35. A.D.Ketley, J.Polymer Sci., B2, 827 (1964).
36. J.P.Kennedy, C.A.Cohen, and W.Naegele, J.Polymer Sci., B2, 1159 (1964).
37. A.D.Ketley and R.J.Ehrig, J.Polymer Sci., A2, 4461 (1964).
38. J.P.Kennedy, J.J.Elliott, and W.Naegele, J.Polymer Sci., A2, 5029 (1964).
39. R.L.Meier, J.Chem.Soc., 3656 (1950).
40. J.P.Kennedy, J.J.Elliott, and B.E.Hudson, Makromol. Chem., 79, 109 (1964).
41. B.A.Krentsel', L.G.Sidorova, M.V.Shishkina, M.M.Kusakov, F.V.Korenevskaya, and V.V.Shchekin, Neftekhimiya, 2, 705 (1962).
42. V.V.Korshak, V.A.Sergeev, V.K.Shitikov, and P.Sh.Burenko, Vysokomol.Soed., 5, 1597 (1963).

Institute of Petrochemical Synthesis,
Academy of Sciences of the USSR,
Moscow

U.D.C. 547.29:547.39

β-ELIMINATION IN THE β-SUBSTITUTED PROPIONIC ACID SERIES

P. F. Butskus and G. I. Denis

CONTENTS

1. β-Substituted propionic acids 839
2. Esters of β-substituted propionic acids 840
3. Amides of β-substituted propionic acids 841
4. Nitriles of β-substituted propionic acids 841
5. Alkylations with the aid of β-substituted propionic acids and their derivatives 843
6. Mechanism of β-eliminations 844

It has long been known that β-substituted propionic acids and their derivatives have a tendency to undergo β-elimination:

$$ACH_2CH_2X \rightarrow AH + CH_2{=}CHX$$

where A = halogen, HO, RO, RS, RSO_2, H_2N, RNH, or $(R)_2N$, etc., and X = COOH, COOR, $CONH_2$, or CN.

These reactions are of both theoretical and practical interest. However, up to recently information on this subject had not been summarised. The present review covers factual information on the β-elimination of β-substituted propionic acids, their esters, amides, and nitriles.

1. β-SUBSTITUTED PROPIONIC ACIDS

β-Halogenopropionic acids are converted into acrylic acid by distillation[1]; by heating under pressure[2] or under vacuum[3]; by heating in the presence of activated charcoal[3] or aluminium oxide[4]; by boiling with water[5] or with aqueous solutions of alkalis[5-11]; and by the action of sodium carbonate[11], lead oxide[11-13] or carbonate[12], alkali metal alkoxides[6], sodium acrylate[14], or diethylaniline[9,10]. Several attempts to synthesise β-alanine and its methyl ester from β-bromopropionic acid led to the preparation of acrylic acid[15]. When β-iodopropionic acid is treated with an excess of silver oxide, a polymer of acrylic acid is formed[16-18].

In 1862 Beilstein noted[12] that, when salts of β-hydroxypropionic acid are heated to 200–250°, salts of acrylic and diacrylic acid are formed. Later this reaction was also observed by Wislicenus[13,19]. Acrylic acid is formed when β-hydroxypropionic acid is heated to boiling, or when the acid itself, or its salts, is distilled with sulphuric acid[12,13,19-22]. When β-hydroxypropionic acid is evaporated with hydrochloric acid, a polymer of acrylic acid is formed[16-18]. Acrylic acid is obtained from a mixture of β-hydroxypropionic acid, diacrylic acid, and acrylic acid polymer[23], and also from 2-hydroxypropiononitrile[24-28].

At 190–225°, and in the presence of alkali or alkaline-earth salts of the same acids, β-alkoxypropionic acids (containing C_1 to C_{17} alkoxy-groups) give acrylic acid in good yield[29]. When β-ethoxypropionic acid is heated in the presence of *p*-toluenesulphonic acid and hydroquinone, a mixture of acrylic acid and its ethyl ester is formed[30,31]. According to the patent literature, 2-dicarboxydiethyl ether gives acrylic acid when it is treated in the gas phase at 150–185° with activated charcoal soaked in phosphoric acid[32]. In an alkaline medium, β-carboxyethyl esters of monohydric and dihydric phenols give decarboxyethylation products[33-38]. When heated for a short time to 180–190° in the presence of hydroquinone, β-acetoxypropionic acid decomposes according to the following reaction[39]:

$$CH_3COOCH_2CH_2COOH \rightarrow CH_3COOH + CH_2{=}CHCOOH.$$

The yield of acrylic acid is 77%. The removal of the β-carboxyethyl group in esters of phosphoric acid[40-43] has been studied. Methods of synthesising α- and β-substituted acrylic acids from α- and β-substituted β-hydroxypropionic acids and their esters at the hydroxy-group have been developed[44-59].

When 2-carboxyethyl aryl sulphones are boiled with 10% sodium hydroxide, cleavage occurs according to the following scheme[60]:

$$ArSO_2CH_2CH_2COOH \rightarrow ArSO_2H + CH_2{=}CHCOOH.$$

Mulder[61] observed that β-aminopropionic acid decomposes into acrylic acid and ammonia when it is heated to about the melting point. β-Diethylaminopropionic acid decomposes in the same way (160°):[62]

$$(C_2H_5)_2NCH_2CH_2COOH \rightarrow (C_2H_5)_2NH + CH_2{=}CHCOOH.$$

When heated to its melting point, the betaine of β-trimethylaminopropionic acid gives ammonium acrylate[63]. The decarboxyethylation of *N*-(2-carboxyethyl)-α-amino-acids has been studied[34]. Heating of 2,2'-dicarboxydiethylamine with phthalic anhydride leads to the formation of *N*-(2-carboxyethyl)phthalimide and acrylic acid in quantitative yield[64].

Attempts to cyclise *N*-(2-carboxyethyl)-*N*-acycl-*p*-anisidines to the corresponding quinolones led to decarboxyethylation[65]. When *N*-(2-naphthyl)-β-aminopropionic acid is heated for 2–3 min at 220°, 1-naphthylamine and acrylic acid are formed[66].

According to Rodionov and coworkers [67], when β-(2-naphthyl)-β-(3-phenylureido)propionic acid is heated with dilute hydrochloric acid, instead of cyclising to the corresponding dihydrouracil, it sometimes forms β-(2-naphthyl)acrylic acid. An attempt to obtain 1-methyl-4-naphthyl-2-thiodihydrouracil from β-(methylamino)-β-(2-naphthyl)propionic acid by heating the latter with potassium thiocyanate in the presence of hydrochloric acid was not successful; β-(2-naphthyl)acrylic acid was the only product isolated from the reaction mixture. In some instances, the cyclisation of β-alkyl- and β-aryl-β-guanidinopropionic acids leads to the elimination of guanidine and the formation of an αβ-unsaturated acid [67,68]. An attempt has been made to synthesise β-(2-thienyl)-β-alanine by the acid hydrolysis of 6-(2-thienyl)dihydrouracil, but β-(2-thienyl)acrylic acid was obtained instead of the amino-acid [69].

When the products of *NN*-dicarboxyethylation of benzenesulphonamide [70], *p*-toluenesulphonamide [71], and sulphanilamide [72] are heated with a 10% aqueous solution of potassium hydroxide, one of the 2-carboxyethyl groups is removed and *N*-monocarboxyethyl derivatives of aryl sulphonamides are formed in 60 and 86% yield:

$$ArSO_2N(CH_2CH_2COOH)_2 \rightarrow ArSO_2NHCH_2CH_2COOH + CH_2{=}CHCOOH.$$

Quantitative elimination of the 2-carboxyethyl group is achieved by treating an alkaline solution of β-indol-1-ylpropionic acid with water vapour superheated to 250–270°. [73] Later this process was observed under analogous conditions by other workers [74]. If water vapour superheated to 280° is passed for 30–40 min through a solution of 1,3-di-(2-carboxyethyl)indole in 50% potassium hydroxide, β-indol-3-ylpropionic acid is formed in 82% yield [75]. 1,3-Di-(2-carboxyethyl)-2-methylindole behaves in the same way under these conditions [75], the yield of its *N*-decarboxyethylated product being 80%. From the foregoing it is clear that the 2-carboxyethyl group can be eliminated if it occurs at the 1-position in indole, but it is stable if it occurs at the 3-position [73–78].

When distilled under reduced pressure, β-indazolylpropionic acid decomposes with the formation of indazole and acrylic acid [79]. Efros and Porai-Koshits obtained benzimidazole by heating β-carboxyethylated benzimidazole with aqueous solutions of acids or alkalis [80]. They were not, however, able to remove the 2-carboxyethyl group from carboxyethylated 2-methylbenzimidazole. When derivatives of pyridine containing a 2-carboxyethyl group at the ring-nitrogen atom are heated above the melting point, or treated with aqueous sodium hydroxide solution, they decompose with the formation of pyridine, 2- and 3-hydroxy-, 2-amino- and 4-methyl-2-amino-pyridines, and also acrylic acid [35,81–83].

Pyrolysis of, or the action of concentrated aqueous sodium hydroxide on, *N*-(2-carboxyethyl)pyrid-2-one gives the decarboxyethylation product and acrylic acid [84]. Attempts to convert some substituted *N*-(2-carboxyethyl)--4-keto-1,2,3,4-tetrahydroquinolines into the corresponding *N*-ethyl-4-keto-1,2,3,4-tetrahydroquinolines have not been successful; decarboxyethylation occurred under all experimental conditions instead of the expected decarboxylation [85].

There are also other references to decarboxyethylation [35,86–93], and to the removal of one aryl group from ββββ-triaryl-substituted propionic acids [94–96]. The bond of the 2-carboxyethyl group with the silicon atom is stronger than the bond of other alkyl groups with this atom [97–100].

2. ESTERS OF β-SUBSTITUTED PROPIONIC ACIDS

Esters of acrylic acid are formed from esters of β-halogenopropionic acids by distilling the latter with concentrated sulphuric [101,102] or phosphoric acid [101]; by heating them with aqueous [103] or alcoholic [103,104] solutions of alkali; by heating them with anhydrous sodium carbonate [102], diethylaniline [8,9], quinoline [105,106], activated charcoal [107], zinc chloride [3,101,108], barium phosphate [101,107], or aluminium oxide [4]. Acrylates are formed from the methyl and ethyl esters of β-hydroxypropionic acid when these are distilled over alkali acetates [109], or heated in the gas phase over silica gel [110], or silicon dioxide saturated with concentrated sulphuric acid [111]. They can also be obtained in yields of up to 90% from the amide [112] and the nitrile [24,25,112–119] of β-hydroxypropionic acid.

Methyl acrylate is obtained in 50% yield from methyl β-methoxypropionate by passing the latter into concentrated sulphuric acid containing an inhibitor at 200°. [120] A similar process proceeds in the gas phase over catalysts [30,121–125]. Ethyl acrylate is obtained from ethyl β-ethoxypropionate [121,126–128]. Acrylates are formed from the esters of oxy-3,3′-dipropionic acid by the action of dilute sulphuric [129] or phosphoric [32] acid, or anhydrous zinc chloride [129] at an elevated temperature. When heated with sodium hydroxide [33], or 2-amino-, [35], or 4-methyl-2-aminopyridines [81], esters of β-aryloxy propionic acid give the corresponding monohydric and dihydric phenols. On being heated with anhydrous potassium carbonate at 100°, ethyl β-hydroxypropionate having the hydroxyl group esterified with *p*-toluenesulphonic acid decomposes almost quantitatively according to the following scheme [130]:

$$p\text{-}CH_3C_6H_4SO_2OCH_2CH_2COOC_2H_5 \rightarrow p\text{-}CH_3C_6H_4SO_2OH + CH_2{=}CHCOOC_2H_5.$$

Acrylates are also obtained from esters of β-acyloxypropionic acids [131–133].

