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Note

A new and convenient synthesis of 15*H*-16,17-dihydrocyclopenta[*a*]phenanthrene derivatives

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Methyl 2-oxocyclopentane-1-carboxylate is selectively C-alkylated with several 2-(3,4-dihydro-1-naphthalenyl)ethyl-4-methylphenylsulphonates to give the corresponding seco-steroids, which on cyclodehydration followed by degradation in 5% Pd-C has afforded the corresponding title compounds.

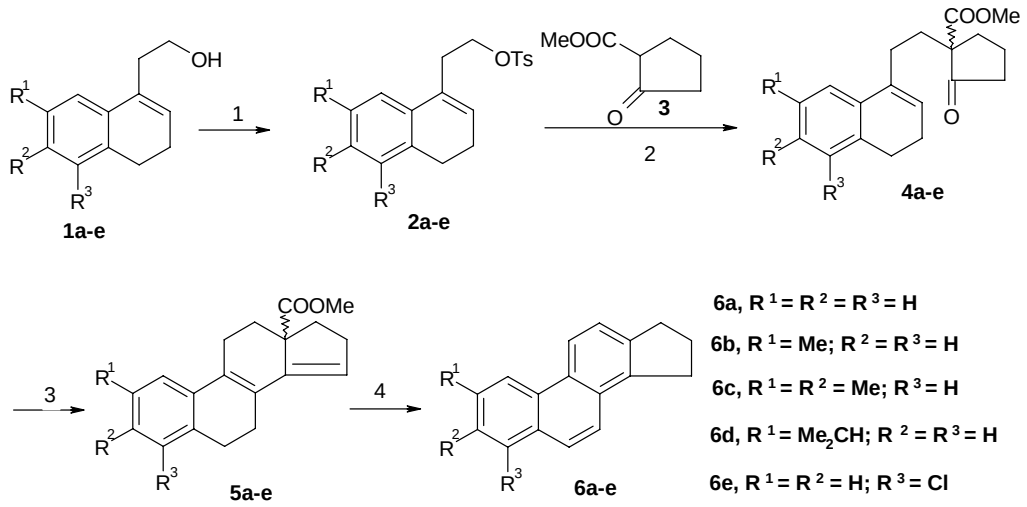
Keywords::2-Oxocyclopentane-1-carboxylate, c-alkylation, methylphenylsulphonates, seco-steroids, cyclopenta-phenanthrene derivatives, Pd-C

IPC: **Int.Cl.**[7] **C 07 J**

Impetus for the syntheses of 15*H*-16,17-dihydrocyclopenta[*a*]phenanthrenes developed due to the presence of some carcinogenic activity[1] and also due to the structural resemblance with the steroids. Moreover, 15*H*-16,17-dihydrocyclopenta[*a*]phenanthrenes have been found to be widely distributed in petroleum, mineral oils, coal, lake sediments and other natural environments[1-4], where they are thought to arise from sterols by microbiological dehydrogenation.[1,4] Though several syntheses[5-17] of 15*H*-16,17-dihydrocyclopenta[*a*]phenanthrenes have been reported, many derivatives are still unknown. All these observations prompted us to develop a new and general synthesis of 15*H*-16,17-dihydrocyclopenta-[*a*]phenanthrenes.

