9. In the course of the work, the following new compounds were prepared: *cis* and *trans* forms of the methyl iodides of 2-*p*-dimethylaminostyryl-4-quinazolone, of 3-methyl-4-quinazolone, of 3-ethyl-4-quinazolone, also of the ethyl iodides of 3-methyl-4-quinazolone, and their bromination products.

New York, N. Y.

[Contribution from the Chemical Laboratory of the University of Illinois]

SOME CONDENSATION REACTIONS INVOLVING THE ELIMINATION OF ESTER GROUPS

By B. L. Souther

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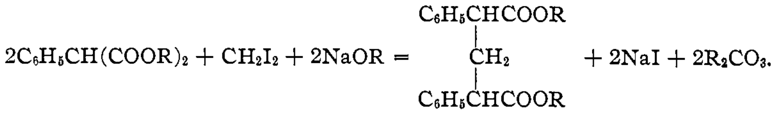
Methylene iodide has been condensed with ethyl malonate giving an excellent yield of ethyl propanetetracarboxylate.[1] A similar reaction applied to substituted malonic esters has not been so successful. Ethyl ethylmalonate[2] gives an indefinitely boiling mixture, although ethyl benzylmalonate forms the expected product, ethyl α,γ-dibenzylpropanetetracarboxylate.[2]

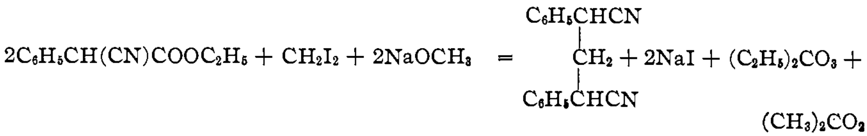
The reactions between methylene iodide, ethyl and methyl phenylmalonates and ethyl phenylcyanoacetate have now been studied. The two esters of phenylmalonic acid react similarly, giving good yields of the esters of α,γ-diphenylglutaric acid instead of esters of α,γ-diphenylpropanetetracarboxylic acid as might be expected. The ester of a tetrabasic acid is probably the primary product of the reaction. It then decomposes in the presence of the sodium alcoholate into the compounds isolated.



$$2C_6H_5CH(COOR)_2 + CH_2I_2 + 2NaOR = \begin{array}{c} C_6H_5CHCOOR \\ | \\ CH_2 \\ | \\ C_6H_5CHCOOR \end{array} + 2NaI + 2R_2CO_3.$$

The carbonic ester was isolated and identified.

When a mixture of sodium methylate, methylene iodide and ethyl phenylcyanoacetate is heated, α,γ-diphenylglutaronitrile is formed. Here, also, the product is apparently a secondary one, arising from a cyano ester by the elimination of two carbethoxyl groups.



$$2C_6H_5CH(CN)COOC_2H_5 + CH_2I_2 + 2NaOCH_3 = \begin{array}{c} C_6H_5CHCN \\ | \\ CH_2 \\ | \\ C_6H_5CHCN \end{array} + 2NaI + (C_2H_5)_2CO_3 + (CH_3)_2CO_3$$

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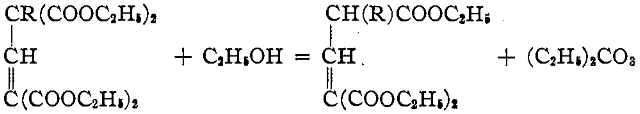
[1] Dressel, *Ann.*, **256**, 175 (1890).

[2] Ref. 1, p. 192.

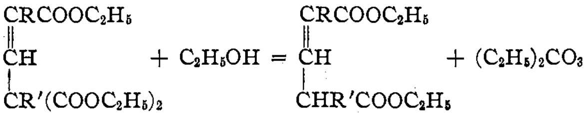
This nitrile[3] is known, having been made in small yield by condensing benzyl cyanide with methylene iodide in the presence of sodium hydroxide.

