TABLE I

2,3-DIALKOXYQUINOXALINES

2,3-Disubstituents	M.p., °C., uncor.	Yield, %	Nitrogen, %		Density d^{25}_4	Refractive index n^{25}_D	Absorption maxima and molecular extinction coefficients[c]		
			Calcd.	Found			$\epsilon \times 10^{-3}$ (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.

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

DEPARTMENT OF CHEMISTRY
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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.

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[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. Exptl. Biol. Med.*, **73**, 401 (1950); M. E. Latham and H. W. Elliott, *J. Pharmacol. Exptl. 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.

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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