The Synthesis of Monomethoxy-6-methyl-7*H*-indeno[2,1-*c*]quinolines

Mumtaz A. Quraishi* [1]

Department of Applied Chemistry, Institute of Technology, Banaras Hindu University, Varanasi-221 005, India

Received November 30, 1987

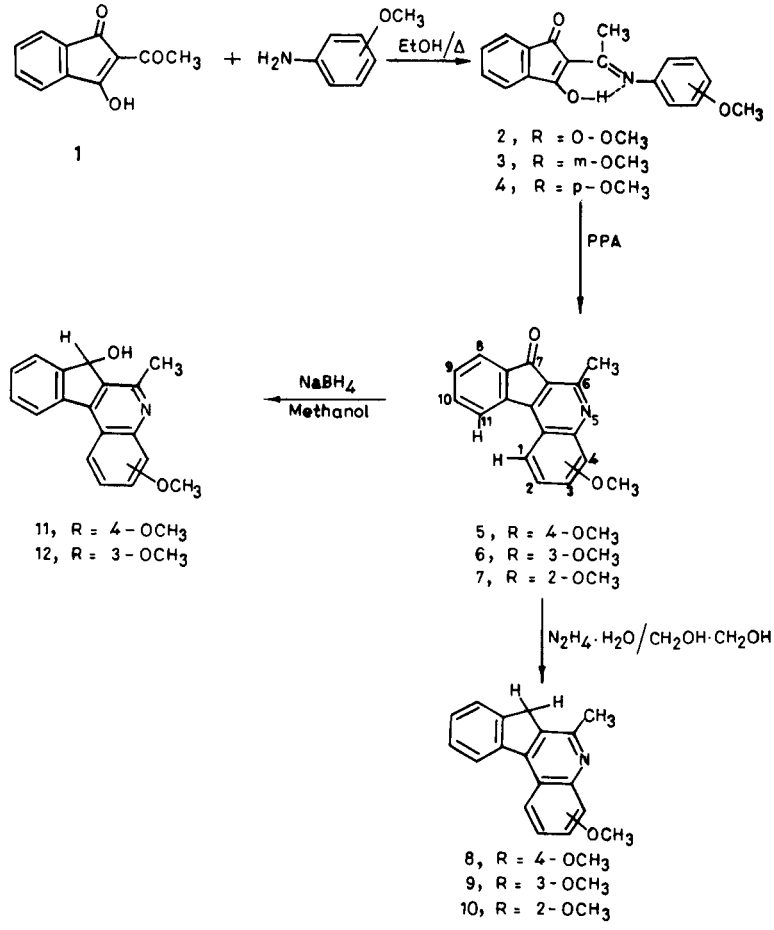
A series of monomethoxy-6-methyl-7*H*-indeno[2,1-*c*]quinolines has been prepared by cyclization of the appropriate 1,3-dioxoindan-2-yl-ethylideneanilines, followed by Wolff-Kishner reduction.

J. Heterocyclic Chem., **26**, 221 (1989).

Azafluorenes and their benz-analogues are reported to possess diverse biological activities [2-5]. Recently some indenoquinoline derivatives have been reported to exhibit significant analgesic and anti-inflammatory activity [6-8]. The reported [9-11] syntheses of Indeno[2,1-*c*]quinoline derivatives are either multisteps or involve substrates which are not readily available. The present paper describes a convenient syntheses of the title compounds (Scheme 1).

The reaction of **1** [12] with *o*-anisidine, *m*-anisidine or *p*-anisidine afforded the required α-(1,3-dioxoindan-2-yl)-*o*-anisidine (**2**) (80% yield), α-(1,3-dioxoindan-2-yl)-*m*-anisidine (**3**) (85% yield), and α-(1,3-dioxoindan-2-yl)-*p*-anisidine (80% yield) respectively. Upon cyclization with polyphosphoric acid compounds **2**, **3** and **4** were transformed into the corresponding ketones namely, 4-methoxy-6-methylindeno[2,1-*c*]quinolin-7(*H*)-one (**5**) 75% yield, 3-methoxy-

Scheme 1



6-methylindeno[2,1-*c*]quinolin-7(*H*)-one (**6**) 72% yield, 2-methoxy-6-methylindeno[2,1-*c*]quinolin-7(*H*)-one (**7**) (70% yield) respectively.