The explanation of these peculiar reactions involving the elimination of ester groups as carbonic esters may be sought in some experiments described by Thorpe[4] and his associates. They have found, for example, that the mono-alkylated esters made from Conrad and Guthzeit's yellow sodium compound[5] react in the manner already described, in the presence of an alcoholic solution of sodium ethylate.



$$\begin{array}{l}CR(COOC_2H_5)_2\\ |\\ CH\\ \|\\ C(COOC_2H_5)_2\end{array} + C_2H_5OH = \begin{array}{l}CH(R)COOC_2H_5\\ |\\ CH\\ \|\\ C(COOC_2H_5)_2\end{array} + (C_2H_5)_2CO_3$$

The ester of the tribasic acid thus formed is stable toward sodium ethylate. It possesses a mobile hydrogen atom. Alkylation gives another compound that will react with sodium ethylate to give ethyl carbonate.



$$\begin{array}{l}CRCOOC_2H_5\\ \|\\ CH\\ |\\ CR'(COOC_2H_5)_2\end{array} + C_2H_5OH = \begin{array}{l}CRCOOC_2H_5\\ \|\\ CH\\ |\\ CHR'COOC_2H_5\end{array} + (C_2H_5)_2CO_3$$

Certain nitriles[4] behave in a similar manner.

In all of these cases the loss of the carbethoxyl group seems to be involved in the peculiar isomerism of the glutaconic acids, for up to the present it has been observed only in compounds of that series, or in compounds of a similar unsaturated character. Thorpe assumes that the driving force in these reactions is the tendency for the molecule to acquire a mobile hydrogen atom. In every case he has mentioned, this explanation applies.

This same explanation may be given for the reactions recorded here. The α-hydrogen atoms in ethyl phenylacetate and in benzyl cyanide are known to be more reactive than those in most esters, and the compounds described here are similar to them. The elimination of ester groups from ethyl propanetetracarboxylate and from ethyl α,γ-dibenzylpropanetetracarboxylate would result in the formation of substances, ethyl glutarate and ethyl α,γ-dibenzylglutarate, respectively, neither of which contains mobile hydrogen atoms. It is therefore to be expected that both of these compounds would be stable in the presence of alcoholates. It is believed that this is the first time that the smooth elimination of ester groups has been observed during the formation of saturated compounds.

The methyl α,γ-diphenylglutarate obtained from the methyl phenylmalonate is a mixture of isomers. This is proved by its behavior on hydrolysis, since it yields a mixture of two acids. Only one of these, the

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[3] Zelinsky and Feldmann, *Ber.*, **22**, 3290 (1890).

[4] Rogerson and Thorpe, *J. Chem. Soc.*, **87**, 1702 (1905). Thole and Thorpe, *ibid.*, **99**, 2187 (1911). Ingold and Thorpe, *ibid.*, **115**, 144 (1919).

[5] Conrad and Guthzeit, *Ann.*, **222**, 258 (1884).

compound of lower melting point, has been previously described, having been obtained from the corresponding nitrile.[3]

Experimental Part

The **Methyl Alcohol** was dehydrated by lime and then treated with magnesium methylate to remove the last traces of water.

The **Methylene Iodide**[6] was obtained by the reduction of iodoform by sodium arsenite.

The **Ethyl Phenylcyano-acetate**[7] was prepared from ethyl carbonate, benzyl cyanide and sodium in 57% yield. It boiled at 139–147° (mostly at 142–143°) at 5mm. pressure.

The **Methyl Phenylmalonate**[8] was made by a modification of Stieglitz and Rising's process. Instead of using sodium as a condensing agent, a very concentrated solution of sodium methylate was employed. To 175 cc. of absolute methyl alcohol 23 g. of sodium was added in portions; about two hours' heating on the steam-bath was required to dissolve it. The solution was then cooled nearly to room temperature and 150 g. of methyl phenylacetate and 118 g. of methyl oxalate were added all at once. The reagents were thoroughly mixed, and within about five minutes the whole mass had solidified. After remaining at room temperature for two or three days, the mixture was refluxed for two hours on the steam-bath. Water, hydrochloric acid and ether were added and all the material was brought into solution by shaking. It was found unnecessary to isolate the sodium compound as was done by Stieglitz and Rising. After the ether solution was dried, the solvent evaporated and the remaining liquid heated to 160° under diminished pressure until no more carbon monoxide was evolved, the dark colored residue was fractionated twice. The white product weighing 127 g. boiled at 145–157° (13 mm.) and melted at 49°. The yield was 61% or, if 35 g. of recovered methyl phenylacetate be considered, 79%.