The action of picric acid on ethyl β-hydroxy-β-(*p*-aminophenyl)propionate gives the picrate of *p*-aminocinnamic acid [134].

When esters of 2-carboxyethyl aryl sulphones are boiled with a 10% aqueous solution of sodium hydroxide, arylsulphinic acids are formed [60]:

$$ArSO_2CH_2CH_2COOR \rightarrow ArSO_2H.$$

It has been shown that a state of mobile equilibrium is established when ethyl acrylate reacts with ammonia [135]:

$$CH_2{=}CHCOOC_2H_5 \underset{-NH_3}{\overset{+NH_3}{\rightleftharpoons}} NH_2CH_2CH_2COOC_2H_5 \underset{+NH_3}{\overset{-NH_3}{\rightleftharpoons}}$$

$$\underset{+NH_3}{\overset{-NH_3}{\rightleftharpoons}} NH(CH_2CH_2COOC_2H_5)_2 \underset{+NH_3}{\overset{-NH_3}{\rightleftharpoons}} N(CH_2CH_2COOC_2H_5)_3.$$

Other investigators have also observed that, when ammonia and amines react with acrylates, a varied mixture of compounds is obtained [136,137]. Dry distillation of the ethyl ester of β-alanine leads to the formation of ethyl acrylate [138]. When ethyl β-(diethylamino)propionate is distilled, it slowly decomposes into diethylamine and ethyl acrylate [139]; its salts decompose more readily; for example, the hydriodide begins to decompose even at 100°, and at 165° this process is instantaneous [62].

When phthalic anhydride is heated with di-[2-(ethoxycarbonyl)ethyl]amine, *N*-[2-(ethoxycarbonyl)ethyl]phthalimide is formed in 75% yield [64]. Ethyl acrylate is formed by heating tri(ethoxycarbonyl)triethylamine [138,140,141], *N*-benzyl- and *N*-benzoyl-di(ethoxycarbonyl)diethylamines [140,141], or by treating ethyl (1-piperidyl)propionate with cyanogen bromide by Braun's method [142]. Oxidation of the addition product of ethyl acrylate and pyrazole gives pyrazole itself [143].

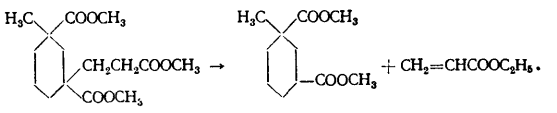
The preparation of an ester of β-(methylamino)-β-phenylpropionic acid is accompanied by the formation of the ester of cinnamic acid [144].

The decomposition products obtained by heating methyl β-(dimethylamino)propionate at 180–185° include acrylic acid. When the methiodide of this ester is heated with alkalis, it decomposes quantitatively into acrylic acid and trimethylamine [63]. When diesters of *NN*-di-(2-carboxyethyl)aryl sulphonamides are heated with 10% aqueous potassium hydroxide, they react according to the following scheme [70-62,92,93]:

$$ArSO_2N(CH_2CH_2COOR)_2 \rightarrow ArSO_2NHCH_2CH_2COOH.$$

The decomposition products obtained in the esterification of *NN*-di-(2-cyanoethyl)-α-amino-acids with hydrogen chloride in ethanol contain *N*-monocarboxyethyl derivatives and ethyl acrylate [145].

Other papers reporting the formation of acrylates from esters of β-substituted propionic acids have also been published [42,65,146-149]. In some reactions a carbon–carbon bond is broken [150,151], for example:



3. AMIDES OF β-SUBSTITUTED PROPIONIC ACIDS

Acrylamide is obtained in yields up to 80–96% from the amides of β-chloro-, [152] β-hydroxy-, [152] β-alkoxy-, [152,153] and β-(dialkylamino)-propionic acids [152,154]; it is also obtained by the following reaction [152,155]:

$$NH_4SO_3OCH_2CH_2CONH_2 \rightarrow CH_2=CHCONH_2 + NH_4HSO_4.$$

The $-CH_2CH_2CONH_2$ group, when located on the nitrogen atom of the pyrrole ring, is also eliminated under certain conditions [156]. Boiling of amides of β-aryloxypropionic acids [33] and amides of 2-carboxyethyl aryl sulphones [60] in aqueous sodium hydroxide gives the corresponding phenols and arylsulphinic acids:

$$ArOCH_2CH_2CONH_2 \rightarrow ArOH,$$
$$ArSO_2CH_2CH_2CONH_2 \rightarrow ArSO_2H.$$

The removal of the 2-carbamoylethyl group from esters of phosphoric acid has been studied [40,41,43].

NN-Disubstituted acrylamides are obtained from the corresponding amino-acid amides (but not anilides) by heating the latter to 180–220°, [136,137,154] for example:

$$(C_2H_5)_2NCH_2CH_2CON(C_2H_5)_2 \rightarrow (C_2H_5)_2NH + CH_2=CHCON(C_2H_5)_2.$$

The piperidide of β-piperidylpropionic acid cannot be separated, as it spontaneously decomposes with the formation of the piperidide of acrylic acid [136]:

$$2C_5H_{11}N + CH_2=CHCOOCH_3 \rightarrow C_5H_{10}N-CH_2CH_2CO-NC_5H_{10} \rightarrow$$
$$\rightarrow C_5H_{11}N + CH_2=CHCONC_5H_{10}.$$

It is noteworthy that when the diamides of *NN*-di-(2-carboxyethyl)aryl sulphonamides are heated with 10% aqueous sodium hydroxide solution, the corresponding monoacids are obtained in 60–76% yield, and not the expected diacids [70-72,92,93]:

$$ArSO_2N(CH_2CH_2CONH_2)_2 \rightarrow ArSO_2NHCH_2CH_2COOH.$$

When the diamide of *NN*-di-(2-carboxyethyl)benzenesulphonamide is heated with a 10% aqueous solutions of ammonia, *N*-(2-carboxyethyl)benzenesulphonamide is obtained in 70% yield; under these conditions, the *NN*-dicarboxyethyl derivative remains unchanged [70].

As Rodionov and Kiseleva [157] have shown, when *N*-benzoyl-β-phenyl-β-alanine is treated with acetic anhydride, cyclisation to the tetrahydropyrimidine derivative is accompanied by the formation of considerable amounts of benzamide and cinnamide:

$$C_6H_5CH(NHCOC_6H_5)CH_2CONH_2 \rightarrow C_6H_5CH=CHCONH_2 + C_6H_5CONH_2.$$

Cinnamic acid has been separated from the reaction mixture obtained by the action of acetic anhydride on the amide of *N*-ethoxycarbonyl-β-phenyl-β-alanine. Rodionov and Yavorskaya [144] have shown that, when β-phenyl-β-(*N*-benzoyl-*N*-methylamino)propionamide is heated with oxalic acid, the main reactior product is cinnamide. When *N* benzoyl-β-piperonyl-β-alanine is heated with thionyl chloride, followed by treatment with ammonia, β-piperonylacrylic acid is formed [158]. Under the same conditions, *N*-benzoyl-β-(1-naphthyl)-β-alanine gives β-(1-naphthyl)acrylamide [159]. Cyclisation of the amides of *N*-methoxycarbonyl-, *N*-acetyl-, and *N*-benzoyl-β-piperonyl-β-alanines gives β-piperonylacrylic acid in addition to the corresponding tetrahydropyrimidines [158]. The dehydrobromination of amides of β-substituted propionic acids has also been studied [160-162].

The pyrolysis of 2-carbamoylethyl hydrogen sulphate [155] and of β-alkoxypropionamides [163,164], leading respectively to the formation of acrylic acid and its nitrile, have been reported. The reaction of 2-carbamoylethyl hydrogen sulphate with alcohols gives the corresponding acrylates [165].

4. NITRILES OF β-SUBSTITUTED PROPIONIC ACIDS

Acrylonitrile is formed in 75–80% yield when β-halogenopropiononitriles are treated with ammonia [166], potassium carbonate [167], alkali hydroxides [168-171], sodium cyanide [172], tertiary aliphatic [166,168-171] and primary aromatic [166,173] amines, and also some heterocyclic bases [166,174]. One of the main methods of preparing acrylonitrile is the dehydration of β-hydroxypropiononitrile [175].

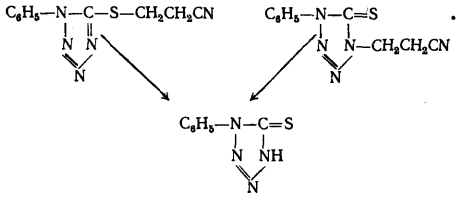
Decyanoethylation of β-alkoxypropiononitriles occurs when these compounds are subjected to reduction [176-180], hydrolysis [181-183], hydration [184] or pyrolysis [185], or when they are treated with organomagnesium compounds [186]. The same reaction occurs on reduction [187,188], hydrolysis [189], and pyrolysis [185] of bis-(2-cyanoethyl) ether, when it is heated in the presence of sodium formate [190] or with an aqueous solution of ammonia [183]. An attempt to cyclise the dicyanoethylation product of decan-1,10-diol to the corresponding iminonitrile by Ziegler's method was not successful, decan-1,10-diol being formed again in 90% yield [191]. When cleavage of the bond between the 2-cyanoethyl group and the oxygen atom occurred, the following were observed amongst the products of cyanoethylation: diethylene glycols [192]; poly(vinyl alcohol) [193,194]; some monosaccharides [195] and polysaccharides [196,197]; alicyclic [198], aromatic [178,199], and heterocyclic [200] alcohols; and phenols [35,36,81,176,185,201-207]. The product of the interaction of acrylonitrile with benzaldehyde in an alkaline medium eliminates acrylonitrile [208]. Other instances are also known of the breaking of the bond of the 2-cyanoethyl group with an oxygen atom in acid [185,209] and alkaline [175,187,209-214] media. Alkaline agents act as catalysts accelerating both the direct cyanoethylation of alcohols and the reverse reaction [215].

In the preparation of acrylonitrile from 2-hydroxypropiononitrile, the latter is sometimes esterified and the acrylonitrile is eliminated catalytically or thermally [175,216-222]. For example:

$$CH_3COOCH_2CH_2CN \rightarrow CH_3COOH + CH_2{=}CHCN,$$
$$p\text{-}CH_3C_6H_4SO_2OCH_2CH_2CN \rightarrow p\text{-}CH_3C_6H_4SO_2OH + CH_2{=}CHCN.$$

The removal of the 2-cyanoethyl group from phosphoric acid esters has been studied [40-43,223-245].

Decyanoethylation is observed when β-alkylthiopropiononitriles are hydrolysed by alkali [246], or when they are treated with organomagnesium compounds [247]; decyanoethylation also occurs when bis-2-cyanoethyl sulphide is reduced by Vyshnegradskii's method [187]. Sulphones containing a cyanoethyl group are unstable in an alkaline medium and are readily decomposed by dilute alkali at room temperature to give acrylonitrile [60,248]. In the cyanoethylation of 1-phenyltetrazoline-5-thione, facile decyanoethylation of *S*- and *N*-isomers was observed [249]:



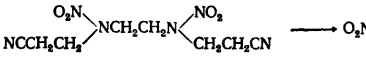
Many investigators [188,211,250-257] have studied the mobile equilibrium in the cyanoethylation of ammonia with acrylonitrile and have established the proportions of products of mono-, di-, and tri-cyanoethylation in relation to the reaction procedure and the proportions of the initial compounds. The products of this reaction undergo decyanoethylation on storage [250], when heated [211,252,258], on catalytic reduction [188,254], and when treated with ammonia [252,255,259]. Di-(2-cyanoethyl)-amine gives *N*-(2-cyanoethyl)acetamide [253] with acetic anhydride; with phthalic anhydride at 200° it gives cyanoethylated phthalimide [64]; and with perylene-3,4,9,10-tetracarboxylic acid at 230° it gives the dicyanoethylated di-imide of this acid [260,261]. When di-(2-cyanoethyl)amine reacts with chlorotriphenylmethane, a molecule of acrylonitrile is eliminated [262].

