canted from the amalgam and decolorized with a few drops of alcohol. The solvent is removed with steam and the residue is crystallized once from acetic acid. The results are tabulated below.

TABLE I

THE INDENE MIXTURES FROM THE SODIUM COMPOUNDS

Source of indene mixture	M. p. of indene mixture, °C.	Composition, % of 1-*p*-tolyl-2,3-diphenylindene
III through Na comp.	137	50
V through Na comp.	138	52
IV through Na comp.	140	56
a	152	90
b	137	50

[a] One-half gram of 1,2-diphenyl-3-*p*-tolylindene boiled with 15 ml. of 90% alcohol containing 5% of potassium hydroxide dissolves completely only after fifteen minutes. Then a solid separates slowly, and after an additional hour of boiling no further change can be noticed. The solution is cooled, the crystalline deposit is washed with a little alcohol and water and dried.

[b] As a check on the method, a mixture of equal parts of the two indenes was crystallized once from acetic acid. The melting point of the mixture so obtained shows that its composition was unchanged by this treatment.

Summary

1,2-Diphenyl-3-*p*-tolylindenol and 1-*p*-tolyl-2,3-diphenylindenol both yield the same methyl ether, presumably derived from the former, when treated with methanol–sulfuric acid. This ether is cleaved by sodium amalgam, and the resulting sodium compound hydrolyzes to a mixture of approximately equal parts of 1,2-diphenyl-3-*p*-tolylindene and 1-*p*-tolyl-2,3-diphenylindene. Each of these indenes reacts with sodium amalgam to give a sodium compound whose hydrolysis results in the formation of the same mixture of indenes.

1,2-Diphenyl-3-*p*-tolylindene rearranges to its less soluble isomer to the extent of 90% when boiled with dilute alcoholic potassium hydroxide.

The conclusion is drawn that the anion present in solutions of the metal salt of the indenes is labile, its structure being fixed only after it has combined with a proton.

MINNEAPOLIS, MINNESOTA RECEIVED DECEMBER 23, 1933

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF DELAWARE]

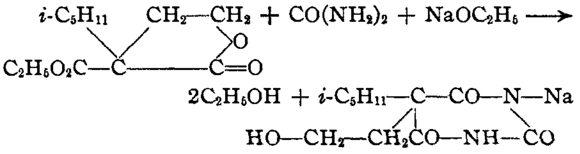
Some 5-β-Ethyl Substituted Derivatives of Barbituric Acid[1]

BY EDWARD F. ROSENBERG, RALPH F. KNEELAND AND GLENN S. SKINNER

In 1922 some work was initiated by one of us[2] which was directed toward the synthesis of 5-phenyl 5-β-ethyl substituted barbituric acids. It was desired ultimately to prepare a 5-vinyl 5-alkyl derivative. These experiments showed that the series of reactions employed go much more smoothly if the phenyl radical is replaced by ethyl. More recently Cope and McElvain[3] report failure to obtain 5-vinyl-5-ethylbarbituric acid by the condensation of vinylethylmalonic ester with urea.

In the present work these experiments have been resumed using in place of phenyl the C_4 and C_5 radicals of the paraffin series since such derivatives of barbituric acid are among the most effective hypnotics. It has been found possible to substitute ethylene bromide for ethylene chloroiodide in the condensation with both *n*-butyl- and isoamylmalonic ester with satisfactory results. The isoamyl-β-bromoethylmalonic ester, however, was largely decomposed to the lactone upon distillation unless the pressure was below 3 mm. In the case of the chloroethyl isoamyl ester a negligible amount of decomposition during the distillation was indicated by the analysis for chlorine. In our experience either benzene or ether is satisfactory as a medium. The yield fluctuates widely with the variation of the equivalent proportions of the reagents. This will be reported in more detail in a later communication.

The lactone was found to condense with urea to form 5-isoamyl-5-β-hydroxyethylbarbituric acid in 75% yield. The method should be general and will be investigated further. This condensation gives better yields if the reaction mixture is refluxed for relatively short periods of time followed by distillation of the alcohol.



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[1] Most of the experimental work here reported formed portions of theses presented for the degree of Master of Science in the University of Delaware by Edward F. Rosenberg, 1930, and Ralph F. Kneeland, 1933.

[2] Voorhees and Skinner, THIS JOURNAL, **47**, 1124 (1925).

[3] Cope and McElvain, *ibid.*, **54**, 4311 (1932).

Experimental Part

β-Halogenoethyl Alkyl Malonic Esters.—These compounds were prepared by the action of ethylene chloroiodide or ethylene bromide on the sodium derivative of the alkyl malonic ester in ether or benzene. About five days of refluxing were required for the reaction to go to completion in ether while in some cases the reaction in benzene was complete in thirty-six hours. In one experiment using ethylene chloroiodide the evolved gas was identified as vinyl chloride by converting it to 1,2-dibromochloroethane. As an illustration of the results obtained from one of the better runs, 9.2 g. of sodium, 150.4 g. of ethylene bromide, 172.8 g. of *n*-butylmalonic ester in 500 cc. of dry benzene yielded 89.2 g. of recovered *n*-butylmalonic ester and 102.8 g. of β-bromoethyl-*n*-butylmalonic ester, corresponding to a yield of 79% based on sodium or 82% based on the malonic ester disappearing in the reaction.