Methyl α, γ-Diphenylglutarate.—A solution of sodium methylate prepared from 11.5 g. of sodium and 100 cc. of methyl alcohol was heated on a steam-bath with 67 g. of methylene iodide and 104 g. of methyl phenylmalonate. In a few hours a gelatinous precipitate of sodium iodide began to separate. After three days' heating the alcohol was distilled from the steam-bath, water was added and the organic compounds were removed with ether. The ether solution was dried with calcium chloride and the solvent evaporated. When the residue was heated under diminished pressure, some methylene iodide and other low-boiling substances distilled. Then the temperature rose rapidly and the product distilled between 202° and 210°, mostly at 205° and 210° (6 mm.). It weighed 48.5 g., which was a 61.5% yield.

From one preparation of the ester a small amount of crystals separated. They melted at 53–55° and were very soluble in all of the common solvents except water.

The composition of the distillate was determined.

Analysis. Subs., 0.1858: CO_2, 0.4960; H_2O, 0.1037. Calc. for $C_{19}H_{20}O_4$: C, 73.1; H, 6.4. Found: C, 73.0; H, 6.3.

The methyl alcohol which was removed by heating the reaction mixture on the steam-bath contained methyl carbonate. This was obtained by pouring the mixture into a saturated solution of calcium chloride. The insoluble portion was separated and fractionated. In this way about 1 g. of liquid boiling at 70° to 90° was isolated. The impure methyl carbonate was then treated with 2 cc. of concd. ammonium hydroxide solution in a sealed tube for four hours at 170–180°. The ester layer had disappeared

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[6] *Univ. Illinois Bull.*, **16,** No. 43, p. 29 (1919).

[7] Hessler, *Am. Chem. J.*, **32,** 120 (1904).

[8] THIS JOURNAL, **40,** 727 (1918).

at the end of that time and, on spontaneous evaporation of the liquid, crystals remained. These were purified by crystallization from absolute ethyl alcohol and identified as urea by a mixed melting point with a known specimen.

Ethyl α,γ-Diphenylglutarate.—This ester was made in the same way as the methyl; yield, 64%. In one experiment in which alcohol-free sodium ethylate was used as the condensing agent, the yield was only 32%. The pure ester boiled at 216–217° (7mm.).

Analysis. Subs., 0.2757: CO_2, 0.7509; H_2O, 0.1715. Calc. for $C_{21}H_{24}O_4$: C, 74.1; H, 7.1. Found: C, 74.3; H, 7.0.

The Isomeric α,γ-Diphenylglutaric Acids.—A solution of 1.5 g. of sodium in a mixture of 20 cc. of ordinary methyl alcohol and 1 cc. of water was allowed to react with 6.5 g. of methyl α,γ-diphenylglutarate. In about three minutes a solid appeared and soon the whole mass had solidified. The next day anhydrous ether was added and the salt filtered off. It was washed well with ether and then dried on the steam-bath. It weighed 4.3 g. The salt was then dissolved in water and the solution decolorized with boneblack. When hydrochloric acid was added dropwise from a buret to the hot solution, the acid precipitated. It was necessary for the acid to be added slowly, and as soon as precipitation started, to wait for the compound to crystallize before more was added, for otherwise the product came down as a putty-like mass which was very slow to crystallize. For the same reason all of the ether had to be removed from the salt before it was dissolved in water. The crude acid melted at 161–162° and weighed 3.3 g. A specimen that had been crystallized from hot water melted at 164.5–165.5°. The literature gives 164°.

The mother liquor from the sodium salt and the wash ether were evaporated on the steam-bath. Water was then added, the dark colored solution treated with boneblack and the organic acid precipitated as described above. It weighed 1.9 g. and melted indefinitely at 169–180°. It was best purified by recrystallization from a mixture of chloroform and petroleum ether. The melting point was then 185–186.5°. The new acid is very soluble in methyl, ethyl and *n*-butyl alcohols, and in ether, but is insoluble in petroleum ether. A mixed melting point of the two acids was 151–158°.

Equivalent weight. Calc. for $C_{17}H_{16}O_4$, 142.1. Isomer melting at 164.5–165.5°. Subs., 0.2357: 16.72 cc. of 0.0989 *N* NaOH. Found: 142.2. Isomer melting at 185–186.5°. Subs., 0.2357: 16.32 cc. of 0.0989 *N* NaOH. Found: 142.3.