As is well known, hydrazine hydrate reacts vigorously with acrylonitrile, adding four molecules of the latter. However, when this product of the tetracyanoethylation of hydrazine is distilled under a high vacuum, it loses two molecules of acrylonitrile and is converted into a mixture of isomers of dicyanoethylated hydrazine [211]. Dibenzoyl--(2-cyanoethyl)hydrazine is formed by the action of benzoyl chloride on *unsym*-di-(2-cyanoethyl)hydrazine [263]. Kost and coworkers observed that, when (2-cyanoethyl)hydrazine is heated with mesityl oxide, 3,5,5-trimethylpyrazoline and acrylonitrile are formed [264]. It is known that *N*-cyanoethylated hydrazones undergo decyanoethylation in an alkaline medium [265], as do dicyanoethylated guanidines on cyclisation [266].

The decyanoethylation of some *N*-substituted β-aminopropiononitriles on distillation indicates the weakness of the bond between the cyanoethyl group and the nitrogen atom [250,254,267-270]. When the product of cyanoethylation of *N*-methyldodecylamine is heated for several hours at 250–275°, it decomposes almost quantitatively into the initial amine and acrylonitrile [271,272]:

$$CH_3(CH_2)_{11}N(CH_3)CH_2CH_2CN \rightarrow CH_3(CH_2)_{11}NHCH_3 + CH_2{=}CHCN.$$

When dicyanoethylated ethylenedinitramine is heated with aqueous alkali, the initial nitramine is formed in 82% yield [273]:



Decyanoethylation is observed when some β-alkylaminopropiononitriles are heated in the presence of water; it is also brought about by catalytic hydrogenation [275], by hydrolysis in an acid medium [276], and by other reactions [277,278].

On being heated, β-(diethylamino)propiononitrile decomposes into diethylammonium chloride and acrylonitrile [279,280]. Quaternary ammonium salts obtained from β-(dialkylamino)-propiononitriles smoothly eliminate acrylonitrile on pyrolysis [168,281]; in the presence of alkalis the reaction is rapid even at 100°. The yields of acrylonitrile and amines are as high as 90–95%. When the product of cyanoethylation of 2-amino-2-methylpropan-1-ol is alkylated with ethyl iodide, acrylonitrile separates [282]:

$$HOCH_2C(CH_3)_2NHCH_2CH_2CN + C_2H_5I \rightarrow HOCH_2C(CH_3)_2NHC_2H_5HI + CH_2{=}CHCN.$$

Methylation of β-(benzylamino)propiononitrile with a mixture of formaldehyde and formic acid gives *NN*-dimethylbenzylamine in 38% yield [283]:

$$C_6H_5CH_2NHCH_2CH_2CN + 2CH_2O + 2HCOOH \rightarrow$$
$$\rightarrow C_6H_5CH_2N(CH_3)_2 + CH_2{=}CHCN + 2CO_2 + 2H_2O.$$

Under the same conditions, the products of monocyanoethylation of tetramethylenediamine and hexamethylenediamine are converted into the corresponding tetramethyl derivatives of the diamines [284].

When the products of dicyanoethylation of a number of carboxylic acid amides are heated, especially in the presence of basic agents, *N*-monocyanoethylated amides are formed [35,64,70-72,81,92,93,250,285-293]:

$$RCON(CH_2CH_2CN)_2 \rightarrow RCONHCH_2CH_2CN + CH_2{=}CHCN,$$
$$RSO_2N(CH_2CH_2CN)_2 \rightarrow RSO_2NHCH_2CH_2CN + CH_2{=}CHCN.$$

Alkaline hydrolysis of *NN*-dicyanoethylated sulphonamides gives the corresponding *N*-monocarboxyethylated derivatives in yields up to 90%. [70-72,92,93,285,294-296]

$$RSO_2N(CH_2CH_2CN)_2 \rightarrow RSO_2NHCH_2CH_2COOH.$$

Under these conditions arylsulphonamides containing aryl and cyanoethyl groups at the nitrogen atom lose the cyanoethyl group [297]. Decyanoethylation may occur in the synthesis of *N*-cyanoethylated polyamides [298].

Recently, great attention has been paid to the decyanoethylation of the products of *N*-mono- and *NN*-di-cyanoethylation of amino-acids and their derivatives [35,81,145,205-207,250,278,299-313]. When two cyanoethyl groups are attached to a nitrogen atom, the first is removed more readily, and under milder conditions, than the second. By a suitable choice of reaction conditions, either one or two groups can be removed from the dicyanoethylation products. Some reactions of *N*-mono- and *NN*-di-cyanoethylated α-amino-acids, such as hydrolysis and cyclisation, are accompanied by decyanoethylation.

Some investigators [314] consider that the cyanoethyl group may be eliminated from dicyanoethylated aromatic amines, when these are cyclised. Decyanoethylation products have also been observed after the decomposition of β-arylaminopropiononitriles in acid or alkaline media [167,250,315-319].

Some derivatives of *N*-(2-cyanoethyl)pyrrole lose the cyanoethyl group when they are heated with sodium ethylate in absolute ethanol at 150°. When β-(5-ethoxycarbonyl-3--formyl-2,4-dimethylpyrrol-1-yl)propiononitrile is reduced by Kishner's method, 2,3,4-trimethylpyrrole is formed[156].

When heated in a vacuum to 250°, 1,3-di-(2-cyanoethyl)-indole eliminates acrylonitrile, giving a quantitative yield of 3-(2-cyanoethyl)indole, which is not decomposed by distillation in vacuum[73]. When heated with a concentrated solution of potassium hydroxide, *N*-(2-cyanoethyl)indole is hydrolysed to the corresponding acid; the decyanoethylation product, indole, is also formed in 10% yield. Under similar conditions, some derivatives of *N*-(2-cyanoethyl)-indole also give the corresponding indole derivatives[74,320]. Under certain conditions *N*-(2-cyanoethyl)indole can form indoline and acrylonitrile[321,322]. Heating of cyanoethylated benzimidazole with aqueous solutions of acids or alkalis leads to benzimidazole[80], and when 5-amino-1-(2-cyanoethyl)tetrazole is heated with aqueous barium hydroxide, 5-aminotetrazole is formed[323]. Pyrolysis of 1-(2-cyanoethyl)-6-methylpyrid-2-one gives 6-methylpyrid-2-one and acrylonitrile[324].

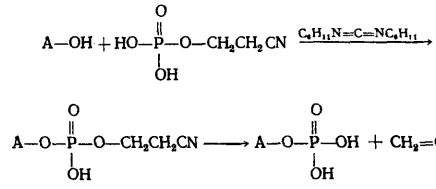
The cyanoethylation products of the following compounds have been decyanoethylated: pyrrolidine[325], derivatives of pyrazole[326,327], piperidine[251,278,325], morpholine[254], anabasine[328], phenothiazine[329,330], its benzo-derivative[331] and oxidation product[332], phenoxazine[331], phenoselenazine[333], tetrahydroharmine[334,335], 2-hydroxyquinoxaline[366], isocyanuric acid[337], dihydrobenzthiopyranoindole[339], and pteridine derivatives[339]. Attempts to remove the cyanoethyl group from 1-(2-cyanoethyl)-1,2,3,4-tetrahydro-4-ketoquinoline by means of bases have been unsuccessful. However, when this compound is treated with a mixture of concentrated hydrochloric acid and an excess of acetic anhydride, 1-acetyl-1,2,3,4-tetrahydro-4-ketoquinoline is obtained[314].

The bond between the 2-cyanoethyl group and the phosphorus atom has been studied in the mono-, di-, and tri-cyanoethylation products of phosphine, and also in their *P*-substituted derivatives. Although Rauhut and coworkers[340] were unable to remove the cyanoethyl group from the compounds mentioned above, other workers[341-344] have shown that *P*-cyanoethylated compounds can be decyanoethylated.

Halides of tri(2-cyanoethyl)tin are obtained by the action of halogens on tetra-(2-cyanoethyl)tin; under certain conditions the nitrile group is hydrolysed and two cyanoethyl groups are eliminated[345].

If a carbon–carbon bond is formed in cyanoethylation, it is usually very difficult to remove the 2-cyanoethyl group[250,346-348]. Under certain conditions, succinic acid dinitrile (the product of cyanoethylation of hydrocyanic acid) decomposes into hydrocyanic acid and acrylonitrile[211,349-351], the latter being obtained in up to 94% yield. Alkaline hydrolysis of tricyanoethylated nitromethane gives γ-ketopimelic acid, and a molecule of acrylonitrile is eliminated[211]. Some *C*-cyanoethylated compounds eliminate the cyanoethyl group under the conditions of the Fischer reaction[352].

Because acrylonitrile is readily eliminated from β-substituted propiononitriles, the 2-cyanoethyl group can be used as a protective group. It was used in this way for the cross--linking of two pyrazole nuclei by means of a methylene bridge attached to the 4-positions of both rings[326,327]; it has also been used in the synthesis of secondary amines[271,272], peptides[353], and monoesters of phosphoric acid[245]. 2-Cyanoethyl phosphate has been widely used in the synthesis of phosphate esters[223-243]. When the diesters of phosphoric acid formed are treated with mild alkali (barium hydroxide or 3 *N* aqueous lithium hydroxide at 100° for 15 min), acrylonitrile is eliminated and the monoester is formed. This method of phosphorylation is used in the synthesis of a number of nucleotides:



where A is a nucleoside residue.

Attempts have been made to use acrylonitrile for blocking sulphydryl groups of proteins[306,354]. The reaction in which *NN*-dicyanoethylated products are decyanoethylated has been used as the basis of a method for synthesising some *N*-monocyanoethylated compounds that are difficult or impossible to obtain by direct cyanoethylation with acrylonitrile[71,92,93,250,301].

5. ALKYLATIONS WITH THE AID OF β-SUBSTITUTED PROPIONIC ACIDS AND THEIR DERIVATIVES

The readiness with which β-elimination occurs in the β-substituted propionic acid series suggests that many alkylations carried out with the aid of β-substituted propionic acids and their derivatives proceed through a stage in which unsaturated compounds — acrylic acid, its ester, amide, or nitrile — are formed. This has been confirmed by studies of the mechanism and kinetics of these reactions[167,168,171,173,213,279,280,318,319,355-357].

