TABLE I

2,3-DIALKOXYQUINOXALINES

2,3-Disubstituents	M.p., °C., uncor.	Yield, %	Nitrogen, % Calcd.	Nitrogen, % Found	Density d^{25}_4	Refractive index $n^{25}D$	Absorption maxima and molecular extinction coefficients[c] $\epsilon \times 10^{-3}$ (λ, 246 mμ)	$\epsilon \times 10^{-3}$ (λ, 300–302 mμ)	$\epsilon \times 10^{-3}$ (λ, 312 mμ)
OCH_3	92–93[a]	82	14.7	14.6	...	....	13.6	4.9	9.8
OCH_2CH_3	77–78[b]	70	12.8	12.9	...	....	14.5	5.3	9.7
$OCH_2CH_2CH_3$	53–54	71	11.4	11.1	...	....	14.7	5.9	10.1
$OCH(CH_3)_2$	93–94	55	11.4	11.1	...	....	14.7	6.5	12.4
$OCH_2CH_2CH_2CH_3$	50–51	45	10.2	10.2	...	....	15.8	6.5	10.2
$OCH_2CH(CH_3)_2$	liq.	76	10.2	10.4	1.040	1.5370	15.6	6.5	9.9
$OCH_2CH_2CH_2CH_2CH_3$	liq.	68	9.3	9.4	1.022	1.5304	15.8	6.5	10.1
$OCH_2CH_2CH(CH_3)_2$	liq.	79	9.3	9.6	1.014	1.5290	15.7	6.6	10.1
$OCH_2CH_2CH_2CH_2CH_2CH_3$	60–65	60	8.5	8.5	...	....	14.7	7.5	10.8

[a] Stevens, Pfister and Wolf[2a] reported a melting point of 92–93°. [b] Gowenlock, Newbold and Spring[2b] reported a melting point of 78°. [c] Solvent, 95% ethanol.

The time of heating varied from 1 hour for the dimethoxy derivative to 11 hours for the di-*n*-hexoxy derivative of quinoxaline. The yield was then worked up by two different procedures.

If the alkoxy group contained less than four carbon atoms, 20 ml. of water was added to the reaction mixture, and the precipitated 2,3-dialkoxyquinoxaline was filtered off and washed several times with water. One recrystallization from ethanol–water gave pure material.

If the alkoxy group had four or more carbon atoms, the reaction mixture was steam distilled to remove excess alcohol. The residue was then extracted with ethyl ether, treated with decolorizing charcoal, and the ether evaporated. The colorless oils were purified by distillation at 1 mm. from a Hickman vacuum still.[5]

Following this treatment, 2,3-di-*n*-butoxyquinoxaline was recrystallized from ethanol–water; 2,3-diisobutoxy-, 2,3-di-*n*-amoxy- and 2,3-diisoamoxyquinoxaline remained in a liquid state as colorless, very viscous oils that could not be distilled through a conventional distillation apparatus. 2,3-Di-*n*-hexoxyquinoxaline slowly solidified in about 10 days to a wax-like solid that could not be recrystallized from any solvent.

Absorption Spectra.—The ultraviolet absorption spectra, condensed in Table I, were obtained on a Beckman model DU quartz spectrophotometer.

(5) K. Hickman and C. Sanford, *J. Phys. Chem.*, **34**, 637 (1930).

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF MIAMI
CORAL GABLES, FLORIDA

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The Preparation of Morphine-N-methyl-C^{14}

BY HENRY RAPOPORT, CALVIN H. LOVELL AND BERT M. TOLBERT

In order to study the metabolic fate and mode of action of morphine and codeine in both the addict and non-addict, a program was initiated for the preparation of these alkaloids labeled at various parts of the molecule with radioactive carbon. The preparation[1] of codeine-3-methoxy-C^{14} and some results on its metabolism[2] in the rat have been reported. The present report is concerned with the preparation of morphine-N-methyl-C^{14}.

Since codeine-N-methyl-C^{14} can be readily prepared in the manner described by von Braun[3] the most attractive path to the corresponding morphine compound would be through cleavage of the 3-methoxyl group. Although this cleavage reaction has been used to convert some codeine derivatives to their morphine analogs, no successful application of this reaction to codeine itself has been reported. The usual ether-cleaving reagents (concentrated hydrogen iodide and hydrogen bromide, in aqueous solution or in glacial acetic acid) appear to be too drastic. However, pyridine hydrochloride, which has been used recently to prepare desoxymorphines from desoxycodeines,[4] under carefully controlled conditions effected the cleavage of codeine to morphine in a reasonable yield (22%), and hence was applied to the preparation of morphine-N-methyl-C^{14} from codeine-N-methyl-C^{14}.

