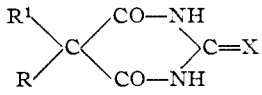
TABLE II

BARBITURIC ACIDS CONTAINING THE 3-THIENYL SUBSTITUENT



R	R¹	X	M.p., °C.	Yield, %	Formula	Sulfur, % Calcd.	Sulfur, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
3-Thenyl	H	O	207–207.5	95	$C_9H_8O_3N_2S$	14.30	13.96	12.50	12.55
3-Thenyl	Ethyl	O	162–163	20[a]	$C_{11}H_{12}O_3N_2S$	12.71	13.05	11.11	11.05
3-Thenyl	Allyl	O	155.5–156.5	77	$C_{12}H_{12}O_3N_2S$	12.13	11.85	10.60	11.04
3-Thenyl	Ethyl	S	170–171	57	$C_{11}H_{12}O_2N_2S_2$	23.89	23.81	10.44	10.32
3-Thenyl	Allyl	S	155–155.5	55	$C_{12}H_{12}O_2N_2S_2$	22.86	22.71	9.99	9.75
3-Thienyl	Ethyl	O	192–194	45	$C_{10}H_{10}O_3N_2S$	13.45	13.40	11.76	11.92
3-Thienyl	Allyl	O	133–134	31	$C_{11}H_{10}O_3N_2S$	12.82	12.64	11.20	11.01

[a] After separation of hydrate.

crude product was dissolved in 10% sodium carbonate and reprecipitated with hydrochloric acid without much loss in weight or improvement in melting range. Careful fractional crystallization from water gave 3 g. of white glistening plates, melting at 177–178° without decomposition, which analyzed correctly for a monohydrate.

Anal. Calcd. for $C_{11}H_{12}O_3N_2S \cdot H_2O$: S, 11.86; N, 10.37. Found: S, 11.70; N, 10.21.

Several attempts to dehydrate this material by vacuum desiccation or recrystallization from absolute ethanol were unsuccessful. Concentration of the aqueous mother liquors and cooling caused the deposition of 2.9 g. of crystals melting at 162–163° which analyzed correctly for the desired product. Properties of the barbituric acids are reported in Table II.

Attempted Preparation of 5-(3-Thenal)-barbituric Acid.—When 25.4 g. (0.1 mole) of diethyl 3-thenalmalonate was allowed to react with urea in the usual way, 17.4 g. of a bright yellow crystalline product was obtained which melted at 161–162° after recrystallizing from water. Attempted recrystallization from absolute ethanol resulted in extensive decomposition, and vacuum desiccation at 100° did not alter the compound. It was soluble in 10% sodium carbonate solution with the evolution of carbon dioxide, and was reprecipitated with acid. This substance analyzed correctly for a dihydrate of thenalbarbituric acid.

Anal. Calcd. for $C_9H_8O_3N_2S \cdot 2H_2O$: S, 12.42; N, 10.85. Found: S, 12.26; N, 10.81.

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The Preparation of β-Aminoglutaric Acid and β-Aminoadipic Acid

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Prior to 1953, β-aminodicarboxylic acids were not mentioned in the chemical literature. Recently, a number of publications have appeared on the preparation of this class of compounds. The syntheses[2–4] are based on the reduction of substituted hydrazones of the appropriate β-keto esters, on the action of hydrazoic acid upon β-substituted γ-keto esters[5] such as ethyl cyclopentanone-2-acetate and on the oxidative cleavage[6] of 4-acetamidocyclohexanol. Some of these methods are rather tedious; in many cases the yields are low, and the starting materials are not readily available.

None of these workers seem to have considered the addition of ammonia to an activated double bond in an acid or an acid derivative, although Scheibler[7] had prepared β-aminobutyric acid from crotonic acid and ammonia more than 40 years ago.

In preliminary experiments a 7.7% yield of β-aminoglutaric acid (I) resulted when diethyl glutaconate (II) was heated at 100–110° for 20 hours with excess ammonium hydroxide in a sealed tube. Ruheman[8] had investigated this reaction with II and its α-benzyl derivative and reported the isolation of an unspecified amount of "benzyldihydroxypyridine" from the latter reaction.

A 60% yield of diethyl β-aminoglutarate(III) was realized when ammonia was introduced into an anhydrous ethanol solution of II. The presence of excess ammonia at all times apparently suppressed the formation of secondary and tertiary amino esters that could result from further reactions of III with the unsaturated ester; no trace of these potential by-products was found.

The preparation of I also was attempted *via* addition of phthalimide to II. This method had been employed successfully for the preparation of β-amino acids from unsaturated nitriles[9] or aldehydes.[10] However, all efforts to effect the addition were unsuccessful. Reactions were carried out in ethanolic solutions of sodium ethoxide and *t*-butyl alcohol solutions of potassium *t*-butoxide at both 30° and the reflux temperatures of the solvents (78 and 83°, respectively).