Reduction of **5**, **6** and **7** was accomplished by refluxing with hydrazine hydrate in ethylene glycol and 4-methoxy-6-methyl-7(*H*)-indeno[2,1-*c*]quinoline (**8**) (60% yield), 3-methoxy-6-methyl-7(*H*)-indeno[2,1-*c*]quinoline (**9**) (50% yield), 2-methoxyl-6-methyl-7(*H*)-indeno[2,1-*c*]quinoline (**10**) (53% yield) respectively were obtained.

Reduction of **5** and **6** with sodium borohydride afforded the corresponding alcohols, 7-hydroxy-4-methoxy-6-methyl-7*H*-indeno[2,1-*c*]quinoline **11** (42% yield) and 7-hydroxy-3-methoxy-6-methyl-7*H*-indeno[2,1-*c*]quinoline **12** (42% yield) respectively.

EXPERIMENTAL

Melting points were taken in open capillaries and are uncorrected. The ir spectra in Nujol were recorded on a Beckman IR-20 spectrophotometer (ν max in cm^{-1}). The ^1H-nmr spectra were recorded in deuteriochloroform and are reported in ppm relative to TMS.

α-(1,3-Dioxoindan-2-yl)ethyliden-*o*-anisidine (**2**).

A mixture of 2-acetylindane-1,3-dione (**1**, 1.88 g, 0.01 mole) and *o*-anisidine (1.08 g, 0.01 mole) in absolute ethanol (30 ml) was refluxed for 3 hours. After cooling, the resulting solid was collected by filtration and the filtrate was evaporated under reduced pressure. The residue was recrystallized from ethanol to give 1.5 g (80% yield) of **2**, mp 137; ^1H nmr (deuteriochloroform): 2.60 (s, 3H, CH_3) 3.94 (s, 3H, OCH_3) 6.98-7.38 (m, 4H, ArH) 7.48-7.85 (m, 4H, ArH) 12.38 (br, 1H, OH exchangeable with deuterium oxide); ir (Nujol): 1690, 1630 cm^{-1}).

Anal. Calcd. for $C_{18}H_{15}NO_3$: C, 73.72; H, 5.11; N, 4.77. Found: C, 73.50; H, 5.32; N, 4.68.

4-Methoxy-6-methylindeno[2,1-*c*]quinolin-7(*H*)-one (**5**).

The anil **3** (2.0 g, 0.006 mole) was added to freshly prepared polyphosphoric acid (20 ml) and heated to 120 for 1.5 hours. After cooling, the reaction mixture was poured into ice cold water and the aqueous layer was made alkaline with ammonium hydroxide. The aqueous layer was extracted with chloroform, and the extracts dried over anhydrous magnesium sulphate. The solvent was distilled and the residue crystallized from a petroleum ether-benzene mixture to afford yellow needles of **5** (1.5 g, 75% yield), mp 182; ^1H nmr (deuteriochloroform): 2.92 (s, 3H, CH_3) 4.22 (s, 3H, OCH_3) 7.30-7.78 (m, 5H, ArH) 7.96 (dd, 1H) 8.20 (dd, 1H, J = 8 and 2.5 Hz, H-1); ir: 1700 cm^{-1}.

Anal. Calcd. for $C_{18}H_{13}NO_2$: C, 78.54; H, 4.72; N, 5.09. Found: C, 78.48; H, 4.59; N, 5.12.

4-Methoxy-6-methyl-7(*H*)-indeno[2,1-*c*]quinoline (**8**).

