tion from methanol afforded 0.55 g. (53%) of white needles, m.p. 46.8–48.0°. The analytical sample was obtained by one further recrystallization from methanol yielding white needles, m.p. 47.3–48.3°.

Anal. Calc'd for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found (G): C, 88.02; H, 11.73.

ANN ARBOR, MICH.

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

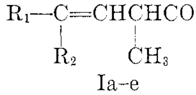
Olefinic Stability and Tautomeric Equilibria. I. Branched-Chain Unsaturated Esters[1]

KENNETH L. RINEHART, JR. AND LLOYD J. DOLBY

Received Aug. 6, 1956

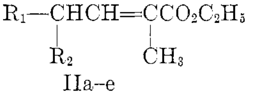
The equilibria between conjugated and unconjugated isomers in two highly branched γ-alkyl unsaturated ester systems have been investigated. The proportion of unconjugated olefin has been shown to decrease with increasing branching in the γ-substituent. These results have been correlated with a number of earlier data and evidence has been presented supporting an interpretation in terms of steric interactions.

It was recently reported that the alkoxide-catalyzed isomerization of ethyl 4-ethyl-2-methyl-3-octenoate (Ib) leads to an equilibrium mixture containing approximately one third of this ester (or its glycol analog) and two thirds of the corresponding conjugated ester, ethyl 4-ethyl-2-methyl-2-octenoate (IIb).[2] The substitution of other *n*-alkyl groups for ethyl or *n*-butyl in the γ-position exerted little effect on the position of equilibrium in this system (Ic–IIc). However, when ethyl was replaced by methyl, the proportion of unconjugated isomer (Ia) in the equilibrated mixture with IIa was reported to be 56%.



$R_1\text{—}\underset{R_2}{C}{=}CH\underset{CH_3}{CH}CO_2C_2H_5$

Ia–e



$R_1\text{—}\underset{R_2}{CH}CH{=}\underset{CH_3}{C}CO_2C_2H_5$

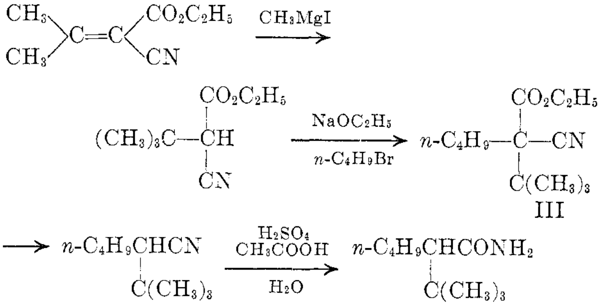
IIa–e

Ia, IIa: $R_1 = n\text{-}C_{10}H_{21}$, $R_2 = CH_3$
Ib, IIb: $R_1 = n\text{-}C_4H_9$, $R_2 = C_2H_5$
Ic, IIc: $R_1 = n\text{-}C_7H_{15}$, $R_2 = n\text{-}C_7H_{15}$
Id, IId: $R_1 = n\text{-}C_4H_9$, $R_2 = iso\text{-}C_3H_7$
Ie, IIe: $R_1 = n\text{-}C_4H_9$, $R_2 = tert\text{-}C_4H_9$

Enhanced hyperconjugative stabilization of the β,γ-double bond by the methyl group and reduced strain of the *cis*-type about the β,γ-double bond were considered as alternative explanations of the higher proportion of unconjugated isomer found in the equilibrated γ-methyl compounds. To examine these alternatives in systems containing more highly branched substituents, the corresponding esters with γ-isopropyl and γ-*tert*-butyl substituents (Id–IId and Ie–IIe, respectively) have been synthesized and the equilibrium mixtures of the two isomers determined after isomerization.[3]

SYNTHESIS

Unsaturated esters required for these studies were prepared by dehydration of the β-hydroxy esters (VIIIa, VIIIb) formed in the Reformatsky reaction of the corresponding α-alkyl aldehydes (VIIa, VIIb) with ethyl α-bromopropionate. The aldehydes were obtained by Rosenmund reduction of the corresponding acid chlorides. Branched acids were prepared *via* modifications of the malonic ester synthesis. Thus, the synthesis of 2-*tert*-butylhexanoic acid (VIb) *via* ethyl isopropylidenecyanoacetate, ethyl *tert*-butylcyanoacetate and the dialkylcyanoacetate (III) is shown in the series of equations below. The corresponding 2-isopropylhexanoic acid (VIa) was prepared by a reaction sequence which is not shown, but which involved successive alkylations of malonic ester with isopropyl bromide and *n*-butyl bromide, followed by alkaline hydrolysis, acidification and decarboxylation.



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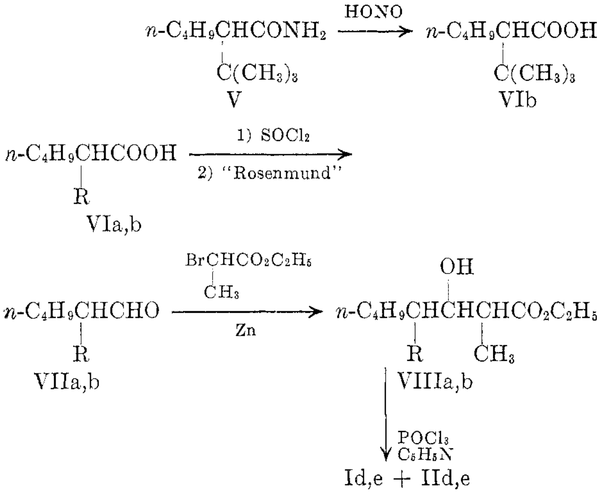
(1) Presented in part at the 130th National Meeting of the AMERICAN CHEMICAL SOCIETY, Atlantic City, Sept. 16–21, 1956.

(2) J. Cason and K. L. Rinehart, Jr., *J. Org. Chem.*, **20**, 1591 (1955).

(3) The α-methyl substituent has been retained both as a point of reference throughout the series and to prevent thermal equilibration of the two isomers during distillation of the isomerized mixtures. Such equilibration is known to occur in the absence of an α-alkyl group [J. Cason, N. L. Allinger, and C. F. Allen, *J. Org. Chem.*, **18**, 857 (1953)]. The α,γ-dialkyl system is further convenient in that no addition of alkoxide to the double bond has been found to occur for these compounds [*cf.* R. P. Linstead and E. G. Noble, *J. Chem. Soc.*, 610 (1934); R. P. Linstead, *J. Chem. Soc.*, 2498 (1929)].



$$\underset{\text{V}}{n\text{-}C_4H_9\underset{C(CH_3)_3}{CH}CONH_2} \xrightarrow{HONO} \underset{\text{VIb}}{n\text{-}C_4H_9\underset{C(CH_3)_3}{CH}COOH}$$

$$\underset{\text{VIa,b}}{n\text{-}C_4H_9\underset{R}{CH}COOH} \xrightarrow[2)\ \text{"Rosenmund"}]{1)\ SOCl_2}$$

$$\underset{\text{VIIa,b}}{n\text{-}C_4H_9\underset{R}{CH}CHO} \xrightarrow[Zn]{Br\underset{CH_3}{CH}CO_2C_2H_5} \underset{\text{VIIIa,b}}{n\text{-}C_4H_9\underset{R}{CH}\overset{OH}{CH}\underset{CH_3}{CH}CO_2C_2H_5} \xrightarrow[C_5H_5N]{POCl_3} \text{Id,e} + \text{IId,e}$$

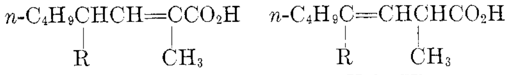
VI–VIIIa: R = *iso*-C_3H_7
VI–VIIIb: R = *tert*-C_4H_9

Alkylation of ethyl *tert*-butylcyanoacetate proceeded smoothly with sodium ethoxide as base (in contrast to the alkylation of isopropylmalonic ester, which required the stronger base potassium *tert*-butoxide). The ease of alkylation of the former compound despite the bulky *tert*-butyl group is explained by the stronger activation of the *alpha* hydrogen by the adjacent nitrile group. Hydrolysis of the α-*tert*-butyl nitrile (IV) gave the amide (V), which resisted further hydrolysis during 48 hours in a refluxing mixture of sulfuric acid, acetic acid, and water. Steric inhibition of amide hydrolysis has been observed previously[4a–d] and is to be expected with the bulky *tert*-butyl group in the position adjacent to the amide.[5] Treatment of the amide with nitrous acid,[4c, 4d, 4e] however, gave the desired acid (VIb) in 80% yield.

Over-all yields from aldehyde (VII) to the mixed unsaturated esters (I, II) were about 65%. Dehydration, effected with phosphorus oxychloride and pyridine, gave approximately equal quantities of conjugated and unconjugated esters (Id and IId) in the isopropyl series, but only 25% of the conjugated ester (IIe) and a preponderant amount of the β,γ-unsaturated isomer (Ie) in the γ-*tert*-butyl series, as estimated from refractive indices of distillation fractions containing the two isomers. From spectral and distillation data given previously it may be estimated that the corresponding dehydration mixtures of unsaturated esters obtained for the γ-methyl, γ-ethyl and γ-heptyl series (Ia and IIa, Ib and IIb, Ic and IIc) contained approximately 56%, 42%, and 53% of the conjugated esters, respectively.[2] There is, then, no observable trend in the proportion of α,β-unsaturated ester obtained in these dehydration mixtures as the γ-alkyl group is varied progressively from methyl (56%) to ethyl (42%) to isopropyl (50%) to *tert*-butyl (25%). While these relative percentages of the two isomers are, unfortunately, not highly accurate and are based on differing physical methods of analysis, they are presumed correct to within 10%. Within this accuracy it may be noted that the only mixture differing significantly in composition from one containing about 50% of each isomer is that obtained with the *tert*-butyl compounds, where the β,γ-unsaturated isomer was obtained in a ratio of 3:1.

