

A Convenient Synthesis of 7-Methoxymitosene by the Photolysis of Aminobenzoquinones

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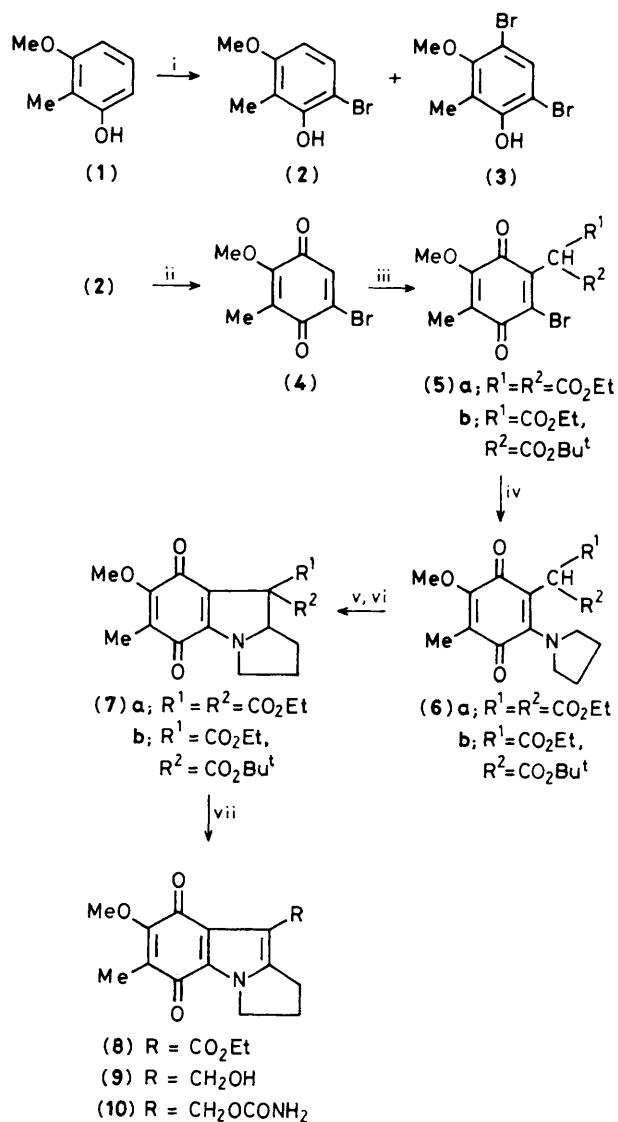
A simple method for the preparation of pyrrolo[1,2-*a*]indoloquinone derivatives using the photolysis of amino-quinones has led to a formal synthesis of 7-methoxymitosene.

In synthetic studies on mitomycin antibiotics,¹ which contain several unique structural features, we have shown that the photolysis of amino-1,4-naphtho- and -benzo-quinones having the active methylene group at the 2-position provides a preparative route to heterocyclic quinones.² In this communication we describe the application of this photo-induced reaction to freshly prepared pyrrolidinylbenzoquinones (**6**) as a simple synthesis of 7-methoxymitosene (**10**).

Our initial approach to (**10**) focused on the preparation of

(**7**) as outlined in Scheme 1. Treatment of the phenol (**1**)³ with bromine-*t*-butylamine⁴ at -78°C afforded the bromophenol (**2**) (60%, m.p. 47°C) in addition to the dibromophenol (**3**) (20%, m.p. 74°C). Compound (**2**) was oxidized with potassium nitrosyldisulphonate-KH₂PO₄($\frac{1}{6}$ M)-acetone-H₂O to give the quinone (**4**)[†] (73%, m.p. 65°C). Treatment of (**4**) with

[†] Satisfactory spectral and analytical data were obtained.