A mixture of the ketone **5** (1 g), ethylene glycol (15 ml) and hydrazine hydrate (2 ml) was heated under reflux first at 120° for 1 hour, and then at 180° for 3 hours. Thereafter the reaction mixture was poured into water. The white solid that precipitated was isolated by filtration, and recrystallized from methanol to afford **8** as colourless needles, 0.6 g (60% yield) mp 148°; ^1H nmr (deuteriochloroform): 2.75 (s, 3H, CH_3), 3.80 (s, 2H, CH_2) 4.20 (s, 3H, OCH_3) 7.27-7.66 (m, 5H, ArH) 8.20-8.55 (m, 2H, H-1 and H-11).

Anal. Calcd. for $C_{18}H_{15}NO$: C, 82.75; H, 5.74; N, 5.36. Found: C, 82.62; H, 5.68; N, 5.30.

7-Hydroxy-4-methoxy-6-methyl-7(*H*)-indeno[2,1-*c*]quinoline (**11**).

A mixture of **5** (0.5 g, 0.0019 mole), methanol (20 ml) and sodium borohydride (0.2 g) was stirred at room temperature for 1 hour, poured into water and the solid thus precipitated, and upon crystallization from benzene gave **11** (0.2 g, 42% yield) mp 168°; ^1H nmr (deuteriochloroform): 2.92 (s, 3H, CH_3), 4.04 (s, 3H, OCH_3), 5.30 (, 1H), 7.28-7.73 (m, 5H, ArH) 7.94-8.15 (2 dd, 2H, H-1 and H-11); ir (potassium bromide): 3150 cm^{-1}.

Anal. Calcd. for $C_{18}H_{15}NO_2$: C, 77.97; H, 5.41; N, 5.05. Found: C, 78.28; H, 5.18; N, 5.16.

α-(1,3-Dioxoindan-2-yl)ethylidene-*m*-anisidine (**3**).

This compound was prepared from **1** (3 g, 0.02 mole) and *m*-anisidine (2.46 g, 0.02 mole) in ethanol (50 ml) in a similar manner to that described for the preparation of **2**, 1.6 g, (85% yield) of **3** was obtained as light green crystals, mp 148°; ^1H nmr (deuteriochloroform): 2.37 (s, 3H, CH_3), 3.86 (s, 3H, OCH_3), 6.88-7.23 (m, 4H, ArH) 7.38-7.68 (m, 4H, ArH), 12.38 (br, 1H, OH exchangeable); ir (Nujol): 1690, 1630 cm^{-1}.

Anal. Calcd. for $C_{18}H_{15}NO_3$: C, 73.72; H, 5.11; N, 4.77. Found: C, 73.74; H, 5.38; N, 4.82.

Compound **6** was prepared as described for 5 using 2 g (0.006 mole) of anil **3**, to provide 1.4 g of **6** (72% yield) as yellow solid which was crystallized from benzene, mp 178°; ^1H nmr (deuteriochloroform): 2.86 (s, 3H, CH_3), 4.18 (s, 3H, OCH_3), 7.12-7.72 (m, 5H, ArH) 7.84 (dd, 1H, H-11), 8.0 (d, 1H, J = 8 Hz, H-1); ir (Nujol): 1700 cm^{-1}.

Anal. Calcd. for $C_{18}H_{13}NO_2$: C, 78.54; H, 4.72; N, 5.09. Found: C, 78.66; H, 4.80; N, 4.88.

3-Methoxy-6-methyl-7(*H*)-indeno[2,1-*c*]quinoline (**9**).

This compound wa prepared from **6** following exactly the same procedure as described for **8** (0.5 g, 50% yield), mp 142°; ^1H nmr (deuteriochloroform): 2.76 (s, 3H, CH_3), 3.80 (s, 2H, CH_2), 4.05 (s, 3H, OCH_3), 7.22-7.74 (m, 4H, ArH), 7.85 (d, 1H), 8.28-8.56 (dd, 2H, J = 8 and 2.5 Hz H-1 and H-11).