There are two reports[11–12] in the literature which describe the addition of amines to 2-hexenedinitrile, the latter being obtained by isomerization of 3-hexenedinitrile (IV). Langkammerer found that ammonia and primary amines did not give the expected products. However, when compound IV was suspended in excess ammonium hydroxide, and gaseous ammonia was passed through the solution, β-aminoadipic acid was isolated in yields of 40.5 and 62%, depending on the methods employed for isolating the free acid.

(1) Abstracted from a thesis by William A. Swarts submitted to the Faculty of the Graduate School of Purdue University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) J. Gootjes and W. Th. Nauta, *Rec. trav. chim.*, **72**, 721 (1953).

(3) L. Birkofer and I. Storch, *Chem. Ber.*, **86**, 32 (1953).

(4) A. Romeo and L. Magni, *Atti acad. nazl. Lincei, Rend., Classe, sci. fis., mat. e nat.*, **14**, 423 (1953); *C. A.*, **48**, 10592 (1954).

(5) L. Birkofer and I. Storch, *Chem. Ber.*, **86**, 749 (1953).

(6) J. H. Billman and J. A. Buehler, THIS JOURNAL, **75**, 1345 (1953).

(7) H. Scheibler, *Ber.*, **45**, 2278 (1912).

(8) S. Ruheman and R. S. Morrell, *J. Chem. Soc.*, **59**, 743 (1891); **63**, 259 (1893).

(9) V. M. Rodionov and N. G. Yartseva, *Bull. acad. sci., U.R.S.S., Classe sci. chim.*, 251 (1948); *C.A.*, **42**, 4942 (1948).

(10) O. A. Moe and D. T. Warner, THIS JOURNAL, **71**, 1251 (1949).

(11) C. M. Langkammerer, U. S. Patent 2,532,561 (1950); *C. A.*, **45**, 2967 (1951).

(12) H. F. Piepenbrink, *Ann.*, **572**, 83 (1951).

Experimental[13]

Ethyl β-Aminoglutarate Hydrochloride.—Absolute ethanol was saturated with dry ammonia and diethyl glutaconate[14] (15 g., 0.08 mole) was added in one portion. The temperature was maintained at 50–55° while ammonia was passed through the solution continually for 36 hours. Removal of ammonia and ethanol *in vacuo* afforded a slightly green-yellow oil which was taken up in 100 ml. of dry ether. Some gummy material remained; it was removed from the solution and washed with two 50-ml. portions of ether. The washings were combined with the ethereal solution and upon addition of dry hydrogen chloride an oil separated which soon crystallized. Dissolution in chloroform followed by reprecipitation with ether afforded a total of 12.0 g. (62%) of ethyl β-aminoglutarate hydrochloride, m.p. 83.5–84.5°.

Anal. Calcd. for $C_9H_{18}NO_4Cl$: C, 45.1; H, 7.52; N, 5.85. Found: C, 44.80; H, 7.58; N, 6.00.

β-Aminoglutaric Acid.—The crude amino ester was heated with excess 37% hydrochloric acid on the steam-bath for two hours. The solution was then concentrated *in vacuo* to a thick slurry, distilled water was added and the resulting solution evaporated *in vacuo* to dryness. Any unchanged glutaconic acid was extracted with boiling ether and the residue was then redissolved in water. The amino acid precipitated when the *p*H was adjusted to about 3.5 with base. Crystallization with water in the presence of Norite and Celite gave β-aminoglutaric acid, m.p. 295° dec. (lit.[2] value 276–280° dec.). An additional amount of the acid was obtained by extracting the Norite and Celite residue several times with boiling water. The total yield was 69%.

Anal. Calcd. for $C_5H_9O_4N$: C, 40.81; H, 6.17; N, 9.52. Found: C, 40.35; H, 6.27; N, 9.50.

β-Aminoadipic Acid.—Ammonia was passed continually through a reaction mixture containing 210 ml. of 28% ammonium hydroxide and 21.2 g. (0.2 mole) of 3-hexenedinitrile which had been recrystallized from both benzene and water. The temperature was raised slowly to 75° where it was maintained for about 24 hours. Ammonia and water were then removed *in vacuo* and this operation was repeated by adding and evaporating more water until all of the ammonia was removed. The remaining oil was hydrolyzed at reflux with 200 ml. of 18% hydrochloric acid in the presence of Norite and Celite. The precipitate was extracted with two 100-ml. portions of distilled water and the extracts combined with the filtrate from the hydrolysis. The solution then was concentrated *in vacuo* and this operation was repeated by adding additional amounts of water until the excess hydrochloric acid was removed. A thick slurry remained from which the isolation of the free amino acid was carried out in two ways:

