1,3-DIOXANE-4,6-DIONES IN ORGANIC SYNTHESIS (REVIEW)

M. F. Strozhev, I. É. Lielbriedis, and O. Ya. Neiland

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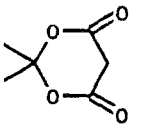
Material dealing with methods for obtaining 1,3-dioxane-4,6-diones and their derivatives, methods for cleaving the 1,3-dioxane ring, and, within the framework of a synthone approach, trends in their utilization in organic synthesis is correlated.

Steady interest in the chemistry and synthetic possibilities of cyclic malonates — 1,3-dioxane-4,6-diones — has been observed in the last decades. This has been promoted by both the successful use of dioxanediones in organic synthesis and by individual reports of the functional ability of 1,3-dioxane-4,6-diones to introduce specific fragments into the molecules of organic compounds; this makes it possible to regard them as synthetic equivalents of a number of synthones. However, previous reviews [1-3] devoted to the chemistry and individual derivatives of 1,3-dioxane-4,6-diones, as well as to certain trends in their utilization in organic synthesis, are incomplete, unsystematized, and do not take into account the examination of 1,3-dioxane-4,6-diones as synthetic agents. This is why we have written this review.

The limited size of this review makes it impossible to examine in detail all 1,3-dioxane-4,6-dione derivatives and their properties and interconversions, and these data are therefore presented in a maximally condensed and schematized form. The examination of the synthetic possibilities of 1,3-dioxane-4,6-diones is primarily emphasized.

1,3-Dioxane-4,6-diones are cyclic malonates — malonic acid acylals. Their first representative, viz., 2,2-dimethyl-1,3-dioxane-4,6-dione (1, Meldrum's acid, isopropylidene malonate), which was obtained in 1908 [4], was for a long time considered to be oxetane derivative **2** [5-11], and its true structure was not established until 1948 [12].



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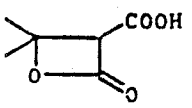

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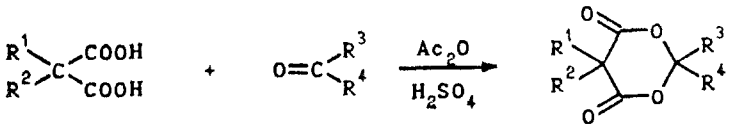
1. Methods for the Synthesis of 1,3-Dioxane-4,6-diones

1.1. Formation of the 1,3-Dioxane Ring

Ring formation is a general method for obtaining 1,3-dioxane-4,6-diones **3**:



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The carbonyl compounds can be aliphatic [4, 13-17] or aromatic [15] ketones and aromatic aldehydes [11, 15, 16]. The reaction is ineffective for all alkanals [5]. Compound **1** is formed in 48-60% yields by the methods of Meldrum [4] or Ott [5], as well as by slight modifications of these methods [8, 11, 12, 17]. A study of the reaction mechanism [18] made it possible to propose the optimum method for obtaining Meldrum's acid **1** (in 92% yield): acetic anhydride is added dropwise with cooling to a mixture of malonic acid, acetone, and sulfuric acid. There are also other methods for obtaining **1**: condensation of malonic acid with isopropenyl acetate in the presence of H_2SO_4 (50% yield) [12]; condensation of carbon suboxide C_3O_2 with oxalic acid and acetone in the presence of H_2O_4 [19].

The condensation of alkyl- [14, 20-22], dialkyl- [14, 23, 24], aryl- and hetaryl- [13, 14, 25, 26], alkylaryl- [13], and arylidenemalonic [27] acids with acetone or isopropenyl acetate has been used for the synthesis of 5-substituted derivatives of **1**.

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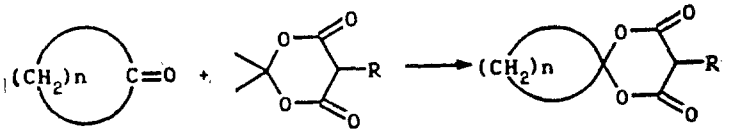
1.2. Substitution of the Carbon Atom in the 2 Position of 1,3-Dioxane-4,6-diones

The thermolysis of **1** and 5-alkyl-2,2-dimethyl-1,3-dioxane-4,6-diones (**4**) in the presence of cycloalkanones in a neutral medium leads to substitution of the isopropylidene fragment in the 1,3-dioxane ring and the formation of 2-spirocycloalkane-1,3-dioxane-4,6-diones **5** (R = H, Alk; n = 4, 5) in 45-90% yields [28].



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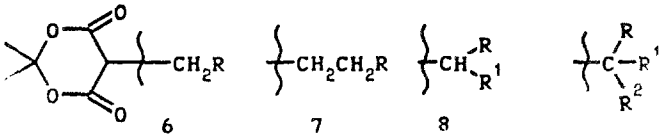
1.3. Substitution and Transformations at the Carbon Atom in the 5 Position of 1,3-Dioxane-4,6-diones

1.3.1. Alkyl Derivatives. The alkylation of the anion of **1** with alkyl halides leads to primarily 5,5-dialkyl derivatives [5, 29-32] in high yields (65-97%) under interphase-catalysis conditions [33]. It has been shown that the primary factor for monoalkylation is the steric factor rather than the electronic factor [30]; the introduction of a second alkyl substituent is facilitated significantly if there is already an alkyl substituent in the ring; dibromoalkanes alkylate Meldrum's acid **1** to give 5,5-spiro compounds [29, 31]. The alkylation of **1** with α-bromo ketones in DMF gives exclusively a monoalkylation product [34]. Alkenes with an activated double bond add dioxanedione **1** to give a mixture of mono- and disubstituted derivatives [35, 36], while catalytic [rhodium(0) complexes] addition to isoprene gives exclusively the monosubstituted derivative [37]. Mannich bases [22] and 1,1-substituted derivatives of cyclopropane and bicyclo[n.1.0]alkanes [38-44] are used as alkylating agents. There are a number of reductive methods for obtaining **4**: reduction of 5-acyl-2,2-dimethyl-1,3-dioxane-4,6-diones (→**6**) [45], 5,5-spirocyclopropene derivatives of **1** (→**7**) [23, 46, 47], and 5-methylene derivatives of **1** (→**8**) [48], and the reductive alkylation of Meldrum's acid **1** by ketones in the presence of complexes of borane with amines (→**8**) [49]. Grignard reagents add to the double bond of 5-methylene-2,2-dimethyl-1,3-dioxane-4,6-diones to give **9** [50, 51].



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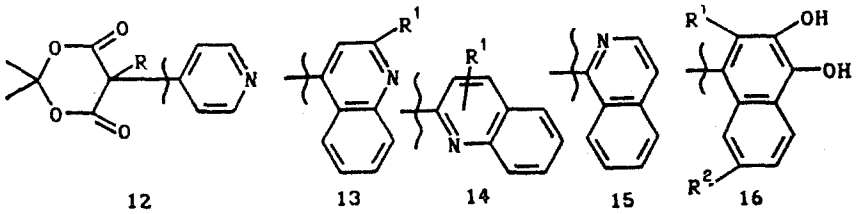
Treatment of **1** and **4** with diazomethane leads to ring-cleavage products: acetone and substituted methyl malonates [52, 53].

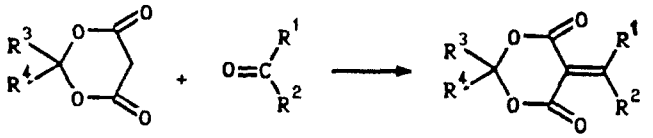
1.3.2. Aryl Derivatives. The direct arylation of 1,3-dioxane-4,6-diones has the following modifications:

1. The use of diaryliodonium salts as alkylating agents. The arylation of the anions of **1** and **4** gives 5,5-diaryl- or 5-alkyl-5-aryl-2,2-dimethyl-1,3-dioxane-4,6-diones (**10** or **11**) in 65-95% yields [54].
2. The use of aryllead triacetates. Compounds **10** (7-17% yields) and **11** (29-95% yields) were obtained [25, 55].
3. The reaction of dioxanediones **1** and **4** with 4-(1H)-pyridones (→**12**, R = Alk, 40-57% yields) [32], 4-chloroquinolines (→**13**, R = H, Alk, 38-51% yields) [56], or quinoline and isoquinoline N-oxides (→**14**, R = H, Alk, 48-84% yields; →**15**, R = H, 93% yield) [57] in acetic anhydride.
4. The reaction of o-naphthoquinones with Meldrum's acid **1** in a methanol solution of an alkali leads to 1,2-dihydroxynaphthalene derivatives **16** (in 53-63% yields) [58].



12 13 14 15 16

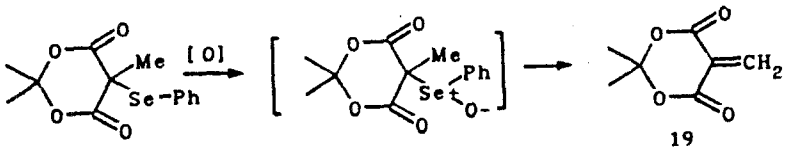
1.3.3. Arylidene and Alkylidene Derivatives. Carbonyl compounds react with 5-unsubstituted 1,3-dioxane-4,6-diones **17** in the presence of bases to give substituted 5-methylenedioxanediones **18**:



17 18

This reaction with Meldrum's acid **1** proceeds readily for aromatic aldehydes (52-96% yields) [59, 60], higher aliphatic aldehydes and aldehydes with a branched hydrocarbon chain (66-81% yields) [60], and aliphatic ketones (25-45% yields) [27]. Aromatic ketones require activation by means of a catalyst ($TiCl_4$/pyridine, 18-72% yields) [61] or prior conversion to ketimines (38-55% yields) [62-66]. Compounds **18** are obtained in good yields when vinylogs of aromatic aldehydes (33-78% yields) [60] and conjugated ketones (monohydrazones of β-dicarbonyl compounds and their vinylogs, 50-95% yields) [67,68] are used. Complex aliphatic ketones undergo condensation with Meldrum's acid **1** in the presence of a catalyst ($TiCl_4$/pyridine) [69, 70]. The condensation proceeds without a solvent in the presence of catalysts — kaolin clays (80-95% yields) [71] and neutral Al_2O_3 (40-95% yields) [72]. Other 1,3-dioxane-4,6-diones **17** (R^3, R^4 = H, Alk, Ph) and their 2-spiro analogs undergo condensation with aromatic aldehydes to give products in 40-88% yields [73, 74].

2,2-Dimethyl-5-methylene-1,3-dioxane-4,6-dione (**19**) was obtained from the 5-methyl-5-phenylseleno derivative of **1** in the form of a polymer [75].