Anal. Calcd. for $C_{18}H_{15}NO$: C, 82.75; H, 5.74; N, 5.36. Found: C, 82.86; H, 5.83; N, 5.41.

7-Hydroxy-2-methoxy-6-methyl-7(*H*)-indeno[2,1-*c*]quinoline (**12**).

This compound was prepared from **6** (0.5 g, 0.0012 mole) in a similar manner to that as described for **11** and 0.2 g (42% yield) was obtained as a white solid, mp 172°; ^1H nmr (deuteriochloroform): 2.85 (s, 3H, CH_3), 4.02 (s, 3H, OCH_3), 5.26 (s, 1H), 7.14-7.68 (m, 5H, ArH), 7.88-8.00 (m, 2H, ArH); ir (potassium bromide): 3130 cm^{-1}.

Anal. Calcd. for $C_{18}H_{15}NO_2$: C, 77.97; H, 5.41; N, 5.05. Found: C, 78.12; H, 5.28; N, 5.12.

α-(1,3-Dioxoindan-2-yl)ethylidene-*p*-anisidine (**4**).

A similar procedure was adopted for the preparation **4** using **1** (3 g, 0.02 mole) and *p*-anisidine (2.46 g, 0.02 mole). The product, 1.50 g (80% yield), was obtained as a green solid mp 162°; ^1H nmr (deuteriochloroform): 2.36 (s, 3H, CH_3), 3.84 (s, 3H, OCH_3, 7.12 (d, 2H, H-2', M-6'), 7.24 (d, 2H, H-3' and H-5'), 7.48-7.78 (m, 4H, ArH) 12.38 (br, 1H, OH exchangeable with deuterium oxide); ir (Nujol): 1690, 1630 cm^{-1}.

Anal. Calcd. for $C_{18}H_{15}NO_3$: C, 73.72; H, 5.11; N, 4.77. Found: C, 73.52; H, 4.94; N, 4.81.

2-Methoxy-6-methylindeno[2,1-*c*]quinolin-7(*H*)-one (**7**).

Compound **7** was prepared, in a similar manner as that described for **5**, from **4** (2 g, 0.06 mole) to afford 1.2 g (62% yield) of **7** as yellow needles, mp 210°; ^1H nmr (deuteriochloroform): 2.84 (s, 3H, CH_3), 4.12 (s, 3H, OCH_3), 7.28-7.72 (m, 4H, ArH), 7.78-7.92 (m, 2H, ArH), 8.10 (d, 1H, J = 2.5 Hz); ir (Nujol): 1700 cm^{-1}.

Anal. Calcd. for $C_{18}H_{13}NO_2$: C, 78.54; H, 4.72; N, 5.09. Found: C, 78.66; H, 4.46; N, 5.16.

2-Methoxy-6-methyl-7(*H*)-indeno[2,1-*c*]quinoline (**10**).

Compound **10** was prepared from **7** (0.5 g, 0.0019 mole) following the procedure as described for **9** and crystallized from methanol as colourless needles (0.25 g, 53% yield) mp 164°; ^1H nmr (deuteriochloroform): 2.72 (s, 2H, CH_3), 3.80 (s, 2H, CH_2), 4.18 (s, 3H, OCH_3), 7.28-7.68 (m, 5H, ArH), 7.96 (d, 1H, J = 2.5 Hz, H-4), 8.18-8.38 (br, 2H, H-1 and H-11).

Anal. Calcd. for $C_{18}H_{15}NO$: C, 82.75; H, 5.74; N, 5.36. Found: C, 82.58; H, 5.58; N, 5.42.

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[1] Address for correspondence, G/1 Arvind Colony, Banaras Hindu University, Varanasi-221 005, India.

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