When β-(methylthio)propionic acid is treated with hydrochloric acid, it forms di-(2-carboxyethyl) sulphide and dimethyl sulphide[358]. Under similar conditions, the hydrolysis of the methyl esters of β-(methylthio)- and β-(ethylthio)-propionic acids proceeds in the same way[358,359]; methanethiol and ethanethiol can be obtained by alkaline hydrolysis of these esters. When ethyl β-(methylamino)-propionate is heated to 130–140°, *NN*-bis-(2-ethoxycarbonylethyl)methylamine is formed[360]:

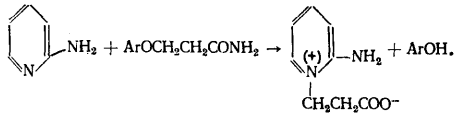
$$2\,CH_3NHCH_2CH_2COOC_2H_5 \rightarrow CH_3N(CH_2CH_2COOC_2H_5)_2 + CH_3NH_2.$$

When 2-carbamoylethyl hydrogen sulphate reacts with aliphatic and heterocyclic amines, carbamoylethylation of the amines takes place[155]. The amide of *N*-(2-carboxyethyl)-*p*-toluidine is formed when the following compounds are heated with *p*-toluidine in water at 100°; the amides of β-(alkylamino)- and β-aryloxy-propionic acids; the amides of *N*-mono-(2-carboxyethyl)-α-amino-acids and the diamides of *NN*-di-(2-carboxyethyl)-α-amino-acids; analogous derivatives of β-alanine; and sulphones containing the 2-carbamoylethyl group[60,361-363].

$$p\text{-}CH_3C_6H_4NH_2 + RCH_2CH_2CONH_2 \rightarrow p\text{-}CH_3C_6H_4NHCH_2CH_2CONH_2 + RH.$$

The products that have been obtained by the reaction of 2-carbamoylethyl hydrogen sulphate with alcohols and

phenols include acrylic acid, β-alkoxy- and β-aryloxy--propionic acids and the esters of these [165]. β-Arylpropionamides react with α-amino- [35] and γ-methyl-α-amino--pyrimidines [81] according to the following scheme:



It is interesting that when the 2-cyanoethyl ether of 2-naphthol is heated in benzene in the presence of alkali, the 2-cyanoethyl group is transferred from the oxygen atom to a carbon atom and 1-(2-cyanoethyl)-2-naphthol is formed [202,364,365]. An analogous reaction occurs with doubly cyanoethylated resorcinol [202]. When 1-phenyltetrazoline--5-thione is cyanoethylated, the *S*-isomer is converted to the *N*-isomer [249]. Attempts to transfer the cyanoethyl group in the indole ring from the nitrogen to the β-position have not been successful [75].

When diethylene glycol [192], acetamide [211], arylsulphamides [70,72,92,93,366], α-amino-acids [304,307,311], and phenylacetonitrile [348] are heated with their dicyanoethylation products, the 2-cyanoethyl groups are redistributed, and monocyanoethylated derivatives are formed, for example:

$$ArSO_2NH_2 + ArSO_2N(CH_2CH_2CN)_2 \rightarrow 2\,ArSO_2NHCH_2CH_2CN,$$
$$C_6H_5CH_2CN + C_6H_5C(CN)(CH_2CH_2CN)_2 \rightarrow 2\,C_6H_5CH(CN)CH_2CH_2CN.$$

Acetophenone with its tricyanoethylated derivatives gives mono- and di-cyanoethylation products [348]. When *unsym*--di-(2-cyanoethyl)hydrazine is treated with phenylisocyanate, a certain amount of *sym*-di-(2-cyanoethyl)hydrazine derivative is formed [367].

The occurrence of mobile equilibrium and reversibility in cyanoethylations is particularly well exemplified by the reaction of acrylonitrile with alcohols [175,210-212,250,368]. When β-alkoxypropiononitriles are heated or set aside with aliphatic or aliphatic–aromatic alcohols in the presence of alkalis or alkoxides, transcyanoethylation occurs [213,250,369,370]:

$$ROCH_2CH_2CN + R'OH \rightarrow R'OCH_2CH_2CN + ROH.$$

β-Alkoxypropiononitriles behave in the same way under the conditions of Vyshnegradskii's reaction [187]. Some β-alkoxypropiononitriles are used as cyanoethylating agents [35,81,182 201,202,213,250,371-377]. Bis-(2-cyanoethyl) ether has been used for the cyanoethylation of hydrogen sulphide [378], thiols and thiophenols [379], ketones [380], and aromatic amines [201,374]. 2-Cyanoethyl esters have been used for the cyanoethylation of aliphatic amines [381], benzene [219,382], resorcinol (in the nucleus) [383], pyrrole [384], and piperidine [385]. Much work has been done on *N*-substituted β-aminopropiononitriles as agents for the cyanoethylation of alcohols [168,371], malonic ester [376], triethyl phosphite [386], dimedone [387], aliphatic [371] and aromatic [167,201,206,279,280,373,388-391] amines, indole [73], piperidine [371], 9,10-dihydrophenanthridine [392], morpholine [376], pyrazolines [393], and pyrazolones [394]. β-Halogeno- [250] and β-hydroxy-propiononitriles [250] are used as cyanoethylation agents, as are also some products of the cyanoethylation of nitrogen-containing heterocyclic bases [250,388].

With the exception of *C*-cyanoethylated compounds, other β-substituted propiononitriles (β-halogeno-, β-alkoxy-, β-aryloxy-, and β-alkylamino-propiononitriles, *S*-cyanoethylated compounds, *N*-mono- and *NN*-di-cyanoethylated amino-acids, *NN*-dicyanoethylated arylsulphamides, cyanoethylation products of peptides and proteins) react with aromatic amines in water at 100° to form decyanoethylation and transcyanoethylation products [70-72,90-93,167,201,202,205-207 213,250,279,280,302-304,318,319,335,355,356,373,374,388-391,395]:

$$XCH_2CH_2CN + ArNH_2 \rightarrow ArNHCH_2CH_2CN + XH,$$

where X = halogen, RO, ArO, RS, ArS, $ArSO_2$, RNH, $(R)_2N$, HOOCCH(R)NH, etc. The reaction of β-substituted propiononitriles with 2-amino- [35] and 4-methyl-2-aminopyridines [81] has been studied.

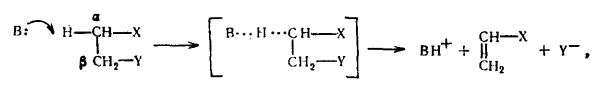
Products of the cyanoethylation of alcohols and aliphatic amines have been used instead of acrylonitrile in the reaction with phenylhydrazine for the synthesis of 3-amino-1--phenylpyrazoline [396]. The reaction of β-(dimethylamino)-propiononitrile with *p*-tolylhydrazine proceeds in the same way [397].

The use of β-substituted propiononitriles as cyanoethylating agents sometimes makes it possible to obtain cyanoethylated compounds when acrylonitrile cannot be used or when it gives low yields [250].

6. MECHANISM OF β-ELIMINATIONS

In most of the papers cited in this review, β-elimination was not the object of the investigation, but was only observed in studies on other problems. There are only a few papers in which some conclusions have been drawn as to possible reaction mechanisms or in which reaction kinetics have been studied [40,171,213,250,274,280,318,319,355-359]. These scattered data may be used, together with the general principles of the mechanisms of elimination reactions [398-401], to set up an approximate scheme of possible mechanisms for the reactions considered here.

The most important and the most widely studied class of β-elimination reactions in the β-substituted propionic acid series is that in which cleavage occurs under the action of basic agents. These reactions appear to proceed by a bimolecular elimination mechanism (*E*2) with an "*E*1 with B-like" transition state, in which rupture of the C–H bond precedes elimination of the β-substituent:

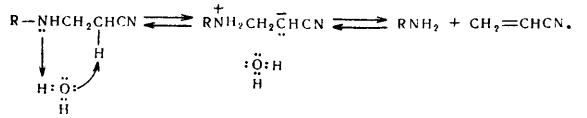


where X = COOH, COOR, $CONH_2$, CN; and Y = halogen, RO, ArO, AcO, H_2PO_3O, $(R)_2N$, $(R)_3N^+$, etc. However, it can happen that, under favourable conditions (low basicity of the agent B, low activating effect of the group X, and the presence in the β-position of substituents that facilitate rupture of the C–Y bond), there is a change to a synchronous or even *E*1-like bimolecular elimination mechanism [401].

The activating effect of the group X on the rate of elimination decreases in the order CN > $CONH_2$ > COOH, COOR. The particular ease with which decyanoethylation occurs in comparison with the removal of the 2-carboxyethyl, 2-carbamoylethyl, and 2-alkoxycarbonylethyl groups appears to be due to the high negative inductive effect (*-I*) of the nitrile group.

The scheme proposed by Bekhli [280] for the cleavage of β-dialkylaminopropiononitriles by a monomolecular mechanism (*E*1) does not appear to be valid. It was later shown that this reaction does not take place in the absence of basic agents [213]. It is also known that ammonium salts have little tendency to undergo cleavage by an *E*1 mechanism [401].

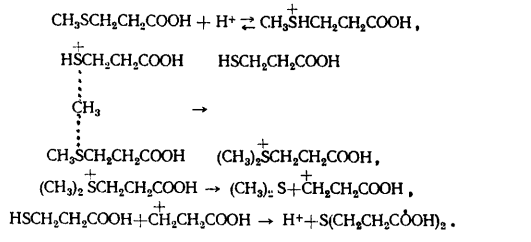
To explain the catalytic effect of water on the decyanoethylation of β-alkylaminopropiononitriles, a scheme has been proposed in which the water molecules act as a "proton carrier"[274]:



However, it is most probable that an $E2$ mechanism also operates here.

The scheme for nucleophilic bimolecular elimination does not appear to cover β-elimination reactions of β-hydroxy-, β-alkoxy-, β-aryloxy-, β-acyloxy-, and β-mercapto--propionic acids and their derivatives in an acid medium. The elimination may proceed through an oxonium ion. However, because of the lack of experimental results, it is not possible to advance a more detailed mechanism.

Challenger and coworkers have described a very interesting reaction of this type[358,359]. They observed that, when β-methylthiopropionic acid or its methyl ester is boiled with 6 N hydrochloric acid, extensive cleavage occurs with the formation of dimethyl sulphide and di-(2-carboxyethyl) sulphide. They propose the following mechanism for this reaction, which they have confirmed by numerous experimental results:



Up to now numerous pyrolytic cleavage reactions of β-halogeno-, β-hydroxy-, β-alkoxy, and β-acyloxy-propionic acids, and their esters, amides, and nitriles have not been studied at all. It may be supposed that they proceed by an "intramolecular elimination" (E_i) mechanism with a cyclic transition state, or by a radical mechanism similar to that of other pyrolytic eliminations[401]. However, cleavage of β-substituted propionic acids and their derivatives occurs at 150–250°, that is, at a temperature 100–200 deg lower than the temperature required for pyrolysis of the simplest alkyl halides, alcohols, and esters. This is probably due to the greater ease with which a hydrogen atom is eliminated from the propionic acids, arising from the effects of the carboxyl, ester, amide, and nitrile groups.

In conclusion it should be noted that at present it is still not possible to explain all the regularities and isolated anomalies of β-elimination. For example, the present review does not consider possible causes of the greater mobility of one 2-cyanoethyl group in the products of NN-dicyanoethylation, the effect of the β-substituent on ease of cleavage, isolated cases of carbon–carbon bond rupture, etc. More serious experimental work is required, with the use of physicochemical methods and kinetics studies, for the elucidation of the mechanism of β-elimination in the β-substituted propionic acid series.