Towards this end, 2-(3,4-dihydro-1-naphthalenyl)-ethanols **1a-e** were reacted with the 4-methylphenyl-sulphonyl chloride in presence of pyridine in $CHCl_3$ to afford the corresponding 2-(3,4-dihydro-1-naphthalenyl)ethyl-4-methylphenylsulphonates **2a-e** following the known literature procedure.[18] Methyl 2-oxocyclopentane-1-carboxylate **3** was then C-alkylated with **2a-e** using Na in xylene under reflux for 12 hr to afford the corresponding seco-steroids **4a-e** for the first time. ^{1}H NMR spectra of all these seco-steroids showed 3H singlet for COOMe group. IR spectra showed two C=O frequencies, one at ~1725 for methyl ester and other at ~1750 cm^{-1} for cyclopentanone ring and MS spectra of **4a** and **4b** showed their corresponding molecular ion peak thus confirming the selective C-alkylation of **3** with **2a-e** to afford **4a-e**. These seco-steroids **4a-e** were then subjected to cyclodehydration by heating in PPA on a steam bath for 90 min to afford the corresponding gonane steroids **5a-e** in a reasonably good yield. The structures of **5a-e** were ascertained from their elemental analysis and spectroscopic data. IR spectra of these compounds showed only one C=O str. frequency for methyl ester and the mass spectra of **5a-c** showed the corresponding molecular ion peak and base peak at M-60 for the loss of neutral HCOOMe. The feasibility of converting **5a-e** to the title compounds **6a-e** at higher temperature with 5% Pd-C was then explored. Mitra *et al.*[19] have used such type of degradation reaction for the synthesis of chrysene derivative. Hence, we believe, that similarly at higher temperature **5a-e** would undergo simultaneous or tandem pyrolytic elimination of HCOOMe and dehydrogenation at ring B to afford the corresponding title compounds **6a-e**. We heated **5a-e** with 5% Pd-C at 250°C for 15 min and the reaction after work-up afforded the corresponding title compounds **6a-e** in reasonably good yields (**Scheme I, Table I**). Mass spectra of **6b**, **6c** and **6e** showed the corresponding molecular ion peak as a base peak and ^{1}H NMR spectra showed presence of signals for C-16 and C-17 protons and disappearance of 3H singlet for OCH_3 of methyl ester thus confirming the dehydrogenation at ring B and pyrolytic elimination of HCOOMe of **5a-e** to give the corresponding title compounds **6a-e**.

In conclusion, the present work provides a new synthesis of the title compounds **6a-e** which involves 4-methylphenylsulphonylation of 2-(3,4-dihydro-1-naphthalenyl)ethanols **1a-e**, selective C-alkylation of **3** with **2a-e** employing Na in xylene, cyclodehydration of **4a-e** in PPA to afford the corresponding gonane steroids **5a-e** and then finally degradation of **5a-e** with 5% Pd-C. Thus, the work described for the synthesis of title compounds is new, general and utilizes easily accessible materials.



Reagents and conditions: (1) *p*-TsCl, C_5H_5N, $CHCl_3$, 10°C (**1a**) and r.t. (**1b-e**), 3.25 hr. 2) Na / xylene, reflux. (3) PPA, steam bath, 90 min. 4) 5% Pd-C, 250°C, 15 min.

Scheme I

Table I — Synthesis of **2a-e**, **4a-e**, **5a-e** and **6a-e**.

Compd	R^1	R^2	R^3	Mp (°C)	Yield[a] (%)
2a	H	H	H	51[18]	85
2b	CH_3	H	H	Oil[18]	84
2c	CH_3	CH_3	H	Oil	88
2d	$CH(CH_3)_2$	H	H	Oil	78
2e	H	H	Cl	Oil[18]	84
4a	H	H	H	Oil	50
4b	CH_3	H	H	Oil	45
4c	CH_3	CH_3	H	Oil	50
4d	$CH(CH_3)_2$	H	H	Oil	49
4e	H	H	Cl	Oil	52
5a	H	H	H	Oil	69
5b	CH_3	H	H	Oil	68
5c	CH_3	CH_3	H	Oil	72
5d	$CH(CH_3)_2$	H	H	Oil	61
5e	H	H	Cl	Oil	64
6a	H	H	H	135[19]	61
6b	CH_3	H	H	104	59
6c	CH_3	CH_3	H	145	62
6d	$CH(CH_3)_2$	H	H	94	45
6e	H	H	Cl	172	56

[a] Yield refers to purified product.

Experimental Section

Reagents were of LR grade and were used without further purification. Column chromatography was carried out using silica gel (S. D. Fine Chemicals, India) 60-120 mesh. The melting points (uncorrected) were determined on a Gallenkamp melting apparatus. The IR spectra were recorded on a Shimadzu FT IR-4200 spectrometer either as oil film or KBr discs. ^{1}H NMR spectra were recorded at 60 MHz on a Varian EM-360L instrument with TMS as an internal standard in $CDCl_3$ solution. Electron impact spectra were recorded on a Katros MS-80. Elemental analyses were carried out on a Carlo Enra EA-1108 elemental analyser. Boiling point of petroleum ether used was in the range of 60-80°C.