Preferential formation of the unconjugated isomer in the dehydration of the γ-*tert*-butyl-β-hydroxy ester contrasts markedly with its lack of stability in the isomerizations described in the next section. It is also surprising in light of the recent work of Brown, Moritani, and Nakagawa, who have shown that both E_1 elimination[6] and E_2 elimination[7] proceed to give an increasing proportion of the isomeric olefin with the double bond further removed from the bulky group as the size of the group is increased. Factors influencing the dehydration, a rate-controlled process, have not been investigated for the present compounds and the mechanism of dehydration is in doubt, although at least a portion of the dehydration has been shown to occur *via* a β-alkyl phosphate.[8]

The isomeric unsaturated esters in each series were first purified by careful fractional distillation. The best samples of conjugated ester obtained from distillation were then further refined by saponification and partial re-esterification, which eliminated small quantities of the more readily esterified unconjugated acid.[2,8a] Similarly, partial esterification of the best distillation samples of unconjugated acids gave highly pure β,γ-unsaturated esters, which could be readily separated from the unesterified α,β-unsaturated acids. By this proce-



$$\underset{\text{IXa, Xa}}{n\text{-}C_4H_9\underset{R}{CH}CH{=}\underset{CH_3}{C}CO_2H} \qquad \underset{\text{IXb, Xb}}{n\text{-}C_4H_9\underset{R}{C}{=}CH\underset{CH_3}{CH}CO_2H}$$

IXa,b: R = *iso*-C_3H_7
Xa,b: R = *tert*-C_4H_9

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(4) (*a*) J. Cason and H. J. Wolfhagen, *J. Org. Chem.*, **14,** 155 (1949); (*b*) J. Cason, C. Gastaldo, D. L. Glusker, J. Allinger, and L. B. Ash, *J. Org. Chem.*, **18,** 1129 (1953); (*c*) N. Sperber, D. Papa, and E. Schwenk, *J. Am. Chem. Soc.*, **70,** 3091 (1948); (*d*) F. C. B. Marshall, *J. Chem. Soc.*, 2754 (1930); (*e*) W. E. Parham, W. N. Moulton and A. Zuckerbraun, *J. Org. Chem.*, **21,** 72 (1956).

(5) It may be noted that the empirical "rule of six" proposed by Newman [M. S. Newman, *J. Am. Chem. Soc.*, **72,** 4783 (1950); M. S. Newman, *Steric Effects in Organic Chemistry*, John Wiley and Sons, New York, 1956, pp. 206, 227] correlates amide hydrolysis and other carbonyl addition reactions with the degree of branching in aliphatic acids and their derivatives.

(6) (*a*) H. C. Brown and I. Moritani, *J. Am. Chem. Soc.*, **77,** 3607 (1955); (*b*) H. C. Brown and M. Nakagawa, *J. Am. Chem. Soc.*, **77,** 3610 (1955); (*c*) H. C. Brown and M. Nakagawa, *J. Am. Chem. Soc.*, **77,** 3614 (1955); (*d*) H. C. Brown and I. Moritani, *J. Am. Chem. Soc.*, **77,** 3623 (1955).

(7) (*a*) H. C. Brown, I. Moritani, and M. Nakagawa, *J. Am. Chem. Soc.*, **78,** 2190 (1956); (*b*) H. C. Brown and I. Moritani, *J. Am. Chem. Soc.*, **78,** 2203 (1956).

(8) K. L. Rinehart, Jr., Ph.D. dissertation, University of California, Berkeley, June, 1954, p. 42.

(8a) J. J. Sudborough and E. R. Thomas, *J. Chem. Soc.*, **99,** 2307 (1911).

TABLE I

PHYSICAL PROPERTIES OF 2,4-DIALKYLOCTENOIC ACIDS AND ESTERS

Compound	B.P., °C./Mm.	n_D^{25}	ε (mμ)
4-Isopropyl-2-methyl-2-octenoic acid	121–122/1.4	1.4639	13,900 (220)[a]
4-Isopropyl-2-methyl-3-octenoic acid	107–108/0.9	1.4507	2120 (220)
Ethyl 4-isopropyl-2-methyl-2-octenoate	95–96/2.5	1.4488	13,200 (218)[a]
Ethyl 4-isopropyl-2-methyl-3-octenoate	85–85.5/2.6	1.4368	1950 (218)
4-*tert*-Butyl-2-methyl-2-octenoic acid	128–130/1.4	M.p. 74–75°	13,800 (220)[a]
4-*tert*-Butyl-2-methyl-3-octenoic acid	110–111/0.9	1.4541	1925 (220)
Ethyl 4-*tert*-butyl-2-methyl-2-octenoate[b]	101–102/2.4	1.4513	12,860 (218)[a]
Ethyl 4-*tert*-butyl-2-methyl-3-octenoate	88–90/2.6	1.4395	2040 (218)

[a] Maximum. [b] Estimated to contain *ca.* 3% of saturated lactone (*cf.* Experimental).

dure, both the isomeric esters (Id and IId, Ie and IIe) and acids (IXa,b and Xa,b) were obtained for each homolog; physical properties are summarized in Table I.

Ultraviolet absorption spectra and refractive indices are seen to be quite different for the isomeric compounds. Refractive indices were employed in estimating the composition of the dehydration mixtures described above, while the ultraviolet absorption spectra of the isomeric acids IXa and IXb, Xa and Xb (*cf.* Fig. 1) were used for the calculation of the composition of isomerization mixtures, described in the next section. The conjugated isomer has a strong maximum near 220 mμ, in agreement with earlier observations for acids of this type.[2] The unconjugated acid has no strong absorption in this region. The spectra obtained for the unconjugated isomers in the present study have somewhat lower absorption than those described earlier, which indicates the higher state of purity achieved by the partial esterification procedure. While Fig. 1 gives the spectra of the isopropyl compounds IXa and IXb only, those of the *tert*-butyl compounds are nearly identical with these. The corresponding conjugated and unconjugated esters show similar spectral properties (*cf.* Table I).

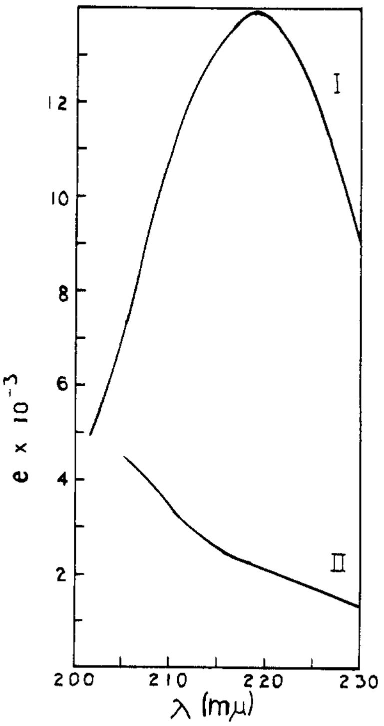

FIG. 1.—ULTRAVIOLET ABSORPTION SPECTRA OF ISOMERIC UNSATURATED ACIDS. I. 4-Isopropyl-2-methyl-2-octenoic acid. II. 4-Isopropyl-2-methyl-3-octenoic acid.

RESULTS OF EQUILIBRATIONS

The unsaturated esters were isomerized, employing sodium glycolate in refluxing ethylene glycol. Previous studies on the γ-ethyl analogs had shown that 27 hr. is a sufficient period to insure complete equilibration in esters of this type[2]; however, a somewhat longer time (36–41 hr.) was employed in the present studies to allow for the more highly branched substituents.

The work-up procedure after isomerization gives a mixture of isomeric unsaturated acids and the spectra of pertinent acids have been given in Fig. 1. From the absorption of the mixed acids isolated, compositions of the equilibrated mixtures have been calculated, as explained in the Experimental section.[9]

Two runs were made with the γ-isopropyl compounds to insure complete equilibration; the equilibrated mixtures were identical from the two runs and were calculated to contain 77% of the α,β-unsaturated isomer. The ultraviolet spectra of the equilibrated mixed γ-isopropyl acids IXa,b are given in Fig. 2, together with a theoretical spectrum calculated for a mixture of 77% conjugated isomer and 23% of the unconjugated compound; the three spectra are very nearly identical. The product from the γ-*tert*-butyl isomers contained 86% of α,β-unsaturated acid. Pertinent data are presented in Table II.

In order to insure that contamination of the

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(9) The present ultraviolet method of analysis is similar to that employed by Bateman and Cunneen[10] and is more convenient and reliable than the iodine or bromine addition procedures employed by earlier investigators of tautomeric unsaturated acids and esters [R. P. Linstead and J. T. W. Mann, *J. Chem. Soc.*, 723 (1931); G. A. R. Kon, R. P. Linstead and J. M. Wright, *J. Chem. Soc.*, 599 (1934)].

(10) L. Bateman and J. I. Cunneen, *J. Chem. Soc.*, 2283 (1951).

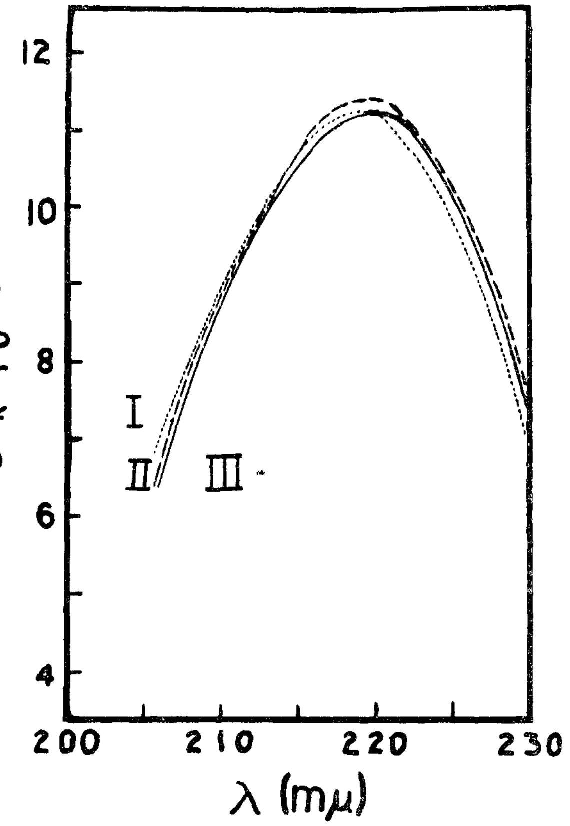


FIG. 2.—ULTRAVIOLET SPECTRA OF MIXTURES OF 4-ISOPROPYL-2-METHYL-2 (AND -3)-OCTENOIC ACIDS. I. Theoretical curve for a mixture containing 77% of the conjugated acid. II. Mixed acids isolated after 36 hours of equilibration by 3.4 N sodium glycolate in refluxing ethylene glycol (Run I). III. Mixed acids isolated after 39 hours of equilibration by 3.4 N sodium glycolate in refluxing ethylene glycol (Run II).

