-Tetramethyl- (+)	75–76				22.0 (25°)	(650)
dimethyl ester		117–117.5/0.2 mm.			18.01 (24°)	(650)
$C_{18}H_{34}O_4$:						
2,9-Dibutyl-						(57, 736)
3,7-Dibutyl-						(59)
3,8-Dibutyl-						
meso	56–57					(59)
(±)	59–60					(59)
dimethyl ester		164–170/1 mm.				(59)
$C_{19}H_{36}O_4$:						
2-Nonyl-						(443)
Undecanedioic acids						
$C_{12}H_{22}O_4$:						
2-Methyl-	80–80.5					(164)
3-Methyl-	40–42	210–215/5 mm.				(164)
dimethyl ester		174–178/15 mm.				(164)
$C_{13}H_{24}O_4$:						
4,8-Dimethyl-		190/0.2 mm.				(354)
6,6-Dimethyl-	71					(43)
$C_{15}H_{28}O_4$:						
2,2,10,10-Tetramethyl-	75–77					(1)
diamide	152–157					(1)
2,5,5,9-Tetramethyl-						
dimethyl ester		120–124/0.18 mm.	1.4460 (23°)			(641, 642)
bis(*p*-bromobenzylisothiouronium) salt	158					(641, 642)
2,6,6,9-Tetramethyl-						
dimethyl ester		147–154/1.5 mm.	1.4462 (20°)			(641, 642)
bis(*p*-bromobenzylisothiouronium) salt	160.5					(219, 641, 642)
$C_{19}H_{36}O_4$:						
2-Octyl-						(443)
Dodecanedioic acids						
$C_{13}H_{24}O_4$:						
2-Methyl-						
dimethyl ester		187–188/13 mm.				(164)
diethyl ester		197/12 mm.				(164)
3-Methyl-		210–211/1 mm.				(164)
dimethyl ester		175–176/8 mm.				(164)
diethyl ester		187–189/8 mm.				(164)
4-Methyl-	71					(601)
diethyl ester		140/0.5 mm.				(601)
6-Methyl-						
dimethyl ester		180–187/10 mm.				(603)
$C_{14}H_{26}O_4$:						
4,9-Dimethyl-	94.5–95.5					(303)
$C_{16}H_{30}O_4$:						
2,2,11,11-Tetramethyl-	86–88					(1)
diamide	170–176					(1)
Tridecanedioic acids						
$C_{14}H_{26}O_4$:						
2-Methyl-	87.5–88.5					(164)

