presence of 1% benzoyl peroxide was studied. Methacrylylsucrose is the most reactive, undecylenoylsucrose is slightly reactive, the crotonyl and allyloxycarbonyl derivatives show intermediate reactivity; furoylsucrose and cinnamoylsucrose do not polymerize at all.

Copolymerization of these esters with styrene and methyl methacrylate in the presence of 1% benzoyl peroxide also was studied.

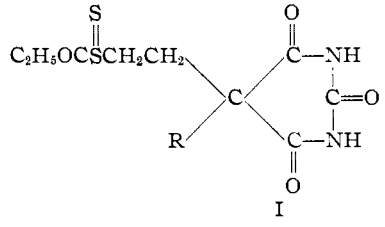
PHILADELPHIA 18, PA. RECEIVED JULY 7, 1949

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF DELAWARE]

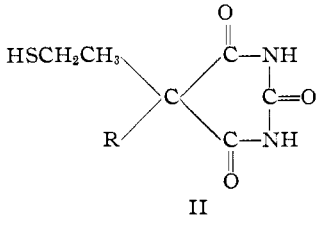
5-Alkyl-5-(β-mercaptoethyl)-barbituric Acids. α-Ethyl-α-carboxethyl-γ-thiobutyrolactone

BY GLENN S. SKINNER AND JOHN B. BICKING

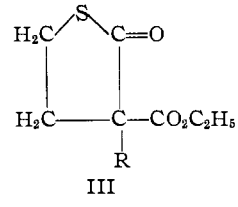
The preparation of 5-alkyl-5-(β-mercaptoethyl)-barbituric acids was undertaken to compare them with the corresponding hydroxyl compounds. Since 5-alkyl-5-(β-bromoethyl)-barbituric acids[1] can be prepared in good yields from the lactone esters, since the methylxanthate had already been prepared[2] from one of the bromo compounds, and since it is known that an aliphatic mercaptan can be prepared in good yield from a xanthate,[3] the first experiments were conducted with potassium methylxanthate. On account of relatively poorer yields as well as lesser stability of both the methylxanthate and the corresponding barbituric acid derivative, potassium ethylxanthate was employed for most of the work. The xanthate derivative (I) was readily converted to the desired β-mercaptoethyl derivative (II) by hydrolysis or ammonolysis. Ammonolysis appeared to be superior both as to yield and quality of product.



I



II



III

It seemed also of interest to determine whether an α-alkyl-α-carboxethyl-γ-thiobutyrolactone (III) could be condensed with urea in a manner analogous to that of an α-alkyl-α-carboxethyl-γ-butyrolactone.[4] A search of the literature failed to reveal any thiolactones derivable from a geminal dibasic acid. The methods reported for making simple thiolactones[5] did not appear suitable. Ethyl β-bromoethylethylmalonate was therefore treated with potassium ethylxanthate and the product was decomposed to the desired thiolactone ester by heating under diminished pressure. This gave 5-ethyl-5-(β-mercaptoethyl)-barbituric acid by condensation with urea.

BARBITURIC ACIDS RR'C(CONH)$_2$CO

R	R'	M. p., °C.	Sulfur, % Calcd.	Found
$HOCH_2CH_2$-	n-C_6H_{11}-	150–151	11.56[a]	11.48[a]
$BrCH_2CH_2$-	n-C_3H_7-	169.5–170	28.84[b]	28.88[b]
$BrCH_2CH_2$-	n-C_6H_{11}-	155.5–156.5	26.19[b]	26.19[b]
$CH_3OCSSCH_2CH_2$-	n-C_3H_7-	165.5–167	21.07	21.20
$C_2H_5OCSSCH_2CH_2$-	C_2H_5-	132.5–134	21.07	20.86
$C_2H_5OCSSCH_2CH_2$-	n-C_3H_7-	139–141	20.14	19.93
$C_2H_5OCSSCH_2CH_2$-	n-C_4H_9-	145.5–146.5	19.29	19.32
$C_2H_5OCSSHG_2CH_2$-	n-C_5H_{11}-	141–142	18.51	18.36
$HSCH_2CH_2$-	C_2H_5-	147–148	14.83	14.62
$HSCH_2CH_2$-	n-C_3H_7-	146–147.5	13.92	13.85
$HSCH_2CH_2$-	n-C_4H_9-	125.5–127	13.12	13.06
$HSCH_2CH_2$-	n-C_5H_{11}-	133–134	12.41	12.36
$HSCH_2CH_2$-	iso-C_5H_{11}-	124–126	12.41	12.29

[a] Nitrogen. [b] Bromine.