TABLE II

RESULTS OF EQUILIBRATIONS OF UNSATURATED ESTERS

Compound	Reflux Time, Hr.[a]	Per Cent of Conjugated Isomer Before equilibration	After equilibration
4-Isopropyl-2-methyl-octenoates			
Run I	36	27	78
Run II	39	67	77
4-*tert*-Butyl-2-methyl-octenoates	41	16	86

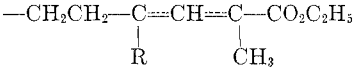
[a] All equilibrations were performed with 3.4*N* sodium glycolate in refluxing ethylene glycol.

isomerization mixtures by nonequilibrating material was absent, the infrared spectra of the equilibrated γ-isopropyl acids (77% conjugated isomer) were examined and shown to be nearly identical with that of pure 4-ethyl-2-methyl-2-octenoic acid (IXa) except for minor differences in those regions where strong bands are shown by the corresponding 3-octenoic acid.

The equilibrium constant, K_{obs}, has been calculated for each of the isomerizations from the relative proportions of conjugated and unconjugated isomers measured by the spectral determinations. These are given in Table III, together with the corresponding constants for the γ-methyl and γ-ethyl compounds studied previously.

TABLE III

EQUILIBRIUM CONSTANTS AND FREE ENERGY DIFFERENCES FOR ISOMERIC UNSATURATED ESTERS



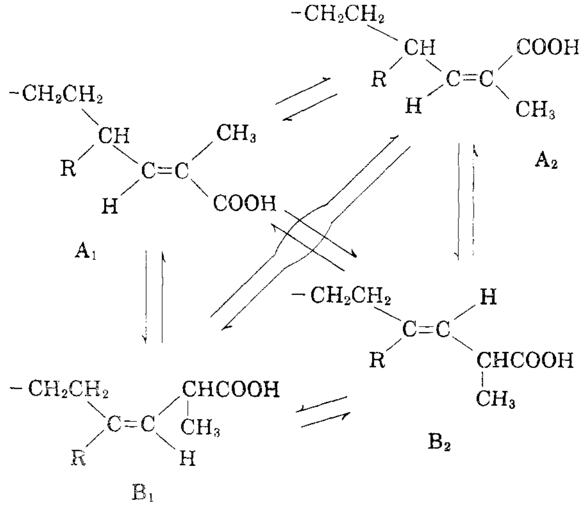
$$—CH_2CH_2—\underset{R}{\underset{|}{C}}\cdots CH\cdots\underset{CH_3}{\underset{|}{C}}—CO_2C_2H_5$$

R	Conjugated Isomer, %	K_{obs}[a]	K_{corr}[b]	−ΔF,[c] Kcal.
CH_3	45	0.82	1.9–2.7	0.60–0.93
C_2H_5	68	2.1	4.2	1.33
iso-C_3H_7	78	3.5	4.9–6.1	1.48–1.68
tert-C_4H_9	86	6.1	6 1	1 68

[a] $K_{obs} = \frac{A_1 + A_2}{B_1 + B_2}$; A_1 and A_2 are *trans* and *cis* α,β-unsaturated isomers, respectively. B_1 and B_2 are *trans* and *cis* β,γ-unsaturated isomers, respectively. [b] $K_{corr} = \frac{A_1}{B_1}$. [c] $\Delta F = -RT \ln K_{corr}$; T = 468°K.

It is apparent that the observed equilibrium constants are in reality a measure and summation of six distinct and separate equilibria, since both α,β- and β,γ-unsaturated forms exist as *trans* and *cis* isomers, A_1 and A_2, B_1 and B_2, respectively, and each can isomerize *via* an enolate ion to any of the others. Thus,

$$K_{obs} = \frac{A_1 + A_2}{B_1 + B_2}.$$



R = CH_3, C_2H_5, *iso*-C_3H_7, *tert*-C_4H_9

In order to compare the effect of the methyl, ethyl, isopropyl, and *tert*-butyl substituents in a single series of compounds it is desirable to isolate a single equilibrium from the six above. For each of the pairs of *trans* isomers A_1 and B_1 there has been calculated a corrected equilibrium constant, $K_{\text{corr}} = A_1/B_1$, and from these constants the free energy differences between the pairs of *trans* isomers.[11] The results of these calculations are also given in Table III.

In calculating K_{corr} from K_{obs} it has been assumed that none of the *cis* conjugated isomer A_2 is present. The pure conjugated acids in the present series have physical constants nearly identical to those of the *trans* isomers described by Cason and Kalm, who studied both *cis*- and *trans*-2-methyl-2-alkenoic acids.[12] In particular, the ultraviolet absorption spectra of the *trans* compounds of these authors showed maxima at 217 mμ, ϵ_{max} 13,600 (in good agreement with the present spectral data in Table I), while the *cis* isomers had λ_{max} 218 mμ, ϵ_{max} 8,800. After isomerization of the present compounds the absorption maxima (11,300 for the γ-isopropyl mixtures, 12,200 for the γ-*tert*-butyl) remained considerably above that of the *cis* compounds (8800) and, as indicated above, the spectra were nearly identical in shape with that calculated for a mixture of *trans* conjugated and mixed unconjugated isomers. Further, as indicated above, the infrared spectrum of the isomerized γ-isopropyl acids agrees well with that of the pure conjugated acid, and it in turn with that of the *trans* isomer of Cason and Kalm, which is different from the spectrum of the *cis* isomer, particularly in the regions 1475–1425 cm.$^{-1}$ and 1300–1265 cm.$^{-1}$ Then

$$K_{\text{obs}} = \frac{A_1}{B_1 + B_2} = \frac{K_{\text{corr}}}{1 + K'}, \text{ where } K' = \frac{B_2}{B_1}$$

The value of K' differs for each of the systems studied and can only be approximately estimated since pure *cis* and *trans* isomers of this type have not been obtained and would be expected to be not only difficultly separable, but very similar in properties. However, two limiting cases are apparent among the present isomerides. For the γ-*tert*-butyl compounds, K' may be taken as zero and $K_{\text{obs}} = K_{\text{corr}}$, since in the *cis*-isomer B_2 the bulky *tert*-butyl group would exhibit very large steric interactions with the propionate group. That this approximation is reasonable is shown by molecular models (Stuart-Briegleb), from which the *cis*-isomer cannot be made. It may also be noted that Brown and Nakagawa obtained an 83:1:*trans*:*cis* ratio of the isomeric 4,4-dimethyl-2-pentenes (*sym*-*tert*-butylmethylethylenes) from the solvolytic elimination of 2-(4,4-dimethylpentyl)-*p*-bromobenzenesulfonate (*cf.* Table IV).[6c]

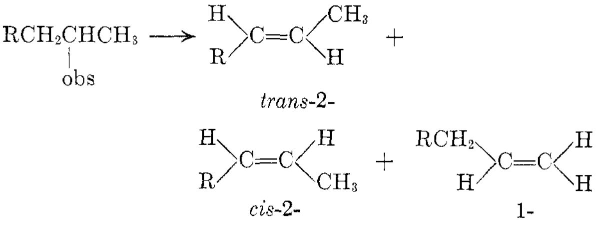
The other limiting case is that of the γ-ethyl compounds, where the two β,γ-unsaturated isomers should be formed in equivalent amounts, as the effect of *n*-alkyl substitution is nearly identical to that of ethyl.[2] Here $K' = 1$ and $K_{\text{corr}} = 2\ K_{\text{obs}}$.

For the γ-methyl and γ-isopropyl esters, estimation of K' is more difficult, although K' is certainly greater than unity for the methyl compounds and less than unity for the isopropyl isomers. Brown and Nakagawa have determined the relative amounts of *cis* and *trans* olefins formed in E_1 eliminations and from these data an estimate may be obtained of the relative effects of varying alkyl groups on olefin stability (Table IV).[6c] It may be seen that $r = trans/cis$ is 1.39 for *sym*-methylethylethylene, 1.08 for *sym*-dimethylethylene and 1.94 for *sym*-isopropylmethylethylene. While these values may not involve equilibrium mixtures the relative effects for the various isomers undoubtedly parallel the equilibria involved. Thus, to compare the relative interaction of isopropyl and ethyl, $r_{\text{ethyl}}/r_{\text{isopropyl}} = 1.39/1.94$ is taken as a first approximation to K', and $K_{\text{corr}} = 1.71\ K_{\text{obs}}$. Since the α-propionate group attached to the double bond (β-carbon) in the present compounds is larger than the methyl group of the compounds investigated by Brown and Nakagawa, the *cis* interaction in the esters under consideration would be considerably larger. To correct for this effect a second approximation may be introduced, $r_{\text{methyl}}/r_{\text{isopropyl}} = 1.08/1.94$, where the bulk of an isopropyl group has been assumed to approximate that of the α-propionate group of the esters investigated. Then, to this second approximation,

$$K_{\text{obs}} = \frac{K_{\text{corr}}}{1 + (1.39/1.94)(1.08/1.94)};\ K_{\text{corr}} = 1.40\ K_{\text{obs}}$$

TABLE IV

COMPOSITION OF OLEFINS FORMED IN SOLVOLYSIS OF ALKYL BROSYLATES[a]



R	Per Cent of Total Olefin *trans*-2, %	*cis*-2, %	1-	r^c	1-/2-
CH_3[b]	46.5	43.5	10.3	1.08	0.11
C_2H_5	48.8	35.5	15.7	1.39	0.19
iso-C_3H_7	53.0	27.3	19.7	1.94	0.25
tert-C_4H_9	74.8	0.9	24 3	83	0.32

[a] Data of Brown and Nakagawa.[6c] Solvolysis in anhydrous acetic acid at 70°. [b] Tosylate. [c] $r = trans\text{-}2/cis\text{-}2$.

Similarly, for the γ-methyl compounds $r_{\text{ethyl}}/r_{\text{methyl}} = 1.39/1.08$ and $K_{\text{corr}} = 2.29\ K_{\text{obs}}$ (first approximation) and $K_{\text{corr}} = 3.32\ K_{\text{obs}}$ (second approximation). Both the first and second (underlined) ap-

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[11] The trans α,β-unsaturated isomer is that with the β-alkyl group *trans* to the carboxyl. In the present discussions we have taken the *trans* β,γ-unsaturated isomer to be that with the varied alkyl group (methyl, ethyl, isopropyl, *tert*-butyl) *trans* to the propionate residue.

[12] J. Cason and M. J. Kalm, *J. Org. Chem.*, **19**, 1947 (1954).

proximations of the equilibrium constants and free energy differences in the two series are given in Table III.

DISCUSSION

From the data presented in Table III it is apparent that the stability of an olefinic system depends upon the nature of the alkyl substituents at the double bond. The relative stabilizing effect of an alkyl group decreases from methyl through *tert*-butyl and may be summarized methyl > ethyl > isopropyl > *tert*-butyl. The over-all effect is rather large and the summation of the various equilibria involved (K_{obs}) shifts from an equilibrium slightly favoring the unconjugated isomer (γ-methyl substituent) to one in which the unconjugated compound is present in only small amount (γ-*tert*-butyl substituent).

