

A Common Aziridinium Ion Intermediate in the Solvolysis of Halogeno-codeinone and -neopinone Acetals

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Summary Treatment of the dimethyl acetal of either 14-bromocodeinone or 7-iodoneopinone with silver perchlorate in benzene gives an aziridinium salt believed to be an intermediate leading to 9-substituted indolino-codeinone derivatives in the solvolysis of either acetal.

SOLVOLYSIS of 14-bromocodeine¹ and 7-iodoneopine² derivatives is believed to proceed, at least in part, *via* an aziridinium ion intermediate. At present, this belief rests

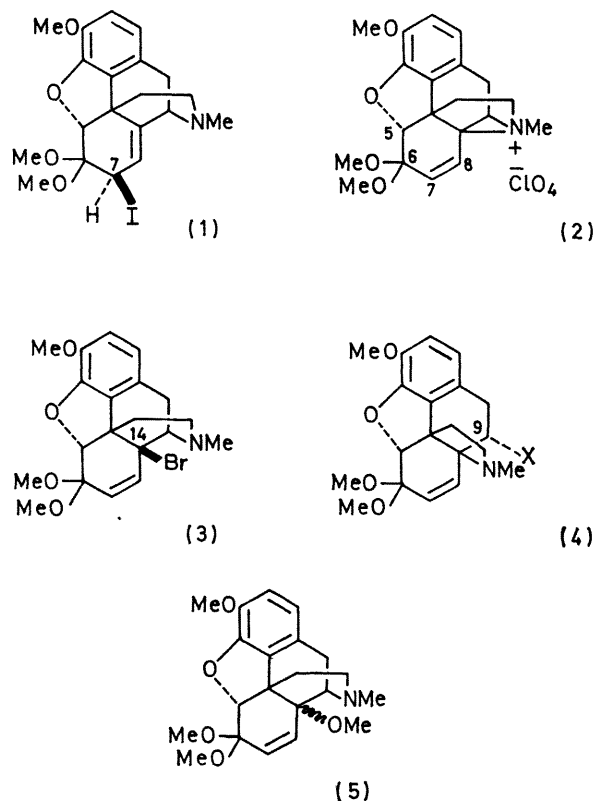
solely on the isolation of products resulting, formally, from a 1,2-migration of nitrogen. We have now prepared an aziridinium salt of appropriate structure and shown that it has the reactivity required for the postulated intermediate.

7- β -Iodoneopinone dimethyl acetal³ (1) was treated³ in benzene at room temperature with silver perchlorate (1 equiv). An immediate precipitation of silver iodide was observed. Filtration and evaporation of the filtrate gave

the amorphous perchlorate (2). The structure (2) was deduced from the following characteristic n.m.r. bands: τ (CDCl₃) 3.58 (d, J 10.5 Hz, 8-H); 3.96 (d, J 10.5 Hz, 7-H); 5.06 (s, 5-H); 6.20, 6.60, and 6.94 (s, MeO); and 6.60 (s, MeN⁺). The low-field position of olefinic and *N*-methyl signals was indicative^{3,4} of positively charged nitrogen: no bands characteristic of starting material were detected. Significantly, the same aziridinium salt (n.m.r. comparison) was obtained from 14-bromocodeinone dimethyl acetal⁵ (3) under the same conditions. Treatment of the salt, in dimethylformamide, separately with aqueous sodium cyanide and aqueous sodium acetate gave, respectively, the indolinocodeinone derivatives (4; X = CN) and (4; X = OAc) obtainable directly² from the iodo-compound (1) with the same reagents.

If the aziridinium salt (2) is an obligatory intermediate then solvolysis of the halides (1) and (3) should give the same yield[†] of rearranged product. Heinisch *et al.*⁶ have recently reported that the bromo-compound (3) reacts in methanol containing sodium carbonate (1 equiv) to give (23% yield) a 14-methoxycodeinone dimethyl acetal (5), m.p. 104–105°, convertible into the corresponding enone, m.p. 159–160°. We have repeated this experiment and obtained (21%) an acetal, m.p. 104–104.5°, giving an enone, m.p. 158.5–159.5°. The same compound was formed (27%) from the iodo-derivative (1) under identical conditions. However, we believe this acetal to have the rearranged structure (4; X = OMe) and to be formed from the common aziridinium ion (2) in both solvolyses. The n.m.r. spectrum of the enone showed a triplet, τ (CDCl₃) 6.45 (J 2.6 Hz), attributable^{1,2} to 9-H; other signals appeared at τ 3.22, 3.81 (AB q, J 10.8 Hz, 8-H and 7-H); 5.32 (s, 5-H); 6.14 and 6.94 (s, MeO); and 7.44 (s, MeN). Nucleophilic substitution at C-9 of indolinocodeinone derivatives may also involve an aziridinium intermediate since treatment of 9- α -hydroxyindolinocodeinone [enone corresponding to (4; X = OH)] with methanesulphonyl chloride in pyridine gave 9- α -chloroindolinocodeinone, m.p. 116–

120°, displaying a double-doublet, τ 5.68 (J 2.7 and 3.3 Hz, 9-H), indicative of substitution with retention of configuration.



We thank Reckitt and Colman Ltd. for financial support.

(Received, July 21st, 1971; Com. 1260.)

[†] Indolinocodeinone derivatives are not the sole products of solvolysis: the yield varies with both nucleophile and solvent.

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⁴ G. A. Olah and P. J. Szilagy, *J. Amer. Chem. Soc.*, 1969, **91**, 2949.

⁵ W. Fleischhacker, F. Vieböck, and F. Zeidler, *Monatsh.*, 1970, **101**, 1215.

⁶ G. Heinisch, V. Klintz, and F. Vieböck, *Monatsh.*, 1971, **102**, 530.