Novel Stereospecific Synthesis of a Potential Intermediate for Preparation of Tetracyclic Diterpenes from Dihydrobenzocyclobutene Derivatives

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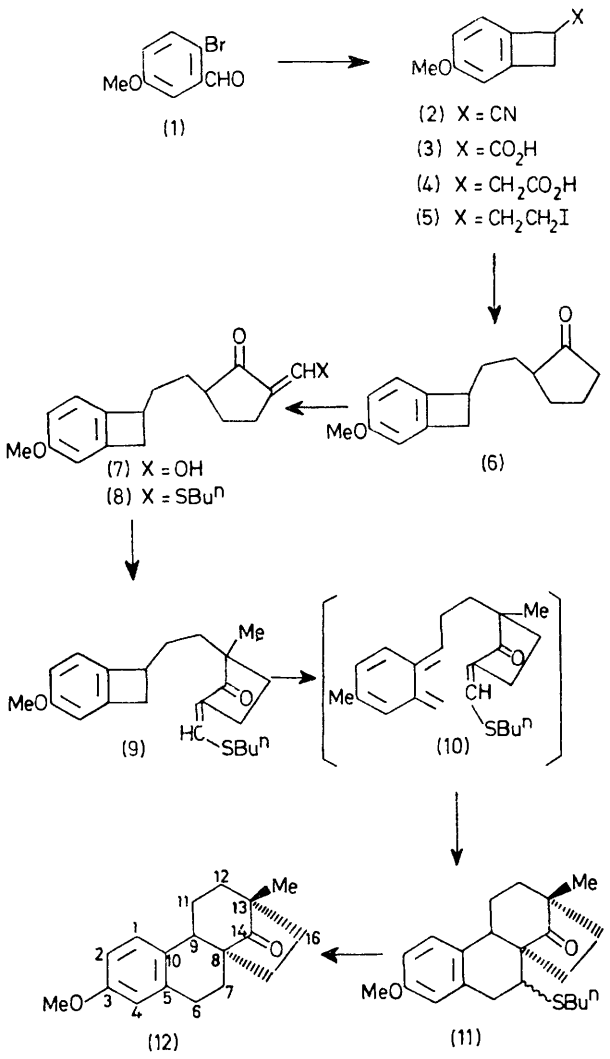
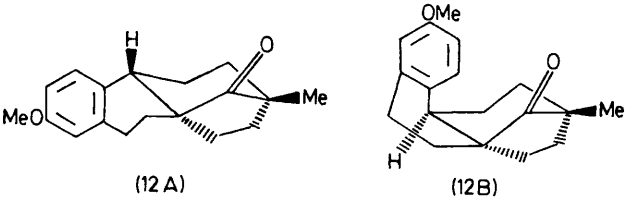
Summary A potential intermediate, the ethano-octahydromethoxymethylphenanthrenone (**12**), for the synthesis of tetracyclic diterpenoids has been stereospecifically synthesised by an intramolecular cycloaddition of the *o*-quinodimethane (**10**) derived thermally from 5-n-butylthiomethylene-2-[2-(4-methoxydihydrobenzocyclobutenyl)ethyl]-2-methylcyclopentanone, followed by desulphurisation.

THE bridged bicyclo[3.2.1]octane is an integral part of the structure of a large class of tetracyclic diterpenoids[1] and many types of approach to the synthesis of this ring system have been reported. In connection with our interest[2] in the synthetic development of electrocyclic reactions or cycloadditions[3] starting from *o*-quinodimethanes based on dihydrobenzocyclobutenes,[4] we investigated a novel route to the potential intermediate (**12**) for the synthesis of tetracyclic diterpenes. The acid (**3**), synthesised

from the aldehyde (**1**) *via* the cyano-compound (**2**) by our method,[5] was converted by a standard procedure[6] into the acetic acid derivative (**4**), which was transformed into the iodide (**5**).[7] Condensation of (**5**) with the pyrrolidine enamine of cyclopentanone in boiling benzene for 23 h gave the cyclopentanone (**6**) [ν_{max}($CHCl_3$) 1725 cm^{-1}, *m/e* 244 (M^+)] in 60% yield. Reaction of (**6**) with ethyl formate in the presence of NaH in benzene, followed by treatment of the resulting hydroxymethylenecyclopentanone (**7**) [ν_{max}($CHCl_3$) 1665 cm^{-1}, *m/e* 272 (M^+)] with Bu^nSH in the presence of toluene-*p*-sulphonic acid,[9] afforded the sulphide (**8**) [ν_{max}($CHCl_3$) 1680 cm^{-1}, *m/e* 334 (M^+)] in 79% yield. A methyl group was introduced at the C–2 position in compound (**8**) by reaction with MeI in Bu^tOH in the presence of Bu^tOK at room temperature for 17 h to give, in 48% yield, the key intermediate (**9**) [ν_{max} ($CHCl_3$) 1680 cm^{-1}, δ (CCl_4) 1·00 (3H, s, Me), 3·73 (3H, s, OMe), 6·53 (1H, d, *J* 2 Hz, ArH), 6·65 (1H, dd, *J* 2 and 8 Hz, ArH), 6·93 (1H, d, *J* 8 Hz, ArH), and 7·25 (1H, distorted d, *J* 2 Hz, olefinic-H), *m/e* 358 (M^+)].



Heating compound (**9**) in *o*-dichlorobenzene at 180°C for 13 h in a current of nitrogen afforded [*via* the *o*-quinodimethane (**10**)] the tetracyclic compound (**11**) in 65% yield [ν_{max} ($CHCl_3$) 1730 cm^{-1}, δ (CCl_4) 1·05 (3H, s, Me), 3·70 (3H, s, OMe), 6·46 (1H, d, *J* 2 Hz, ArH), 6·55 (1H, dd, *J* 2 and 8 Hz, ArH), and 6·96 (1H, d, *J* 8 Hz, ArH), *m/e* 358 (M^+)], desulphurisation of which with Raney nickel in ethanol gave, in 86·2% yield, the potential intermediate (**12**), m.p. 104—105 °C [ν_{max} ($CHCl_3$) 1725 cm^{-1}, δ (CCl_4) 1·00 (3H, s, Me), 3·70 (3H, s, OMe), 6·50 (1H, d, *J* 2 Hz, ArH), 6·55 (1H, dd, *J* 2 and 8 Hz, ArH), and 7·00 (1H, d, *J* 8 Hz, ArH), *m/e* 270 (M^+)]. The 13-Me signal in (**12**) was in the normal position, which showed that the relative configuration of the 13-Me and 9-H was probably *cis*-(**12**A). The stereochemistry of compound (**12**) is thus considered to be *cis*, as in (**12**A), but the alternative *trans*-structure (**12**B) cannot be ruled out.



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