In evaluating the equilibrium constant $K_{obs} = (A_1 + A_2)/(B_1 + B_2)$ the amount of A_2, the *cis* conjugated isomer, has, as indicated above, been assumed to be negligible. The value of K_{obs} depends then on the concentrations of the *trans* conjugated isomer A_1 and of the two unconjugated isomers B_1 and B_2, and thus on the relative stabilities of these three species. A major portion of the change in K_{obs} in this series as the γ-alkyl substituent is made progressively more branched is due to a sharp decrease in the amount of B_2. In this *cis* unconjugated isomer (B_2) a bulky group (as *tert*-butyl) on the same side of the double bond as the α-propionate residue gives rise to strong steric repulsions. Interaction of this type between *cis* alkyl groups has long been recognized to lead to olefin destabilization[6c, 13, 26] and was earlier suggested as the predominant reason for the higher proportion of conjugated isomer found at equilibrium in the γ-ethyl substituted system compared to γ-methyl.[2]

On the other hand, the equilibrium constant $K_{corr} = A_1/B_1$ attempts to estimate the variation in the relative stabilities of the various *trans* unconjugated isomers, as distinct from the recognized increasing instability of the *cis* unconjugated isomers. From these calculations, equilibria between the *trans* isomers A_1 and B_1 are seen to favor the conjugated compound (A_1) in every case. Variations in K_{corr} for the various γ-alkyl unsaturated systems are not large; the equilibrium constant varies from 2.7 to 6.1 and there is a free energy difference of less than 0.8 kcal. between the methyl substituted compound and the *tert*-butyl.[14] These differences, though small, are, however, real and may be interpreted in varying ways.[15]

Bateman and Cunneen, who investigated equilibrations in γ-alkyl-phenylpropenes, observed a similar shift in equilibrium from the unconjugated isomer as the size of the γ-alkyl group was increased.[10] Pertinent data from this work, together with corrections based on relative amounts of *cis* and *trans* isomers similar to those described above, are presented in Table V.[16] These and other authors[17-20] have attributed the decreased stability of the olefins substituted with larger alkyl groups to a loss of carbon-hydrogen (C—H) hyperconjugation in progressing from methyl (with three α-hydrogens) to ethyl (two) to isopropyl (one) to *tert*-butyl (no α-hydrogens), and have assigned a value of 0.2–0.3 kcal. to each possible C—H hyperconjugation structure.[21] Changes in free energy with alteration of the alkyl substituent in the present series are seen to be of the same order of magnitude as those observed by Bateman and Cunneen, and C—H hyperconjugation remains a useful tool for the prediction of relative olefin stability.

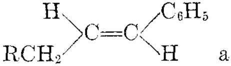
TABLE V

EQUILIBRIUM COMPOSITIONS IN SYSTEMS[a]

$RCH{=}CH{=}CHC_6H_5$

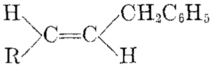
R	% Conjugated Isomer[a]	K_{obs}[b]	K_{corr}[c]	$-\Delta F$,[d] Kcal.
CH_3	82	4.56	4.90	1.38
iso-C_3H_7	89	8.10	8.10	1.82
tert-C_4H_9	91	10.12	9.16	1.93

[a] Data of Bateman and Cunneen.[10] Isomerization in 20% methanolic potassium hydroxide at 165°. [b] $K_{obs} = \frac{A_{trans} + A_{cis}}{B_{trans} + B_{cis}}$. [c] $K_{corr} = A_{trans}/B_{trans}$, where A_{trans} is



$(H)(RCH_2)C{=}C(C_6H_5)(H)$

and B_{trans} is



$(H)(R)C{=}C(CH_2C_6H_5)(H)$

[d] $\Delta F = -RT \ln K_{corr}$; $T = 438°K$.

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[13] A value may be assigned to the *cis*-interaction of two methyl groups, based on heat of hydrogenation data for *cis*- and *trans*-2-butenes, where the difference between the two isomers is 1.0 kcal. [G. B. Kistiakowsky, J. R. Ruhoff, H. A. Smith, and W. E. Vaughan, *J. Am. Chem. Soc.*, **57**, 876 (1935)] (Table VI, D and E).

[14] Although a good bit of approximation has been employed in the estimation of the methyl and isopropyl equilibria, the ethyl and *tert*-butyl figures rest on firmer support. Since K_{corr} and ΔF vary in a direct qualitative fashion throughout the series, discussion may be extended without serious inaccuracy from a comparison of ethyl and *tert*-butyl to the whole series.

[15] It has been assumed that the stability of the conjugated isomer A_1 remains constant throughout the present series. Thus, both conjugation with the carboxyl group and hyperconjugation, the latter treated in detail for the β,γ-unsaturated isomers, do not vary for the α,β-unsaturated isomers. Further, steric interaction, judged from models, does not differ significantly for the variously substituted esters.

[16] The first indication of the lessened stabilizing effect of higher alkyl substituents relative to methyl is to be found in the work of Linstead [A. A. Goldberg and R. P. Linstead, *J. Chem. Soc.*, 2343 (1928)] (Table VII, B, C, and D).

[17] (*a*) C. K. Ingold, *Structure and Mechanism in Organic Chemistry*, Cornell University Press, Ithaca, New York, 1953, p. 564. (*b*) P. B. D. de la Mare, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 22 (1948).

[18] F. Becker, *Fortschr. chem. Forsch.*, **3**, 187 (1955).

[19] J. W. Baker, *Hyperconjugation*, Oxford University Press, London, 1952, p. 64.

[20] E. R. Alexander, *Principles of Ionic Organic Reactions*, John Wiley and Sons, New York, 1950, p. 283.

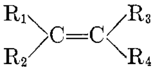
[21] Bateman and Cunneen attributed 0.3 kcal. to each C—H hyperconjugation structure in their phenyl-propenes, but only 0.2 kcal. to each structure in unsaturated esters, nitriles and acids.

There are certain theoretical considerations, however, which lead one to question seriously the validity of C—H hyperconjugation as the true reason for the enhanced stability of methyl over *tert*-butyl substituted olefins. There seems little doubt that alkyl substitution generally enhances the stability of a double bond. Thus, the studies of Kistiakowsky (*cf.* Table VI) have shown that the heat of hydrogenation of *trans*-2-butene, with two alkyl substituents, is 2.7 kcal. more than that of 1-butene, with one substituent (Table VI, E and C, respectively). Further, in progressing from ethene to 1-propene to *trans*-2-butene (Table VI, A, B, and E), the heat of hydrogenation is progressively reduced by about 2.6 kcal. per additional alkyl substituent and additional, somewhat smaller effects are observed with further methyl substitution (Table VI, F and G).

Similarly, the position of equilibrium in isomerized unsaturated acids was early shown to depend on the degree of substitution at each of the centers of unsaturation and while the equilibrium mixture of butenoic acids (no *alpha* or *gamma* substituents—Table VII, A) contained 98% of the conjugated

TABLE VI

HEATS OF HYDROGENATION OF OLEFINS[a]

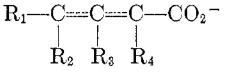


Compound	R_1	R_2	R_3	R_4	Heat of Hydrogenation,[a] Kcal.
A Ethene	H	H	H	H	32.8[b]
B Propene	CH_3	H	H	H	30.1[c]
C 1-Butene	C_2H_5	H	H	H	30.3[c]
D *cis*-2-Butene	CH_3	H	CH_3	H	28.6[c]
E *trans*-2-Butene	CH_3	H	H	CH_3	27.5[c]
F 2-Methyl-2-butene	CH_3	CH_3	CH_3	H	26.9[d]
G 2,3-Dimethyl-2-butene	CH_3	CH_3	CH_3	CH_3	26.6[d]
H 3-Methyl-1-butene	*iso*-C_3H_7	H	H	H	30.3[e]
I 3,3-Dimethyl-1-butene	*tert*-C_4H_9	H	H	H	30.3[e]
J 2-Methyl-1-butene	C_2H_5	CH_3	H	H	28.5[d]
K 2,4,4-Trimethyl-2-pentene	*tert*-C_4H_9	H	CH_3	CH_3	28.4[e]
L 2,4,4-Trimethyl-1-pentene	*neo*-C_5H_{11}	CH_3	H	H	27.2[e]

[a] Data of Kistiakowsky *et al.* Heats of hydrogenation are for gaseous reactants and products at 1 atmosphere and 82°C. [b] G. B. Kistiakowsky, H. Romeyn, Jr., J. R. Ruhoff, H. A. Smith, and W. E. Vaughan, *J. Am. Chem. Soc.*, **57**, 65 (1935). [c] G. B. Kistiakowsky, J. R. Ruhoff, H. A. Smith and W. E. Vaughan, *J. Am. Chem. Soc.*, **57**, 876 (1935). [d] G. B. Kistiakowsky, J. R. Ruhoff, H. A. Smith and W. E. Vaughan, *J. Am. Chem. Soc.*, **58**, 137 (1936). [e] M. A. Dolliver, T. L. Gresham, G. B. Kistiakowsky and W. E. Vaughan, *J. Am. Chem. Soc.*, **59**, 831 (1937).

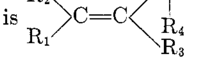
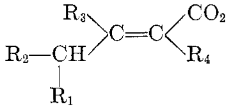
TABLE VII

EQUILIBRIUM COMPOSITIONS IN UNSATURATED SYSTEMS[a]



$$R_1—\underset{R_2}{\underset{|}{C}}\overset{}{=\!=}\underset{R_3}{\underset{|}{C}}\overset{}{=\!=}\underset{R_4}{\underset{|}{C}}—CO_2^-$$

Item	R_1	R_2	R_3	R_4	% α,β[a]	K_{obs}[b]	K_{corr}[c]	$-\Delta F$,[d] Kcal.
A	H	H	H	H	98	49	98.0	3.40
B	CH_3	H	H	H	68	2.12	2.55	0.70
C	C_2H_5	H	H	H	74	2.85	3.30	0.89
D	*iso*-C_3H_7	H	H	H	82[e]	4.56	5.07	1.21
E	CH_3	CH_3	H	H	6[f]	0.064	0.128	1.48
F	CH_3	H	H	CH_3	81[f]	4.26	4.88	1.17
G	CH_3	H	C_2H_5	H	21[g]	0.266	0.532	0.47
H	C_2H_5	H	*n*-C_3H_7	H	34[h]	0.515	1.03	0.02
I	*iso*-C_3H_7	H	*iso*-C_4H_9	H	49[f]	0.96	1.92	0.50

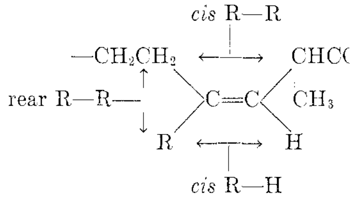
[a] From data of Kon, Linstead *et al.* Isomerizations conducted in aqueous potassium hydroxide (10 equivalents) at 100°C. [*cf.* R. P. Linstead and E. G. Noble, *J. Chem. Soc.*, 614 (1934)]. [b] $K_{obs} = \frac{\text{total, } \alpha,\beta\text{-unsaturated isomers}}{\text{total, } \beta,\gamma\text{-unsaturated isomers}}$. [c] $K_{corr} = \frac{A_1}{B_1}$, where A_1 is  and B_1 is . [d] $\Delta F = -RT \ln K_{corr}$; $T = 373°K$. [e] R. Fittig, *Ann.*, **283,** 47 (1894). Cited in Ref. (16) in text. [f] Ref. (16) in text. [g] G. A. R. Kon, E. Leton, R. P. Linstead and L. G. B. Parsons, *J. Chem. Soc.*, 1411 (1931). [h] Ref. (9) in text.

isomer, the pentenoic acids (one *gamma* substituent) contained 68% and the 4-methylpentenoic acids (two *gamma* substituents) only 6% (Table VII, B and E, respectively). Conversely, *alpha* substitution, as in 2-methylpentenoic acids (Table VII, F) gave a shift to higher percentages of conjugated isomer (81%).

