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TRAPPING OF DOPACHROME WITH 2,3-DIHYDRO-1H-CYCLOPENT[b]INDOLE

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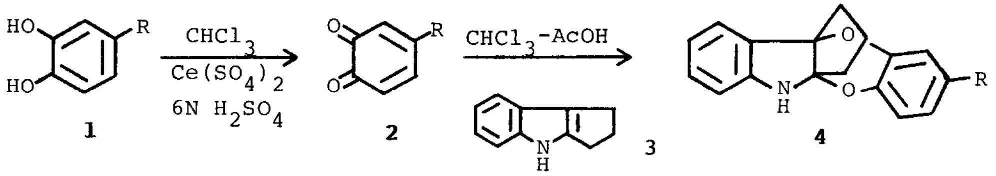
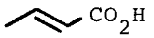
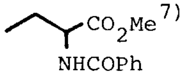
Summary: Dopachrome (6) and related o-benzoquinones including dopaquinone (2d) were trapped, by treating each quinone from the corresponding catechol, with 2,3-dihydro-1H-cyclopent-[b]indole (3) to afford [4.3.3]-propellane adduct.

The melanogenesis route[1] of tyrosine has been shown to follow tyrosine, DOPA, dopaquinone, leuco dopachrome, dopachrome, 5,6-dihydroxyindole, 5,6-indolequinone, melanochrome, and melanin. The existence of three quinoid intermediates, dopaquinone, dopachrome, and 5,6-indolequinone have been proposed spectroscopically, but none of them have been isolated owing to their labilty. Previously we reported trapping of dopaquinone by phenylenediamine[2] or cyclopentadiene.[3] Now we want to report a new trapping method of o-benzoquinones including dopaquinone and dopachrome with 2,3-dihydro-1H-cyclopent-[b]indole.

The method is based on the fact that 2,3-disubstituted indoles reacted rapidly with o-benzoquinones to yield one-to-one adducts.[4] o-Benzoquinones (2) were prepared by the method of Brockhaus[5] from their corresponding catechols (1). To an ice-methanol cooled solution of 1 (4.5 mmol) in 50 ml of chloroform, a precooled (0°C) 6N sulfuric acid solution of cerium (IV) sulfate (9.0 mmol) was added and stirred for one minute. The organic layer was separated, washed with 0.01N sulfuric acid, and dried over magnesium sulfate.

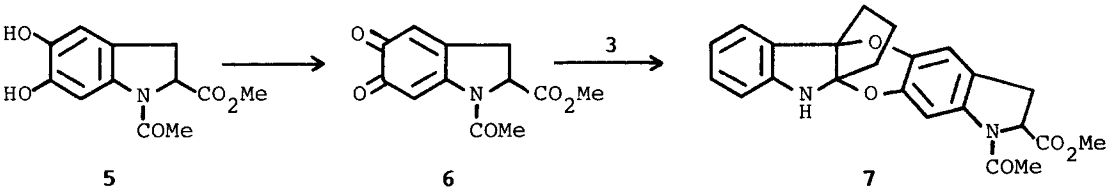
Table 1. Trapping of dopaquinone and related compounds with 2,3-dihydro-1H-cyclopent[b]indole, yield (%).



R :	a		9 %	R :	c		34 %
	b		38 %		d		42 %

To this solution acetic acid (1 ml) and the indole (3, 4.5 mmol) were added. After stirring for one hour at room temperature, the acetic acid was removed with a saturated sodium hydrogen carbonate solution, washed with water, dried and evaporated. Products were purified on silica gel chromatography and recrystallized. (Table 1).

This method was applied to the trap of dopachrome. Methyl N-acetyl-5,6-dihydroxyindoline-2-carboxylate (5) was synthesized from DOPA by the method previously reported.6) The catechol 5 was oxidized to the o-benzoquinone (N-acetyl dopachrome methyl ester) 6 which was trapped with indole 3 to give the adduct 7 in 25% yield.8)



5 6 7

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7) For **4d** (mixture of dl-isomers) : IR (ν_{max}, KBr) 3320, 1740, 1645, 1615 and 1600 cm^{-1}; ^{1}H-NMR (δ, $CDCl_3$) 1.1-2.7 (m, 6H), 3.07 (d, 2H, J=5.8 Hz), 3.60 (s, 1.8H), 3.63 (s, 1.2H), 4.52 (br s, 1H, D_2O exchangeable), 4.97 (dt, 1H, J=5.8, 7.8 Hz), 6.8-7.8 ppm (m, 13H); ^{13}C-NMR (δ, $CDCl_3$) 21.8 (t), 37.3 (t), 39.5 (t), 40.2 (t), 52.2 (q), 53.5 (d), 93.1 (s), 104.1(s), 128.6 (s), 130.0 (s), 133.8 (s), 144.4 (s), 145.2 (s), 148.7 (s), 166.7 (s), 171.9 ppm (s) and aromatic carbons; (found C, 71.37; H, 5.74, N, 5.81%; calcd. for $C_{28}H_{26}N_2O_5$ C, 71.47; H, 5.56; N, 5.95%).

8) For 7 (mixture of dl-isomers) : IR (ν_{max}, KBr) 3300, 1740, 1640 and 1605 cm^{-1}; ^{1}H-NMR (δ, $CDCl_3$) 1.6-2.6 (m, 6H), 2.05 (s, 1.1H), 2.34 (s, 1.9H), 2.9-3.5 (m, 2H), 3.68 (s, 3H), 4.53 (br s, 1H, D_2O exchangeable), 4.7-5.1 (m, 1H), 6.4-7.3 (m, 5H), 7.81 ppm (s, 1H); ^{13}C-NMR (δ , $CDCl_3$) 21.8 (t), 33.0 (t), 39.9 (t), 40.2 (t), 52.4 (q), 52.8 (q), 61.5 (d), 93.4 (s), 103.9 (s), 122.1 (s), 128.5 (s), 137.3 (s), 141.4 (s), 144.7 (s), 148.7 (s), 168.5 (s), 171.7 ppm (s) and aromatic carbons; (found C, 67.85; H, 5.58; N, 6.80%; calcd. for $C_{23}H_{22}N_2O_5$ C, 67.96; H, 5.45; N, 6.89%).

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