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AN INTERESTING APPLICATION OF PHOTOCYCLISATION IN APORHOEADANE ALKALOID SYNTHESIS

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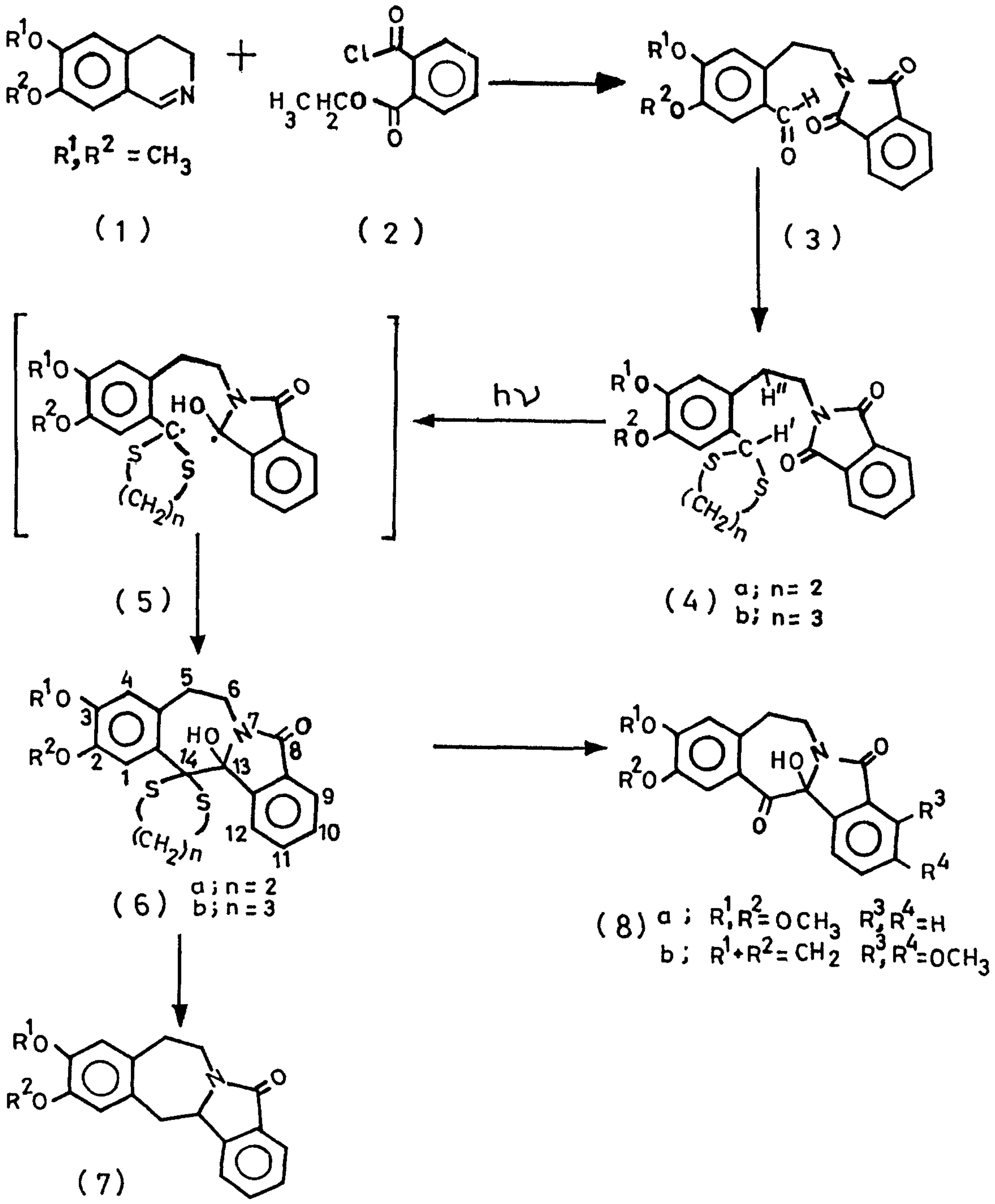
Abstract: Reaction of 2-carboethoxybenzoyl chloride with 3,4-dihydro-6,7-dimethoxyisoquinoline afforded a ring open aldehydic phthalimide(3) which on thioacetal formation and photocyclisation followed by deketalisation gave 8,14-dioxo-13-hydroxyaporhoeadane (8).