Scheme 1. Reagents: i, $Br_2, Bu^tNH_2, -78^\circ C$; ii, $(SO_3K)_2NO, 1/6 M KH_2PO_4, Me_2CO-H_2O$; iii, $TiCl_4(R^1)(R^2)$ ($R^1=R^2=CO_2Et$ or $R^1=CO_2Et, R^2=CO_2Bu^t$), THF; iv, pyrrolidine, $CHCl_3$; v, *hv*, EtOH; vi, $SiO_2, EtOH$; vii, CF_3CO_2H, CH_2Cl_2 .

thallium diethylmalonate in tetrahydrofuran (THF) gave (5a)† (40%, a yellow oil), which reacted with pyrrolidine to yield the amino-quinone (6a)† (85%, a purple oil). A solu-

tion of (6a) in ethanol was irradiated with a high pressure mercury lamp through Pyrex glass. This irradiated solution was retained on a silica gel column for a few days, and then eluted with ethyl acetate to afford (7a)‡ (68%, m.p. $171^\circ C$). De-esterification of (7a) with sodium cyanide or magnesium chloride in dimethyl sulphoxide⁵ followed by oxidation failed to give the required product (8). Therefore, the pyrrolidinylbenzoquinone (6b)† was prepared from (4) and the thallium salt of ethyl t-butylmalonate by the same method in a moderate yield. Photolysis of (6b) afforded the diastereoisomers of the pyrroloindoloquinone, (7b)-(I)‡ (40%, m.p. $103^\circ C$) and (7b)-(II)‡ (32%, m.p. $156^\circ C$), in the ratio 5:4 after chromatography on silica gel. Structural assignments have not yet been made. On treatment with trifluoroacetic acid, however, each stereoisomer was converted into the same product (8)‡ (m.p. $164^\circ C$), which was identical with an authentic sample (lit.⁶ m.p. $165-166^\circ C$). Recently, the transformation of (8) to (9) and 7-methoxymitosene (10) was reported by Coates and MacManus.⁶ Consequently, this sequence constitutes a formal synthesis of 7-methoxymitosene.

Received, 7th March 1983; Com. 295

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‡ Compound (7a): i.r. $\nu_{max}(KBr)$ 1720, 1650 ($C=O$) cm^{-1} ; m/z 377 M^+ ; 1H n.m.r. $\delta(CDCl_3)$ 1.30 (6H, t, J 7.5 Hz, $Me \times 2$), 1.87 (3H, s, Me), 1.70–2.20 (4H, m, $CH_2 \times 2$), 3.63 (2H, m, CH_2N), 4.12 (3H, s, OMe), 4.26 (4H, q, J 7.5 Hz, $OCH_2 \times 2$), 4.80 (1H, m, CHN). Compound (7b)-(I): i.r. $\nu_{max}(KBr)$ 1742, 1723, 1660, 1640, 1580 cm^{-1} ; m/z 405 M^+ ; 1H n.m.r. $\delta(CDCl_3)$ 1.28 (3H, t, J 7.5 Hz, Me), 1.46 (9H, s, Bu^t), 1.84 (3H, s, Me), 1.84–2.20 (4H, m, $CH_2 \times 2$), 3.60 (2H, m, NCH_2), 4.08 (3H, s, OMe), 4.26 (2H, q, J 7.5 Hz, CH_2), 4.80 (1H, m, CH). Compound (7b)-(II): i.r. $\nu_{max}(KBr)$ 1747, 1708, 1650, 1623, 1560 cm^{-1} ; m/z 405 M^+ . The n.m.r. spectrum is very similar to that of (7b)-(I). Compound (8): i.r. $\nu_{max}(KBr)$ 1718, 1662, 1640, 1610 cm^{-1} ; m/z 303 M^+ ; 1H n.m.r. $\delta(CDCl_3)$ 1.36 (3H, t, J 7.5 Hz, Me), 1.96 (3H, s, Me), 2.56 (2H, quintet, J 7.5 Hz, $NCH_2CH_2CH_2$), 3.10 (2H, t, J 7.5 Hz, CH_2), 4.06 (3H, s, OMe), 4.28 (2H, t, J 7.5 Hz, NCH_2), 4.32 (2H, q, J 7.5 Hz, CO_2CH_2Me).