No.	Ester	B. p., °C.	d_4^{20}	d_4^{25}
1	$C_{14}H_{25}O_4Cl$	132 (1 mm.)	1.0381	1.0334
2	$C_{14}H_{25}O_4Br$	145–147 (2 mm.)	1.1576	1.1540
3	$C_{13}H_{23}O_4Br$	127–128 (0.5 mm.)		

No.	n_D^{20}	n_D^{25}	Halogen, % Calcd.	Halogen, % Found
1	1.4454		12.12	12.24
2	1.457		23.71	23.24
3	1.4568	1.4548	24.6	22.9

β-Dimethylaminoethyl Alkyl Malonic Esters.—β-Chloroethyl isoamyl malonic ester (44 g.) and 13.5 g. of dimethylamine heated in 71 cc. of absolute alcohol for forty-eight hours at 100° yielded 1.0 g. of unchanged chloro ester and 23 g. of β-dimethylamino ester; hydrochloride, m. p. 78°. β-Diethylamino isoamyl malonic ester (12 g.) was prepared similarly from 29.5 g. of the β-bromoethyl ester and 19.8 g. of diethylamine in 40 cc. of absolute alcohol; b. p. 141° (1 mm.). β-Bromoethyl *n*-butyl malonic ester (32.3 g.) and 9.0 g. of dimethylamine in 75 cc. of absolute alcohol similarly yielded 3 g. of unchanged ester and 15 g. of the dimethylamino ester. A better yield is obtained at room temperature and the product is not contaminated with a slightly higher boiling by-product, but the reaction is slow, requiring about two weeks. A pure product was obtained by conversion to the hydrochloride. The *n*-butyl derivative crystallized from a mixture of benzene and ligroin melted at 137–138 (corr.); chlorine found, 10.87%; calculated for $C_{15}H_{30}O_4NCl$, 10.95%.

No.	Ester	B. p., °C.	d_4^{20}	d_4^{25}
1	$C_{16}H_{31}O_4N$	152–154 (10 mm.)	0.9548	0.9525
2	$C_{15}H_{29}O_4N$	115 (3 mm.)	.9544	.9500

No.	n_D^{20}	n_D^{25}	Nitrogen, % Calcd.	Nitrogen, % Found
1			4.65	4.79
2	1.4420	1.4400	4.89	4.93

5-β-Alkylaminoethyl-5-alkylbarbituric Acids.—These were more conveniently prepared by a modification of the usual procedure. The reaction mixture was refluxed for one hour on the water-bath followed by distillation of the alcohol. To obtain the hydrochloride of the resulting amino acid the concentrated aqueous solution of the residue from the reaction of the amino ester was made acid to Congo paper with concd. hydrochloric acid. The free amino acids were easily extracted from a concentrated solution neutral to litmus by chloroform. The yield was approximately 90% of the theoretical. The hydrochlorides were purified by crystallization from alcohol and the free amino acids from chloroform. The hydrochloride of the isoamyl derivative melted at 277–280° (sealed tube); chlorine found 11.54%; calculated for $C_{13}H_{24}O_3N_3Cl$, 11.60%. The free amino acid melted at 115–116° (sealed tube). The hydrochloride of the *n*-butyl derivative melted at 244–245° (corr.). The free amino acid melted at 118–119° (heated slowly); nitrogen found 16.2%; calculated for $C_{12}H_{21}O_3N_3$, 16.5.

α-Isoamyl-α-carboxethyl-γ-butyric Lactone.—A sample of the β-bromoethyl derivative of isoamylmalonic ester that had partially decomposed by distillation at 5 mm. was then distilled slowly at about 20 mm. to complete the decomposition. Analysis now showed it to contain only 1.06% bromine. This last portion of bromine was retained rather stubbornly as eleven distillations were required to reduce the bromine content to 0.32%. It was then carefully refractionated and the middle cut was found to give no weighable precipitate of silver bromide (Carius). It was then partially frozen in a carbon dioxide freezing mixture, filtered through a sintered glass filter, followed by distillation of the crystalline portion; b. p. 165–166.5° (18 mm.); d_4^{25} 1.0393; n_D^{20} 1.4492; n_D^{25} 1.4472. Calcd. for $C_{12}H_{20}O_4$: C, 63.11; H, 8.84. Found: C, 63.31; H, 8.66.

β-Hydroxyethylisoamylbarbituric Acid.—A solution of sodium ethoxide was prepared by dissolving 1.9 g. of sodium in 75 cc. of absolute alcohol. Finely powdered fused urea (3.3 g.) and 6.38 g. of the above lactone were added to the cooled solution. The mixture was refluxed for two and one-half hours and the alcohol was distilled on the steam-bath. The residue was dissolved in a small volume of water and precipitated in the cold with hydrochloric acid. The acid was filtered on a small Hirsch funnel with suction and washed with small quantities of water and ligroin. The yield of product melting at 174–175° was 5.1 g. It was conveniently recrystallized by dissolving in an equal weight of boiling alcohol, at once adding four times its weight of boiling water and continuing the boiling until crystallization began; m. p. 177.5–178° (corr.). Calcd. for $C_{11}H_{18}O_4N_2$: N, 11.57. Found: N, 11.63.

Summary

5-β-Ethyl substituted derivatives of 5-*n*-butyl and 5-isoamylbarbituric acids are described. A new method is given for the preparation of a 5-β-hydroxyethyl-5-alkyl-barbituric acid.

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