While it may then be agreed that alkyl substitution on a double bond in general increases the stability of the olefin, the degree to which a particular alkyl group stabilizes the olefin varies. Hyperconjugation of the C—H type has been invoked in this regard as indicated above. Recently, however, C—H hyperconjugation as the most important mode of alkyl electron release in substituted benzenes has been criticized by several authors[22–24] and these criticisms are equally valid in application to the present studies. Schubert and Sweeney have pointed out that in many of those properties which depend least on solvent effect the influence of methyl, ethyl, isopropyl, and *tert*-butyl substituents is very similar and is in the opposite direction to that predicted from C—H hyperconjugation. In particular, the *E*-bands in the ultraviolet spectra of *p*-alkyl nitrobenzenes, acetophenones and benzoic acids, and especially of their conjugated acids and of the triphenylmethylcarbonium ions, showed shifts in wave length and extinction coefficient more in keeping with a greater electron release by *tert*-butyl than methyl. Although these authors did not attempt to distinguish between C—C hyperconjugation and other modes of electron release as the predominating alkyl effect, it is clear that C—H hyperconjugation is not the only variable to be considered.[25] In the present compounds solvent effects should be relatively small since the two isomeric olefins are uncharged; hence by the above reasoning C—H hyperconjugation as a dominant effect is not to be expected. Further evidence against C—H hyperconjugation as the predominating influence may be seen in the heats of hydrogenation of methyl, ethyl, isopropyl, and *tert*-butyl ethylenes (Table VI, B, C, H, and I, respectively), which, within experimental error, are identical.

An alternative explanation of the present observations exists in steric interactions. These have, as indicated above, been recognized as important when involving alkyl-alkyl (R—R) interaction *cis* about a double bond. The magnitude of these effects is often large, as may be assessed by comparing the heats of hydrogenation of the isomeric 2-methyl-2 (and -1)-butenes and the 2,4,4-trimethyl-2(and -1)-pentenes (Table VI, F-J and K-J). In the former pair the 2-isomer is more stable by 1.6 kcal., while in the latter pair the 1-isomer is favored by 1.2 kcal., even though the double bond is less highly substituted. From these data, if methyl-methyl interaction involves about 1.0 kcal. of hindrance,[13] then methyl-*tert*-butyl R-R interaction may be estimated at *ca.* 3.8 kcal.[26]

In the present compounds interaction of the *cis* R-R type remains nearly constant in the β,γ-unsaturated isomer, involving interaction of a *n*-alkyl group with the α-propionate residue. There is, however, an increasing amount of steric repulsion between the β-hydrogen and the γ-alkyl substituent (methyl < ethyl < isopropyl < *tert*-butyl) in the series (*cis* R-H interaction). That such interaction is small is shown by the small increment in ΔF between the variously substituted compounds (0.2–0.4 kcal.). However, interference is not negligible and may be observed in molecular models of the unsaturated esters.



Such models suggest that the influence of branched substituents is somewhat more complex than that of simple R—H repulsion mentioned above. In particular, interaction between the two *gamma* substituents becomes serious with the larger substituents (rear R—R interaction).[26a] The methyl-substituted compound is the only one in which there is no compression of the *n*-alkyl group by the second γ-substituent. In all others there is restriction of rotation of the *n*-alkyl when the second alkyl substituent is in such a conformation as to minimize its interaction with the β-hydrogen (rear R—R repulsion) and there is repulsion by the β-hydrogen when the γ-alkyl substituent is in such a conformation as to minimize its interaction with the *n*-alkyl substituent (*cis* R—H interaction). In the γ-*tert*-butyl compound the total effect reaches a maximum and the compound is effectively locked in one con-

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(22) W. M. Schubert and W. A. Sweeney, *J. Org. Chem.*, **21**, 119 (1956).

(23) A. Burawoy and E. Spinner, *J. Chem. Soc.*, 3752 (1954).

(24) V. J. Shiner, Jr., *J. Am. Chem. Soc.*, **76**, 1603 (1954).

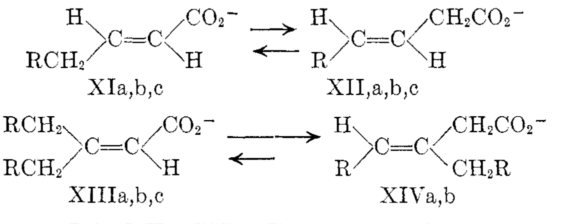
(25) Bateman and Cunneen[10] assigned a value 0.03 kcal. to each C—C hyperconjugation structure and assumed these could be neglected.

(26) Brown has recently assigned a value of 6.0 kcal. to this *cis* methyl-*tert*-butyl strain.[6b]

(26a) Steric compression of a similar nature ("B-strain") has been employed by Brown [for a review, *cf.* H. C. Brown, *J. Chem. Soc.*, 1248 (1956)] to explain the relative basicities of primary, secondary, and tertiary amines and the enhanced solvolytic rates of highly branched tertiary halides. The results in both of these systems were considered to be dut to a relief of strain in going from a tetrahedral to a trigonal state. The present "rear R—R" interaction makes no attempt to evaluate the relative stabilities of the tetrahedral and trigonal states, but is considered as a contributing part of the general steric rigidity about the double bond.

formation, in which there is repulsion of the *tert*-butyl group by both the β-hydrogen and the *n*-butyl group and also an enhanced *n*-butyl-α-propionate (*cis* R—R) interaction. From these considerations it may be been that the steric interactions are quite complex, and involve both primary and secondary effects.

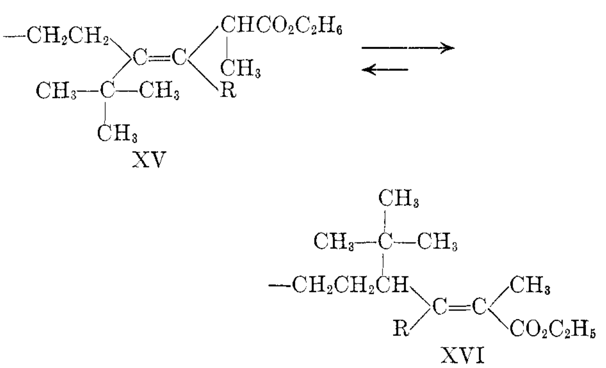
A primary advantage of the steric approach in describing the results of isomerizations of unsaturated systems is that steric interactions are quite useful in explaining a number of anomalies unresolved by the hyperconjugation treatment. Thus, β-alkyl (or phenyl) substitution in an unsaturated ester system has been shown to increase the proportion of unconjugated isomer present at equilibrium (*cf.* Table VII, B *vs.* G, C *vs.* H, D *vs.* I) and this cannot be easily explained by C—H hyperconjugation since the β-substituent can hyperconjugate equally with either an α,β- or a β,γ-double bond.[17,19] A portion of this effect may be ascribed to the presence of a greater number of β,γ-unsaturated isomers present in the mixture, but even after correction for this statistical effect (Table VII) there is a definite shift toward the unconjugated isomer with β-substitution. The equilibria measured by K_{corr} are given below (XI–XII and XIII–XIV), where it may be seen that the introduction of a β-alkyl substituent introduces a *cis* opposition between β-alkyl and carboxylate in the conjugated isomer (XIII) and a *cis* opposition between β-alkyl and γ-alkyl in the unconjugated isomer (XIV).


XIa,b,c XII,a,b,c

XIIIa,b,c XIVa,b

XIa, XIIa, XIIIa, XIVa: R = CH_3
XIb, XIIb, XIIIb, XIVb: R = C_2H_5
XIc, XIIc, XIIIc, XIVc: R = *iso*-C_3H_7

The results of isomerizations of β-substituted systems are readily interpreted if it is assumed that a carboxylate anion exerts a higher degree of repulsion on a *cis*-alkyl group than the repulsion exerted by another alkyl group.[27] If this be the case, then the *relative* effect of carboxylate *vs.* alkyl should decrease in the series methyl > ethyl > isopropyl. That this is indeed so is seen from the data of Table VII. By comparing appropriate systems it is seen that the difference in the free energy between the conjugated and unconjugated isomers without β-substituent and the free energy between the conjugated and unconjugated isomers with β-substituent ($\Delta F_{unsub} - \Delta F_{\beta\text{-sub}}$) is greatest in the case of the γ-methyl systems B and G (Table VII), where this difference is *ca.* 1.2 kcal. In the γ-ethyl systems (Table VII, C and H) the difference amounts to *ca.* 0.9 kcal., while in the γ-isopropyl systems (Table VII, D and I) it is about 0.7 kcal. Thus, in agreement with the above prediction, the order of repulsive effect is $—CO_2^- >$ *iso*-$C_3H_7 > C_2H_5 > CH_3$. On the basis of this explanation it may be predicted that equilibration of a system similar to the present ones with γ-*tert*-butyl group but with a β-alkyl substituent (XV, XVI) would probably lead to a higher proportion of conjugated isomer (XVI) than the present systems without such β-substitution. We hope to report on results in such β-substituted compounds in a future communication.

