Novel Access to 2-Substituted Indoles and a Convenient Synthesis of Secodine-type Alkaloids

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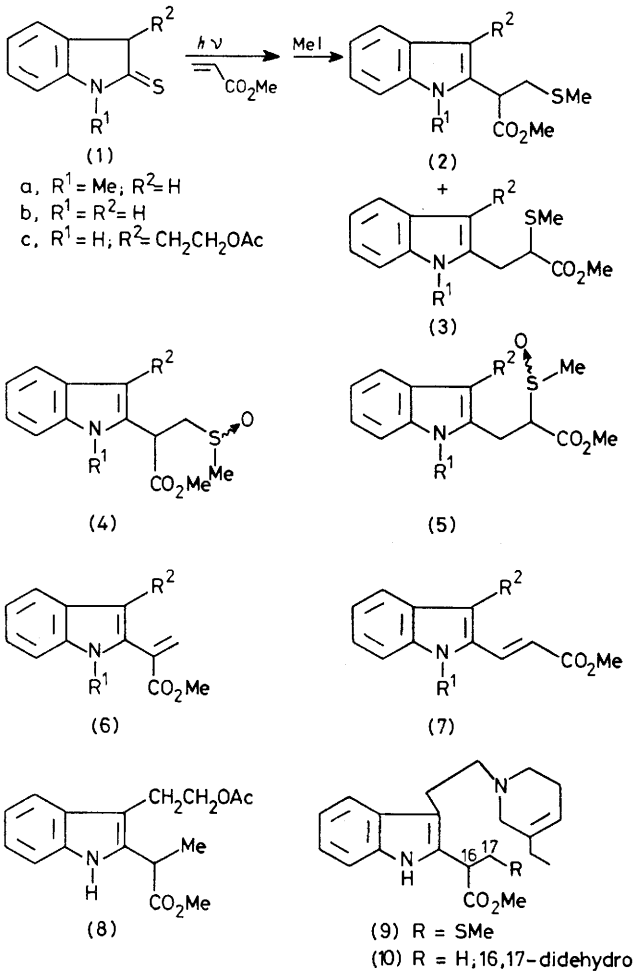
Summary Indoline-2-thiones (**1**) undergo photo-induced addition to methyl acrylate to give 2-substituted indoles and this reaction has been utilised to synthesise dimers of secodine (**10**) which contains an α-acrylic ester function.

IT has been demonstrated[1,2] that a variety of thiones can undergo photo-induced addition to electron-deficient olefins. This ready mode of carbon–carbon bond formation suggested that indoline-2-thiones (**1**) could be attractive substrates for similar reactions to provide 2-substituted indoles. Such an approach offers the possibility of a simple entry to secodine-type alkaloids[3] as illustrated.

Irradiation† of 1-methylindoline-2-thione (**1a**)[4] in dichloromethane solution in the presence of methyl acrylate gave, after methylation (MeI, K_2CO_3, acetone), an inseparable mixture of (**2a**)‡ and (**3a**) (total yield 70%) in the ratio 8:2 as indicated by its ^1H n.m.r. spectrum. Sodium periodate oxidation of the mixture gave two pairs of diastereoisomeric sulphoxides (**4a**) and (**5a**) which could be separated by preparative t.l.c. Upon heating (toluene, 100 °C, 0·5 h) (**4a**) and (**5a**) were transformed into acrylic esters (**6a**)[5] and (**7a**), respectively, which were stable at room temperature.

With (**1b**) as the starting material, the major sulphide (**2b**), m.p. 133 °C, was isolated in 60% yield from a reaction mixture which also contained its isomer (**3b**). Periodate oxidation of (**2b**) led to an unstable pair of sulphoxides which underwent spontaneous elimination of MeSOH at room temperature readily affording two dimers (M^+, m/e 402) of the presumably unstable intermediate (**6b**) (M 201).

By repeating the same sequence of reactions (irradiation with methyl acrylate, *S*-methylation) on compound (**1c**) (oil), synthesised from tryptophyl *O*-acetate according to the procedure of Hino *et al.*,[6] the corresponding 2-substituted derivative (**2c**) was obtained in 60% yield.§ Raney nickel treatment of (**2c**) converted it into (**8**) (oil) whose ^1H n.m.r. spectrum exhibited the expected secondary methyl signal. Compound (**2c**) was de-*O*-acetylated and treated with PBr_3 to yield the corresponding bromide which on reaction with 3-ethylpyridine followed by $NaBH_4$ reduction of the pyridinium salt gave the tetrahydropyridine (**9**) (oil). This compound, a stable derivative of secodine (**10**),[3] was oxidised with *m*-chloroperbenzoic acid (1 equiv.) below −30 °C. The product seemed to be a mixture of secodine dimers on the basis of u.v. data.



† A indoline-2-thione solution (4×10^{-2}M) containing methyl acrylate (10%) was irradiated through Pyrex under nitrogen below 0 °C with a Hanau TQ 150 lamp until the starting material had been consumed. All new compounds gave correct composition by mass spectrometry and the spectral data were consistent with assigned structures.

‡ Only compound (**2a**), m.p. 87 °C, could be partially separated from the mixture by fractional crystallisation.

§ No attempts were made to isolate and characterize the minor compound (**3c**).

This assumption was also supported by the mass spectrum which showed characteristic peaks at *m/e* 338, 214, and 124 (base peak) consistent with the structure of secodine (**10**). These observations are in accord with the previously published work[3] which demonstrated that distillation of secodine dimers afforded unstable secodine. It is very likely that the above synthetic dimers revert to secodine under conditions employed for recording the mass spectra.

In view of this simple access to biogenetically significant secodine-type alkaloids, it should now be possible to prepare other suitably substituted indole derivatives which may serve as appropriate models for cyclisation[7] to *Aspidosperma* or *Iboga*-type alkaloids.

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[1] P. Jouin and J.-L. Fourrey, *Tetrahedron Letters*, 1975, 1329, and references cited therein.
[2] For a review see P. de Mayo, *Accounts Chem. Res.*, 1976, **9**, 52.
[3] G. A. Cordell, G. F. Smith, and G. N. Smith, *Chem. Comm.*, 1970, 189; 191.
[4] T. Hino, K. Tsuneoka, M. Nakagawa, and S. Akaboshi, *Chem. Pharm. Bull (Japad)*, 1969, **17**, 550, and references cited therein.
[5] This compound was obtained through a different route by F. E. Ziegler and E. B. Spitzner, *J. Amer. Chem. Soc.*, 1973, **95**, 7146.
[6] T. Hino, T. Suzuki, S. Takeda, N. Kano, Y. Ishii, A. Sasaki, and M. Nakagawa, *Chem. Pharm. Bull.* (Japan), 1973, **21**, 2739.
[7] A. I. Scott, *Bio-org. Chem.*, 1974, **3**, 398.