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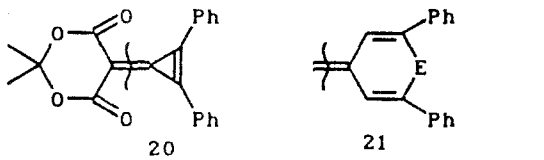
5-Methylene derivatives are formed in the condensation of Meldrum's acid **1** with alkoxycyclopropenylium (→**20**, 53% yield) [76], pyrylium and 4-alkoxypyrylium (→**21**, 97-100% yields) [77-80], and 4-alkoxytelluropyrylium (→**21**, E = Te, 80% yield) salts [81]. The condensation of **1** with the simplest aldehydes and, in the appropriate stoichiometric ratio, with alkylbenzaldehydes gives 5,5′-methylenebis derivatives **22** (R = H, Me, 97-98% yields [29, 52]; R = $AlkC_6H_4$, 27-82% yields [82]). In the presence of indole or proline the condensation of **1** with aldehydes leads to dioxanediones **23** (X = 2-indolyl) [83, 84] and **24** (X = pyrrolidino) [85].



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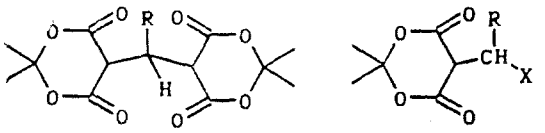
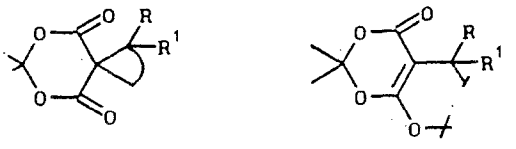


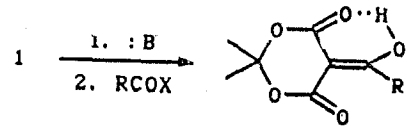
22 23, 24

The activated C=C bond of arylidene and alkylidene derivatives **18** adds π-electron-conjugated systems to give 5,5-spirocycloalkane derivatives of 1,3-dioxane-4,6-diones — structures of the **A** type: diazomethane and diazoacetic ester add to give spiro derivatives of cyclopropane [47, 86-88], the Diels—Alder addition of 1,3-dienes leads to the corresponding spiro derivatives of cyclohexene [89-93], and the [2π+2π]-cycloaddition of cycloalkenes to **18** gives spirocyclobutane derivatives of 1,3-dioxane-4,6-dione [94]. The addition of 5-methylenedioxanediones **18** as heterodienes to alkenes with an activated double bond makes it possible to obtain annelated systems of the **B** type [95-98].



A B

1.3.4. Acyl Derivatives. The anion of **1** is readily acylated to give 5-acyl-2,2-dimethyl-1,3-dioxane-4,6-diones **25** in the stable enol form:



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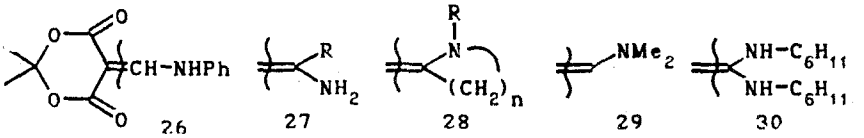
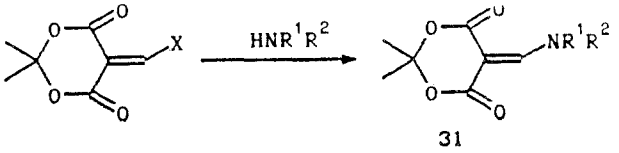
Pyridine or its derivatives are used as bases, and organic acid anhydrides [99], acid chlorides [100-107], and acid bromides [108] are used as acylating agents. The condensation of Meldrum's acid **1** with ethyl orthoformate with subsequent hydrolysis leads to 2,2-dimethyl-5-formyl-1,3-dioxane-4,6-dione [109].

1.3.5. Amino- and Diaminomethylene Derivatives. 5-(Aminomethylene)- and 5-(diaminomethylene)-2,2-dimethyl-1,3-dioxane-4,6-diones are formed in the condensation of Meldrum's acid **1** with ethyl orthoformate and aniline (**26**, 92-95% yields) [110, 111], with imidates and their hydrochlorides (**27**, 7-92% yields) [112-114], with esters of cyclic lactams and their hydrochlorides (**28**, 58-94% yields) [115, 116], with dimethylformamide (DMF) diacetal (**29**, 84% yield) [117], and with dicyclohexylcarbodiimide (**30**, 78% yield) [118].



26 27 28 29 30

The amination of hydroxy and alkoxy derivatives and the transamination of N,N-dimethylaminomethylene derivatives with aliphatic and aromatic amines leads to a large number of N-substituted aminomethylene derivatives **31** in 32-95% yields [109-111, 117, 119, 120].



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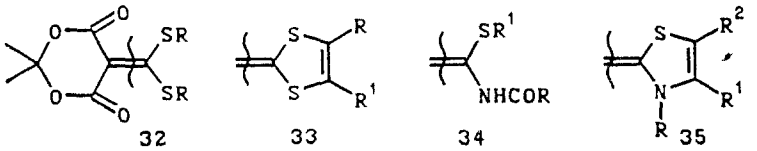
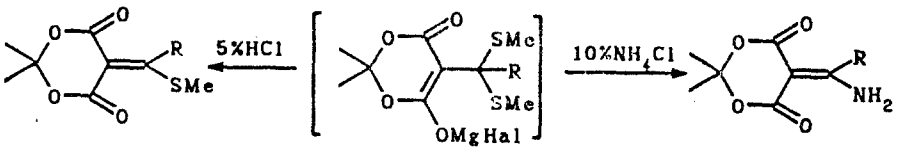
1.3.6. Thio-, Dithio-, and Aminothiomethylene Derivatives. The condensation of Meldrum's acid **1** with carbon disulfide in the presence of sodium hydride [121] or triethylamine [122] with subsequent alkylation leads to 5-[di(alkylthio)methylene]-2,2-dimethyl-1,3-dioxane-4,6-diones **32**, while with 2-alkylthio-1,3-dithiolium salts it leads to 1,3-dithiol-2-ylidene derivatives (**33**, 52-95% yields) [16, 123]. 5-(Aminothiomethylene)-2,2-dimethyl-1,3-dioxane-4,6-diones are formed in the condensation of **1** with acyl isothiocyanates (→**34**) [124] and with 2-methylthio-1,3-thiazolium salts (→**35**) [125, 126].



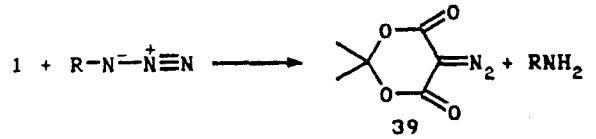
32 33 34 35

5-[Di(methylthio)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione adds Grignard reagents to give intermediate **36**, the subsequent treatment of which leads to β-methylthiomethylene derivatives **37** (52-90% yields) or β-aminomethylene derivatives **38** (53-93% yields) [127].



37 36 38

1.3.7. Diazo Derivatives. The reaction of Meldrum's salt **1** with organic azides that have stable leaving groups as the organic residue leads to 5-diazo-2,2-dimethyl-1,3-dioxane-4,6-dione (**39**) in 45-75% yields.



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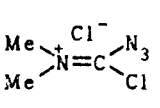
Tosyl azide in the presence of strong bases [128, 129], p-acetamidobenzenesulfonyl azide [130], imino-activated azide **40** [131], and 1-ethyl-2-azidopyridinium tetrafluoroborate, generated in the reaction medium [128, 132, 133], are

used to introduce the diazo group. The photolysis of diazo compound **39** gives "Meldrum's carbene" **41**, which, judging from the products of the reaction with alkenes, exists in the triplet state [134, 135].



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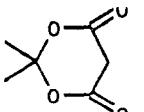

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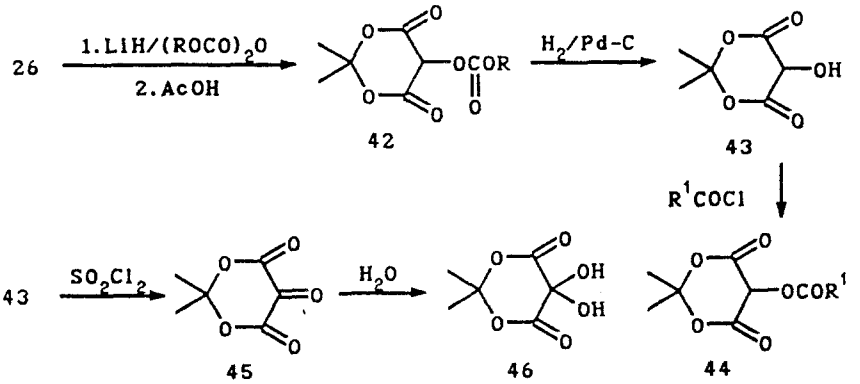
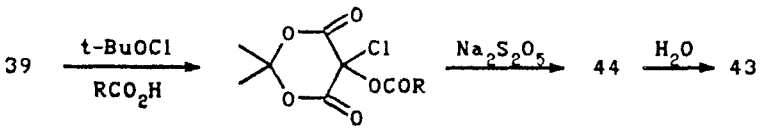
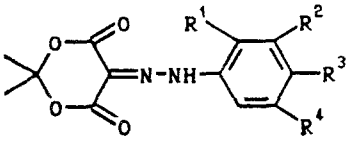
1.3.8. Hydroxy, Oxo, Hydrazo, and Amino Derivatives. 5-Alkoxycarbonyloxy, 5-hydroxy, 5-acyloxy, 5-oxo, and 5,5-dihydroxy derivatives of **1** (**42-45** and **46**) are formed when **26** is used as the starting compound [110]:



Another pathway for obtaining hydroxy derivative **43** is based on the use of 5-diazodioxanedione **39** as the starting compound [136].



The ozonolysis of 2,2-dimethyl-5-(methoxymethylene)-1,3-dioxane-4,6-dione in aprotic solvents gives an ozonide, which is converted to dioxanetrione **45** on treatment with PCl_3 [137]. The oxidation of dimethylsulfonium ylid **52** with an equimolar amount of ozone in methylene chloride leads to DMSO and **45**, which is isolated in the form of phenylhydrazone **48** (all R = H, 55% yield) or as the product (**49**, 69% yield) of condensation with 2-hydroxydimedone [138]. 2,2-R,R-1,3-Dioxane-4,5,6-triones [R = Me, RR = $(CH_2)_n$, n = 4, 5] were obtained in 82-88% yields in the ozonolysis in methylene chloride of the 5-phenyliodonium ylids of the corresponding dioxanediones [139].