Experimental[5]

Morphine-N-methyl-C^{14}.—Cleavage of 1.00 g. of codeine-N-methyl-C^{14} (specific activity 3.56 μc./mg.) was effected by heating with pyridine hydrochloride in the manner previously described for Δ^7-desoxycodeine.[4b] The reaction mixture was dissolved in 20 ml. of water, basified with 10 ml. of 4 *N* sodium hydroxide, and the non-phenolic material was removed by extraction with four 15-ml. portions of chloroform. The combined chloroform extracts were washed with 10 ml. of 0.5 *N* sodium hydroxide and 10 ml. of water, and the aqueous phase, after adding the washings, was adjusted to *p*H 9 and cooled thoroughly to precipitate phenolic material. After filtering and drying, this phenolic material was digested with 75 ml. of methanol, the mixture was filtered hot, and the filtrate was chromatographed on an alumina (Merck and Co., Inc.) column (120 × 11 mm.) using 700 ml. of methanol as eluent. The residue after evaporation of the methanol was dissolved in 10 ml. of 0.2 *N* sodium hydroxide, filtered, and the filtrate was adjusted to *p*H 9, precipitating the crude morphine. After drying, this crude morphine was sublimed (180–190° (0.1 mm.)), and the sublimate was crystallized from absolute ethanol. There was thus obtained a total of 210 mg. (22%) of morphine-N-methyl-C^{14}, m.p. 254–255°, specific activity, 3.75 μc./mg.

(1) F. N. Chang, J. F. Oneto, P. T. Sah, B. M. Tolbert and H. Rapoport, *J. Org. Chem.*, **15**, 634 (1950).

(2) T. K. Adler and M. E. Latham, *Proc. Soc. Expti. Biol. Med.*, **73**, 401 (1950); M. E. Latham and H. W. Elliott, *J. Pharmacol. Expti. Therap.*, **101**, 259 (1951).

(3) J. von Braun, *Ber.*, **47**, 2312 (1914).

(4) (a) H. Rapoport and R. M. Bonner, THIS JOURNAL, **73**, 2872 (1951); (b) H. Rapoport and R. M. Bonner, *ibid.*, **73**, 5485 (1951).

(5) All melting points are corrected.

DEPARTMENT OF CHEMISTRY AND RADIATION LABORATORY
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA

RECEIVED JULY 30, 1951

Preparation of 1,4-Dihydroxy-2-naphthyl Hydroxymethyl Ketone

BY DEAN R. REXFORD

Previous to the appearance of Spruit's excellent work in the preparation of a series of substituted

naphthoquinones and naphthohydroquinones,[1] we had for some time been engaged in the preparation of 1,4-dihydroxy-2-naphthyl hydroxymethyl ketone.[2] This compound represented a suggested structure for bacterial luciferin.[3]

In the course of the work we arrived at a method for the preparation of the compound by a route which differs slightly from that of Spruit[1] and which offers some advantages in terms of the stability of the intermediate compounds,

It was found that 1-hydroxy-4-acetoxy-2-naphthyl methyl ketone[4] can be conveniently brominated to form 1-hydroxy-4-acetoxy-2-naphthyl bromomethyl ketone in satisfactory yield. This compound can be acetylated to form Spruit's 1,4-diacetoxynaphthyl bromomethyl ketone. The indirect hydrolysis of this diacetate to form 1,4-dihydroxy-2-naphthyl hydroxymethyl ketone is best carried out according to Spruit.[1]

Experimental

1-Hydroxy-4-acetoxy-2-naphthyl Bromomethyl Ketone.—To an illuminated solution of 0.655 g. of resublimed 1-hydroxy-4-acetoxy-2-naphthyl methyl ketone in 7 cc. of purified glacial acetic acid[5] was added at room temperature 2.56 cc. of a freshly titrated solution of bromine (2.1 *N*) in the same solvent. Final warming in a warm water-bath completed the reaction in one-half hour (solution negative to wet KI–starch paper).

The reaction mixture on being poured into water deposited a yellow oil which crystallized on the addition of alcohol. The product was recrystallized from 95% ethanol and sublimed (0.1 mm., 120°); m.p. 172° dec. micro. cor.

Anal.[6] Calcd. for $C_{14}H_{11}O_4Br$: C, 52.03; H, 3.43; Br, 24.73. Found: C, 51.94, 52.15; H, 3.78, 3.73; Br, 24.29, 24.58.

1,4-Diacetoxy-2-naphthyl bromomethyl ketone prepared by acetylation of the 1-hydroxy compound with acetic anhydride and zinc chloride and crystallized from absolute ethanol, was identical with the product described by Spruit.[1] The 1-acetoxy group is easily lost by hydrolysis in a work-up involving water.