Chilenine (8b) is an alkaloid having a string of contiguous functionalities appended on to an aporhoeadane skeleton.[1] We report that this structural pattern can very simply be put together through photocyclisation of a thioacetal imide[2] (4).

On stirring a benzene solution of 3,4-dihydro-6,7-dimethoxyisoquinoline (1) (1.0 mmole) and 2-carboethoxybenzoyl chloride (2) (1.2 mmole) with aqueous sodium hydroxide (3.0 mmole) at room temperature for 30 min, the aldehydic imide (3)[3] was obtained in 35% yield[4], m.p. 183°C; ^{1}H NMR ($CDCl_3$) δ 3.49 (t, 2H, Ar-C$\underline{H}_2$-), 3.96 (s, 3H, -OCH_3), 4.06 (s, 3H, -OCH_3), 4.0-4.26 (m, 2H, -C$\underline{H}_2$-N-), 6.8 (s, 1H, H-C_4), 7.53 (s, 1H, H-C_1), 7.66-8.13 (m, 4H, ArH), 10.43 (s, 1H, -C$\underline{H}$O); MS (m/e) 339 (M^+). Reaction with ethane-1,2-dithiol in the presence of BF_3-etherate afforded (4a), m.p. 178°C; yield 85%; ^{1}H NMR ($CDCl_3$) δ 2.96 (t, 2H, Ar-C$\underline{H}_2$), 3.5 (d, 4H, (-S-C$\underline{H}_2$-C$\underline{H}_2$-S-), 3.86 (s, 3H, -OCH_3), 3.96 (s, 3H, -OCH_3), 3.96-4.23(m, 2H, -C$\underline{H}_2$-N-), 6.16 (s, 1H,-S-C$\underline{H}$-S-), 6.7 (s, 1H, H-C_4), 7.5 (s, 1H, H-C_1), 7.66-8.16 (m, 4H, ArH); MS (m/e) 415 (M^+). Irradiation (medium pressure mercury arc, pyrex filter, 1h) of (4a) (1.32 mmole) in acetone (275 ml) furnished[5] (31%) the tetracyclic compound[6] (6a),m.p. 265°C; ^{1}H NMR (DMSO-d_6) δ 2.46-3.73 (m, 7H, Ar-C$\underline{H}_2$-C$\underline{H}$-N-and -S-C$\underline{H}_2$-C$\underline{H}_2$-S-), 3.87 (s, 3H, -OCH_3), 3.90 (s, 3H, -OCH_3), 4.33-4.6 (m, 1H,-C$\underline{H}$-N-), 6.71 (s, 1H, H-C_4), 7.4-7.83 (m, 3H, H-C_{10}, H-C_{11},H-C_{12}), 7.98 (s, 1H, H-C_1), 8.3-8.43 (m, 1H, H-C_9); MS (m/e) 415 (M^+). Treatment of (6a) in ethanol with Raney Nickel led[7] to the aporhoeadane (7), m.p. 159°C; yield 62%; ^{1}H NMR[8] ($CDCl_3$) δ 2.98 (m, 4H, -$\underline{H}_2$C-Ar-C$\underline{H}_2$-), 3.9, 3.96 (s, 6H, 2-OCH_3), 4.2-4.9 (m, 3H, -C$\underline{H}$-N-C$\underline{H}_2$-), 6.8, 6.96 (s, 2H, Aromatic H-C_1, H-C_4), 7.5-7.8, 7.9-8.1 (m, 4H, ArH); MS (m/e) 309 (M^+, base peak). Unmasking of the carbonyl function under standard procedures[9] was unsuccessful,therefore the 1,3-thioacetal (4b) (m.p. 225-226°C; yield 85%; ^{1}H NMR ($CDCl_3$) δ 1.76-2.4 (m, 2H, -S-CH_2-C$\underline{H}_2$-), 2.7-3.56 (m, 6H, 2(-S-C$\underline{H}_2$-) and -C$\underline{H}_2$-Ar), 3.93, 3.98 (s, 6H,2-OCH_3), 3.9-4.26 (m, 2H, -C$\underline{H}_2$-N-), 5.76 (s, 1H, -S-C$\underline{H}$-S-), 6.83 (s, 1H, H-C_4), 7.27 (s, 1H, H-C$_1$), 7.73-8.16 (s, 4H, ArH); MS (m/e) 429 (M$^+$) was prepared and similarly photocyclised under identical conditions.