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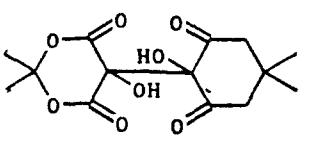

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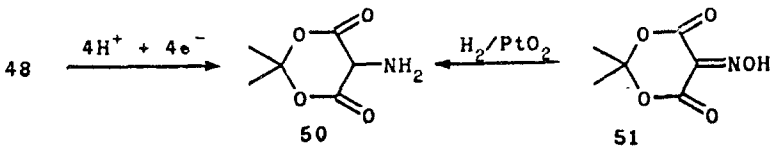
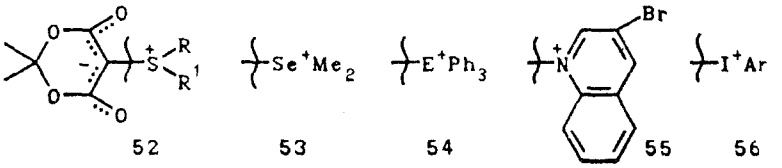
The reaction of Meldrum's acid **1** with arenediazonium salts leads to arylhyrazones **48** in 32-56% yields [14, 140]. The electrochemical reduction of **48** gives 5-amino-2,2-dimethyl-1,3-dioxane-4,6-dione (**50**) [141]. Oxime **51** — an unstable solid substance obtained by the reaction of **1** with sodium nitrite [14, 27] — gives amine **50** when it is reduced.



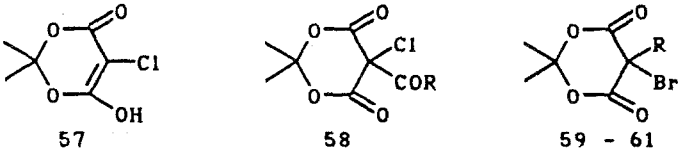
1.3.9. Ylids. Sulfonium ylids **52** are obtained by the following methods: 1) by condensation of Meldrum's acid **1** with sulfoxides by refluxing in acetic anhydride (40-82% yields) [142, 143], with DMSO activated by 3-sulfopropanoic anhydride (80% yield) [144], or with DMSO in the presence of dicyclohexylcarbodiimide and H_3PO_4 (40% yield) [143]; 2) by condensation of 5-bromo-2,2-dimethyl-1,3-dioxane-4,6-dione with DMSO (30-40% yield) [143, 145]; 3) by treatment of phenyliodonium ylid **56** with dimethyl sulfide in anhydrous acetone (44% yield) [146]; 4) by the reaction of **39** with DMSO with UV irradiation (21% yield) [147].

Selenonium ylid **53** is formed in 30% yield in the condensation of Meldrum's acid **1** with dimethyl dibromoselenide [143]. Arsonium ylid **54** (E = As, 40-42% yield) [149] and bismuthonium ylid **54** (E = Bi, 83% yield) [150] are stable compounds. 3-Bromoquinoline 1-oxide reacts with **1** at room temperature in acetic anhydride to give N-ylid **55** in 89-91% yield [57]. The condensation of Meldrum's acid **1** with aryliodoso diacetates leads to aryliodonium ylids **56** in 82-97% yields [146].



52 53 54 55 56

1.3.10. Halo Derivatives. Fluoro- and iodo-1,3-dioxane-4,6-diones have not been obtained. 5-Chloro derivative **57** is formed in 73% yield by treatment of ylids **56** with an equimolar amount of hydrochloric acid in acetone [146]. Treatment of enol **25** with sulfuryl chloride gives 5-acyl-2,2-dimethyl-5-chloro-1,3-dioxane-4,6-dione **58** [151]. The reaction of **1** with bromine in the presence of 1 mole of base leads to 5-bromo derivative **59** (R = H), while 5,5-dibromo derivative **60** (R = Br) is obtained in the presence of 2 moles of base [5, 152]. The bromination of dioxanedione **4** (R = Me) in chloroform in the presence of NaF gives 5-bromo-2,2,5-trimethyl-1,3-dioxane-4,6-dione **61** (R = Me) [20].



57 58 59 - 61

The bromo derivatives are good sources of the bromonium ion: **59** and **60** brominate saturated aldehydes and α,β-unsaturated ketones with high selectivity to give the products in high yields [153], while **61** adds to polyenolates with high regioselectivity in a transfer-alkylation reaction [154-156].

2. Methods for Cleaving the 1,3-Dioxane Ring

The 1,3-dioxane ring is cleaved by hydrolysis (acidic and alkaline), alcoholysis, solvolysis by phenols, and aminolysis and also by pyrolysis (5-diazo-2,2-dimethyl-1,3-dioxane-4,6-dione is cleaved by photolysis).

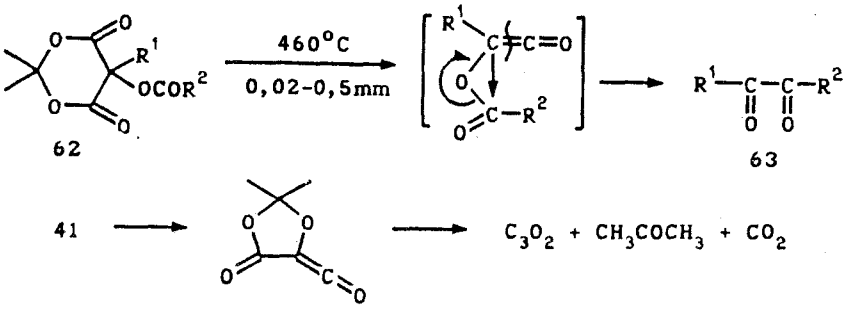
Heating the 5,5-dimethyl derivative of **1** with dilute hydrochloric acid for a few minutes leads to acetone and dimethylmalonic acid [12]. The hydrolysis of **1** in excess alkali gives acetone and sodium malonate [4]. 2,2,5,5-Tetramethyl-1,3-dioxane-4,6-dione reacts with two equivalents of base in an aqueous solution of alkali [157], while titration with a methanol solution of potassium hydroxide includes the reaction with one equivalent of alkali to give the potassium salt of methyl dimethylmalonate [12].

The alcoholysis of **1** with an alcohol solution of hydrogen chloride leads to diethyl malonate at 20°C [14], while refluxing of 5-acyl derivatives **25** gives β-keto carboxylic acid esters (see section 3.2.1). The solvolysis of Meldrum's acid **1** with equimolar amounts of phenols gives equal amounts of malonic acid and a diaryl malonate [158, 159]. Amines react with **1** to give malonic acid monoamides [160]; in some cases ring cleavage is accompanied by decarboxylation and the formation of acetamides [4, 32, 161].

Ketene, acetone, and carbon dioxide are formed in the pyrolysis of Meldrum's acid **1** at 400-600°C [4, 162], while methyleneketenes [11, 69, 75, 83, 158-169], which are unusually reactive particles with a wide range of synthetic applications (see section 3.3), are formed in the pyrolysis of methylene derivatives of **1**. The corresponding acetylenes are obtained under more severe conditions of pyrolysis of the methylene derivatives (temperatures up to 700°C) [164]. The pyrolysis of 5-aminomethylenedioxanediones **27** and **31** gives aminomethyleneketenes [170], while the pyrolysis of arylhydrazones **48** gives aryldiazoketenes, which immediately undergo decarbonylation to give substituted cyanamides [170].

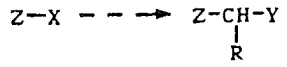
During the pyrolysis of 5-acyloxydioxanediones **62** the intermediate ketenes are decarbonylated to give carbenes, which then undergo rearrangement to α-diketones **63** in 77-92% yields [166].

The photochemically obtained "Meldrum's carbene" **41** undergoes Wolff ring contraction [171-173], while complete destruction occurs under more severe conditions [171].

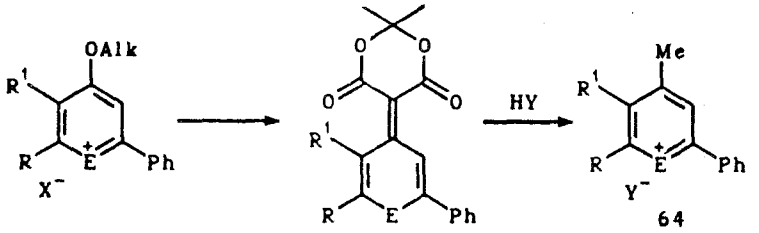


3. Application in Syntheses

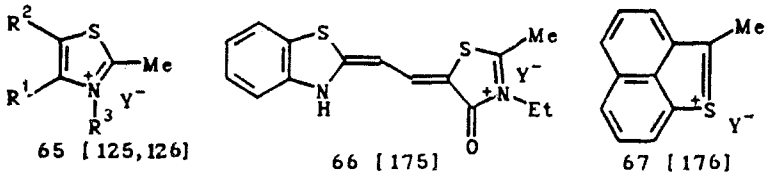
3.1. The $(CH_2)^{2-}$ and $(CHR)^{2-}$ Synthones



5-Methylene, 5-acyl, and 5-aryl derivatives of dioxanediones undergo acidic hydrolysis to give compounds that contain a methyl or alkyl substituent in quantitative yields. The method has been used to obtain **64-67**, which are intermediates in the synthesis of polymethine dyes.

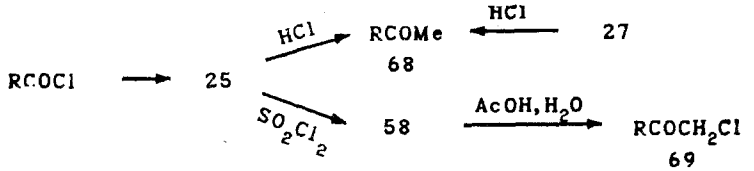


E = O,NMe [78,79], E = Te [81]

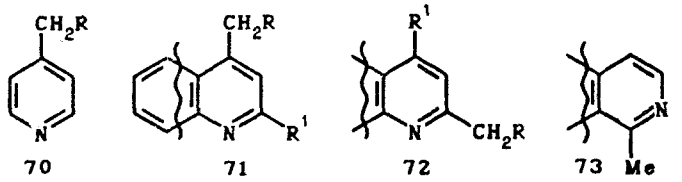


65 [125,126] 66 [175] 67 [176]

The acidic hydrolysis of dioxanediones **25** and **27** leads to alkyl and aralkyl methyl ketones **68** in 30-58% yields [89, 98]. The hydrolysis of chloro derivative **58** in dilute acetic acid leads to 1-chloro-2-alkanones **69** in 20% yield [151].



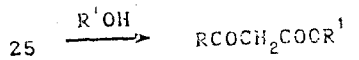
Heating 5-hetaryldioxanediones **12-15** in acids gives the corresponding alkylhetarenes **70** (75-87% yields) [32] and **71-73** (70-95% yields) [56] in high yields.

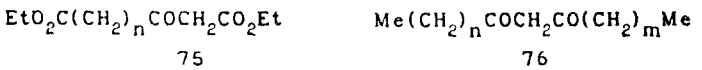


70 71 72 73

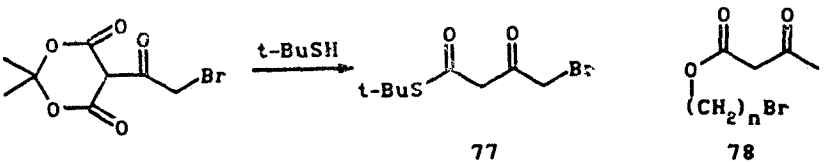
3.2. The $C^{-}H_2$—$C^{+}O$ Synthone

3.2.1. Synthesis of β-Keto Esters. The alcoholysis of 5-acyldioxanediones **25** leads to β-keto carboxylic acid esters **74** in 38-85% yields [99, 100, 105, 107, 177-181]. The method has been used to obtain acylacetates of hydroxy steroids with a labile OH group [104, 182], β-keto dicarboxylic acid esters **75** (n = 2-7, 33-80% yields) [183], and long-chain β-diketones **76** (n = 6, 12; m = 6, 14, 20; 82-95% yields) [106].