(a) On dissolving the above slurry in water and on adjusting the *p*H to about 3.5 with base, a total of 13.1 g. (40.5%) of β-aminoadipic acid m.p. 190–193° dec., precipitated from the solution on standing for several weeks in a refrigerator. An additional 8% of slightly impure acid, m.p. 180–185° dec. (lit.[2,6] values 186–187° dec. and 189–190.5° dec.), was obtained on concentrating the mother liquor, adding a mixture of alcohol and ether and washing the precipitate free of ammonium chloride with ice-cold water, methanol and finally ether.

(b) The above slurry was dissolved in 200 ml. of distilled water and passed through a column of the basic ion-exchange resin, Amberlite IR-4-B. The eluate was basic and was concentrated until the excess ammonia was removed. The concentrate was diluted with water and the fresh solution passed again through the exchange resin. This procedure had to be repeated several times to remove all inorganic matter. In doing this a certain amount of Amberlite had been dissolved by the water and concentration of the final eluate gave a red-brown, gummy semi-solid. Trituration of this magma with 150 ml. of methanol at 25° left 18.7 g. of crude β-aminoadipic acid, m.p. 185–187° dec. Additional amounts of the acid were isolated by evaporating the aqueous methanolic solution and triturating the residue with fresh methanol. The total yield was 20.0 g. (62%).

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(13) All melting points are uncorrected.

(14) E. P. Kohler and G. H. Reid, THIS JOURNAL, **47**, 2807 (1925).

Dehydrocyclization of *o*-Ethyl-, *o*-Allyl- and *o*-Isopropylphenols

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Hansch and co-workers[1,2] recently described this dehydrocyclization reaction, but their yields were low (4–11% for benzofuran over palladium-on-charcoal and chromia-on-charcoal at 600–625°, 8–18% for 3-methylbenzofuran over chromia–copper-on-charcoal at 540–600° and 15–31% for 2-methylbenzofuran over palladium-on-charcoal and platinum-on-charcoal at 525–625°). They reported chromia–alumina to be unsatisfactory due to excessive decomposition of the phenols. On the contrary, we found chromia–alumina to be an effective catalyst, especially in the presence of diluent steam.

The use of diluent steam was found to be beneficial in these dehydrocyclizations, increasing the per pass yield of benzofuran from 16 to 48%, that of 2-methylbenzofuran from 31 to 48%, and that of 3-methylbenzofuran from 12 to 54%. The ultimate yields were increased proportionally. The use of diluent benzene vapor increased the per pass yield of benzofuran from 16 to 21% but decreased the yield of 3-methylbenzofuran from 12 to 7% (again the ultimate yields varied in similar manner). The superiority of steam over benzene vapor as diluent agrees with the findings of Nickels and Corson[3] in the dehydrogenation of ethylnaphthalene.

Certain by-products were identified: phenol and *o*-cresol from *o*-ethylphenol; phenol, *o*-cresol, *o*-ethylphenol and benzofuran from *o*-allyl- and *o*-isopropylphenols. Dihydrobenzofurans were not found.

The dehydrocyclization of these *o*-substituted phenols makes benzofuran and alkylbenzofurans readily available for the first time from easily obtainable starting materials.

Catalyst and Materials.—The chromia–alumina catalyst, 15% Cr_2O_3–85% Al_2O_3, was in the form of $1/8'' \times 1/8''$ pills, purchased from the Harshaw Chemical Co. *o*-Ethyl- and *o*-isopropylphenols were supplied by the Koppers Co., Inc. *o*-Allylphenol was prepared in 83% yield by the rearrangement of *o*-allylphenyl ether.

Apparatus, Analysis and Procedure.—The catalytic apparatus was similar to that described previously.[4] The starting materials and catalysates were distilled through a 27-plate glass column packed with glass helices, and analyzed by infrared absorption.

Procedure A.—The phenol was passed over the catalyst in the absence of diluent. The catalysate was dissolved in 500 cc. of ether, and the solution was extracted with 700 cc. of cold 10% aqueous sodium hydroxide in three portions.

(1) C. Hansch, W. Saltonstall and J. Settle, THIS JOURNAL, **71**, 943 (1949).

(2) C. Hansch, C. Scott and H. Keller, *Ind. Eng. Chem.*, **42**, 2114 (1950).

(3) J. E. Nickels and B. B. Corson, *ibid.*, **43**, 1685 (1951).

(4) J. E. Nickels, G. A. Webb, W. J. Heintzelman and B. B. Corson, *ibid.*, **41**, 563 (1949).