

## Diels-Alder Adducts from Thebaine and Nitroso-arenes

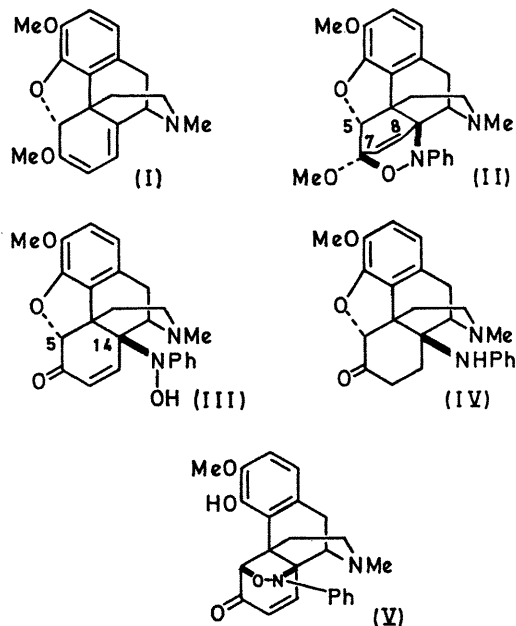
By K. W. BENTLEY, P. HORSEWOOD, G. W. KIRBY,\* and SERJINDER SINGH  
(Chemistry Department, University of Technology, Loughborough, Leicestershire)

**Summary** Thebaine reacts reversibly with nitroso-arenes to form Diels-Alder adducts readily convertible into previously inaccessible derivatives of 14-aminocodeinone.

TREATMENT of thebaine (I) with nitrosobenzene in chloroform at room temp. gave, in high yield, the adduct (II), m.p. 115–118° (decomp.);  $\tau$  3.75 (CDCl<sub>3</sub>) (q, *J* 1.9 Hz, 7-H), 4.64 (d, *J* 9 Hz, 8-H), 5.25 (d, *J* 1 Hz, 5-H), 6.18 and 6.24 (s, MeO), 7.51 (s, MeN). Solutions of the colourless adduct in methanol or chloroform showed a green tint due to partial dissociation; a solution in deuteriochloroform showed weak n.m.r. bands attributable to thebaine. Trituration of the adduct with 1*N*-hydrochloric acid gave 14-(*N*-hydroxyphenylamino)codeinone (III) as the dihydrochloride. The free base had m.p. 127–128°;  $\nu_{\max}$  (CHCl<sub>3</sub>) 3540, 1687 cm.<sup>-1</sup>;  $\lambda_{\max}$  (EtOH) 240 ( $\epsilon$  9,230), 280 (2,510), 350 nm. (sh, 636);  $\tau$  (CDCl<sub>3</sub>) 3.71 and 4.08 (d, *J* 10 Hz, vinyl protons), 5.12 (s, 5-H). Tailing of the long-wavelength, u.v. absorption band of this compound accounted for its pale yellow colour. The mode of attachment of the phenylhydroxylamino-residue at C-14 was established as follows. Acetylation (Ac<sub>2</sub>O, pyridine) of (III) gave an *O*-acetate, m.p. 157–158°;  $\nu_{\max}$  (CHCl<sub>3</sub>) 1773, 1688 cm.<sup>-1</sup>, and catalytic (Pd/C) hydrogenation of (III) gave 14-phenylaminodihydrocodeinone (IV), m.p. 189–190°;  $\nu_{\max}$  (CHCl<sub>3</sub>) 1721 cm.<sup>-1</sup>;  $\tau$  (CDCl<sub>3</sub>) 5.33 (s, 5-H). The ketone (III) rearranged at room temp. in ethanolic sodium ethoxide to the phenol (V), m.p. 197°;  $\nu_{\max}$  (CHCl<sub>3</sub>) 3510, 1685 cm.<sup>-1</sup>;  $\lambda_{\max}$  (EtOH) 235 ( $\epsilon$  10,600), 317 (1220), 361 nm. (872);  $\lambda_{\max}$  (EtOH/EtONa) 254 ( $\epsilon$  12,200), 298 (4370), 361 nm. (1480);  $\tau$  (CDCl<sub>3</sub>) 3.92 (vinyl protons, signals not separated at 60 MHz).

4-Chloro- and 4-methyl-nitrosobenzene also formed

adducts with thebaine. Hydrolysis of the adduct from 4-chloronitrosobenzene gave the expected chloro-analogue of (III). The reactions recorded provide the first route to 14-aminocodeinone derivatives several of which have been found to possess analgaesic properties.



(Received, October 17th, 1969; Com. 1584.)