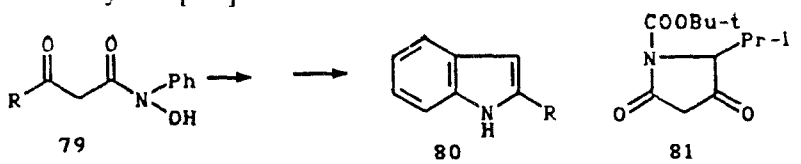




Acylthioacetates such as **77** (76% yield) were obtained by thiolysis of **25** [108].

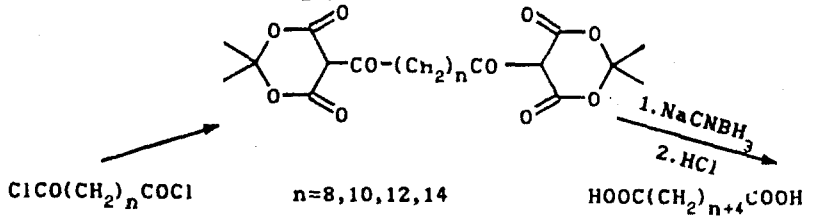


Thioester **77** is used in the synthesis of macrocyclic lactones, as are **78** — products of the alcoholysis of 5-acetyl-2,2-dimethyl-1,3-dioxane-4,6-diones by ω-bromoalkanols (n = 5-11, 41-57% yields) [184]. Refluxing phenylhyroxylamine with **25** (1:1) in acetonitrile leads to N-(acylacetyl)phenylhydroxylamines **79** in 51-95% yields. The introduction of yet another mole of **25** leads to the formation of an N,O-diacylacetyl derivative, which undergoes rearrangement and cyclization to indoles **80** in 21-58% yields [185].



β-Keto acid esters were obtained in 41-58% yields in the alkaline alcoholysis and subsequent acidic treatment of aminomethylene derivatives **27** [112]. Pyrrolidin-2,4-dione **81** was synthesized from L-butoxycarbonylleucine, activated by isopropenyl chloroformate, and Meldrum's acid **1** [186].

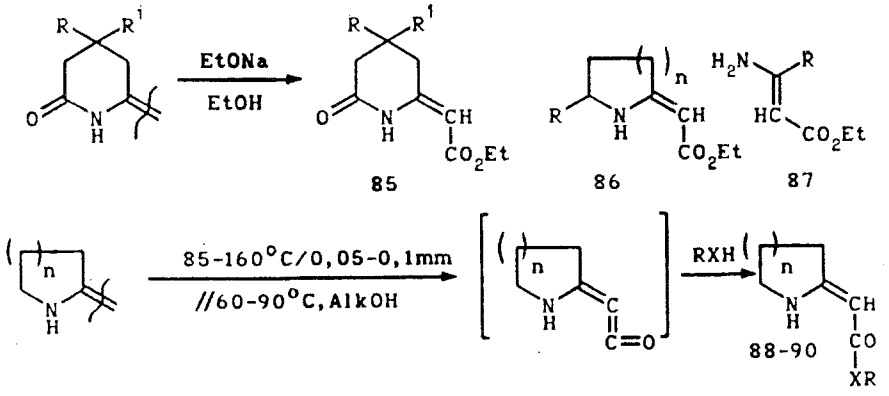
3.2.2. Synthesis of Carboxylic Acids and Their Esters. Adamantylacetic acid [187, 188] and 4-phenyl- and 3-methylbutyric acids [46] were obtained by the acidic hydrolysis of the corresponding dioxanediones **4**. The alkaline hydrolysis of 4-pyridyl derivatives **12** with subsequent acidic treatment at room temperature gives 2-(4-pyridyl)butyric (77% yield) and 2-(4-pyridyl)caproic (84% yield) acids [32]. The ethanolysis of **23** in the presence of pyridine and copper powder leads to 3-(3-indolyl)-3-R-propionic acid esters (R = Alk, Ph; 62-87% yields) [83]. The acidic hydrolysis of dioxanediones **4** is convenient for lengthening the chains of carboxylic acids by a $(CH_2)_2$ fragment; the chain of dicarboxylic acids is lengthened by a $(CH_2)_4$ grouping [102].



The method of acidic hydrolysis of **4** was used to obtain γ-keto acids **82** [R = $(CH_2)_7COOH$] and **83** (R = $CH_2NH_3^+Cl^-$) [189-192].

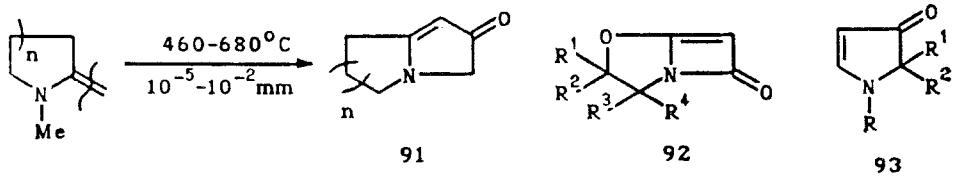
3.3. The C^2—H—C^+O Synthone

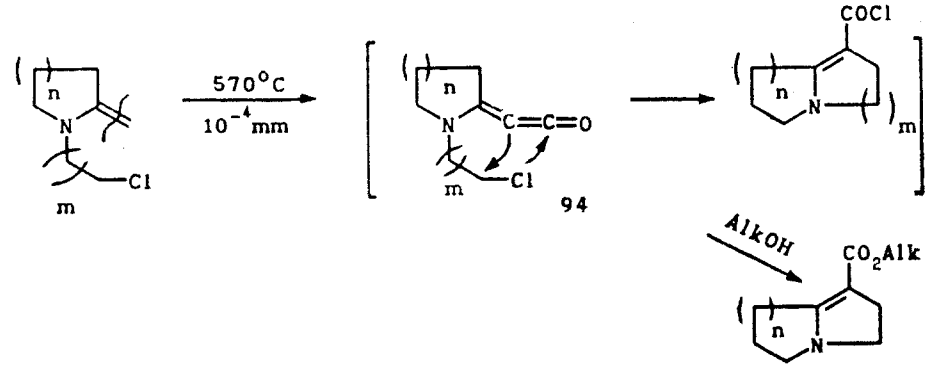
The mild hydrolysis, alcoholysis, or pyrolysis of methylene derivatives of **1** leads to cinnamic acids **84** [59, 73, 82, 193] and esters **85-88** [112, 194, 195], amides **89**, and thioesters **90** of α,β-unsaturated acids [195].



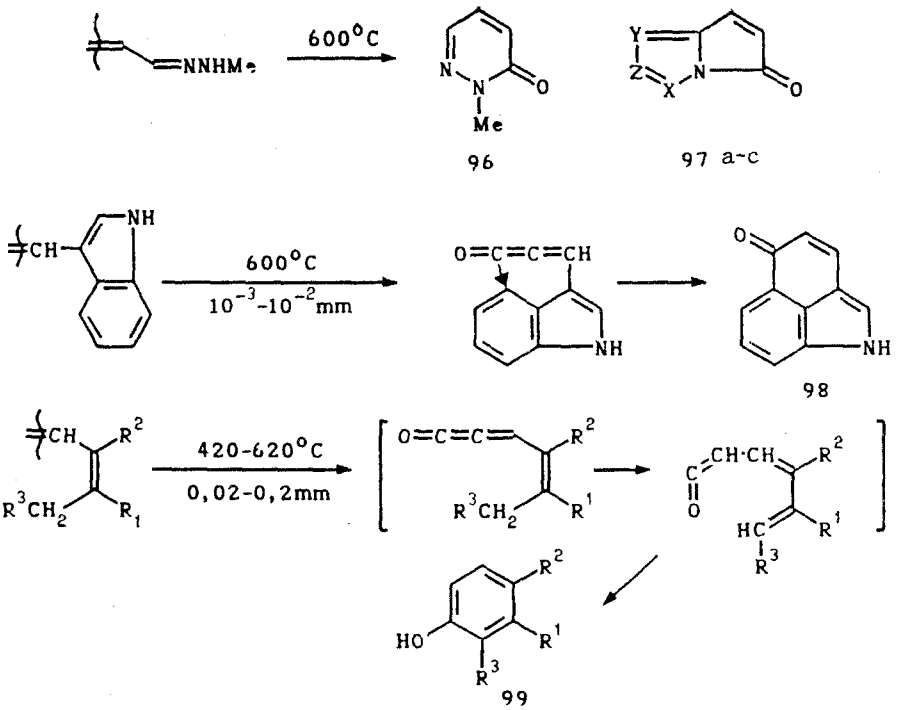
n=1, 2, 3; R=Alk; **88** X=O; **89** X=NH; **90** X=S

The flash-vacuum pyrolysis of methylene derivatives, which proceeds through a step involving a methyleneketene, is accompanied by intramolecular acylation, which leads to stable mono- and polycyclic products with ring sizes from four to six (**91**, n = 1, 2 [196, 197]; **92**, R^1—R^4 = H, Alk, Ph [115]; **93**, R—R^2 = H, Alk, Ph [120, 198, 199]). The cyclization of aminomethyleneketene **94** includes intramolecular substitution of the chlorine atom and leads to bicyclic enamino esters **95** (n, m = 1, 2) [200].



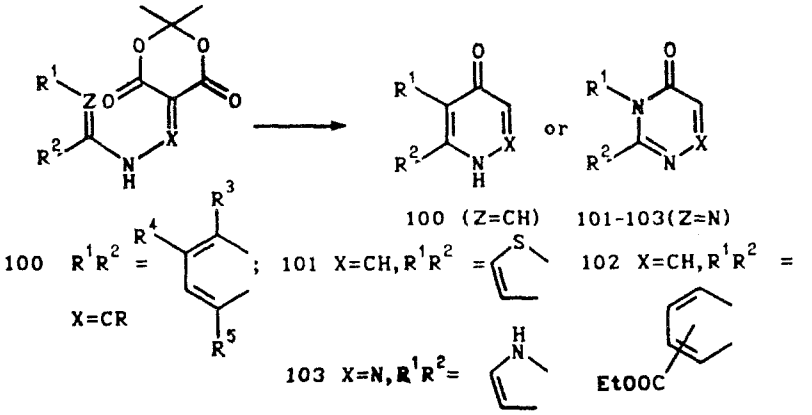


Intramolecular acylation, which takes place at the nitrogen atom, leads to 3-pyridazinone **96** [67] and three isomeric azapyrrazolizinones **97** [201]; structural hindrance to N-acylation directs the synthesis to favor the formation of a product of addition of the intermediate methyleneketene to the carbon atom (**98**) [202]. The C-acylated cyclic products obtained by flash-vacuum pyrolysis from 5-(o-alkylaryliden- and [-hetarylidene])-2,2-dimethyl-1,3-dioxane-4,6-diones are stabilized due to the formation of aromatic systems — arenols **99** [163, 165, 202].