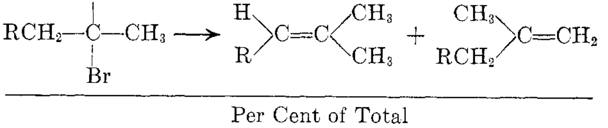

XV

XVI

The present study deals with equilibrium or thermodynamically controlled processes and no attempt has been made to correlate these data with the numerous literature references concerning rate or kinetically controlled processes. It may be noted, however, that the recent work of Brown has shown that an increasing proportion of the less substituted isomer is formed in elimination reactions (both E_1 and E_2) as the size of the alkyl group R to be substituted on the olefin is increased.[6,7] Further, the influence of the branched alkyl in effecting this shift is more pronounced in the second series involving the elimination from a tertiary center (*cf.* Table VIII), than in the series dealing with elimi-

TABLE VIII

COMPOSITION OF OLEFINS FORMED IN SOLVOLYSIS OF ALKYL BROMIDES[a]



R	Per Cent of Total Olefin 2-, %	 1-, %	1-/2-
CH_3	79	21	0.27
C_2H_5	71	29	0.41
iso-C_3H_7	59	41	0.70
tert-C_4H_9	19	81	4.26

[a] Data of Brown and Nakagawa.[6b] Solvolysis in *n*-Butyl Cellosolve at 25°C.

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(27) Judged from bond radii and van der Waal's radii, the size of a carboxylate group is somewhat smaller than an isopropyl group, although the geometry is somewhat different, as the carboxylate is planar rather than tetrahedral. However, the full negative charge of the carboxylate anion might well repel other groups more strongly than the neutral alkyl residues.

nation from a secondary center (Table IV). This has been attributed by Brown to steric repulsion between alkyl R and methyl groups (*cis* R—R) in the former series,[6b] which should be considerably larger than the repulsion between alkyl and hydrogen (*cis* R—H) in the latter series.[6c]

In summary, then, the stability of substituted unsaturated esters is determined largely by the number of alkyl substituents on each isomeric olefin. A more highly branched substituent is generally less effective in stabilizing the double bond, and while this is in agreement with C—H hyperconjugation predictions, steric interactions are believed to offer a somewhat more satisfying explanation of the effect.

EXPERIMENTAL[28]

2-Isopropylhexanoic acid was prepared *via* two malonic ester syntheses. Diethyl isopropylmalonate,[31] obtained in 80% yield by a standard procedure,[32] had b.p. 212–214° (109–112°/21 mm.), n_D^{25} 1.4178 (lit.[32] b.p. 132–135°/44 mm.). The monoalkyl malonic ester was heated for one hour under reflux with potassium *tert*-butoxide[33] before the addition of *n*-butyl bromide. Diethyl *n*-butylisopropylmalonate,[31] which was obtained in 50% yield by this modified procedure, had b.p. 141–142°/28 mm., n_D^{25} 1.4310 (lit.[34] b.p. 136°/14 mm., n_D^{25} 1.4291). The disubstituted malonic ester (154.5 g.) was saponified with refluxing ethanolic potassium hydroxide to give the crude dibasic acid, which was decarboxylated by heating for two hours at 180°. Fractional distillation of the product gave 89.1 g. (74%) of 2-isopropylhexanoic acid, b.p. 121°/12 mm., n_D^{25} 1.4266 (lit.[35] b.p. 125°/10 mm., n_D^{25} 1.4270).

2-Isopropylhexanal was synthesized *via* the Rosenmund reduction of the corresponding acid chloride, prepared according to Bishop.[36] A mixture of 62 g. of 2-isopropylhexanoic acid and 125 g. of thionyl chloride was heated overnight under reflux and excess thionyl chloride was removed under aspirator pressure. Distillation through a short Vigreux column yielded 65 g. (94%) of 2-isopropylhexanoyl chloride, b.p. 75–78°/12 mm., n_D^{25} 1.4336 (lit.[37] b.p. 155–158°).

The procedure of Hershberg and Cason[38] was followed for reduction. In a run employing 65 g. of 2-isopropylhexanoyl chloride, 225 ml. of sodium-dried xylene, 11.2 g. of palladium-barium sulfate catalyst and 0.68 ml. of stock poison reaction had nearly ceased after 9 hrs., when 80% of the theoretical amount of hydrogen chloride had been evolved. The mixture was treated with Norit and filtered and the entire filtrate was fractionally distilled to give 34.6 g. (66%) of 2-isopropylhexanal, b.p. 85–86°/40 mm., n_D^{25} 1.4236. The aldehyde decomposed slowly on standing and gave unsatisfactory elemental analyses.

The *2,4-dinitrophenylhydrazone*[39] had m.p. 140.5–141° after two crystallizations from 95% ethanol.

Anal. Calc'd for $C_{15}H_{22}N_4O_4$: C, 55.88; H, 6.87; N, 17.38. Found: C, 55.82; H, 6.65; N, 17.14.

In a second run the yield of aldehyde was 58%.

Preparation and dehydration of ethyl 4-isopropyl-2-methyl-3-hydroxyoctanoate was effected by a procedure which has previously been described in detail.[2] A solution of 8.3 g. of 2-isopropylhexanal and 28.8 g. of ethyl α-bromopropionate in 83 ml. of sodium-dried benzene was added during one hour to 10.4 g. of zinc foil and 70 ml. of refluxing dry benzene. Refluxing was continued for two additional hours. Work up in the usual manner,[2] followed by fractional distillation, yielded 8.7 g. (61%) of ethyl 4-isopropyl-2-methyl-3-hydroxyoctanoate, b.p. 111°/2.3 mm., n_D^{25} 1.4455.

Anal. Calc'd for $C_{14}H_{28}O_3$: C, 68.41; H, 11.48. Found: C, 68.40; H, 11.23.

In a second run carried out in the same manner as the first, employing 34.6 g. of 2-isopropylhexanal, 120 g. of ethyl α-bromopropionate and 43.1 g. of zinc foil, the crude β-hydroxy ester was not distilled but was combined with the fractionated product from the first run and dehydrated directly to the mixed unsaturated esters, as described in the next paragraph.

The hydroxy ester obtained from the two runs above was dissolved in 312 g. of pyridine and cooled to *ca.* 0°. To the solution was added slowly with vigorous swirling 68 g. of phosphorus oxychloride. The mixture was allowed to stand 18 hours at room temperature, then was heated for $1\frac{1}{2}$ hr. on the steam bath. Work-up in the usual manner, followed by fractional distillation, yielded 44.6 g. (65%, based on total starting aldehyde in the two Reformatsky runs) of mixed unsaturated esters contained in eighteen fractions. These included 5.1 g. of the β,γ-unsaturated ester (96% pure), b.p. 87–90°/2.8 mm., n_D^{25} 1.4372, 33.0 g. of intermediate fractions (containing *ca.* 50% of each isomer), b.p. 90–99°/2.8 mm., and 6.5 g. of the α,β-unsaturated isomer (98% pure), b.p. 97°/2.6 mm., n_D^{25} 1.4489. The composition of the above fractions was estimated from the refractive indices of the pure compounds (*cf.* below); the dehydration mixture thus contained approximately equal quantities of the two isomers.

Ethyl 4-isopropyl-2-methyl-3-octenoate. The best sample of β,γ-unsaturated ester from the fractional distillation in the preceding section (n_D^{25} 1.4372) was saponified with refluxing 2*N* ethanolic potassium hydroxide. The crude acid obtained was dissolved in 22.4 ml. of commercial absolute

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[28] Melting points and boiling points are uncorrected. Unless otherwise noted, distillations were through a 4-ft. Podbielniak-type column.[29] Refractive indices are corrected to 25° using 0.0004/deg.[30] Ultraviolet spectra were determined, in duplicate, with a Beckman quartz spectrophotometer, Model DU; samples were prepared in specially purified heptane in concentrations such that the absorbances were in the range 0.3–0.6. Infrared spectra have been determined for all the compounds described and are on file in the Infrared Laboratory, Department of Chemistry and Chemical Engineering, University of Illinois. We are indebted to Mr. Jozsef Nemeth, Mrs. Maria Benassi and Mrs. Ruby Ju for microanalyses.

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ethanol and 0.95 ml. of concentrated sulfuric acid was added. The solution was allowed to stand for 10 hr. at room temperature and was then diluted with water and extracted with hexane. The hexane extracts were washed with saturated sodium carbonate to remove any unreacted acid. The solution was dried, solvent was removed, and the residue was fractionally distilled to give 3.1 g. of ethyl 4-isopropyl-2-methyl-3-octenoate. A center cut had b.p. 85–85.5°/2.6 mm., n_D^{25} 1.4368. The ultraviolet absorption spectrum has no maximum above 205 mμ and no inflection near 218 mμ (ϵ_{218} 1950).

Anal. Calc'd for $C_{14}H_{26}O_2$: C, 74.28; H, 11.58. Found: C, 73.65; H, 11.66.

4-Isopropyl-2-methyl-3-octenoic acid. A solution of 1.5 g. of pure ethyl 4-isopropyl-2-methyl-3-octenoate (n_D^{25} 1.4368) in 10 ml. of 2*N* ethanolic potassium hydroxide was allowed to stand for 12 hr. at room temperature and was then refluxed for one hour. The usual work-up procedure and fractional distillation yielded 0.8 g. of 4-isopropyl-2-methyl-3-octenoic acid, b.p. 107–108°/0.9 mm., n_D^{25} 1.4507. The ultraviolet absorption spectrum (Fig. 1, Curve II) shows no maximum above 205 mμ and only low absorption near 219 mμ (ϵ_{220} 2120).

Anal. Calc'd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18; eq. wt., 198. Found: C, 72.68; H, 11.53; eq. wt., 195.

4-Isopropyl-2-methyl-2-octenoic acid. A solution of 6.5 g. of the best sample of α,β-unsaturated ester from the fractional distillation above (n_D^{25} 1.4489) was refluxed for 7 hr. in 25 ml. of 2*N* ethanolic potassium hydroxide. The crude acid obtained was allowed to stand for 10 hr. at room temperature in a solution of 48 ml. of absolute ethanol and 2 ml. of concentrated sulfuric acid. The solution was diluted with water and extracted with hexane. The hexane solution was extracted exhaustively with saturated sodium carbonate and the sodium carbonate extracts in turn washed with hexane. Acidification of the sodium carbonate solution then precipitated the conjugated acid, which was worked up in the usual way to give 2.3 g. of 4-isopropyl-2-methyl-2-octenoic acid. A center cut had b.p. 121°/1.4 mm., n_D^{25} 1.4639. The ultraviolet absorption spectrum (Fig. 1, Curve I) has λ_{max} 219 mμ, ϵ_{max} 13,900.