The obtained compound (6b) (m.p. 245°C; yield 30%; ^{1}H NMR (DMSO-d_6) δ 1.43-2.33 (m, 2H, $-S-CH_2-C\underline{H}_2-$), 2.4-3.9 (m, 7H, $2(-C\underline{H}_2-S-)$, $Ar-C\underline{H}_2-C\underline{H}-N-$), 3.97, 4.00 (s, 6H, $2-OCH_3$), 4.26-4.6 (m, 1H, $-C\underline{H}-N-$), 7.06 (s, 1H, $H-C_4$), 7.56-7.96 (m, 3H, $H-C_{10}$, $H-C_{11}$, $H-C_{12}$), 8.2 (s, 1H, $H-C_1$), 8.2-8.4 (m, 1H, $H-C_9$); MS (m/e) 429 (M^+) on treatment with N-chlorosuccinimide-$AgNO_3$ in aqueous acetonitrile[9a] (80%) afforded the aporhoeadane 8a, m.p. 191°C (acetone); yield 38%; ^{1}H NMR ($CDCl_3$) δ 2.9-3.73 (m, 3H, $-C\underline{H}_2-C\underline{H}-N-$), 3.77, 3.90 (s, 6H, $2-OCH_3$), 3.98-4.37 (m, 1H, $-C\underline{H}-N-$), 4.43 (bs, 1H, $-O\underline{H}$, D_2O exchangeable), 6.67 (s, 1H, $H-C_4$), 6.86 (s, 1H, $H-C_1$), 7.26-7.83 (m, 4H, ArH); MS (m/e) 339 (M^+).

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References and Notes

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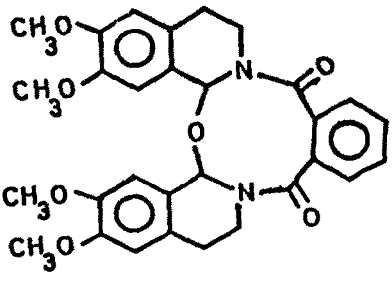
3. All compounds synthesised have satisfactory analytical data.

4. The use of phthaloyl chloride affords a side product m.p. 265°C which is tentatively assigned structure(9).



(9)

5. Progress of the photocyclisation could be monitored by the disappearance of thioacetal methine proton (δ 6.16) in the ^1H NMR spectrum of aliquots.

6. Hydrogen abstraction through a 9-membered ring (H') may not be expected to compete with that through a six membered ring (H"). Substantial formation of (5) on irradiation of (4) is suggestive of the involvement of a sulphur oxygen charge transfer complex[2] in the excited state.

7. For other approaches to the aporhoeadanes; see H.O. Bernhard and V. Snieckus, Tetrahedron Lett., 4867 (1971); S. Ruchirawat, W. Lertwanawatana, S. Thianpatanagul, J.L. Cashaw and V.E. Davis, Tetrahedron Lett., 25, 3485 (1984).

8. The ^1H NMR spectrum is in agreement with that reported for aporhoeadanes; see S. Teitel, W. Klotzer, J. Borgese and A. Brossi, Can. J. Chem., 50, 2022 (1972).

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