General procedure for the synthesis of 4-methylphenylsulphonate 2a-e. To a well-stirred mixture of 4-methylphenylsulphonyl chloride (1.045 g, 5.5 mmole) and dry pyridine (1.58 g, 20 mmole) in dry $CHCl_3$ (25 mL) was added alcohol **1** (5 mmole) in dry $CHCl_3$ (10 mL) at 10°C for **1a** and at r.t. for **1b-1c** during a period of 15 min. After the addition was completed, the mixture was stirred for an additional 3 hr at the same temperature. The reaction mixture was then poured onto a mixture of ice and conc. HCl (50 mL) and the organic layer was separated. The aqueous layer was extracted with $CHCl_3$ (3 × 25 mL) and the combined $CHCl_3$ layer washed with 10% Na_2CO_3 (2 × 25 mL), water (2 × 25 mL) and then dried (anhyd. Na_2SO_4). After the evaporation of the solvent, a brown residue was obtained which was purified by column chromatography [silica gel, pet. ether - $CHCl_3$ (80:20)] to afford the corresponding 4-methylphenylsulphonate **2**. ^{1}H NMR of **2a, 2b** and **2e** were in agreement with the reported data.[18]

2-(3,4-Dihydro-6,7-dimethyl-1-naphthalenyl)ethyl-4-methylphenylsulphonate 2c: IR (oil film): 1181, 1362 (S=O str.) cm^{-1}; ^1H NMR: δ 2.00-2.50 (11H, m), 2.60-3.00 (4H, m), 4.22 (2H, t, *J* = 7 Hz, OCH_2), 5.80 (1H, t, *J* = 5 Hz, C=C-H), 6.85-7.60 (6H, m, Ar-H); Anal. Calcd for $C_{21}H_{24}O_3S$: C, 70.76; H, 6.79; S, 8.99. Found: C, 70.88; H, 6.75; S, 8.96%.

2-[3,4-Dihydro-7-(2-propyl)-1-naphthalenyl]ethyl-4-methylphenylsulphonate 2d: IR (oil film): 1181, 1360 (S=O str.) cm^{-1}; ^1H NMR: δ 1.25 (6H, d, *J* = 7 Hz, $C(CH_3)_2$), 2.10-2.50 (6H, m), 2.60-3.00 (4H, m), 4.15 (2H, t, *J* = 7 Hz, OCH_2), 5.82 (1H, t, *J* = 5 Hz, C=C-H), 6.78-7.72 (7H, m, Ar-H); Anal. Calcd for $C_{22}H_{26}O_3S$: C, 71.32; H, 7.07; S, 8.65. Found: C, 71.21; H, 7.11; S, 8.62%.

General procedure for the synthesis of *seco*-steroids 4a-e. Methyl 2-oxocyclopentanecarboxylate **3** (213 mg, 1.5 mmole) in dry xylene (10 mL) was gradually added to granulated Na metal (35 mg, 1.5 mmole) and the mixture was allowed to stand overnight when a solid cake was formed. To this, **2a-e** (1 mmole) in dry xylene (15 mL) was added in one lot and the mixture refluxed with stirring for 12 hr. The reaction mixture was cooled, diluted with water and the organic layer separated. The aqueous layer was extracted with benzene (3 × 50 mL) and the combined organic extracts were washed with water (2 × 50 mL) and then dried (anhyd. Na_2SO_4). Evaporation of solvent gave a dark oil, which was purified by column chromatography [silica gel; pet. ether - $CHCl_3$ (60:40)] to furnish *seco*-steroids **4a-e**.

Methyl 1-[2-(3,4-dihydro-1-naphthalenyl)ethyl]-2-oxocyclopentanecarboxylate 4a: IR (oil film): 1725 (C=O str. of ester), 1751 (C=O str. of five membered ketone) cm^{-1}; ^1H NMR: δ 1.64-1.92 (6H, m), 2.10-2.84 (8H, m), 3.69 (3H, s, OCH_3), 5.83 (1H, t, *J* = 5 Hz, C=C-H), 6.95-7.43 (4H, m, Ar-H); MS (EI, m/z): 298 (3%, M^+), 267 (3), 157 (15), 156 (100), 143 (10), 141 (47), 129 (22), 128 (47), 127 (7); Anal. Calcd for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43. Found: C, 76.54; H, 7.39%.

Methyl 1-[2-(3,4-dihydro-7-methyl-1-naphthalenyl)ethyl]-2-oxocyclopentanecarboxylate 4b: IR (oil film): 1723 (C=O str. of ester), 1750 (C=O str. of five membered ketone); cm^{-1}; ^1H NMR: δ 1.60-2.00 (6H, m), 2.10-2.90 (11H, m), 3.71 (3H, s, OCH_3), 5.73 (1H, t, *J* = 5 Hz, C=C-H), 6.73-7.10 (3H, m, Ar-H); MS (EI, m/z): 312 (4%, M^+), 235 (2), 171 (17), 170 (100), 169 (10), 156 (21), 155 (60), 154 (26), 153 (13), 143 (21), 142 (39), 141 (28), 128 (13), 115 (10); Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 76.94; H, 7.72%.