1. G. Krestovnikov, Zhur. Russ. Fiz.-Khim. Obshch., 11, 250 (1879).
2. A. Michael, Ber., 34, 4028 (1901).
3. German P. 607483 (1934); Chem. Zentr., 34, II, 1612 (1935).
4. U.S.P. 2210564 (1940); Chem. Abs., 35, 138 (1941).
5. W. Lossen and E. Kowski, Annalen, 342, 128 (1905).
6. W. Schneider and E. Erlenmeyer, Ber., 3, 339 (1870).
7. C. Moureu, Ann. Chim. (France), [7], 2, 158 (1894).
8. C. Moureu, M. Murat, and L. Tampier, Compt. rend., 172, 1267 (1921).
9. C. Moureu, M. Murat, and L. Tampier, Ann. Chim. (France), [9], 15, 221 (1921).
10. H. Staudinger and E. Urech, Helv. Chim. Acta, 12, 1109 (1929).
11. A. Wölk, J. prakt. Chem., [2], 61, 200 (1900).
12. F. Beilstein, Annalen, 122, 366 (1862).
13. J. Wislicenus, Annalen, 166, 6 (1873).
14. C. Rüber and J. Schetelig, Z. physiol. Chem., 48, 345 (1904).
15. F. Winternitz and R. Lachazette, Bull. Soc. chim. France, 664 (1958).
16. E. Klimenko, Zhur. Russ. Fiz.-Khim. Obshch., 12, 102 (1880).
17. E. Klimenko, Zhur. Russ. Fiz.-Khim. Obshch., 22, 100 (1890).
18. E. Klimenko, Zhur. Russ. Fiz.-Khim. Obshch., 26, 411 (1894).
19. J. Wislicenus, Annalen, 174, 285 (1874).
20. W. Moldenhauer, Annalen, 131, 323 (1864).
21. J. vander Burg, Rec. Trav. chim., 41, 21 (1922); Chem. Zentr., III, 1287 (1922).
22. L. Broude, Z. physiol. Chem., 173, 4 (1928).
23. German P. 1151501 (1964); Ref. Zhur. Khim., 17N53P (1965).
24. "Monomery" (Monomers), Collection of Papers Translated from English, Edited by V. V. Korshak, Inostr. Lit., Moscow, 1953, Vol. 2.
25. P. Vaculik, "Chemie Monomerů (Translated into Russian), Edited by I. L. Knunyants, Inostr. Lit., Moscow, 1960, Vol. 1.
26. B. P. 455087 (1936); Chem. Abs., 31, 1433 (1937).
27. U.S.P. 2026894 (1936); Chem. Abs., 30, 1393 (1936).
28. U.S.P. 2425694 (1947); Chem. Abs., 41, 7410 (1947).
29. U.S.P. 3115522 (1963); Ref. Zhur. Khim., 15N31P (1965).
30. German P. 729342 (1942); Chem. Abs., 38, 379 (1944).
31. U.S.P. 2341663 (1944); Chem. Abs., 38, 4272 (1944).
32. U.S.P. 2485510 (1949); Chem. Abs., 44, 7345 (1950).
33. P. F. Butskus and N. V. Raguotene, Zhur. Obshch. Khim., 33, 622 (1963).
34. P. F. Butskus, R. Yu. Stonite, and N. V. Raguotene, Nauch. Trudy Vys. Ucheb. Zaved. Litov. SSR, Khim. i Khim. Tekhnol., 2, 27 (1962).
35. P. F. Butskus, G. I. Denis, and N. V. Raguotene, Zhur. Obshch. Khim., 33, 1236 (1963).
36. E. Simpson, M. Tomlinson, and H. Taylor, J. Chem. Soc., 2239 (1951).
37. T. Gresham, J. Jansen, F. Shaver, R. Bankert, W. Beears, and M. Prendergart, J. Amer. Chem. Soc., 71, 661 (1949).
38. R. Gregory and M. Tomlinson, J. Chem. Soc., 795 (1956).
39. U.S.P. 2459677 (1949); Chem. Abs., 43, 2026 (1949).
40. E. Cherbulize, H. Probst, and J. Rabinowitz, Pharm. Acta Helv., 37, 396 (1962).
41. E. Cherbuliez and J. Rabinowitz, Helv. Chim. Acta, 39, 1844 (1956).
42. E. Cherbuliez, G. Probst, J. Rabinowitz, and S. Sandrin, Helv. Chim. Acta, 41, 1163 (1958).
43. E. Cherbuliez, G. Gordahi, and J. Rabinowitz, Helv. Chim. Acta, 43, 863 (1960).
44. D. Noyce and C. Lane, J. Amer. Chem. Soc., 84, 1653 (1962).
45. D. Noyce, P. King, C. Lane, and W. Reed, J. Amer. Chem. Soc., 84, 1638 (1962).
46. D. Noyce and C. Lane, J. Amer. Chem. Soc., 84, 1641 (1962).
47. D. Noyce and H. Avarbock, J. Amer. Chem. Soc., 84, 1644 (1962).
48. C. Kleber, Annalen, 246, 97 (1888).
49. O. S. Stepanova and V. S. Garkusha-Bozhko, Khim. Prom., Nauk.-Tekhn. Zb., No. 2, 25 (1961).

50. O. S. Stepanova and M. I. Drozdovskaya, Ukrain. Khim. Zhur., 27, 786 (1961).
51. O. S. Stepanova, Zhur. Obshch. Khim., 32, 1026 (1962).
52. E. A. Yatsenko and O. S. Stepanova, Zhur. Obshch. Khim., 23, 3823 (1963).
53. Z. D. Bogatskaya and N. L. Garkovik, Ukrain. Khim. Zhur., 27, 671 (1961).
54. A. V. Bogatskii and N. A. Goryachuk, Ukrain. Khim. Zhur., 27, 782 (1961).
55. A. V. Bogatskii, N. A. Goryachuk, and G. I. Parnak, Zhur. Obshch. Khim., 32, 1498 (1962).
56. A. V. Bogatskii and S. D. Yablonovskaya, Zhur. Obshch. Khim., 32, 3886 (1962).
57. V. P. Gol'mov and N. M. Afanas'ev, Zhur. Obshch. Khim., 22, 1953 (1952).
58. V. P. Gol'mov and N. M. Afanas'ev, Zhur. Obshch. Khim., 23, 1188 (1953).
59. L. I. Zakharkin and N. A. Preobrazhenskii, Zhur. Obshch. Khim., 22, 1890 (1952).
60. P. F. Butskus, R. Yu. Stonite, and A. I. Butskene, Zhur. Vses. Khim. Obshch. im. Mendeleeva, 11, 468 (1966).
61. E. Mulder, Ber., 9, 1902 (1876).
62. B. Flurscheim, J. prakt. Chem., [2], 68, 345 (1903).
63. R. Willstätter, Ber., 35, 584 (1902).
64. S. Chodroff, R. Kapp, and C. Beckmann, J. Amer. Chem. Soc., 69, 256 (1947).
65. R. Elderfield, W. Gensler, T. Bembry, C. Kremer, F. Broady, H. Hageman, and J. Head, J. Amer. Chem. Soc., 68, 1259 (1946).
66. A. K. Purenas and R. S. Baltrushis, Trudy Akad. Nauk Litov. SSR, B3(26), 203 (1961).
67. V. M. Rodionov and B. I. Kurtev, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 268 (1952).
68. V. M. Rodionov and O. S. Urbanskaya, Zhur. Obshch. Khim., 18, 2023 (1948).
69. L. Birkofer abd I. Storch, Ber., 86, 529 (1953).
70. P. F. Butskus and R. Yu. Stonite, Zhur. Obshch. Khim., 32, 1865 (1962).
71. P. F. Butskus and R. Yu. Stonite, Zhur. Obshch. Khim., 33, 624 (1963).
72. P. F. Butskus and R. Yu. Stonite, Zhur. Obshch. Khim., 34, 589 (1964).
73. A. P. Teren'tev, A. N. Kost, and V. A. Smit, Zhur. Obshch. Khim., 25, 1959 (1955).
74. M. Julia and J. Lenzi, Bull. Soc. chim. France, 2267 (1962).
75. A. P. Teren'tev, A. N. Kost, and V. A. Smit, Zhur. Obshch. Khim., 26, 557 (1956).
76. R. Lukes and K. Blaha, Coll. Czech. Chem. Comm., 22, 626 (1957).
77. H. Fritz, J. Org. Chem., 28, 1384 (1963).
78. H. Johnson and D. Crosby, J. Org. Chem., 28, 2030 (1963).
79. K. Auwers and H. Allardt, Ber., 59, 95 (1926).
80. L. S. Efros and B. A. Porai-Koshits, Zhur. Obshch. Khim., 23, 697 (1953).
81. P. F. Butskus, N. V. Raguotene, and A. I. Butskene, Zhur. Obshch. Khim., 34, 3847 (1964).
82. A. Kirpal and B. Wojnar, Ber., 71, 1261 (1938).
83 R. Adams and I. Pachter, J. Amer. Chem. Soc., 74, 4906 (1952).
84. R. Adams and V. Jones, J. Amer. Chem. Soc., 69, 1803 (1947)
85. J. Braunholtz and F. Mann, J. Chem. Soc., 651 (1954).
86. S. Takemura, Chem. Pharm. Bull. (Tokyo), 8, 574 (1960); Chem. Abs., 55, 14475 (1961).
87. Yang Shih-hsien, Chen Ju-yu, Li Wan-lin, Tsao Hui-fang, Ho Min-chang, Hu Sheng-wen, and Tsao Shan-chi, Acta Chim. Sinica, 26, 49 (1960); Chem. Abs., 55, 18589 (1961).
88. U. S. P. 2 846 447 (1958); Chem. Abs., 53, 2192 (1959).
89. S. A. Vartanyan, A. O. Tosunyan, and L. G. Mesropyan, Izv. Akad. Nauk Armyan. SSR, Khim. Nauk, 14, 469 (1961).
90. N. V. Raguotene, Candidate's Thesis, Vilna State University, 1963.
91. N. V. Raguotene, Author's Abstract of Candidate's Thesis. Vilna State University, 1963.
92. R. Yu. Stonite, Candidate's Thesis, Vilna State University, 1963.
93. R. Yu. Stonite, Author's Abstract of Candidate's Thesis, Vilna State University, 1963.
94. J. Wilt and D. Oathoudt, J. Org. Chem., 21, 1550 (1956).
95. J. Wilt and D. Oathoudt, J. Org. Chem., 23, 218 (1958).
96. J. Wilt and D. Oathoudt, J. Org. Chem., 26, 2173 (1961).
97. L. Sommer, N. Marans, G. Goldberg, J. Rockert, and R. Pioch, J. Amer. Chem. Soc., 73, 882 (1951).
98. B. N. Dolgov, E. V. Kukharevskaya, and D. N. Andreev, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 968 (1957).
99. B. N. Dolgov, D. N. Andreev, and V. P. Lyutyi, Dokl. Akad. Nauk SSSR, 118, 501 (1958).
100. D. N. Andreev, B. N. Dolgov, and S. V. Butts, Zhur. Obshch. Khim., 32, 1275 (1962).
101. B. P. 351 518 (1930); Chem. Abs., II, 1923 (1931).
102. German P. 571 524 (1933); Chem. Abs., 27, 4243 (1933).
103. German P. 546 141 (1932); Chem. Zentr., I, 2642 (1932).
104. U. S. P. 1 864 884 (1932); Chem. Abs., 26, 4345 (1932).
105. C. Marvel, J. Amer. Chem. Soc., 62, 3495 (1940).
106. C. Marvel and R. Frank, J. Amer. Chem. Soc., 64, 1675 (1942).
107. French P. 709 627 (1931); Chem. Abs., 26, 994 (1932).
108. A. L. Klebanskii and K. K. Chevychalova, Trudy Gos. Inst. Prikl. Khim., No. 31, 46 (1937).
109. B. P. 531 968 (1941); Chem. Abs., 36, 496 (1942).
110. U. S. P. 1 890 277 (1932); Chem. Abs., 27, 1639 (1933).
111. French P. 707 154 (1931); Chem. Abs., 26, 479 (1932).
112. German P. 365 530 (1919); 571 123 (1928); Fortschr. TheerfarbFabr., 18, 283 (1933).
113. U. S. P. 1 388 016 (1921); Chem. Zentr., IV, 1222 (1921).
114. U. S. P. 1 829 208 (1932); Chem. Abs., 26, 735 (1932).
115. French P. 675 327 (1929); Chem. Abs., 24, 2756 (1930).
116. B. P. 561 969 (1944); Chem. Abs., 40, 593 (1946).
117. S. Iwai, J. Soc. Chem. Ind. Japan, 45, 137 (1942); Chem. Abs., 44, 8858 (1950).
118. G. Kline, Mod. Plastics, 23, 152 (1945); Chem. Abs., 40, 1690 (1946).
119. H. Neher, Ind. Eng. Chem., 28, 267 (1936).
120. German P. 573 724 (1933); Chem. Abs., 28, 483 (1934).
121. U. S. P. 2 457 225 (1948); Chem. Abs., 43, 3442 (1949).
122. U. S. P. 1 890 277 (1932); Chem. Abs., 27, 1639 (1933).
123. German P. 1 124 482 (1962); Ref. Zhur. Khim., 14N48P (1963).
124. German P. 1 124 483 (1962); Ref. Zhur. Khim., 19N22P (1963).
125. German P. 1 126 378 (1962); Ref. Zhur. Khim., 18N28P (1963).
126. U. S. P. 2 393 737 (1946); Chem. Abs., 40, 3127 (1946).
127. B. P. 828 658 (1960); Chem. Abs., 54, 19488 (1960).
128. French P. 1 202 610 (1960); Chem. Zentr., 5094 (1962).
129. U. S. P. 2 390 028 (1945); Chem. Abs., 40, 1866 (1946).
130. G. Clemo and E. Walton, J. Chem. Soc., 723 (1928).
131. R. Burns, D. Jones, and P. Ritchie, J. Chem. Soc., 400 (1935).
132. S. Goldschmidt, H. Spath, and L. Beer, Annalen, 649, 1 (1961).
133. U. S. P. 2 858 330 (1958).
134. V. P. Bronovitskaya and A. Ya. Berlin, in Collected Papers from Zhur. Obshch. Khim., "Problemy Organicheskogo Sinteza" (Problems of Organic Synthesis), Nauka, Moscow–Leningrad, 1965, p. 147.
135. S. McElvain and G. Stork, J. Amer. Chem. Soc., 68, 1049 (1946).