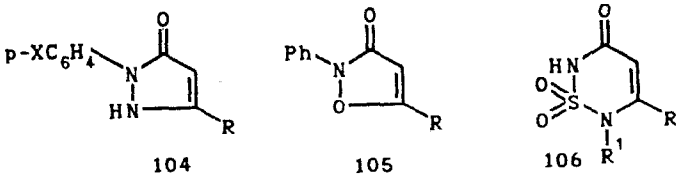


97 a X=Y=CH, Z=N; b X=Z=CH, Y=N; c Y=Z=CH, X=N

The thermal cyclization of 5-[(arylamino)methylene]-2,2-dimethyl-1,3-dioxane-4,6-diones in diphenyl ether leads to 4-quinolones **100** (60-96% yields) [111, 203] and their aza analogs **101** (66% yields) [111], **102** (64-91% yields) [204, 205], and **103** [206] in high yields.

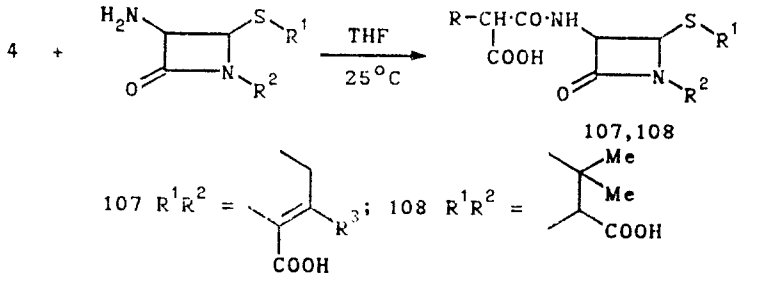


The condensation of 2,2-dimethyl-5-(methylthiomethylene)-1,3-dioxane-4,6-diones **37** with arylhydrazines in diphenyl ether gives 2-aryl-3-pyrazolones **104** (60-82% yields) [207]. 5-Acyl derivatives **25** react with phenylhydroxylamine in the presence of anhydrous p-toluenesulfonic acid in benzene to give 2-phenylisoxazolin-3-ones **105** (76-97% yields) [185, 208]. Sulfonamides condense with **25** to give 1,2,6-thiadiazine 1,1-dioxides **106** [209].

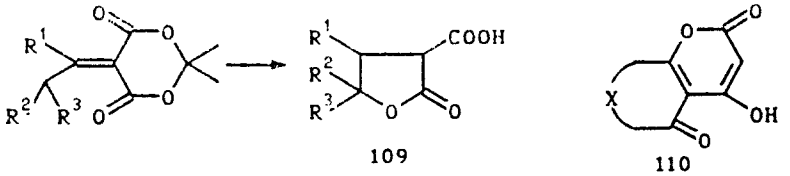


3.4. The $OC^+—CH_2—C^+O$, $OC^+CHR—C^+O$, and $OC^+—C^{2-}—C^+O$ Synthones

2,2-Dimethyl-1,3-dioxane-4,6-dione and its 5-mono- and disubstituted derivatives are used as malonylating agents. The method has been used to obtain α-carboxylated penicillins **107** (33-90% yields) and cephalosporins **108** (40-87% yields) [26].

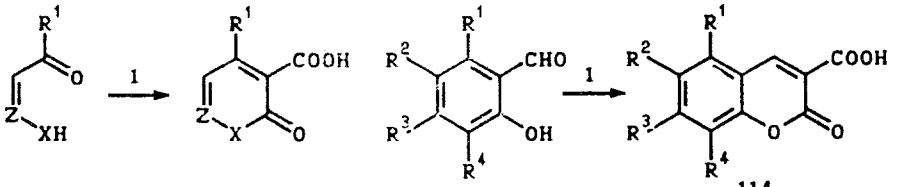


In strongly acidic media (TsOH, H_2SO_4, polyphosphoric acid, $BF_3{\cdot}Et_2O$) cycloalkylidene derivatives are converted to α-carboxy-γ-lactones **109** in 33-100% yields [70, 210]. Meldrum's acid **1** reacts with cyclic β-diketones on heating to 130-135°C to give O,C-malonylation products **110** [11, 212].



109 110

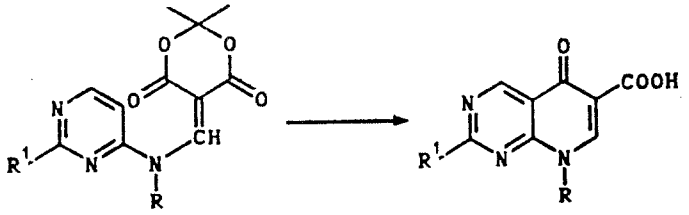
The condensation of dioxanedione **1** with β-dicarbonyl compounds and their amino derivatives, glyoxal monohydrazones, and substituted salicylaldehydes leads to, respectively, α-pyrone derivatives **111** [211], α-pyridone derivatives **112** [211], α-pyridazinone derivatives **113** [213], and coumarin-3-carboxylic acid derivatives **114** [211, 214, 215].



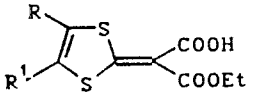
111 - 113 114

111 Z=CR², X=O, R¹=Me; 112 Z=CR², X=NH, NPh, R¹=Me; 113 Z=N, X=N—Bu-*t*, R¹=H

The cyclization of 2,2-dimethyl-5-(pyrimidinylaminomethylene)-1,3-dioxane-4,6-diones in polyphosphoric acid or in the presence of organic derivatives of silicon has been proposed as a method for obtaining pyridopyrimidinecarboxylic acids **115** [216-218].



The alkaline alcoholysis of ylidene derivatives **33** with subsequent treatment with acid is a valuable method for the one-step synthesis of ylidenemalonic acid monoesters **116** (75-93% yields) [123, 219]. The acidic hydrolysis of methylenebis derivatives **22** (R = H, $AlkC_6H_4$) is a convenient method for obtaining tetracarboxylic acids **117** [52, 82].

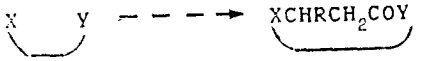


116

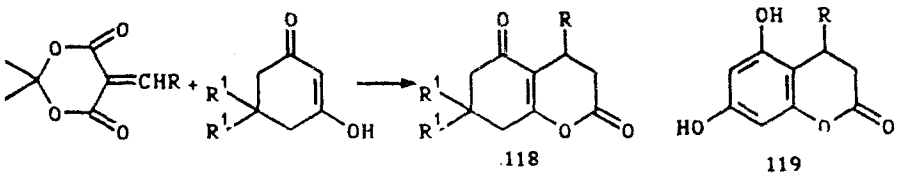
$(COOH)_2CHCHRCH(COOH)_2$

117

3.5. The $C^+HR—CH_2—C^+O$ Synthone

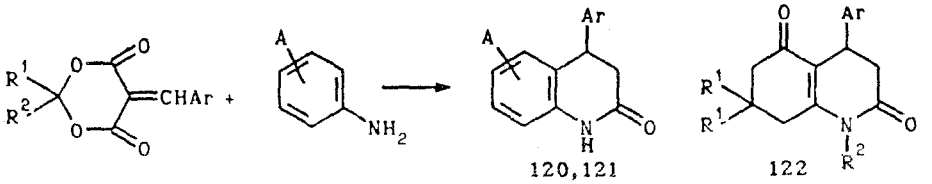


The condensation of 5-arylidene- and 5-alkylidene-1,3-dioxane-4,6-diones with binucleophilic reagents, by introducing the $C^+HRCH_2C^+O$ fragment, makes it possible to obtain heterocycles in one step. Thus hexahydro-5-coumarone derivatives **118** were obtained in 66-82% yields from cyclohexane-1,3-diones [220-222], while dihydrocoumarin derivatives **119** were obtained from floroglucinol [223].



118 **119**

The reaction with anilines and naphthylamines leads to tetrahydro-2-quinolones **120** in 8-25% yields [65] and their benzo analogs **121** in 30-80% yields [62-65, 224-227]. The condensation of 5-arylidene-2,2-dimethyl-1,3-dioxane-4,6-diones with 3-aminocyclohexen-2-ones in alcohols leads to octahydroquinoline-2,5-diones **122** in 34-90% yields [228-232].

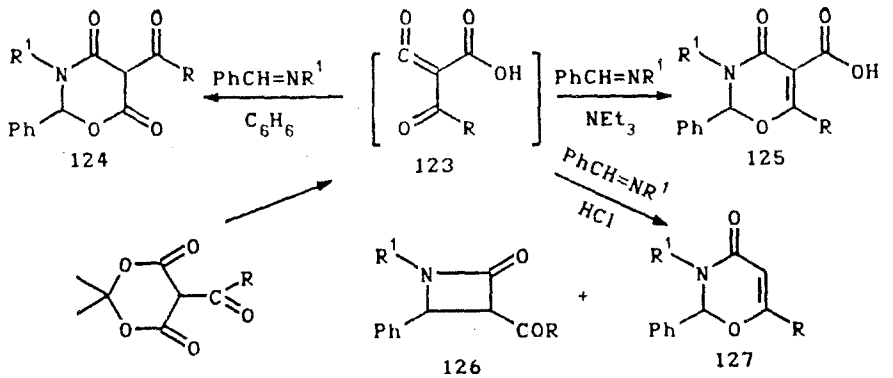


120,121 **122**

$R^1=R^2=Me$, $R^1R^2=(CH_2)_4$, $(CH_2)_5$; **120** A=H, 6-Me; **121** A=5,6- and 7,8 benzo; **122** R^1=H, Me, R^2=H, Me, Ar

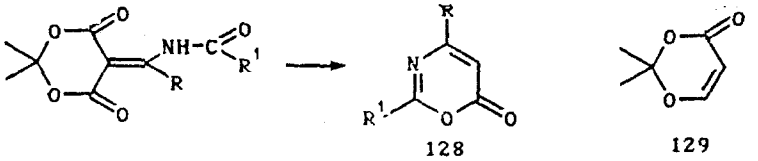
3.6. Acyl Derivatives in the Synthesis of Heterocycles

Splitting out of a molecule of acetone from 5-acyl-2,2-dimethyl-1,3-dioxane-4,6-diones gives intermediate **123**, which, depending on the conditions used, reacts with Schiff bases to give the corresponding addition products: 5-acyl-3,4,5,6-tetrahydro-2H-1,3-oxazine-4,6-diones **124** (54-86% yields), 2,3-dihydro-1,3-oxazine-5-carboxylic acids **125** (24-75% yields), 3-acyl-β-lactams **126** (35-85% yields), and 2,3-dihydro-1,3-oxazin-4-ones **127** (6-34% yields) [233, 234].