Anal. Calc'd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18; eq. wt., 198. Found: C, 72.77; H, 11.41; eq. wt., 200.

Ethyl 4-isopropyl-2-methyl-2-octenoate was prepared by esterifying 1.5 g. of the acid (n_D^{25} 1.4539) in dilute refluxing ethanolic sulfuric acid. Fractional distillation yielded 1.4 g. of the conjugated ester, b.p. 95–96°/2.5 mm., n_D^{25} 1.4488. The ultraviolet absorption spectrum has λ_{max} 217 mμ (ϵ_{max} 13,200).

Anal. Calc'd for $C_{14}H_{26}O_2$: C, 74.28; H, 11.58. Found: C, 73.98; H, 11.68.

Ethyl tert-butylcyanoacetate[31] was prepared by the method of Alexander, McCollum, and Paul.[40] The intermediate ethyl isopropylidenecyanoacetate,[31] prepared according to Cope and Hancock,[41] was obtained in 37% yield, b.p. 117–119°/18 mm., m.p. 28° (lit.[42] m.p. 28°). A solution of 126.2 g. of ethyl isopropylidenecyanoacetate in ether was added to the Grignard reagent from 140 g. of methyl iodide and 24.3 g. of magnesium turnings. The mixture was stirred overnight at room temperature and then refluxed for one hour. The usual work-up procedure gave on fractional distillation 67.4 g. (49%) of ethyl *tert*-butylcyanoacetate, b.p. 87–89°/20 mm., n_D^{25} 1.4246 (lit.[40] b.p. 88°/5 mm., n_D^{25} 1.4258).

Ethyl n-butyl-tert-butylcyanoacetate[31] was prepared by the usual malonic ester alkylation procedure[43] from 99.5 g. of ethyl *tert*-butylcyanoacetate, 14 g. of sodium and 98.5 g. of *n*-butyl bromide. The sodium ethoxide–malonic ester solution was refluxed for one hour before the addition of the butyl bromide and for 9 hr. after the addition. Dilution with water and the usual work-up procedure and fractional distillation yielded 75 g. (56%) of ethyl *n*-butyl-*tert*-butylcyanoacetate, b.p. 121–123°/15 mm., n_D^{25} 1.4401.

Anal. Calc'd for $C_{13}H_{23}NO_2$: C, 69.28; H, 10.28; N, 6.22. Found: C, 69.20; H, 10.15; N, 6.65.

2-tert-Butylhexanenitrile. A solution of 117.2 g. of ethyl *n*-butyl-*tert*-butylcyanoacetate and 135 ml. of 5*N* ethanolic potassium hydroxide was refluxed for 2 hr. The reaction mixture was diluted with water and acidified to give an oily layer. The two phases were separated; when the organic layer was washed with water it solidified to white crystalline *n*-butyl-*tert*-butylcyanoacetic acid. The acid had m.p. 113–114° after recrystallization from hexane.

Anal. Calc'd for $C_{11}H_{19}NO_2$: C, 66.97; H, 9.71; N, 7.10. Found: C, 67.04; H, 9.82; N, 7.29.

The aqueous phase was extracted with ether and the ether extracts were combined with the solid acid, then washed with water, and dried over sodium sulfate. Ether was removed by flash distillation and the cyano acid was decarboxylated by heating for two hours at 195°. The resulting 2-*tert*-butylhexanenitrile was distilled rapidly at atmospheric pressure, b.p. 202°, then fractionally re-distilled to yield 73.0 g. (92%) of nitrile, b.p. 99–100°/31 mm., n_D^{25} 1.4241.

Anal. Calc'd for $C_{10}H_{19}N$: C, 78.36; H, 12.50; N, 9.14. Found: C, 78.65; H, 12.48; N, 9.33.

2-tert-Butylhexanoic acid was prepared by the method of Parham.[4e] A solution composed of 30 g. of 2-*tert*-butylhexanenitrile, 30 g. of concentrated sulfuric acid, 120 g. of glacial acetic acid, and 60 g. of water was heated for 48 hr. under reflux. The cooled reaction mixture was poured over ice to give a white solid, which was extracted from the aqueous layer with ether. The ether extracts were extracted with saturated sodium carbonate; however, acidification of the carbonate extracts yielded no organic acid. Ether was removed by distillation to give 31.1 g. (93%) of 2-*tert*-butylhexanamide. A small sample was crystallized twice from acetone as long transparent needles, m.p. 102–103°.

Anal. Calc'd for $C_{10}H_{21}NO$: C, 70.12; H, 12.36; N, 8.17. Found: C, 69.97; H, 12.26; N, 8.37.

The amide obtained above (31.1 g.) was mixed with 165 ml. of concentrated sulfuric acid and 150 ml. of glacial acetic acid. The resulting mixture was cooled to 0° and a solution of 12.3 g. of sodium nitrite in the minimum amount of water was added with mechanical stirring. The reaction was allowed to warm to room temperature, and was then heated to 60°; evolution of nitrogen began at 36°. After gas evolution had ceased, the mixture was cooled to 0° and the diazotization procedure was repeated. The reaction mixture was then decanted slowly into 300 ml. of ice water. The oily layer which formed was extracted into hexane. Removal of solvent and fractional distillation yielded 25.4 g. (81%) of 2-*tert*-butylhexanoic acid, b.p. 120–124°/7 mm., n_D^{25} 1.4304.

Anal. Calc'd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.72. Found: C, 69.36; H, 11.93.

In a second run a solution of 35.2 g. of nitrile, 35 g. of concentrated sulfuric acid, 75 g. of acetic acid, and 35 g. of water was refluxed for three days. The intermediate amide was not isolated but was diazotized directly. To the crude reaction mixture was added 97 ml. of concentrated sulfuric acid. The resulting mixture was cooled to 0° and diazotized twice with 15.8 g. quantities of sodium nitrite solution, as above. Work-up as before and fractional distillation yielded 31 g. (78%) of 2-*tert*-butylhexanoic acid.

2-tert-Butylhexanal was prepared by Rosenmund reduc-

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(40) E. R. Alexander, J. D. McCollum, and D. E. Paul, *J. Am. Chem. Soc.*, **72**, 4791 (1950).

(41) A. C. Cope and E. M. Hancock, *Org. Syntheses*, **Coll. Vol. 3**, 399 (1955). For an alternative procedure, *cf.* F. S. Prout, R. J. Hartman, E. P.-Y. Huang, C. J. Korpics, and G. R. Tichelaar, *Org. Syntheses*, **35**, 7 (1955); F. S. Prout, *J. Org. Chem.*, **18**, 928 (1953).

(42) G. Komppa, *Ber.*, **33**, 3530 (1900).

(43) C. S. Marvel, *Org. Syntheses*, **Coll. Vol. 3**, 495 (1955).

tion of the acid chloride, as described for 2-isopropylhexanal above. The intermediate 2-*tert*-butylhexanoyl chloride, from 56.4 g. of 2-*tert*-butylhexanoic acid and 117 g. of thionyl chloride, was obtained in 94% yield (59 g.) after distillation through a short Vigreux column, b.p. 95°/20 mm., n_{D}^{25} 1.4393. The acid chloride (59 g.) was converted to the aldehyde, employing 10.25 g. of palladium-barium sulfate and 0.62 ml. of sulfur-quinoline poison in 210 ml. of sodium-dried xylene. The reaction appeared complete after $8^{1}/_{2}$ hr., when 79% of the theoretical amount of hydrogen chloride had been evolved. Work-up and fractional distillation of the entire solution yielded 28.6 g. (59%) of 2-*tert*-butylhexanal. A center cut had b.p. 85–86°/23 mm., n_{D}^{25} 1.4280.

The *2,4-dinitrophenylhydrazone* had m.p. 163–164° after two crystallizations from 95% ethanol.

Anal. Calc'd for $C_{16}H_{24}N_4O_4$: C, 57.12; H, 7.19; N, 16.66. Found: C, 57.38; H, 6.89; N, 16.71.

An unsuccessful attempt was made to prepare 2-*tert*-butylhexanal *via* lithium aluminum hydride reduction of 2-*tert*-butylhexanenitrile. A solution of 0.684 g. of lithium aluminum hydride in 100 ml. of ether was added at dry ice-temperature to 11.3 g. of the nitrile in 100 ml. of ether. After the mixture had been stirred for one hour at this temperature it was allowed to warm to room temperature. Hydrolysis at 0° and distillation of the product gave only recovered starting nitrile.

Preparation and dehydration of ethyl 4-tert-butyl-2-methyl-3-hydroxyoctanoate. This β-hydroxy ester was prepared by the Reformatsky reaction as described above for the preparation of ethyl 4-isopropyl-2-methyl-3-hydroxyoctanoate. The present sequence employed 28.0 g. of 2-*tert*-butylhexanal, 100 g. of ethyl α-bromopropionate and 35.8 g. of zinc foil. A small portion of the hydroxy ester was distilled through a 3-ft. modified Vigreux column,[44] b.p. 114°/2 mm., n_{D}^{25} 1.4482.

Anal. Calc'd for $C_{15}H_{30}O_3$: C, 69.72; H, 11.70. Found: C, 69.86; H, 11.57.

This material was combined with the undistilled crude hydroxy ester and dehydrated as described for the γ-isopropyl hydroxy ester. In this case 285 g. of pyridine and 62 g. of phosphorus oxychloride were employed. After the usual work-up procedure, the product was fractionally distilled to yield 26.5 g. (62%) of mixed unsaturated esters, obtained in 16 small fractions. The composition of each fraction was estimated from the refractive indices for the pure conjugated and unconjugated esters given below. Thus, there were obtained 16.6 g. of β,γ-unsaturated ester (96% pure) b.p. 89–92°/2.4 mm., n_{D}^{25} 1.4399, 4.5 g. of intermediate fractions (containing 28% of α,β-unsaturated ester), b.p. 89–94°/2.2 mm. and 5.4 g. of α,β-unsaturated ester (88% pure) b.p. 94–95°/2.2 mm., n_{D}^{25} 1.4502. From the composition of these fractions it was estimated that the dehydration gave a mixture containing only 25% of the conjugated isomer.

Ethyl 4-tert-butyl-2-methyl-3-octenoate was obtained in pure form by the partial esterification method described above for ethyl 4-isopropyl-2-methyl-3-octenoate. From 16.6 g. of β,γ-unsaturated ester (n_{D}^{25} 1.4399) there was obtained after saponification and partial esterification 12.9 g. of pure ethyl 4-*tert*-butyl-2-methyl-3-octenoate; the best sample had b.p. 88–90°/2.6 mm., n_{D}^{25} 1.4395. The ultraviolet absorption spectrum showed no maximum above 205 mμ and only low absorption at 218 mμ (ϵ_{218} 2040).