136. K. Binovic, Bull. Soc. chim. France, 206 (1949).
137. R. Rieber, Compt. rend., 231, 291 (1950).
138. E. Abderhalden and A. Fodor, Z. physiol. Chem., 85, 117 (1913).
139. R. Fuson, J. Amer. Chem. Soc., 50, 1444 (1928).
140. S. Morosawa, J. Chem. Soc. Japan, Pure Chem. Sect., 79, 1269 (1958); Chem. Zentr., 17 062 (1959).
141. S. Morosawa and A. Yokoo, Bull. Chem. Soc. Japan, 36, 179 (1963); Ref. Zhur. Khim., 22Zh186 (1963).
142. J. Braun, Ber., 42, 2035 (1909).
143. H. Reimlinger and J. Oth, Ber., 97, 331 (1964).
144. V. M. Rodionov and E. V. Yavorskaya, Zhur. Obshch. Khim., 23, 983 (1953).
145. L. McKinney, E. Uhing, E. Setzkorn, and J. Cowan, J. Amer. Chem. Soc., 74, 5183 (1952).
146. R. Adams and A. Schrecker, J. Amer. Chem. Soc., 71, 1186 (1949).
147. C. Weisel, R. Taylor, H. Mosher, and F. Whitmore, J. Amer. Chem. Soc., 67, 1071 (1945).
148. N. Harper, A. Beckett, and A. Balon, J. Chem. Soc., 2704 (1960).
149. R. Hinton, F. Mann, and D. Todd, J. Chem. Soc., 5454 (1961).
150. E. Bullock, B. Gregory, A. Johnson, P. Brignell, U. Eisner, and H. Williams, Proc. Chem. Soc., 122 (1962).
151. A. Kundu, N. Kundu, and Ph. Dutta, J. Chem. Soc., 2749 (1965).
152. E. Carpenter and H. Davis, J. Appl. Chem., 7, 671 (1957).
153. German P. 1 046 608 (1958); Chem. Zentr., 9732 (1959).
154. J. Erickson, J. Amer. Chem. Soc., 74, 6281 (1952).
155. A. A. Michurin and E. N. Zil'berman, Zhur. Org. Khim., 1, 711 (1965).
156. H. Fischer and H. Loewe, Annalen, 615, 124 (1958).
157. V. M. Rodionov and V. V. Kiseleva, Zhur. Obshch. Khim., 18, 1912 (1948).
158. V. M. Rodionov and V. V. Kiseleva, Zhur. Obshch. Khim., 26, 1133 (1956).
159. V. M. Rodionov, L. V. Antik, and N. A. Kravchenko, Zhur. Obshch. Khim., 23, 1836 (1953).
160. I. L. Knunyants and N. P. Gambaryan, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 1037 (1955).
161. I. L. Knunyants, E. E. Rytslin, and N. P. Gambaryan, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 527 (1960).
162. I. L. Knunyants, E. E. Rytslin, and N. P. Gambaryan, Zhur. Obshch. Khim., 32, 1262 (1962).
163. Canad. P. 510 228 (1955); Ref. Zhur. Khim., 54 664P (1957).
164. B. P. 703 398, 703 399 (1954); Ref. Zhur. Khim., 10 737P (1956).
165. E. N. Zil'berman and A. A. Michurin, Zhur. Obshch. Khim., 33, 2766 (1963).
166. S. Heininger, J. Org. Chem., 22, 704 (1957).
167. A. F. Bekhli, Zhur. Obshch. Khim., 27, 698 (1957).
168. A. P. Terent'ev, A. N. Kost, and S. M. Gurvich, Zhur. Obshch. Khim., 23, 615 (1953).
169. A. P. Terent'ev and P. F. Butskus, Zhur. Obshch. Khim., 27, 2591 (1957).
170. P. F. Butskus, Zhur. Obshch. Khim., 30, 1816 (1960).
171. G. I. Denis, S. I. Ionaitis, and P. F. Butskus, Zhur. Obshch. Khim., 34, 2477 (1964).
172. G. Ham and J. Stevens, J. Org. Chem., 27, 4638 (1962).
173. P. F. Butskus, G. I. Denis, and A. I. Butskene, Zhur. Obshch. Khim., 34, 4119 (1964).
174. I. Kh. Fel'dman and A. V. Voropaeva, Zhur. Obshch. Khim., 33, 269 (1963).
175. A. P. Terent'ev and A. N. Kost, in "Reaktsii i Metody Issledovaniya Organicheskikh Soedinenii" (Reactions and Methods of Investigating Organic Compounds), Vol. 2, Goskhimizdat, Moscow–Leningrad, 1952, p. 47.
176. L. Soffer and E. Parrotta, J. Amer. Chem. Soc., 76, 3580 (1954).
177. L. Soffer, M. Katz, and E. Parrotta, J. Amer. Chem. Soc., 78, 6120 (1956).
178. W. Utermohlen, J. Amer. Chem. Soc., 67, 1505 (1945).
179. R. Christian, H. Brown, and R. Hixon, J. Amer. Chem. Soc., 69, 1961 (1947).
180. F. Buckle and B. Saunders, J. Chem. Soc., 2774 (1949).
181. I. N. Nazarov and G. A. Shvekhgeimer, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 1221 (1956).
182. U. S. P. 2 335 605 (1943); Chem. Abs., 38, 2970 (1944).
183. U. S. P. 2 335 653 (1943); Chem. Abs., 38, 2970 (1944).
184. I. N. Nazarov and G. A. Shvekhgeimer, Zhur. Obshch. Khim., 24, 157 (1954).
185. E. Müller (Editor), "Methoden der organischen Chemie (Houben-Weyl)", Thieme, Stuttgart, 1952, Vol. 8, p. 539.
186. M. F. Shostakovskii, L. M. Kaliberdo, and N. V. Komarov, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 703 (1961).
187. A. N. Kost and V. G. Yashunskii, Zhur. Obshch. Khim., 23, 230 (1953).
188. O. Wiedeman and W. Montgomery, J. Amer. Chem. Soc., 67, 1994 (1945).
189. C. Berther, Ber., 92, 2616 (1959).
190. U. S. P. 2 832 798 (1958); Chem. Abs., 52, 16 195 (1958).
191. C. Allen and J. Van Allan, J. Org. Chem., 14, 754 (1949).
192. U. S. P. 2 853 510 (1958); Ref. Zhur. Khim., 35 786P (1960).
193. J. Wright and L. Minsk, J. Amer. Chem. Soc., 75, 98 (1953).
194. M. Negishi, I. Sekiguchi, and S. I. Okada, J. Soc. Textile Cellulose Ind., 12, 479 (1956); Chem. Abs., 51, 8040 (1957).
195. S. N. Danilov and A. A. Lopatenok, Zhur. Obshch. Khim., 32, 3611 (1962).
196. S. N. Danilov and A. A. Lopatenok, Zhur. Obshch. Khim., 28, 3184 (1958).
197. O. Moe, S. Miller, and M. Buckley, J. Amer. Chem. Soc., 74, 1325 (1952).
198. T. Takahashi, M. Hori, and K. Okumara, J. Pharm. Soc. Japan, 78, 1 (1958); Ref. Zhur. Khim., 1199 (1959).
199. O. Grummitt and D. Marsh, J. Amer. Chem. Soc., 71, 4156 (1949).
200. J. Griffing and L. Salisbury, J. Amer. Chem. Soc., 70, 3416 (1948).
201. P. F. Butskus and G. I. Denis, Nauch. Dokl. Vys. Shkoly, Khim. i Khim. Tekhnol., 743 (1958).
202. P. F. Butskus and G. I. Denis, Zhur. Obshch. Khim., 30, 1321 (1960).
203. A. Fitton and G. Ramage, J. Chem. Soc., 4870 (1962).
204. J. Colonge, G. Descotes, and R. Puthet, Bull. Soc. chim. France, 553 (1963).
205 P. F. Butskus and N. V. Raguotene, Zhur. Obshch. Khim., 31, 3639 (1961).
206. P. F. Butskus and N. V. Raguotene, Zhur. Obshch. Khim., 32, 1816 (1962).
207. P. F. Butskus, Zhur. Obshch. Khim., 34, 2093 (1964).
208. H. Wassermann, B. Suryanarayana, and D. Grasetti, J. Amer. Chem. Soc., 78, 2808 (1956).
209. H. Zahn and W. Gerstner, Ber., 88, 1731 (1955).
210. H. Bruson, in "Organic Reactions" (Edited by R. Adams), Wiley, New York, Vol. 5, p. 79.
211. O. Bayer, Angew. Chem., 61, 229 (1949).
212. A. P. Terent'ev, A. N. Kost, and A. M. Berlin, Zhur. Obshch. Khim., 26, 719 (1956).
213. G. Denis and P. Butskus, Nauch. Trudy Vys. Ucheb. Zaved. Litov. SSR, Khim. i Khim. Tekhnol., 5, 39 (1964).
214. V. M. Vdovin, R. Sultanov, E. D. Lubuzh, and A. D. Petrov, Dokl. Akad. Nauk SSSR, 138, 831 (1961).
215. "Preparativnaya Organicheskaya Khimiya" (Preparative Organic Chemistry). Translated into Russian from the Polish under the Editorship of N. S. Vul'fson, Goskhimizdat, Moscow, 1959, p. 586.
216. B. P. 424 885 (1933); Chem. Zentr., I, 2439 (1936).

