Novel Photochemical Aporphine Synthesis *via* Spirodienone Rearrangement: (±)-Boldine

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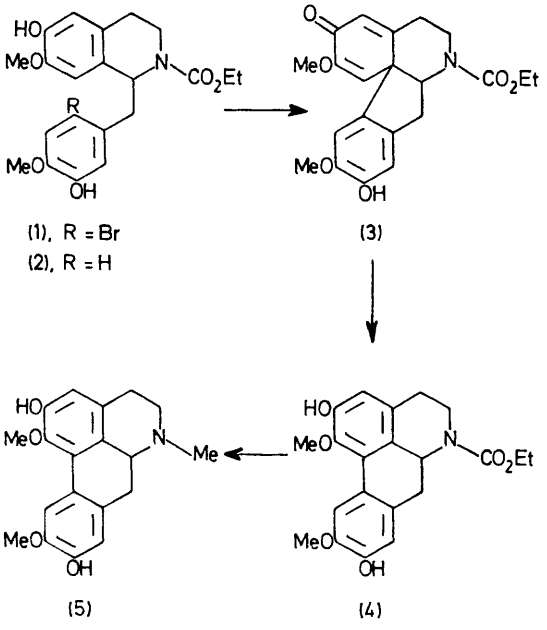
Summary The first synthesis of (±)-boldine (**5**), by photocyclization of the (±)-bromodiphenol (**1**) to the (±)-spirodienone (**3**), followed by rearrangement to (±)-*N*-ethoxycarbonylnorboldine (**4**) and reduction with $LiAlH_4$, is reported.

THE past decade has witnessed the discovery of several photochemical syntheses of aporphine alkaloids, which have proceeded by several different mechanistic pathways.[1] We describe here a novel photochemical synthesis of (±)-boldine (**5**), which proceeds *via* the intermediacy of the proerythrinadienone (**3**).

Photolysis† of the (±)-bromodiphenol (**1**)[2] in a solution of NaOH in absolute ethanol for 14 h gave the (±)-spirodienone (**3**), 34%,‡ m.p. 183—184·5 °C (lit.[3] 144—146 °C),



(**1**), R = Br
(**2**), R = H

(**3**)

(**5**) (**4**)

and (±)-*N*-ethoxycarbonylnorboldine (**4**),§ 5%, m.p. 197—199 °C (EtOH–Et_2O), u.v. λ_{max} (EtOH) 304 (log ϵ 4·15), 284 (4·15), and 216 (4·61) nm; i.r. λ_{max} 2·83 and 5·96 μm; δ ($CDCl_3$) 7·96 (1H, s, H-11), 6·85 (1H, s, H-8), 6·70 (1H, s, H-3), 3·93 (3H, s, C-10 OMe), 3·59 (3H, s, C-1 OMe), 4·20 (2H, q, OCH_2-Me), and 1·29 (3H, t, OCH_2Me); *m/e* 385 (100%, M^+), 355 (64), 340 (4), 323 (5), 310 (12), 296 (14), 283 (31), and 269 (27), along with (±)-*N*-ethoxycarbonylnorprotosinomenine (**2**), 15%, m.p. 153—154 °C (lit.[3] 148–150 °C) and the starting material (**1**), 8%. Treatment of (**4**) with $LiAlH_4$ in tetrahydrofuran under reflux for 18 h yielded (±)-boldine (**5**), isolated as the hydrobromide, 78%, m.p. 189—191 °C (free base, m.p. 159—162 °C). The u.v., n.m.r., and mass spectra were in good agreement with those reported for naturally occurring (+)-boldine.[4] When a solution of (**1**) and sodium acetate in absolute ethanol was irradiated for 15 h, (**3**) and (**4**) were isolated in 7 and 22% yield, respectively, along with (**2**), 22%, and the starting material (**1**), 9%.

These results led us to consider that photochemical transformation of the (±)-bromodiphenol (**1**) into (±)-*N*-ethoxycarbonylnorboldine (**4**) may proceed *via* the spirodienone intermediate (**3**). A solution of the (±)-spirodienone (**3**) and NaOH in absolute ethanol was irradiated for 3·5 h, whereupon (**4**) was isolated in 6% yield along with starting material, 50%. On the other hand, photolysis of (**3**) in a solution of sodium acetate in absolute ethanol for 4 h yielded (**4**), 44%, along with recovered (**3**), 10%. This ready photochemical rearrangement of (**3**) to (**4**) supports the proposed intermediacy of the spirodienone in the photochemical conversion of the (±)-bromodiphenol (**1**) into (±)-*N*-ethoxycarbonylnorboldine (**4**) and constitutes the first reported synthesis of an aporphine *via* rearrangement of a proerythrinadienone.¶ Furthermore, the demonstrated sequence (**1**) → (**3**) → (**4**) → (**5**) constitutes the first total synthesis of (±)-boldine.

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† Photolyses were carried out in a quartz vessel under N_2 and irradiation with GE G15T8 germicidal lamps. Products were separated by preparative t.l.c. using plates pre-coated with silica gel 60 F-254 (EM Reagents).

‡ The spirodienone (**3**) was obtained in *ca.* 2% yield as a powder by phenolic oxidation[3] and *ca.* 18% yield as an oil by photolytic synthesis[2] under somewhat different conditions. The product with m.p. 183—184·5 °C was characterized as (**3**) by comparison of the u.v., i.r., n.m.r., and mass spectra with those reported in ref. 3.

§ All new compounds were characterized by concordant analytical and spectral data. The structural formulae containing asymmetric atoms refer to racemic compounds.

¶ An unsuccessful attempt to convert the spirodienone (**3**) into an aporphine derivative by acid-catalysed rearrangement has been reported (ref. 2).

[1] For a recent review, see M. Shamma, 'The Isoquinoline Alkaloids,' Academic Press, New York, 1972, ch. 10; S. M. Kupchan and P. F. O'Brien, *J.C.S. Chem. Comm.*, 1973, 915.
[2] T. Kametani, K. Takahashi, T. Honda, M. Ihara, and K. Fukumoto, *Chem. and Pharm. Bull. (Japan)*, 1972, **20**, 1793.
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[4] M. Shamma, *Experientia*, 1960, **16**, 484; A. H. Jackson and J. A. Martin, *J. Chem. Soc. (C)*, 1966, 2181 and 2222.