(1) C. P. J. Spruit, *Rec. trav. chim.*, **67**, 285 (1948).

(2) F. H. Johnson, D. R. Rexford and E. N. Harvey, *J. Cellular Comp. Physiol.*, **33**, No. 1, 133 (1949).

(3) C. P. J. Spruit, Thesis, "Naphthothinonen en Bioluminescentie," Drukker ij Fa. Schotanus & Jens, Utrecht, 1946.

(4) C. P. J. Spruit, *Rec. trav. chim.*, **66**, 655 (1947).

(5) Fractionated from acetic anhydride. Several other solvents were tried. Specially purified acetic acid appeared to yield the purest product.

(6) Analyses by Joseph F. Alicino, P. O. Box 267, Metuchen, N. J.

FRICK CHEMICAL LABORATORY
PRINCETON UNIVERSITY
PRINCETON, N. Y.

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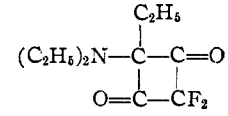
Reactions of Polyfluoro Olefins. IV,[1] Reaction with Triethylamine[2]

BY KARL E. RAPP

Reaction between triethylamine and chlorotrifluoroethylene was undetectable when this amine was used as an alkaline catalyst in the anionic addition of thiols to the polyfluoro olefin.[3]

When triethylamine was used to catalyze the addition of 1-butanethiol to hexafluorocyclobutene, however, an interesting and unexpected side reaction involving the tertiary amine occurred. This reaction was shown to take place independently of the addition reactions reported by Rapp, *et al.*[3] The product of the reaction was an extremely hygroscopic crystalline solid which reacted readily with water, moist air or absolute methanol with the evolution of heat and hydrogen fluoride. Because of this reactivity, the extent to which purification for analysis could be carried was somewhat limited. On the other hand, the white crystalline solid resulting from hydrolysis was so stable that it could be employed as a calibration reference in the development of an analytical procedure for the determination of organic fluoride.[4]

Elemental analysis of the stable hydrolyzed compound and determination of its molecular weight strongly indicated a molecular composition of $C_{10}H_{15}NO_2F_2$. Although attempts to prepare an oxime or *p*-nitrophenylhydrazone were unsuccessful, a possible diketone structure



satisfying both composition and valence requirements might be expected to possess the low water-solubility responsible for the initial precipitation of the compound when the amine-catalyzed butanethiol reaction mixture was washed with water. Consideration of a means by which a structure of this type might be attained would initially involve the formation of a quaternary ammonium fluoride by a fluorine substitution reaction in contrast to the addition mechanism followed by primary and secondary amines.[5] Analysis of the somewhat impure reactive product agreed fairly well with the composition, $C_{10}H_{15}NF_6$. Existence of such a quaternary salt was further substantiated by the reaction with absolute methanol to form an active methoxy derivative which was extremely soluble in methanol and was converted to the stable hydrolysis product immediately by dilution of its methanol solution with water or within a few hours when exposed in the solid form to normally moist air. Acceptance of the suggested diketone structure would require a shift of an ethyl radical from nitrogen to the adjacent carbon of the ring during the removal of hydrogen fluoride by hydrolysis of either the quaternary fluoride or its methoxy derivative.

Experimental

Reaction in the Presence of 1-Butanethiol.—As described in a previous report[3] the closed cylinder was charged with 1-butanethiol, hexafluorocyclobutene and triethylamine in a molar ratio of 1:1.1:1.1. The reactants were shaken at a temperature of 46° for 48 hr. although there was evidence of heat-evolution at the Dry Ice charging temperature. At the end of this period the reaction mixture was transferred to a separatory funnel and acidified with concentrated hydrochloric acid. At the time, the relatively small amount of

(1) The previous paper in this series is: J. T. Barr, K. E. Rapp, R. L. Pruett, C. T. Bahner, J. D. Gibson and R. H. Lafferty, Jr., THIS JOURNAL, **72**, 4480 (1950).

(2) This document is based on work performed for the Atomic Energy Commission by Carbide and Carbon Chemicals Company a Division of Union Carbide and Carbon Corporation, at Oak Ridge, Tennessee.

(3) K. E. Rapp, R. L. Pruett, J. T. Barr, C. T. Bahner, J. D. Gibson and R. H. Lafferty, Jr., THIS JOURNAL, **72**, 3642 (1950).

(4) R. R. Rickard, F. L. Ball and W. W. Harris, *Anal. Chem.*, **23**, 919 (1951).

(5) R. L. Pruett, J. T. Barr, K. E. Rapp, C. T. Bahner, J. D. Gibson and R. H. Lafferty, Jr., THIS JOURNAL, **72**, 3646 (1950).