217. U.S.P. 2208328 (1940); Chem.Abs., 35, 139 (1941).
218. U.S.P. 2452672 (1949); Chem.Abs., 43, 2220 (1949).
219. G.Clemo and E.Walton, J.Chem.Soc., 723 (1928).
220. R.Burns, D.Jones, and P.Ritchie, J.Chem.Soc., 400 (1935).
221. P.Ritchie, J.Chem.Soc., 1054 (1935).
222. E.Sakellarios, Helv.Chim.Acta, 29, 1675 (1946).
223. P.Gilham and G.Tener, Chem.and Ind., 542 (1959).
224. J.Montgomery and H.Thomas, J.Org.Chem., 26, 1926 (1961).
225. G.Weimann and H.Khorana, J.Amer.Chem.Soc., 84, 419 (1962).
226. G.Weimann and H.Khorana, J.Amer.Chem.Soc., 84, 4329 (1962).
227. H.Thomas, K.Newson, and J.Montgomery, J.Org.Chem., 27, 192 (1962).
228. G.Tener, J.Amer.Chem.Soc., 83, 159 (1961).
229. F.Cramer, W.Saenger, K.-H.Scheit, and J.Tennigkeit, Annalen, 679, 156 (1964).
230. J.Roy, D.Kvam, J.Dahl, and R.Parks, J.Biol.Chem., 236, 1158 (1961).
231. J.Smrt and F.Šorm, Coll.Czech.Chem.Comm., 28, 887 (1963).
232. J.Smrt and F.Šorm, Coll.Czech.Chem.Comm., 28, 2415 (1963).
233. J.Smrt and F.Šorm, Coll.Czech.Chem.Comm., 29, 2971 (1964).
234. J.Moffatt, J.Amer.Chem.Soc., 85, 1118 (1963).
235. K.Scheit and W.Kampe, Ber., 98, 1045 (1965).
236. D.Straus, J.Amer.Chem.Soc., 87, 1375 (1965).
237. H.Machleidt, E.Cohnen, and R.Tschesche, Annalen, 655, 70 (1962).
238. D.Remy, A.Sunthankar, and C.Heidelberger, J.Org.Chem., 27, 2491 (1962).
239. K.Scheit and W.Kampe, Angew.Chem., 683 (1964).
240. G.Pfeiderer, C.Woenckhaus, K.Scholtz, and H.Feller, Annalen, 675, 205 (1964).
241. N.K.Kochetkov, E.I.Budovskii, V.N.Shibaev, and M.A.Grachev, Izv.Akad.Nauk SSSR, Ser.Khim., 1592 (1963).
242. W.Wehrli, D.Verheyden, and J.Moffatt, J.Amer.Chem.Soc., 87, 2265 (1965).
243. R.Letsinger and V.Mahadevan, J.Amer.Chem.Soc., 87, 3526 (1965).
244. E.Ohtsuka, M.Moon, and H.Khorana, J.Amer.Chem.Soc., 87, 2956 (1965).
245. H.Witzel, H.Mirbach, and K.Dimroth, Angew.Chem., 72, 751 (1960).
246. L.Rapoport, A.Smith, and M.Newman, J.Amer.Chem.Soc., 69, 693 (1947).
247. M.Weiss and M.O'Donghue, J.Amer.Chem.Soc., 79, 4771 (1957).
248. O.Achmatowicz and J.Michalski, Roczniki Chem., 30, 243 (1956).
249. V.L.Nirenburg and I.Ya.Postovskii, Zhur.Obshch.Khim., 34, 3200 (1964).
250. P.F.Butskus, Uspekhi Khim., 30, 1352 (1961) [Russ.Chem.Rev., 583 (1961)].
251. A.N.Kost, Uch.Zap.Moskov.Gos.Univ., VI, No. 131, 37 (1950).
252. A.P.Terent'ev, K.I.Chursina, and A.N.Kost, Zhur.Obshch.Khim., 20, 1073 (1950).
253. U.S.P. 2401429 (1946); Chem.Abs., 40, 5447 (1946).
254. F.Withmore, H.Mosher, R.Adams, R.Taylor, E.Chapin, C.Weisel, and W.Janko, J.Amer.Chem.Soc., 66, 725 (1944).
255. J.Ford, S.Buc, and J.Greiner, J.Amer.Chem.Soc., 69, 844 (1947).
256. E.Smolin and L.Beegle, Ind.Eng.Chem., 50, 1115 (1958).
257. S.Buc, J.Ford, and E.Wise, J.Amer.Chem.Soc., 67, 92 (1945).
258. E.Müller (Editor), "Methoden der organischen Chemie" (Houben-Weyl), Thieme, Stuttgart, 1957, Vol. 11/1, p.272.
259. U.S.P. 2334163; Chem.Abs., 38, 2667 (1944).
260. U.S.P. 2794805 (1957); Chem.Abs., 51, 14279 (1957).
261. W.Schmidt-Nickels, J.prakt.Chem., [4], 6, 139 (1958).
262. P.F.Butskus, Izv.Vys.Ucheb.Zaved., Khim.i Khim.Tekhnol., 2, 51 (1959).
263. M.Mugno and M.Bornengo, Gazzetta, 86, 451 (1956).
264. A.N.Kost, S.I.Suminov, and V.V.Ershov, Zhur.Obshch.Khim., 30, 498 (1960).
265. W.Hahn, Soc.Sci.Lodz.Acta Chim., 8, 37 (1962); Ref.Zhur.Khim., 1Zh109 (1964).
266. M.Kreling and A.McKay, Canad.J.Chem., 40, 143 (1962).
267. U.S.P. 2368521 (1945); Chem.Abs., 40, 352 (1946).
268. O.Ya.Fedotova, M.I.Shtil'man, and I.P.Losev, Zhur.Obshch.Khim., 34, 181 (1964).
269. O.Ya.Fedotova, M.I.Shtil'man, and I P.Losev, Zhur.Obshch.Khim., 34, 189 (1964).
270. O.Ya.Fedotova, M.I.Shtil'man, and I.P.Losev, Zhur.Obshch.Khim., 32, 3214 (1962).
271. U.S.P. 2627526 (1953); Ref.Zhur.Khim., 47292P (1954).
272. P.Dubrow and H.Harwood, J.Org.Chem., 17, 1043 (1952).
273. L.Lissinger and M.Schwartz, J.Org.Chem., 23, 1342 (1958).
274. K.Taylor, W.Selcer, P.Montgomery, and R.Hughes, J.Amer.Chem.Soc., 81, 5333 (1959).
275. A.Kotelko, Acta.Polon.Pharm., 19, 215 (1962); Ref.Zhur.Khim., 19Zh214 (1963).
276. C.Mannich and E.Ganz, Ber., 55, 3486 (1922).
277. D.Tarbell, N.Shakespeare, C.Claus, and J Bunnett, J.Amer.Chem.Soc., 68, 1217 (1946).
278. P.F.Butskus, Izv.Vys.Ucheb.Zaved., Khim.i Khim.Tekhnol., 3, 1108 (1960).
279. A.F.Bekhli, Zhur.Obshch.Khim., 21, 86 (1951).
280. A.F.Bekhli, Zhur.Obshch.Khim., 28, 204 (1958).
281. A.T.Babayan, G.T.Martirosyan, D.V.Grigoryan, and E.A.Grigoryan, Izv.Akad.Nauk Armyan.SSR, Khim.Nauka, 16, 449 (1963).
282. G.Bachman and R.Mayhew, J.Org.Chem., 10, 245 (1945).
283. J.King and F.McMillan, J.Amer.Chem.Soc., 68, 1468 (1946).
284. S.G.Kuznetsov and D.V.Ioffe, in Collected Papers from Zhur.Obshch.Khim., "Biologicheskie Aktivnye Soedineniya" (Biologically Active Compounds), Nauka, Moscow–Leningrad, 1965, p.144.
285. U.S.P. 2885435 (1959); Chem.Abs., 53, 21698 (1959).
286. U.S.P. 2927126 (1960).
287. U.S.P. 3017425 (1962); Chem.Abs., 57, 668 (1962)
288. A.E.Kretov, M.S.Rovinskii, and B.S.Evchik, Zhur.Org.Khim., 1, 950 (1965).
289. A.N.Pudovik and G.P.Krupnov, Zhur.Obshch.Khim., 33, 1654 (1963).
290. L.Pursglove, J.Org.Chem., 24, 576 (1959).
291. W.Schulter and D.Guth, J.Org.Chem., 23, 1047 (1958).
292. S.Peterson and E.Müller, Ber., 81, 31 (1948).
293. J.Lynn, J.Amer.Chem.Soc., 78, 5829 (1956).
294. G.Misra and R.Asthana, J.prakt.Chem., [4], 3, 4 (1956).
295. G.Misra and R.Asthana, J.prakt.Chem., [4], 4, 270 (1957).
296. H.Bruson and T.Riener, J.Amer.Chem.Soc., 70, 214 (1948).
297. Z.F.Solomko, L.G.Gergel', S.A.Volkova, and M.S.Malinovskii, Zhur.Obshch.Khim., 34, 1964 (1964).
298. O.Ya.Fedotova, M.I.Shtil'man, I.P.Losev, V.M.Bogdanova, and T.V.Zelenetskaya, in Collected Papers, "Geterotsepnye Vysokomolekulyarnye Soedineniya" (Hetero-Chain High-Molecular Weight Compounds), Nauka, Moscow, 1963, p.139.