124 **123** **125** **126** **127**

2,4-Disubstituted 1,3-oxazin-6-ones **128** are formed in 32-93% yields in the thermal cyclization of [5-(acylamino)methylene]-2,2-dimethyl-1,3-dioxane-4,6-diones [114]. The thermolysis of 2,2-dimethyl-5-formyl-1,3-dioxane-4,6-dione in toluene leads to 2,2-dimethyl-1,3-dioxin-4-one **129** — an intermediate in the synthesis of prostaglandins [235].



128 **129**

Material involving the description of a number of physical and chemical properties (acid—base equilibria, keto—enol tautomerism, spectral and structural characteristics, the results of kinetic experiments) of 1,3-dioxane-4,6-diones, which is necessary for comparing the characteristics of the initial state of synthesis (the reactants) and the final state (the products) and for elucidating the mechanisms of reactions with the participation of 1,3-dioxane-4,6-diones, was beyond the scope of the present review. The further development of the problems involved in the synthone approach, which makes it possible to conceive of organic synthesis as being the introduction of predesignated fragments into the molecules of compounds, will lead, in all likelihood, to the publication in the near future of research devoted to the possibilities and limitations of the applicability (right up to the specific conditions) of synthetic agents similar to the 1,3-dioxane-4,6-diones described in this review and also specialized research on the cataloging of synthetic agents for the construction of organic molecules and molecular designing.

LITERATURE CITED

1. H. McNab, *Chem. Soc. Rev.*, **7**, 345 (1978).
2. X. Huang, *Yutszi Khuasyué*, 329 (1986).
3. A. Said, *Inf. Chim.*, No. 261, 251 (1985).
4. A. N. Meldrum, *J. Chem. Soc.*, **93**, 598 (1908).
5. E. Ott, *Ann.*, **401**, 159 (1913).
6. A. Michael and J. Ress, *J. Am. Chem. Soc.*, **55**, 3084 (1933).
7. N. S. Vul'fson, *Zh. Obshch. Khim.*, **19**, 1904 (1949).
8. N. S. Vul'fson, *Zh. Obshch. Khim.*, **20**, 425 (1950).
9. N. S. Vul'fson, *Zh. Obshch. Khim.*, **20**, 435 (1950).
10. N. S. Vul'fson, *Zh. Obshch. Khim.*, **20**, 595 (1950).
11. A. Michael and N. Weiner, *J. Am. Chem. Soc.*, **58**, 680 (1936).
12. D. Davidson and S. A. Bernhard, *J. Am. Chem. Soc.*, **70**, 3426 (1948).
13. P. J. Scheuer and S. G. Cohen, *J. Am. Chem. Soc.*, **80**, 4933 (1958).
14. B. Eistert and F. Geiss, *Chem. Ber.*, **94**, 929 (1961).
15. A. N. Kost, I. N. Khaimov, Yu. Dkzhurakulov, K. Kh. Khaidarov, L. D. Lebedeva, and A. L. Kotov, *Khim. Geterotsikl. Soedin.*, No. 11, 1482 (1975).
16. K. Ogawa, A. Nakai, N. Ohayashi, and A. Mitani, Japanese Patent Application No. 61-137883; *Ref. Zh. Khim.*, 20O84P (1987).
17. A. M. Shul'ga and P. V. Ponomarev, *Khim. Geterotsikl. Soedin.*, No. 7, 924 (1984).
18. A. G. Relenyi, D. E. Wallick, and J. D. Streit, US Patent No. 4613671.
19. T. Kappe and E. Ziegler, *Angew. Chem.*, **43**, 491 (1974).
20. K. Pihlaja and M. S. Seilo, *Acta Chem. Scand.*, **22**, 3053 (1968).
21. K. Pihlaja and M. S. Seilo, *Acta Chem. Scand.*, **23**, 3003 (1969).
22. R. T. Jacobs, A. D. Wright, and F. X. Smith, *J. Org. Chem.*, **47**, 3769 (1982).
23. S. Danishevsky and R. K. Singh, *J. Am. Chem. Soc.*, **97**, 3239 (1975).
24. S. Danishevsky and R. K. Singh, *J. Org. Chem.*, **40**, 3807 (1975).
25. J. T. Pinhey and R. A. Rowe, *Tetrahedron Lett.*, No. 10, 965 (1980).
26. P. Crooy, R. De Neys, J. Eliaers, R. Liveyns, G. Simonet, and I. Vandervelle, *Bull. Soc. Chim. Belg.*, **86**, 991 (1977).
27. G. Swoboda, J. Swoboda, and F. Wessely, *Monatsh. Chem.*, **95**, 1238 (1964).
28. E. Ziegler, H. Junek, and H. Kroboth, *Monatsh. Chem.*, **107**, 317 (1976).
29. J. A. Hedge, C. W. Kruse, and A. R. Snyder, *J. Org. Chem.*, **26**, 992 (1961).
30. R. B. Mane and K. G. S. Rao, *Chem. Ind.*, No. 18, 786 (1976).
31. D. G. Desai and R. B. Mane, *Chem. Ind.*, No. 20, 809 (1982).
32. F. X. Smith and G. G. Evans, *Tetrahedron Lett.*, No. 13, 1237 (1972).
33. C.-C. Chan and X. Huang, *Synthesis*, No. 6, 452 (1982).
34. N. E. Kravchenko, "C-Acyl derivatives of 2-phenyl-2-oxazolin-5-one and Meldrum's acid in organic synthesis," Author's Abstract of Master's Thesis, Moscow (1989).
35. C.-C. Chan and X. Huang, *Synthesis*, No. 3, 224 (1982).
36. Q. Zhong, J.-G. Shau, and C.-Q. Liu, *Yutszi Khuasyué*, **8**, 466 (1988); *Ref. Zh. Khim.*, 5Zh203 (1989).
37. G. Mignani, D. Morel, and Y. Colleville, *Tetrahedron Lett.*, No. 51, 6337 (1985).
38. E. Vilsmaier and K. Joerg, *Chem. Ber.*, **117**, 2910 (1984).
39. E. Vilsmaier, K. Joerg, and R. Nauert, *Chem. Ber.*, **117**, 2928 (1984).

40. E. Vilsmaier, K. Joerg, and G. Maas, *Chem. Ber.*, **117**, 2947 (1984).
41. J. Weidner, E. Vilsmaier, and R. Fries, *Monatsh. Chem.*, **118**, 1039 (1987).
42. J. Weidner, E. Vilsmaier, and C. Henn, *Monatsh. Chem.*, **118**, 1147 (1987).
43. T. Stamm, E. Vilsmaier, G. Maas, and E. Anders, *Chem. Ber.*, **121**, 1487 (1988).
44. J. Weidner and E. Vilsmaier, *Monatsh. Chem.*, **118**, 1057 (1987).
45. C. F. Nutaitis, R. A. Schultz, I. Obaza, and F. X. Smith, *J. Org. Chem.*, **45**, 4606 (1980).
46. G. Adametz, J. Swoboda, and F. Wessely, *Monatsh. Chem.*, **93**, 1453 (1962).
47. G. Bilek, O. Saiko, H. Stephen, and F. Wessely, *Monatsh. Chem.*, **97**, 633 (1966).
48. A. D. Wright, M. L. Haslego, and F. X. Smith, *Tetrahedron Lett.*, No. 25, 2325 (1979).
49. D. M. Hrubowchak and F. X. Smith, *Tetrahedron Lett.*, No. 45, 4951 (1983).
50. M. L. Haslego and F. X. Smith, *Synth. Commun.*, **10**, 421 (1980).
51. X. Huang, C.-C. Chan, and Q.-L. Wu, *Tetrahedron Lett.*, No. 1, 75 (1982).
52. S. I. Zav'yalov, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, No. 12, 2185 (1961).
53. G. A. Bihlmaier, P. Schuster, and O. E. Polansky, *Monatsh. Chem.*, **97**, 145 (1966).
54. Z.-C. Chen, Y.-Y. Jin, and P. J. Stang, *J. Org. Chem.*, **52**, 4115 (1987).
55. R. P. Kopinski, J. T. Pinhey, and B. A. Rowe, *Austral. J. Chem.*, **37**, 1245 (1984).
56. A. Scovill and F. X. Smith, *J. Heterocycl. Chem.*, **14**, 1081 (1977).
57. M. M. Yousif, S. Saeki, and M. Hamana, *Chem. Pharm. Bull.*, **30**, 1680 (1982).
58. A. N. Grinev and I. K. Arsenichev, *Zh. Org. Khim.*, **21**, 1315 (1985).
59. E. J. Corey, *J. Am. Chem. Soc.*, **74**, 5897 (1952).
60. P. Schuster, O. E. Polansky, and F. Wessely, *Monatsh. Chem.*, **95**, 53 (1964).
61. C. J. Baxter and R. F. C. Brown, *Austral. J. Chem.*, **28**, 1551 (1975).
62. G. A. Bihlmaier, F. J. Kunz, and O. E. Polansky, *Monatsh. Chem.*, **97**, 1293 (1966).
63. Ya. A. Strod, I. É. Lielbriedis, and O. Ya. Neiland, Summaries of Papers Presented at the 4th All-Union Conference on the Chemistry of Dicarbonyl Compounds [in Russian], Riga (1976), p. 161.
64. Ya. A. Strods, Ya. A. Miller, I. É. Lielbriedis, and O. Ya. Neiland, *Izv. Akad. Nauk Latv. SSR, Ser. Khim.*, No. 3, 350 (1977).
65. Ya. A. Strods, I. É. Lielbriedis, and O. Ya. Neiland, *Izv. Akad. Nauk Latv. SSR, Ser. Khim.*, No. 2, 225 (1978).
66. Ya. A. Strods, V. P. Tsiekure, V. É. Kampars, I. É. Lielbriedis, and O. Ya. Neiland, *Khim. Geterotsikl. Soedin.*, No. 10, 1369 (1978).
67. H. McNab and J. Stobie, *J. Chem. Soc., Perkin 1*, No. 8, 1845 (1982).
68. H. McNab, L. C. Monahan, and A. Gray, *Chem. Commun.*, No. 3, 140 (1987).
69. R. F. C. Brown, K. J. Coulton, F. W. Eastwood, B. M. Gatehouse, L. W. Guddatt, M. Pffenninger, and J. Rainbaw, *Austral. J. Chem.*, **37**, 2509 (1984).
70. E. Campaigne and J. C. Beckmann, *Synthesis*, No. 5, 385 (1978).
71. M. T. Thorat, M. H. Jagdale, R. B. Mane, M. M. Salunkhe, and P. P. Wadagaonkar, *Current Sci.*, **56**, 771 (1987).
72. D. Villemin, *Chem. Ind.*, No. 12, 478 (1983).
73. I. É. Lielbriedis and É. Yu. Gudrinietse, *Izv. Akad. Nauk Latv. SSR, Ser. Khim.*, No. 2, 193 (1964).
74. I. N. Khaimov, Yu. Dzhurakulov, and A. N. Kost, *Fiziol. Akt. Veshchestva*, No. 10, 70 (1978).
75. R. F. C. Brown, F. W. Eastwood, and G. L. McMullen, *Austral. J. Chem.*, **30**, 179 (1977).
76. T. Eicher, T. Pfister, and N. Kruger, *Org. Prep. Proc. Intern.*, **6**, 63 (1974).
77. B. Eistert, A. Schmidt, and T. I. Arackal, *Chem. Ber.*, **109**, 1549 (1976).
78. J. A. Van Allan and G. A. Reynolds, *J. Heterocycl. Chem.*, **8**, 803 (1971).
79. J. A. Van Allan and G. A. Reynolds, *J. Heterocycl. Chem.*, **9**, 669 (1972).
80. J. R. Wilt, G. A. Reynolds, and J. A. Van Allan, *Tetrahedron*, **29**, 795 (1973).
81. M. R. Detty and B. J. Murray, *J. Org. Chem.*, **47**, 5235 (1982).
82. L. P. Zalukaev, I. K. Anokhina, and G. M. Mozhaev, All-Union Institute of Scientific and Technical Information Deposited Paper No. 6606—73 (16.08.73), Voronezh State University, Voronezh (1973).
83. Y. Oikawa, H. Hirasawa, and O. Yonemitsu, *Tetrahedron Lett.*, No. 20, 1759 (1978).
84. Y. Oikawa, H. Hirasawa, and O. Yonemitsu, *Chem. Pharm. Bull.*, **30**, 3092 (1982).
85. B. R. Chhabra, M. L. Bolte, and W. D. Crow, *Austral. J. Chem.*, **37**, 1795 (1984).
86. P. Schuster, F. Wessely, and A. Stephen, *Monatsh. Chem.*, **98**, 1772 (1967).
87. H. Peham, O. E. Polansky, and F. Wessely, *Monatsh. Chem.*, **98**, 1665 (1967).
88. F. Neirlich, P. Schuster, and O. E. Polansky, *Monatsh. Chem.*, **102**, 438 (1971).
89. F. J. Kunz and O. E. Polansky, *Monatsh. Chem.*, **100**, 920 (1969).
90. W. G. Dauben, A. P. Kozikowski, and W. T. Zimmerman, *Tetrahedron Lett.*, No. 8, 515 (1975).