Pharmacological screening tests indicated that the above compounds are not suitable for anesthesia or hypnosis.

To determine whether a lactone ester gives the expected value for the parachor α-n-amyl-α-carboxethyl-γ-butyrolactone was selected. The ring method[6] for determining the surface tension and the previously determined value for the density[7] were used. The surface tension was found to be $\gamma^{25°}$ = 33.95 dynes/cm. and the parachor calculated from this value is [P] = 529.4. The parachor calculated from the atomic and structural contributions [P] = 531.3 reveals no marked effect due to the lactone ring.

Experimental

5-Alkyl-5-(β-alkylxanthoethyl)-barbituric Acids.—In a typical experiment 9.2 g. (0.030 mole) of 5-n-amyl-5-β-bromoethylbarbituric acid and 5.3 g. (0.033 mole) of freshly prepared potassium ethylxanthate were dissolved in 120 cc. of absolute alcohol contained in a 200 cc., r. b. flask surrounded by a water-bath at 45°. After five

(1) Skinner, THIS JOURNAL, **69**, 322 (1937).
(2) Skinner, Stokes and Spiller, *ibid.*, **69**, 3083 (1947).
(3) Loven and Johansson, *Ber.*, **48**, 1257 (1915).
(4) Rosenberg, Kneeland and Skinner, THIS JOURNAL, **56**, 1339 (1934).
(5) Fries and Mengel, *Ber.*, **45**, 3408 (1912); Holmberg and Schjänberg, *C. A.*, **35**, 2113 (1941).
(6) Harkins and Jordan, THIS JOURNAL, **52**, 1751 (1930).
(7) Skinner and Mitchell, *ibid.*, **67**, 1252 (1945).

hours the solvent was removed by distillation under diminished pressure. The white solid residue was washed thoroughly with ice-cold water while being filtered with suction. The crude product (11.0 g.) was crystallized from benzene, yield 9.4 g. (85%), m. p. 141–142°.

5-Alkyl-5-β-mercaptoethylbarbituric Acids.—Typical experiments were made using the crude 5-*n*-amyl-5-(β-ethylxanthoethyl)-barbituric acid made from 15.3 g. (0.050 mole) of the bromo acid.

Procedure A.—The crude xanthoethylbarbituric acid was dissolved in 70 cc. of 10% sodium hydroxide and kept at 45–50° for one and one-half hours. The solution was cooled and acidified to congo red by careful addition of hydrochloric acid. The precipitated oil was stirred vigorously while it crystallized. The product (11.5 g.) was crystallized from a mixture (2:1) of benzene and toluene, yield 9.0 g., m. p. 129–132°. Two recrystallizations raised the melting point to 133–134°.

Procedure B.—To a solution of the crude xanthoethylbarbituric acid in 20 cc. of 10% sodium hydroxide 50 cc. of aqua ammonia (0.90) were added with stirring. After standing seven hours at room temperature the solution was extracted with chloroform and the aqueous layer was made acid to congo red with hydrochloric acid. The precipitated oil crystallized when cooled in an ice-bath with vigorous stirring, yield 12 g. One recrystallization from the benzene-toluene mixture gave 10.2 g. (79%) of the product, m. p. 130–132.5°. Another recrystallization raised the melting point to 133–134°.

All of the mercapto acids gave a positive test for a mercaptan in alkaline solution with sodium nitroprusside. These acids had not suffered oxidation to the disulfides as indicated by molecular weight determinations (Rast). Calcd. as mercaptan: ethyl deriv. 216, *n*-amyl deriv. 258. Calcd. as disulfide: ethyl deriv. 430, *n*-amyl deriv. 514. Found: ethyl deriv. 227, *n*-amyl deriv. 241.

α-Ethyl-α-carboxethyl-γ-thiobutyrolactone.—Ethyl β-bromoethylethylmalonate was prepared in the usual way and the fraction distilling at 101–114° (0.5 mm.) was employed. The analysis for bromine indicated that 97.6% of it was the desired product.