299. P. F. Butskus, Izv. Vys. Ucheb. Zaved., Khim. i Khim. Tekhnol., 3, 122 (1960).
300. P. F. Butskus, G. I. Denis, A. I. Butskene, Izv. Vys. Ucheb. Zaved., Khim. i Khim. Tekhnol., 3, 469 (1960).
301. P. F. Butskus, Izv. Vys. Ucheb. Zaved., Khim. i Khim. Tekhnol., 3, 124 (1960).
302. P. F. Butskus and G. I. Denis, Nauch. Dokl. Vys. Shkoly, Khim. i Khim. Tekhnol., No. 1, 130 (1958).
303. P. F. Butskus, N. V. Raguotene, G. I. Denis, and A. I. Butskene, Zhur. Obshch. Khim., 32, 738 (1962).
304. P. F. Butskus and N. V. Raguotene, Zhur. Obshch. Khim., 34, 593 (1964).
305. P. F. Butskus and N. V. Raguotene, Nauch. Trudy Vys. Ucheb. Zaved. Litov. SSR, Khim. i Khim. Tekhnol., 1, 81 (1961).
306. E. D. Levin and V. M. Stepanov, Zhur. Obshch. Khim., 34, 2468 (1964).
307. P. F. Butskus and G. I. Denis, Zhur. Obshch. Khim., 30, 1317 (1960).
308. P. F. Butskus, N. V. Raguotene, and A. I. Butskene, Zhur. Vses. Khim. Obshch. im. Mendeleeva, 11, 466 (1966).
309. P. F. Butskus, N. V. Raguotene, and A. I. Butskene, Zhur. Vses. Khim. Obshch. im. Mendeleeva, 11, 478 (1966).
310. P. F. Butskus, Uspekhi Khim., 31, 559 (1962) [Russ. Chem. Rev., 283 (1962)].
311. P. F Butskus, Candidate's Thesis, Moscow State University, 1954.
312. L. McKinney, E. Uhing, E. Setzkorn, and J. Cowan, J. Amer. Chem. Soc., 73, 1641 (1951).
313. L. McKinney, E. Setzkorn, and E. Uhing, J. Amer. Chem. Soc., 74, 1942 (1952).
314. W. Johnson and W. DeAcetis, J. Amer. Chem. Soc., 75, 2766 (1953).
315. J. Allison, J. Braunholtz, and F. Mann, J. Chem. Soc., 403 (1954).
316. G. Proctor and R. Thomson, J. Chem. Soc., 2312 (1957).
317. A. P. Terent'ev, A. N. Kost, and V. M. Potapov, Zhur. Obshch. Khim., 18, 82 (1948).
318. A. F. Bekhli, Author's Abstract of Doctor's Thesis, Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow, 1959.
319. A. F. Bekhli, Doctor's Thesis, Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow, 1959.
320. A. N. Grinev, N. E. Rodzevich, and A. P. Terent'ev, Zhur. Obshch. Khim., 27, 1690 (1957).
321. H. Rapoport and J. Tretter, J. Org. Chem., 23, 248 (1958).
322. B. Astill and V. Boekelheide, J. Org. Chem., 23, 316 (1958).
323. D. Renn and R. Herbst, J. Org. Chem., 24, 473 (1959).
324. R. Adams and A. Schrecker, J. Amer. Chem. Soc., 71, 1186 (1949).
325. L. Horner and A. Mentrup, Annalen, 646, 49 (1961).
326. I. I. Grandberg, Author's Abstract of Doctor's Thesis, Moscow State University, Moscow, 1962.
327. I. I. Grandberg and A. N. Kost, Zhur. Obshch. Khim., 31, 3700 (1961).
328. E. Kh. Timbekov and A. S. Sadykov, Zhur. Obshch. Khim., 25, 786 (1955).
329. N. Smith, J. Org. Chem., 15, 1125 (1950).
330. E. Godefroi and E. Wittle, J. Org. Chem., 21, 1163 (1956).
331. P. Müller, N. Buu-Hoi, and R. Rips, J. Org. Chem., 24, 1699 (1959).
332. N. Smith, J. Org. Chem., 16, 415 (1951).
333. P. Müller, N. Buu-Hoi, and R. Rips, J. Org. Chem., 24, 37 (1959).
334. A. L. Mndzhoyan and S. G. Agbalyan, Izv. Akad. Nauk Armyan. SSR, Khim. Nauka, 13, 297 (1960).
335. S. G. Agbalyan, Izv. Akad. Nauk Armyan. SSR, Khim. Nauka, 14, 277 (1961).
336. G. Cheeseman, J. Chem. Soc., 1246 (1961).
337. T. Frazier, E. Little, and B. Lloyd, J. Org. Chem., 25, 1944 (1960).
338. N. F. Kucherova, L. A. Aksanova, N. M. Sharkova, and V. A. Zagorevskii, Zhur. Obshch. Khim., 33, 3662 (1963).
339. W. Curran and R. Angier, J. Org. Chem., 27, 1366 (1962).
340. M. Rauhut, I. Hechenbleikner, H. Currier, F. Schaefer, and V. Wystrach, J. Amer. Chem. Soc., 81, 1103 (1959).
341. M. Grayson, P. Keough, and G. Johnson, J. Amer. Chem. Soc., 81, 4803 (1959).
342. L. Horner and A. Mentrup, Annalen, 646, 65 (1961).
343. B. P. 886 505 (1962); Chem. Abs., 56, 15 548 (1962).
344. E. V. Kuznetsov, T. V. Sorokina, and R. K. Valetdinov, Zhur. Obshch. Khim., 33, 2631 (1963).
345. L. V. Kaabak and A. P. Tomilov, Zhur. Obshch. Khim., 33, 2808 (1963).
346. I. N. Nazarov, G. A. Shvekhgeimer, and V. A. Rudenko, Zhur. Obshch. Khim., 24, 319 (1954).
347. G. Badger, J. Cook, and T. Walker, J. Chem. Soc., 1141 (1949).
348. A. Campbell and I. Stevens, J. Chem. Soc., 959 (1956).
349. U. S. P. 2 407 848 (1946); Chem. Abs., 41, 987 (1947).
350. U. S. P. 2 410 820 (1946); Chem. Abs., 41, 1235 (1947).
351. U. S. P. 2 429 459 (1947); Chem. Abs., 42, 1962 (1948).
352. A. N. Kost, L. G. Yudin, and Ch'iu K'i-chu, Zhur. Obshch. Khim., 34, 3444 (1964).
353. P. F. Butskus and A. I. Butskene, Zhur. Obshch. Khim., 33, 3775 (1963).
354. L. Weil and T. Seibles, Arch. Biochem. Biophys., 95, 470 (1961).
355. G. I. Denis, Candidate's Thesis, Vilna State University, 1961.
356. G. I. Denis, Author's Abstract of Candidate's Thesis, Vilna State University, 1961.
357. A. N. Kost, Doctor's Thesis, Moscow State University, Moscow, 1956.
358. F. Challenger and H. Hollingworth, J. Chem. Soc., 61 (1959).
359. F. Challenger and H. Hollingworth, Chem. and Ind., 463 (1954).
360. W. Thomas and S. McElvain, J. Amer. Chem. Soc., 54, 3295 (1932).
361. P. F. Butskus and A. I. Butskene, Zhur. Obshch. Khim., 34, 1407 (1964).
362. P. F. Butskus and A. I. Butskene, Zhur. Org. Khim., 2, 864 (1966).
363. P. F. Butskus and A. I. Butskene, Zhur. Vses. Khim. Obshch. im. Mendeleeva, 10, 706 (1965).
364. P. F. Butskus, Zhur. Obshch. Khim., 33, 1381 (1963).
365. J. Lichtenberger, J. Core, and R. Geyer, Bull. Soc. chim. France, 997 (1962).
366. A. E. Kretov and N. P. Romazanovich, Zhur Obshch. Khim., 28, 1059 (1958).
367. M. Jorio, Gazzetta, 94, 1391 (1964).
368. J. McGregor and C. Pugh, J. Chem. Soc., 535 (1945).
369. A. Takamizawa, J. Pharm. Soc. Japan, 74, 759 (1954); Ref. Zhur. Khim., 49543 (1959).
370. Jap. P. 3811 (1955); Ref. Zhur. Khim., 55 477 (1957).
371. A. P. Terent'ev, A. N. Kost, and S. M. Gurvich, Zhur. Obshch. Khim., 22, 1977 (1952).
372. German P. 1 003 740 (1957); Chem. Abs., 53, 18 867 (1959).
373. P. F. Butskus and R. Yu. Stonite, Zhur. Obshch. Khim., 31, 3638 (1961).
374. P. F. Butskus, R. Yu. Stonite, G. I. Denis, and A. I. Butskene, Zhur. Obshch. Khim., 32, 820 (1962).
375. U. S. P. 2 425 693 (1947); Chem. Abs., 41, 7410 (1947).
376. R. Oda, M. Nomura, and S. Tanimoto, Bull. Inst. Chem. Res. Kyoto Univ., 32, 231 (1954); Chem. Abs., 50, 7112 (1956).
377. W. Johnson, J. Collins, R. Pappo. M. Rubin, P. Kropp, W. Johns, J. Pike, and W. Bartmann, J. Amer. Chem. Soc., 85, 1409 (1963).

378. U.S.P. 2 790 821 (1957); Chem. Abs., 51, 15 550 (1957).
379. U.S.P. 2 790 818 (1957); Chem. Abs., 51, 15 573 (1957).
380. U.S.P. 2 770 640 (1956); Chem. Abs., 51, 8792 (1957).
381. P. F. Butskus and R. Yu. Stonite, Nauch. Trudy Vys. Ucheb. Zavod. Litov. SSR, Khim. i Khim. Tekhnol., 1, 68 (1961).
382. A. N. Kost, B. M. Sheiman, and V. K. Kuskov, Izv. Vys. Ucheb. Zaved., Khim. i Khim. Tekhnol., 4, 87 (1961).
383. E. Chapman and H. Stephen, J. Chem. Soc., 885 (1925).
384. G. Clemo and G. Ramage, J. Chem. Soc., 49 (1931).
385. G. Clemo, J. Ormston, and G. Ramage, J. Chem. Soc., 3185 (1931).
386. T. Shono and R. Oda, J. Chem. Soc. Japan, Ind. Chem. Sect., 60, 21 (1957); Ref. Zhur. Khim., 39 716 (1958).
387. L. Bradford, E. Meek, J. Turnbull, and W. Wilson, Chem. and Ind., 839 (1951).
388. R. Bates, J. Cymerman-Craig, M. Moyle, and R. Young, J. Chem. Soc., 388 (1956).
389. L. Bauer and J. Cymerman, Chem. and Ind., 615 (1951).
390. L. Bauer, J. Cymerman, and W. Sheldon, J. Chem. Soc., 3311 (1951).
391. J. Cymerman-Craig, M. Moyle, A. Nicholson, and R. Werner, J. Chem. Soc., 3628 (1955).
392. R. Bates and J. Cymerman-Craig, J. Chem. Soc., 1153 (1954).
393. A. N. Kost, V. V. Ershov, and S. I. Suminov, Zhur. Obshch. Khim., 27, 2514 (1957).
394. A. N. Kost, S. I. Suminov, R. S. Sagitullin, and V. V. Ershov, Zhur. Obshch. Khim., 30, 2286 (1960).
395. P. F. Butskus, Zhur. Obshch. Khim., 30, 1814 (1960).
396. A. N. Kost and V. V. Ershov, Zhur. Obshch. Khim., 26, 3132 (1956).
397. A. N. Kost, Yu. V. Konnova, V. V. Ershov, and E. G. Rukhadze, Zhur. Obshch. Khim., 29, 498 (1959).
398. C. K. Ingold, "Structure and Mechanism in Organic Chemistry" (Translated into Russian; Edited by I. L. Knunyants and Ya. F. Komissarov), Inostr. Lit., Moscow, 1959.
399. J. Bunnett, Angew. Chem., 74, 731 (1962).
400. W. Kirmse, Angew. Chem., 77, 1 (1965).
401. D. V. Banthorpe, "Elimination Reactions", Elsevier, Amsterdam, 1963.

Vilna State Pedagogic Institute

Vilna State University

U. D. C. 547.7 : 547.9

GIBBERELLINS

N. Ya. Grigor'eva and V. F. Kucherov

CONTENTS

I. Gibberellins — natural phytohormones 850

II. Structure and chemical features of the gibberellins 851

III. Biogenesis of the gibberellins and their place among other natural polycyclic compounds 857

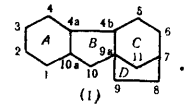
IV. Approach to an explanation of the mechanism of action of the gibberellins on higher plants 859

This review is devoted to the gibberellins — a new class of natural compound, the ever increasing interest in which is due to their high physiological activity as phytohormones.

The present article will be concerned with the chemical and biochemical aspects of the problem of the gibberellins. For a detailed analysis of the various physiological changes which can be observed in higher plants under the action of gibberellins, the reader is referred to several papers which have appeared in Soviet scientific literature [1-8].

I. GIBBERELLINS — NATURAL PHYTOHORMONES

The gibberellins, tetracyclic carboxylic acids, the structure of which is based on the hydrocarbon gibbane (I), were discovered by Japanese scientists investigating the reasons for the "bakanae" disease of rice ("foolish seedling disease"):



(I)

As long ago as 1898, Hori [9] established that the hypertrophic growth of the vegetative organs of rice seedlings which is typical of "bakanae" is caused by a fungus, the conidial stage of which was later named *Fusarium moniliforme* Sheld., the ascomycetous stage being named *Gibberella fujikuroi* Saw. In 1926, Kurosawa showed [10] that a similar physiological effect was produced by treating the seedlings with a culture medium of the fungus, free from mycelia, and in 1938 Yabuta and Sumiki [11] isolated as a crystalline material the active principles of the culture liquid of *Gibberella f.*, which they named gibberellin A and gibberellin B.

Subsequently the Japanese biochemists intensively studied the chemical structure and physiological properties of the preparations isolated, but their work only became known outside Japan in the 'fifties, when it gave an impetus to the development of studies in the field of gibberellins in other countries.

The first success in these investigations was the development of methods for the chromatographic purification of the crude preparation of gibberellin, which allowed Curtis and Cross [12] and also Stodola and coworkers [13] to isolate a pure substance with a high physiological activity, which was named gibberellic acid (GAc) or gibberellin A_3 (GA_3). The methods of fermentation and isolation which were developed out of Cross and Stodola's studies formed the basis of the industrial method of making GAc and made it an available substance [14,15]. Somewhat later, two other pure, physiologically active substances were isolated from the crude gibberellin preparation: gibberellins A_1 [16-18] and A_2 [17-19] (GA_1 and GA_2)†, and from the culture liquid of new strains of *Gibberella f.* the gibberellins A_4 (GA_4) [19-21], A_7 (GA_7) [22], A_9 (GA_9) [22], and A_{10} (GA_{10}) [23] were obtained (see Table 1).

† The numbering of the first three gibberellins is determined by the order of their elution from columns during chromatography on a Celite 545 : Norite A mixture (1 : 1). The numbering of the other gibberellins (see below) was determined by the sequence in which they were isolated from natural sources.