91. J. F. Businkai, D. M. Hrubowchak, and F. X. Smith, *Tetrahedron Lett.*, No. 27, 3195 (1985).
92. G. A. Kraus and M. E. Krolski, *J. Org. Chem.*, **51**, 3347 (1986).
93. M. Benzing, E. Vilsmaier, H. Martini, G. Michaels, and E. Anders, *Chem. Ber.*, **122**, 1277 (1989).
94. J. Leitich, H. Partale, and O. E. Polansky, *Chem. Ber.*, **112**, 3293 (1979).
95. J. Bitter, J. Leitich, H. Partale, O. E. Polansky, W. Riemer, U. Ritter-Thomas, B. Schlamann, and B. Stilkerieg, *Chem. Ber.*, **113**, 1020 (1980).
96. L. F. Tietze, H. Stegelmeier, K. Harms, and T. Brumby, *Angew. Chem.*, **94**, 868 (1982).
97. L. F. Tietze, M. Bratz, R. Machinek, and G. V. Kiedrowski, *J. Org. Chem.*, **52**, 1638 (1987).
98. L. F. Tietze, H. Denzer, X. Holdgrün, and M. Neumann, *Angew. Chem.*, **99**, 1309 (1987).
99. R. P. Houghton and D. J. Lapham, *Synthesis*, No. 6, 451 (1982).
100. Y. Oikawa, K. Sugano, and Y. Yonemitsu, *J. Org. Chem.*, **43**, 2087 (1978).
101. D. G. Desai and R. B. Mane, *Indian J. Chem., B*, **20**, 504 (1981).
102. J. Obaza and F. X. Smith, *Synth. Commun.*, **12**, 19 (1982).
103. T. P. Emel'yanova, G. M. Segal', and I. V. Torgov, *Biorg. Khim.*, **10**, 100 (1984).
104. B. M. Seletskii, G. M. Segal', and I. V. Torgov, *Bioorg. Khim.*, **10**, 104 (1984).
105. S. I. Zav'yalov, O. V. Dorofeeva, and O. K. Taganova, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 7, 1691 (1985).
106. G. Biondi and M. Grugni, *Gazz. Chim. Ital.*, **115**, 11 (1985).
107. D. H. Grayson and M. R. T. Tuite, *J. Chem. Soc., Perkin 1*, No. 12, 2137 (1986).
108. S. V. Ley and P. R. Woodward, *Tetrahedron Lett.*, No. 3, 345 (1987).
109. G. A. Bihlmaier, G. Derflinger, J. Derkosch, and O. E. Polansky, *Monatsh. Chem.*, **98**, 564 (1967).
110. G. Bouillon and K. Schank, *Chem. Ber.*, **113**, 2630 (1980).
111. R. Cassis, R. Tapia, and J. A. Valderrama, *Synth. Commun.*, **15**, 125 (1985).
112. J.-P. Celerier, E. Deloisy, P. Kapron, G. Lhommet, and P. Maitte, *Synthesis*, No. 2, 130 (1981).
113. P. Kapron, G. Lhommet, and P. Maitte, *Tetrahedron Lett.*, **22**, 2255 (1981).
114. Y. Yamamoto, Y. Morita, and K. Minami, *Chem. Pharm. Bull.*, **34**, 1980 (1986).
115. M. Huche and G. Lhommet, *J. Heterocycl. Chem.*, **23**, 701 (1986).
116. J.-P. Celerier, E. Deloisy, G. Lhommet, and P. Maitter, *J. Org. Chem.*, **44**, 3089 (1979).
117. T. V. Stezhko, N. P. Solov'eva, E. F. Kuleshova, and V. G. Granik, *Khim. Geterotsikl. Soedin.*, No. 2, 184 (1988).
118. A. Stephen, *Monatsh. Chem.*, **97**, 695 (1966).
119. H. McNab and L. C. Monahan, *J. Chem. Soc., Perkin 1*, No. 4, 863 (1988).
120. Mitsui Petrochem. Ind., Ltd., Japanese Patent No. 58-46084; *Chem. Abstr.*, **99**, 1755806 (1983).
121. F. Bellini and J. Bagli, US Patent No. 4547516; *Ref. Zh. Khim.*, 12091 (1986).
122. X. Huang and B.-C. Chen, *Synthesis*, No. 11, 967 (1988).
123. Ya. N. Kreitsberga, É. V. Vilyuma, V. Yu. Khodorkovskii, and O. Ya. Neiland, *Khim. Geterotsikl. Soedin.*, No. 12, 1621 (1988).
124. M. Augustin and E. Günther, *Z. Chem.*, **27**, 68 (1987).
125. E. D. Sych, O. V. Moreiko, and G. G. Dyadyusha, *Khim. Geterotsikl. Soedin.*, No. 3, 341 (1977).
126. Yu. P. Kovtun, A. D. Kachkovskii, and N. N. Romanov, *Khim. Geterotsikl. Soedin.*, No. 3, 418 (1988).
127. X. Huang and B.-C. Chen, *Synthesis*, No. 5, 480 (1987).
128. M. Regitz, A. Liedhegener, and D. Stadler, *Ann.*, **713**, 101 (1968).
129. M. Regitz and D. Stadler, *Ann.*, **687**, 214 (1965).
130. J. S. Baum, D. A. Shook, H. M. L. Davies, and H. D. Smith, *Synth. Commun.*, **17**, 1709 (1987).
131. V. B. Kokel and H. G. Viehe, *Angew. Chem., Int. Ed.*, **19**, 716 (1980).
132. H. Balli, R. Lön, V. Müller, H. Rempfler, and A. Sezen-Gezgin, *Helv. Chim. Acta*, **61**, 97 (1978).
133. H. J. Monteiro, *Synth. Commun.*, **17**, 983 (1987).
134. M. Jones, W. Ando, M. E. Hendrick, A. Kulczinski, P. M. Howley, K. F. Hummel, and D. S. Malament, *J. Am. Chem. Soc.*, **94**, 7469 (1972).
135. T. Livinghouse and R. V. Stevens, *J. Am. Chem. Soc.*, **100**, 6479 (1978).
136. K. Schank and R. Blattner, *Chem. Ber.*, **114**, 1958 (1981).
137. K. Schank and C. Schuhknecht, *Chem. Ber.*, **115**, 2000 (1982).
138. K. Schank and C. Schuhknecht, *Chem. Ber.*, **115**, 3032 (1982).
139. K. Schank and C. Lick, *Synthesis*, No. 5, 392 (1983).
140. A. A. Fadda, M. M. Yousif, A. M. El-Housini, and M. S. El-Housini, *Indian J. Text. Res.*, **9**, No. 3, 115 (1984).
141. K. V. Rao, C. S. Venkatachalam, and C. Kalidas, *Indian J. Chem.*, **26A**, 202 (1987).
142. A. Hochrainer, *Monatsh. Chem.*, **97**, 823 (1966).