Methyl 1-[2-(3,4-dihydro-6,7-dimethyl-1-naphthalenyl)ethyl]-2-oxocyclopentanecarboxylate 4c: IR (oil film): 1726 (C=O str. of ester), 1752 (C=O str. of five membered ketone) cm^{-1}; ^1H NMR: δ 1.62-2.00 (6H, m), 2.10-2.85 (14H, m), 3.68 (3H, s, OCH_3), 5.76 (1H, t, *J* = 5 Hz, C=C-H), 6.82 (1H, s, Ar-H5), 7.10 (1H, s, Ar-H8); Anal. Calcd for $C_{21}H_{26}O_3$: C, 77.27; H, 8.03. Found: C, 77.17; H, 8.07%.

Methyl 1-[2-{3,4-dihydro-7-(2-propyl)-1-naphthalenyl}ethyl]-2-oxocyclopentanecarboxylate 4d: IR (oil film): 1724 (C=O str. of ester), 1752 (C=O str. of five membered ketone) cm^{-1}; ^1H NMR: δ 1.25 (6H, d, *J* = 7 Hz, $C(CH_3)_2$), 1.62-2.00 (6H, m), 2.10-2.85 (9H, m), 3.66 (3H, s, OCH_3), 5.73 (1H, t, *J* = 5 Hz, C=C-H), 6.90-7.10 (2H, m, Ar-H5 and Ar-H6), 7.40 (1H, s, Ar-H8); Anal. Calcd for $C_{22}H_{28}O_3$: C, 77.61; H, 8.29. Found: C, 77.57; H, 8.32%.

Methyl 1-[2-(5-chloro-3,4-dihydro-1-naphthalenyl)ethyl]-2-oxocyclopentanecarboxylate 4e: IR (oil film): 1725 (C=O str. of ester), 1751 (C=O str. of five membered ketone) cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz): δ 1.65-1.95 (6H, m), 2.00-2.85 (8H, m), 3.69 (3H, s, OCH_3), 5.81 (1H, t, *J* = 5 Hz, C=C-H), 6.95-7.20 (2H, m, Ar-H5 and Ar-H6), 7.50 (1H, s, Ar-H8); Anal. Calcd for $C_{19}H_{21}O_3Cl$: C, 68.57; H, 6.36; Cl, 10.65. Found: C, 68.48; H, 6.40; Cl, 10.60%.

General procedure for the synthesis of gonane steroids 5a-e. A mixture of seco-steroid **4a-e** (125 mg) and PPA (10 g) was heated on a steam-bath for 90 min. The reaction mixture was poured onto ice and allowed to stand overnight. It was extracted with EtOAc (3 × 25 mL). The combined EtOAc extracts were washed with 10% Na_2CO_3 (2 × 25 mL), water (2 × 25 mL) and then dried (anhyd. Na_2SO_4). Evaporation of solvent gave a dark oil, which was purified by column chromatography [silica gel, pet. ether : $CHCl_3$ (75:25)] to furnish gonane steroids **5a-e**.

Methyl 6,7,11,12,16,17-hexahydro-13*H*-cyclopenta[*a*]phenanthrene-13-carboxylate 5a: IR (oil film): 1726 (C=O str.) cm^{-1}; ^1H NMR: δ 1.50-1.90 (4H, m), 2.00-2.80 (8H, m), 3.69 (3H, s, OCH_3), 6.86-7.70 (5H, m, Ar-H and C=C-H); MS (EI, m/z): 280 (26%, M^+), 221 (23), 220 (100), 219 (17), 192 (26), 191 (30); 179 (17), 178 (19), 165 (19); Anal. Calcd for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.34; H, 7.24%.

Methyl 6,7,11,12,16,17-hexahydro-7-methyl-13*H*-cyclopenta[*a*]phenanthrene-13-carboxylate 5b: IR (oil film): 1725 (C=O str.) cm^{-1}; ^1H NMR: δ 1.57-1.95

(4H, m), 2.06-2.84 (11H, m), 3.70 (3H, s, OCH_3), 6.92-7.22 (2H, m, Ar-H and C=C-H); 7.54-7.71 (2H, m, Ar-H); MS (EI, m/z): 294 (30%, M^+), 235 (30), 234 (100), 233 (13), 205 (26), 193 (13), 191 (17), 189 (10); Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.66; H, 7.51%.