TABLE 6—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
Tridecanedioic acids—*Continued*						
	°C.	°C.				
dimethyl ester		185/9 mm.				(164)
3-Methyl-	68.5-69.5					(164)
dimethyl ester		182-185/9 mm.				(164)
4-Methyl-	47	190-200/0.5 mm.				(601)
$C_{16}H_{28}O_4$:						
2,12-Dimethyl-	67-68	225-226/1-1.5 mm.				(163)
dimethyl ester		167-168/1.5 mm.				(163)
$C_{17}H_{32}O_4$:						
2,2,12,12-Tetramethyl-	57-59					(1)
diamide	156-162					(1)
3,3,11,11-Tetramethyl-	117					(663)
Tetradecanedioic acids						
$C_{16}H_{28}O_4$:						
3-Methyl-	75.2	239-241/4 mm.				(164)
dimethyl ester		194-196/9 mm.				(164)
diethyl ester		205-207/9 mm.				(164)
4-Methyl-	76-77					(601)
5-Methyl-	74-75					(601)
$C_{16}H_{30}O_4$:						
2,13-Dimethyl-	111-111.4					(163)
dimethyl ester		179-180/3.5 mm.				(163)
diethyl ester		190-191/3.5 mm.				(163)
3,12-Dimethyl-	77	210-220/0.02 mm.				(196, 481)
dimethyl ester		162-166/0.18 mm.	1.4571 (20°)			(196)
$C_{18}H_{34}O_4$:						
2,2,13,13-Tetramethyl-	84-86					(1)
diamide	172-178					(1)
3,6,9,12-Tetramethyl- (3L, 6D, 9L, 12D)	34-35				−7.6 (21°)	(649)
dimethyl ester		146-148/0.5 mm.			−7.02 (20°)	(649)
diamide	123.2-123.8					(649)
$C_{22}H_{42}O_4$:						
3,3,6,6,9,9,12,12-Octamethyl-	135					(76)
dimethyl ester		137/0.5 mm.	1.4560 (20°)			(76)
Pentadecanedioic acids						
$C_{16}H_{30}O_4$:						
2-Methyl-	93.5-94.5					(164)
diethyl ester		158-164/0.08 mm.	1.4460 (17.5°)			(664)
dimethyl ester		193-195/5 mm.				(164)
3-Methyl-	76-77	215-220/1 mm.				(164)
dimethyl ester		203-204/8 mm.				(164)
diethyl ester		167-173/0.12 mm.				(665)
4-Methyl-	69-69.6	226-227/3 mm.				(164)
5-Methyl-	54-55	229-230/2.5 mm.				(601)
dimethyl ester		210-215/14 mm.				(164)
$C_{17}H_{32}O_4$:						
3,13-Dimethyl-	63-64	202-205/0.05 mm.				(163, 480)
diethyl ester		170-174/0.1 mm.	1.4655 (20°)			(480)
dimethyl ester		209/0.9 mm.				(163)
Hexadecanedioic acids						
$C_{17}H_{32}O_4$:						
2-Methyl-	89-90	223-225/0.2 mm.				(164)

TABLE 6—*Continued*

Compound	Melting Point	Boiling Point	n_D^t	d_4^t	$[\alpha]_D^t$	References
Hexadecanedioic acids—*Continued*						
	°C.	°C.				
dimethyl ester		210-213/8 mm.				(164)
3-Methyl- (±)	77.2-77.4					(164)
dimethyl ester		198-200/3.5 mm.				(164)
diethyl ester		209-211/3.5 mm.				(164)
(+)	78.6-79.0				4.46 (25°)	(652)
(−)	79.0-79.4				−4.48 (24°)	(652)
4-Methyl-	78-78.4	238-240/1 mm.				(164)
dimethyl ester		203-204/4 mm.				(164)
diethyl ester		223-225/8 mm.				(164)
5-Methyl-	78.8-79					(164)
dimethyl ester		200-202/3 mm.				(164)
diethyl ester		234-236/9 mm.				(164)
8-Methyl-	77-78					(603)
dimethyl ester		187-193/1 mm.				(603)
$C_{18}H_{34}O_4$:						
2,15-Dimethyl-	83-84, 110-110.5					(163)
3,14-Dimethyl-	81-81.5					(163)
dimethyl ester	13	178-183/1.5 mm.				(163)
$C_{20}H_{38}O_4$:						
2,6,11,15-Tetramethyl-						(354)
Heptadecanedioic acids						
$C_{18}H_{36}O_4$:						
2,16-Dimethyl-	65-67, 80-81					(163)
4,14-Dimethyl-	40-43, 48-51, 59-60					(163)
Octadecanedioic acid						
$C_{20}H_{38}O_4$:						
4,15-Dimethyl-	104-105					(163)
dimethyl ester		205-207/1.7 mm.		0.9518 (15°)		(163)
Eicosanedioic acid						
$C_{24}H_{46}O_4$:						
4,8,13,17-Tetramethyl-		220/0.1 mm.				(354)
diamide	127					(354)
Hexacosanedioic acid						
$C_{30}H_{58}O_4$:						
3,12,15,24-Tetramethyl-		235-240/0.21 mm.				(196)
Octacosanedioic acid						
$C_{32}H_{62}O_4$:						
3,13,16,26-Tetramethyl- dimethyl ester		245-255/0.08 mm.	1.4722 (20°)			(196)