143. A. Hochrainer and F. Wessely, *Monatsh. Chem.*, **97**, 1 (1966).
144. K. Schank and C. Schuhknecht, *Synthesis*, No. 9, 678 (1978).
145. A. Hochrainer and F. Wessely, *Tetrahedron Lett.*, No. 12, 721 (1965).
146. O. Ya. Neiland and B. Ya. Karele, *Zh. Org. Khim.*, **7**, 1611 (1971).
147. V. A. Nikolaev, Yu. Frenkh, and I. K. Korobitsyna, *Zh. Org. Khim.*, **14**, 1433 (1978).
148. E. Ernstbrunner and D. Lloyd, *Ann.*, **753**, 196 (1971).
149. I. Gosney and D. Lloyd, *Tetrahedron*, **29**, 1697 (1973).
150. A. Suzuki, T. Murafuji, and T. Ogawa, *Chem. Lett.*, No. 5, 847 (1988).
151. S. I. Zav'yalov, T. I. Ezhova, and T. K. Budkova, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 9, 2165 (1981).
152. H. R. Snyder and C. W. Kruse, *J. Am. Chem. Soc.*, **80**, 1942 (1958).
153. R. Bloch, *Synthesis*, No. 2, 140 (1978).
154. L. S. Melvin and B. M. Trost, *J. Am. Chem. Soc.*, **94**, 1790 (1972).
155. B. M. Trost and L. S. Melvin, *J. Am. Chem. Soc.*, **98**, 1204 (1976).
156. B. M. Trost and L. S. Melvin, *Croat. Chem. Acta*, **58**, 601 (1985).
157. K. Pihlaja and I. Ketola, *Finn. Chem. Lett.*, Nos. 4-5, 123 (1976).
158. H. Junek, E. Ziegler, U. Herzog, and H. Kroboth, *Synthesis*, No. 5, 332 (1976).
159. G. Uray, H. Junek, and E. Ziegler, *Monatsh. Chem.*, **108**, 423 (1977).
160. C. D. Hurd and S. Hayao, *J. Am. Chem. Soc.*, **76**, 5563 (1954).
161. A. R. Butler, *J. Chem. Res.*, **50**, 855 (1978).
162. R. F. C. Brown, F. W. Eastwood, and K. J. Harrington, *Austral. J. Chem.*, **27**, 2373 (1974).
163. R. F. C. Brown and G. L. McMullen, *Austral. J. Chem.*, **27**, 2385 (1974).
164. R. F. C. Brown, F. W. Eastwood, K. J. Harrington, and G. L. McMullen, *Austral. J. Chem.*, **27**, 2393 (1974).
165. G. J. Baxter, R. F. C. Brown, and G. L. McMullen, *Austral. J. Chem.*, **27**, 2605 (1974).
166. R. F. C. Brown, F. W. Eastwood, S. T. Lim, and G. L. McMullen, *Austral. J. Chem.*, **29**, 1705 (1976).
167. C. Westrup, G. Gross, H. M. Berstermann, and P. Lorenčak, *J. Org. Chem.*, **50**, 2877 (1985).
168. C. Wentrup, R. Blanch, H. Briehl, and G. Gross, *J. Am. Chem. Soc.*, **110**, 1874 (1988).
169. C. Wentrup and P. Lorenčak, *J. Am. Chem. Soc.*, **110**, 1880 (1988).
170. H. Briehl, A. Lukosch, and C. Wentrup, *J. Org. Chem.*, **49**, 2772 (1984).
171. S. L. Kammula, H. L. Tracer, P. B. Shevlin, and M. Jones, *J. Org. Chem.*, **42**, 2931 (1977).
172. V. A. Nikolaev, N. N. Khimich, and I. K. Korobitsyna, *Khim. Geterotsikl. Soedin.*, No. 3, 321 (1985).
173. N. N. Khimich, V. A. Nikolaev, N. E. Glushkova, and I. K. Korobitsyna, Summaries of Papers Presented at the All-Union Conference on the Chemistry of Carbenes [in Russian], Moscow (1987), p. 74.
174. Yu. P. Kovtun and N. N. Romanov, *Khim. Geterotsikl. Soedin.*, No. 11, 1547 (1988).
175. Yu. A. Slominskii, A. I. Tolmachev, and L. M. Shulezhko, *Ukr. Khim. Zh.*, **41**, 284 (1975).
176. N. P. Vasilenko, F. A. Mikhailenko, and A. G. Maidannik, *Khim. Geterotsikl. Soedin.*, No. 3, 418 (1987).
177. M. Sato, N. Yoneda, N. Katagiri, H. Watanabe, and C. Kaneko, *Synthesis*, No. 8, 672 (1986).
178. T. Kaneko, M. Sato, and S. Katagiri, Japanese Patent Application No. 62-61952; *Ref. Zh. Khim.*, 9O3P (1988).
179. T. Kaneko, M. Sato, and S. Katagiri, Japanese Patent Application No. 62-61953; *Ref. Zh. Khim.*, 9O4P (1988).
180. O. A. Kozhich, G. M. Segal', and I. V. Torgov, *Bioorg. Khim.*, **9**, 1663 (1983).
181. N. Khouki, M. Vaultier, and R. Carrie, *Tetrahedron*, **43**, 1811 (1987).
182. B. M. Seletskii (Seletsky), G. M. Segal' (Segal), and I. V. Torgov, *Croat. Chem. Acta*, **58**, 699 (1985).
183. H.-W. Smidt and M. Klade, *Org. Prep. Proc. Intern.*, **20**, 184 (1988).
184. R. I. Sims, S. A. Tischler, and L. Weiler, *Tetrahedron Lett.*, No. 3, 253 (1983).
185. K. Mohri, Y. Oikawa, K. Hirao, and O. Yonemitsu, *Chem. Pharm. Bull.*, **30**, 3097 (1982).
186. P. Jonin, B. Castro, I. Poncet, and D. Nisato, *Peptides, 1986: Proceedings of the 19th European Peptide Symposium (Berlin)*, New York (1987), p. 659; *Ref. Zh. Khim.*, 20E159 (1987).
187. E. K. Novitskaya, N. V. Smirnova, and A. P. Skoldinov, *Zh. Org. Khim.*, **10**, 131 (1974).
188. E. K. Novitskaya, N. V. Smirnova, and A. P. Skoldinov, *Zh. Org. Khim.*, **12**, 576 (1976).
189. S. I. Zav'yalov and N. E. Knyaz'kova, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 1, 215 (1983).
190. S. I. Zav'yalov and N. E. Kravchenko, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 2, 454 (1984).
191. S. I. Zav'yalov and A. G. Zavozin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 8, 1796 (1987).
192. S. I. Zav'yalov, G. I. Ezhova, and N. E. Kravchenko, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 3, 667 (1987).
193. E. Winkert, E. L. Michelotti, and J. S. Pyrek, *J. Org. Chem.*, **49**, 1832 (1984).
194. D. Bacos, J. J. Basselier, J. P. Celerier, C. Lange, E. Marx, G. Lhommet, P. Escoubas, M. Lemaire, and J. L. Clement, *Tetrahedron Lett.*, No. 25, 3061 (1988).

195. J. P. Celerier, G. Lhommet, and P. Maitte, *Tetrahedron Lett.*, No. 10, 963 (1981).
196. P. Lorenčak, J. C. Pommelet, J. Chuche, and C. Wentrup, *Chem. Commun.*, No. 5, 369 (1986).
197. H. Dhimane, J. C. Pommelet, J. Chuche, G. Lhommet, M. G. Richaud, and M. Haddad, *Tetrahedron Lett.*, No. 7, 833 (1985).
198. G. L. Hickson, E. M. Keith, J. C. Martin, H. McNab, L. C. Monahan, and M. D. Walkinshaw, *J. Chem. Soc., Perkin 1*, No. 8, 1465 (1986).
199. H. McNab and L. C. Monahan, *Chem. Commun.*, No. 3, 138 (1987).
200. H. Dhimane, J. C. Pommelet, J. Chuche, G. Lhommet, and M. Haddad, *Tetrahedron Lett.*, No. 8, 885 (1987).
201. H. McNab, *J. Chem. Soc., Perkin 1*, No. 3, 653 (1987).
202. D. W. M. Benzies, P. M. Fresneda, R. A. Jones, and H. McNab, *J. Chem. Soc., Perkin 1*, No. 9, 1651 (1986).
203. B. C. Chen, X. Huang, and I. Wang, *Synthesis*, No. 5, 482 (1987).
204. O. H. Abdirizak, I. Hermecz, and Z. Meszaros, *Magyar. Kem. Fol.*, **84**, 494 (1978).
205. G. Horvath, I. Hermecz, A. Horvath, M. Pongor-Csakvari, and L. Pusztay, *J. Heterocycl. Chem.*, **22**, 481 (1985).
206. J. Farras, E. Fos, R. Ramos, and J. Vilarrosa, *J. Org. Chem.*, **53**, 887 (1988).
207. B. C. Chen and X. Huang, *Synth. Commun.*, **17**, 1519 (1987).
208. K. Mohri, Y. Oikawa, K. Hirao, and O. Yonemitsu, *Heterocycles*, **19**, 521 (1982).
209. I. Iwataki, S. Makizawa, and K. Saito, Japanese Patent Application No. 61-19808; *Ref. Zh. Khim.*, 6O73P (1988).
210. E. Campaigne, P. Raval, and J. C. Beckman, *J. Heterocycl. Chem.*, **15**, 1261 (1978).
211. H. Junek, E. Ziegler, and U. Herzog, *Monatsh. Chem.*, **102**, 1096 (1971).
212. E. Ziegler, H. Junek, and U. Herzog, *Monatsh. Chem.*, **102**, 1626 (1971).
213. J. J. Lyons and H. McNab, *J. Chem. Soc., Perkin 1*, No. 3, 649 (1987).
214. V. Armstrong, O. Soto, J. A. Valderrama, and R. Tapia, *Synth. Commun.*, **18**, 717 (1988).
215. E. A. Shirokova, G. M. Segal', and I. V. Torgov, *Bioorg. Khim.*, **14**, 236 (1988).
216. Mitsui Petrochem. Ind., Ltd., Japanese Patent No. 56-99480; *Chem. Abstr.*, **95**, 220080 (1981).
217. Mitsui Petrochem. Ind., Ltd., Japanese Patent No. 58-85887; *Chem. Abstr.*, **99**, 139962 (1983).
218. Mitsui Petrochem. Ind., Ltd., Japanese Patent No. 58-46085; *Chem. Abstr.*, **99**, 175802 (1983).
219. Ya. N. Kreitsberga and O. Ya. Neiland, *Khim. Geterotsikl. Soedin.*, No. 7, 898 (1989).
220. P. Margaretha, *Tetrahedron Lett.*, No. 17, 1449 (1970).
221. P. Margaretha, *Angew. Chem.*, **84**, 308 (1972).
222. K. Hobel and P. Margaretha, *Helv. Chim. Acta*, **70**, 995 (1987).
223. V. Nair, *Synth. Commun.*, **17**, 723 (1987).
224. O. Ya. Neiland, I. É. Lielbriedis, and Ya. A. Strods, USSR Author's Certificate No. 507570; *Byull. Izobret.*, No. 11, 72 (1976).
225. Ya. A. Strods, I. É. Lielbriedis, and O. Ya. Neiland, *Khim. Geterotsikl. Soedin.*, No. 7, 977 (1977).
226. Ya. A. Strods, R. B. Kampare, I. É. Lielbriedis, and O. Ya. Neiland, *Khim. Geterotsikl. Soedin.*, No. 7, 973 (1977).
227. Ya. A. Strods, "Polynuclear heterocycles based on cyclic β-dicarbonyl compounds and azomethines," Author's Master's Dissertation Abstract, Riga (1977).
228. I. É. Lielbriedis and G. Ya. Dubur, Summaries of Papers Presented at the 5th All-Union Conference on the Chemistry of Dicarbonyl Compounds [in Russian], Riga (1981), p. 131.
229. M. F. Strozhev, Ya. A. Miller, and I. É. Lielbriedis, Summaries of Papers Presented at the 6th All-Union Conference on the Chemistry of Dicarbonyl Compounds [in Russian], Riga (1986), p. 182.
230. M. F. Strozhev, I. É. Lielbriedis, and O. Ya. Neiland, *Khim. Geterotsikl. Soedin.*, No. 6, 786 (1990).
231. M. F. Strozhev and I. É. Lielbriedis, *Khim. Geterotsikl. Soedin.*, No. 7, 947 (1990).
232. I. É. Lielbriedis, R. B. Kampare, and G. Ya. Dubur, *Latv. Khim. Zh.*, No. 2, 212 (1990).
233. Y. Yamamoto, Y. Watanabe, and S. Ohnishi, *Chem. Pharm. Bull.*, **35**, 1860 (1987).
234. Y. Yamamoto and Y. Watanabe, *Chem. Pharm. Bull.*, **35**, 1871 (1987).
235. T. Kaneko, M. Sato, and H. Ogasawara, Japanese Patent Application No. 61-17580; *Ref. Zh. Khim.*, 1O75P (1987).