To a solution of 48 g. (0.30 mole) of freshly prepared potassium ethylxanthate in 650 cc. of ethyl alcohol was added 74 g. (0.25 mole) of ethyl β-bromoethylethylmalonate with good mixing. After heating at 50° for twelve hours and allowing to stand at room temperature for eleven hours the amount of potassium bromide removed by filtration corresponded to the amount expected. Removal of the solvent under diminished pressure left 82.5 g. (98%) of a yellow, viscous oil possessing a nauseating odor. It contained only a trace of bromine.

Eighty grams of the oil were heated in a bath at 200° (40 mm.) for one hour. Toward the end of this period, distillation of a more volatile material began to occur. The residue was then distilled (30–7 mm., bath 160–190°). Refractionation of the distillate gave 32.5 g. of crude thiolactone. The analysis for sulfur indicated that the thiolactone comprised 92.5% of the product. It was purified by two recrystallizations from petroleum ether at dry ice temperature, b. p. 115–116° (5 mm.), 123–125° (7 mm.); d^{20}_4 1.1377, d^{25}_4 1.1346; $n^{20}D$ 1.4887, $n^{25}D$ 1.4860; $[M]^{25}\gamma$ 51.18 (Lorentz–Lorenz), $[M]^{25}\gamma$ 51.21 (calcd. from Eisenlohr's values).

Anal. Calcd. for $C_9H_{14}O_3S$: S, 15.85. Found: S, 15.63.

Condensation of α-Ethyl-α-carboxethyl-γ-thiobutyrolactone with Urea.—To an ice-cold solution of sodium ethoxide prepared from 3.5 g. of sodium and 50 cc. of absolute alcohol was added 6.0 g. of urea and then dropwise with stirring 10.1 g. of α-ethyl-α-carboxethyl-γ-thiobutyrolactone. The urea dissolved after three hours. The reaction mixture remained as a viscous solution after forty hours at room temperature. The product obtained by distillation of the solvent and acidification in the usual way partially crystallized. After removal of the liquid with petroleum ether the crude solid product weighed 6 g. Crystallization from benzene, dissolution in aqueous sodium hydroxide, and precipitation with hydrochloric acid gave 2.8 g. of crystals, m. p. 146–148°. The melting point was not lowered when mixed with a sample of 5-ethyl-5-β-mercaptoethylbarbituric acid prepared from the bromo acid. Further work is in progress.

Summary

1. 5-Alkyl-5-β-mercaptoethylbarbituric acids have been prepared from 5-alkyl-5-β-bromoethylbarbituric acids.

2. An α-carboxethyl-γ-thiobutyrolactone is described. It has been condensed with urea to give a β-mercaptoethylbarbituric acid.

NEWARK, DELAWARE RECEIVED AUGUST 6, 1949

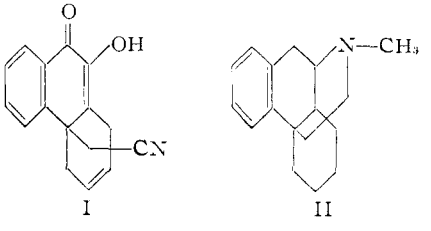
[CONTRIBUTION FROM THE MARIAN EDWARDS PARK LABORATORY OF BRYN MAWR COLLEGE AND THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

The Synthesis of Ring Systems Related to Morphine. IV. N-Methylisomorphinane*

BY MARSHALL GATES, R. B. WOODWARD, WILLIAM F. NEWHALL AND ROSEMARIE KÜNZLI

The synthesis of 9,10-dioxo-13-cyanomethyl-5,8,9,10,13,14-hexahydrophenanthrene (I) and a preliminary account of its conversion to the tetracyclic tertiary base II which we now call N-methylisomorphinane, and which has, or is stereoisomeric with, the carbon–nitrogen skeleton present in morphine, have been the subjects of the first two papers of this series.[1a]

The present paper is concerned with a reinterpretation of the reaction path leading from I to II, with the detailed description of these reactions, and with an improved procedure for the preparation of I.



I II

The adduct I on hydrogenation over copper–chromium oxide at moderate temperature and

* Taken in part from a dissertation presented by William F. Newhall to the faculty of Bryn Mawr College in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(1) (a) Gates and Newhall, THIS JOURNAL, **70**, 2261 (1948); (b) *Experientia*, **5**, 285 (1949).