α,γ-Diphenylglutaronitrile.—A solution of 3.5 g. of sodium in 40 cc. of methyl alcohol was mixed with 28 g. of ethyl phenylcyano-acetate and 20 g. of methylene iodide. After remaining at room temperature for two hours the solution was heated for five hours on the steam-bath. At the end of this period, it was only slightly alkaline to moist litmus paper and the mixture was poured into dil. hydrochloric acid. The product was extracted with ether and the solution washed with water, dried with calcium chloride and then distilled. A small amount of low-boiling material came over first, and finally the product which consisted of 14 g. of yellowish oil that boiled at 220–227° (5 mm.). This oil was dissolved in warm alcohol and the solution allowed to concentrate spontaneously. A white crystalline product weighing 11.5 g. was obtained; m. p., 66°, yield, 54%. Another run gave a 39% yield.

The same substance was obtained by a modification of Zelinsky and Feldmann's method.[3] Instead of steam-distilling the product, vacuum distillation was used. The yield was the same as reported by them. A pure acid could not be obtained by the hydrolysis of the nitrile under a variety of conditions.

Summary

1. An improved method for the preparation of methyl phenylmalonate is given.

2. Methylene iodide has been condensed with methyl and ethyl phenylmalonates and with ethyl phenylcyano-acetate, giving good yields of esters of α,γ-diphenylglutaric acid and α,γ-diphenylglutaronitrile, respectively. These reactions involve the elimination of ester group as carbonic esters.
3. A new isomer of α,γ-diphenylglutaric acid has been obtained.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE ABBOTT LABORATORIES]

PREPARATION AND HYDROLYSIS OF SUBSTITUTED CYANAMIDES: DI-N-BUTYLCYANAMIDE AND DIALLYLCYANAMIDE

BY E. B. VLIET

RECEIVED FEBRUARY 18, 1924

In searching for a method of preparing di-*n*-butylamine and diallylamine in relatively pure form, free from primary and tertiary amines, the hydrolysis of disubstituted cyanamides was investigated. Diethylamine has been formed in this manner by the action of acids and alkalies on diethylcyanamide,[1,2] while di-*iso*-amylcyanamide and dibenzylcyanamide have been converted into the corresponding amines by treatment with hydrochloric acid at 140–150°.[3] However, this method of obtaining secondary amines is handicapped by the lack of a practical method for preparing disubstituted cyanamides.

Dialkylcyanamides have been prepared by the reaction of dialkylamines with chlorocyanogen or bromocyanogen,[4,5] the reaction of dialkylchloroamines with potassium cyanide,[6] and the action of bromine on a mixture of dialkylamines and potassium cyanide.[7,8] Dimethylcyanamide has been obtained[9] from dimethylsulfate and free cyanamide, H_2CN_2. It is obvious that these methods are not practical.

Dialkylcyanamides have also been prepared by the action of alkyl halides on disilvercyanamide[10] and on disodiumcyanamide.[2,3] Since disodiumcyanamide cannot be obtained on the market and is difficult to prepare, these methods could not be considered.

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[1] Cahours and Cloëz, *Ann.*, **90**, 96 (1854).

[2] Fileti and Schiff, *Ber.*, 10, 427 (1877).

[3] Traube and Engelhardt, *Ber.*, **44**, 3149 (1911).

[4] Ref. 1, p. 95.

[5] Wallach, *Ber.*, **32**, 1873 (1899).

[6] Berg, *Compt. rend.*, **114**, 483, 1379 (1892); **116**, 327, 887 (1893); *Bull. soc. chim.*, [3] **7**, 548 (1892); *Ann. chim. phys.*, [7] **3**, 352 (1894).

[7] Chancel, *Compt. rend.*, **116**, 329 (1893); *Bull. soc. chim.*, [3] **9**, 239 (1893).

[8] McKee, *Am. Chem. J.*, **36**, 209 (1906).

[9] Diels and Gollmann, *Ber.*, **44**, 3165 (1911).

[10] Lime nitrogen contains approximately 55% of $CaCN_2$, 20% of CaO, 12% of graphite, and small amounts of various impurities. It should be protected from moisture in order to prevent slow polymerization to dicyanodiamide. It is advisable to obtain fresh lime nitrogen for the syntheses reported.