Anal. Calc'd for $C_{15}H_{28}O_2$: C, 74.92; H, 11.77. Found: C, 74.80; H, 11.66.

4-tert-Butyl-2-methyl-3-octenoic acid was prepared by saponification in ethanolic potassium hydroxide of 3.0 g. of ethyl 4-*tert*-butyl-2-methyl-3-octenoate (n_{D}^{25} 1.4395). The pure acid (1.2 g.) had b.p. 109–111°/0.9 mm., n_{D}^{25} 1.4541. The ultraviolet spectrum shows no inflection point above 205 mμ and only low absorption near 220 mμ (ϵ_{220} 2120).

Anal. Calc'd for $C_{13}H_{24}O_2$: C, 73.53; H, 11.39; eq. wt., 212. Found: C, 73.98; H, 11.35; eq. wt., 211.

4-tert-Butyl-2-methyl-2-octenoic acid was initially purified by partially esterifying the acid obtained on saponification of the high-boiling distillation fraction above (n_{D}^{25} 1.4502), as previously described for the isopropyl conjugated acid. The unsaturated acid obtained in this manner had b.p. 130°/1.5 mm., m.p. 68–70° and the ultraviolet absorption spectrum ($\lambda_{\max}$ 220 mμ, $\epsilon_{\max}$ 11,800) showed it to be relatively impure.

The unconjugated isomer was accordingly removed by a procedure involving lactonization, as has been previously described.[2] A mixture of 7.5 g. of 4-*tert*-butyl-2-methyl-2-(and 3-) octenoic acids (consisting of 86% of the Δ^2 isomer), 35 ml. of ethylene glycol and 2.5 ml. of concentrated sulfuric acid was refluxed for 40 hr. The reaction mixture was poured into water and the mixture of conjugated glycol ester and lactone was isolated in the usual manner. Saponification of this mixture and fractional distillation yielded 1.5 g. of pure 4-*tert*-butyl-2-methyl-2-octenoic acid, b.p. 129–130°/1.3 mm., m.p. 74–75°. The ultraviolet spectrum of this sample had $\lambda_{\max}$ 220 mμ, $\epsilon_{\max}$ 13,800.

Anal. Calc'd for $C_{13}H_{24}O_2$: C, 73.53; H, 11.39; eq. wt., 212. Found: C, 73.50; H, 11.63; eq. wt., 216.

Ethyl 4-tert-butyl-2-methyl-2-octenoate was obtained in somewhat impure form by esterification of the acid (m.p. 68–70°) obtained from the partial esterification technique above. From 1.0 g. of acid there was obtained 0.8 g. of ethyl 4-*tert*-butyl-2-methyl-2-octenoate, b.p. 101–102°/2.4 mm., n_{D}^{25} 1.4513. Although there were no bands in the infrared spectrum indicating presence of β,γ-unsaturated ester, a small shoulder at 1775 cm.$^{-1}$ is indicative of the presence of saturated γ-lactone.[2] The ultraviolet absorption spectrum ($\lambda_{\max}$ 218 mμ, $\epsilon_{\max}$ 12,860) shows the sample to contain *ca.* 3% of unconjugated material.

Anal. Calc'd for $C_{15}H_{28}O_2$: C, 74.92; H, 11.77. Found: C, 74.73; H, 11.51.

Determination of the composition of mixtures of α,β- and β,γ-unsaturated acids and esters. A. Ultraviolet absorption spectra. In the isomerization experiments described below, mixtures of conjugated and unconjugated unsaturated acids were obtained. Ultraviolet spectra of these mixtures were determined and compared algebraically and graphically with the spectra of the pure isomeric acids given above. In the algebraic method the extinction coefficient of the mixture was determined at the wave length for which the two pure isomers show the maximum differential between their extinction coefficients. For both the isopropyl and *tert*-butyl acids this wave length is 220 mμ. The compositions of mixtures were then calculated from the following formula.[2]

For 4-isopropyl-2-methyl-2(and -3)-octenoic acids:

$$139X + 21.2(1 - X) = \epsilon'_{220}$$

For 4-*tert*-butyl-2(and -3)-octenoic acids:

$$138X + 19.2(1 - X) = \epsilon'_{220}$$

In each case X is the fraction of conjugated isomer, while $\epsilon'_{220} = \epsilon_{220} \times 10^{-2}$ for the mixture of acids.

For each mixture analyzed in this manner, a theoretical curve was prepared, based on the percentage calculated from the above formulas of the two isomers present in the mixture and the observed spectra of the pure isomers in the range of high absorption (205–230 mμ). In each case the theoretical curves so prepared were in excellent agreement with those obtained for the equilibration mixtures (*cf.* Fig. 2). Thus, the shapes of the curves[2] confirm the compositions calculated algebraically.

B. Refractive indices. For mixtures of unsaturated isomeric esters, obtained from fractional distillation of the dehydration products above, the composition was estimated algebraically from the refractive indices of the mixture and of

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(44) Ref. (29), p. 245.

the two pure isomeric esters. A linear dependence of refractive index on composition was assumed. While this method is subject to distortion by small amounts of impurities and is not so accurate as that employing the ultraviolet spectra, it has the advantages of speed and simplicity and was also employed in roughly estimating the composition of the mixtures of unsaturated acids obtained from equilibrations.

Equilibrations of mixed esters were performed according to a previously described procedure.[2]

A. Ethyl 4-isopropyl-3-methyl-2(and -3)-octenoates. Run I. A solution of 3.4*N* sodium glycolate was prepared in a metal flask by dissolving 5.8 g. of sodium in 75 ml. of anhydrous ethylene glycol. This had been previously dried by distilling 150 ml. of glycol from over sodium into the metal flask and then redistilling half of this quantity to remove last traces of water. To the sodium glycolate solution was added 10 g. of a mixture of ethyl 4-isopropyl-2-methyl-2(and -3)-octenoates (n_D^{25} 1.4410) containing *ca.* 27% of the conjugated isomer. The resulting mixture was refluxed for 36 hours, cooled, and diluted with water, then refluxed an additional hour to saponify the glycol esters. The reaction mixture was poured into water, acidified, and worked up in the usual manner. The mixed acids, which were distilled rapidly, weighed 8.1 g. and had b.p. 115–124°/1 mm., n_D^{25} 1.4602. A small sample taken just prior to distillation had n_D^{25} 1.4605, showing that no separation of isomers had occurred during distillation. From the refractive index of the distilled mixture it was estimated to contain 72% of the conjugated isomer. The ultraviolet absorption spectrum (Fig. 2, Curve II) has ϵ_{220} 11,270, from which the mixture may be calculated to contain 78% of the α,β-unsaturated isomer.

Run 2. The second run was performed in the same manner as the first. A mixture of 10 g. of mixed γ-isopropyl unsaturated esters (n_D^{25} 1.4488), containing 67% of conjugated isomer, and 75 ml. of 3.4*N* sodium glycolate solution was heated for 39 hr. under reflux, then diluted with water and worked up as before. The mixed unsaturated acids obtained weighed 8.1 g. and had b.p. 114–130°/1 mm., n_D^{25} 1.4602. From the refractive index the mixture was estimated to contain 72% of the conjugated isomer. The ultraviolet absorption spectrum (Fig. 2, Curve III) has ϵ_{220} 11,170, from which it may be calculated that the mixture contains 77% of the α,β-unsaturated isomer.

B. Ethyl 4-tert-butyl-2-methyl-2(and -3)-octenoates. The same procedure was employed as that described above for the γ-isopropyl esters. A mixture of 10 g. of mixed γ-*tert*-butyl esters (n_D^{25} 1.4413), containing *ca.* 16% of the conjugated isomer, and 75 ml. of 3.4*N* sodium glycolate solution was heated for 41 hr. under reflux and worked up as above. The isomerized product was distilled to give 7.9 g. of a solid mixture of acids, b.p. 115–135°/0.9 mm. The ultraviolet spectrum had ϵ_{220} 12,200, from which the mixture may be calculated to contain 86% of the conjugated isomer. The shape of the absorption spectrum between 205 and 230 mμ also agrees well with that calculated for a hypothetical mixture containing 86% of the conjugated acid.

URBANA, ILL.

[CONTRIBUTION FROM KOPPERS CO., INC., MONOMER FELLOWSHIP AT MELLON INSTITUTE]

Isomerization Accompanying the Acetylation of *p-t*-Butyltoluene

W. J. HEINTZELMAN AND B. B. CORSON

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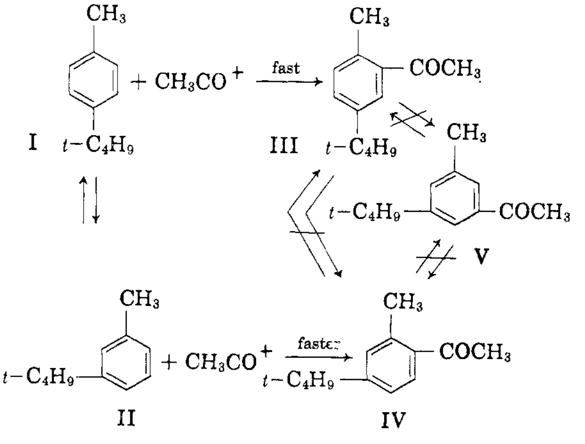
By suitable choice of the order of addition of the reactants, the acetylation of *p-t*-butyltoluene can be directed to give either 2-methyl-4-*t*-butylacetophenone or 2-methyl-5-*t*-butylacetophenone.

There is considerable confusion in the literature concerning the orientation of the ketones resulting from the aluminum chloride catalyzed acetylation of certain *p*-dialkylbenzenes in which one or both of the alkyl groups are secondary or tertiary. It has been variously reported that the product is a 2,4-dialkylacetophenone,[1–5] a 2,5-dialkylacetophenone,[5,6] and a mixture of 2,4- and 2,5-dialkylacetophenones.[7] These conclusions were based on nonquantitative data—the isolation of ketone derivatives, often in small yield.

We have investigated the acetylation of *p-t*-butyltoluene under a variety of conditions and determined the composition of the acetylated products by means of infrared spectrometry. Our results support a mechanism in which the rate-determining step is the ionization of acetyl chloride and the rate of acetylation of *p-t*-butyltoluene is slower than the rate of acetylation of *m-t*-butyltoluene.

It was further shown that 2-methyl-4-*t*-butylacetophenone (IV) and 2-methyl-5-*t*-butylacetophe-

$$CH_3COCl + AlCl_3 \overset{slow}{\rightleftarrows} CH_3CO^+ + AlCl_4^-$$



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