Methyl 6,7,11,12,16,17-hexahydro-6,7-dimethyl-13*H*-cyclopenta[*a*]phenanthrene-13-carboxylate 5c: IR (oil film): 1726 (C=O str.) cm^{-1}; ^1H NMR: δ 1.54-1.93 (4H, m), 2.03-2.84 (14H, m), 3.71 (3H, s, OCH_3), 7.12-7.28 (2H, m, Ar-H and C=C-H); 7.71 (1H, s, Ar-H1); MS (EI, m/z): 308 (30%, M^+), 249 (37), 248 (100), 247 (10), 233 (15), 207 (10), 205 (15), 193 (7), 191 (12), 189 (12); Anal. Calcd for $C_{21}H_{24}O_2$: C, 81.78; H, 7.84. Found: C, 81.88; H, 7.80%.

Methyl 6,7,11,12,16,17-hexahydro-7-(2-propyl)-13*H*-cyclopenta[*a*]phenanthrene-13-carboxylate 5d: IR (oil film): 1726 (C=O str.) cm^{-1}; ^1H NMR: δ 1.25 (6H, d, J = 7 Hz, $C(CH_3)_2$), 1.50-1.95 (4H, m), 2.00-2.80 (9H, m), 3.69 (3H, s, OCH_3), 6.85-7.70 (4H, m, Ar-H and C=C-H); Anal. Calcd for $C_{22}H_{26}O_2$: C, 81.95; H, 8.13. Found: C, 81.89; H, 8.16%.

Methyl 5-chloro-6,7,11,12,16,17-hexahydro-13*H*-cyclopenta[*a*]phenanthrene-13-carboxylate 5e: IR (oil film): 1728 (C=O str.) cm^{-1}; ^1H NMR: δ 1.48-1.90 (4H, m), 2.00-2.80 (8H, m), 3.71 (3H, s, OCH_3), 6.80-7.75 (4H, m, Ar-H and C=C-H); Anal. Calcd for $C_{19}H_{19}O_2Cl$: C, 72.49; H, 6.08; Cl, 11.26. Found: C, 72.44; H, 6.12; Cl, 11.31%.

General procedure for the synthesis of title compounds 6a-e. Gonane steroids **5a-e** (60 mg) was heated with 5% Pd-C (30 mg) at 250°C for 15 min. It was extracted with hot EtOAc (4 × 50 mL). The combined EtOAc extracts were filtered to remove traces of catalyst. Evaporation of solvent gave a light brown residue, which was purified by column chromatography [silica gel, pet. ether] to furnish the title compound **6a-e**. ^1H NMR of 16,17-dihydro-15*H*-cyclopenta[*a*]phenanthrene **6a** was in agreement with the reported data.[21]

16,17-Dihydro-7-methyl-15*H*-cyclopenta[*a*]phenanthrene 6b: IR (KBr): 1460, 1500, 1600 (aromatic C=C str.) cm^{-1}; ^1H NMR: δ 2.32 (2H, m, H16), 3.10 (3H, s, CH_3), 3.15-3.38 (4H, m, H15, H17), 7.46-7.97 (5H, m, Ar-H), 8.31-8.56 (2H, m, H1 and H11); MS (EI, m/z): 232 (100%, M^+), 231 (30), 217 (39), 216 (26), 215 (34), 202 (17), 114 (13), 110 (18); 101 (24); Anal. Calcd for $C_{18}H_{16}$: C, 93.06; H, 6.94. Found: C, 92.97; H, 6.98%.

16,17-Dihydro-6,7-dimethyl-15*H*-cyclopenta[*a*]-phenanthrene 6c: IR (KBr): 1500, 1600 (aromatic C=C str.) cm^{-1}; ^1H NMR: δ 2.33 (2H, m, H16), 3.13 (6H, combined singlet, CH_3), 3.19-3.40 (4H, m, H15, H17), 7.52-7.98 (4H, m, Ar-H), 8.38-8.61 (2H, m, H1 and H11); MS (EI, m/z): 246 (100%), 231 (42), 216 (19), 215 (28), 202 (14), 114 (14), 110 (16); Anal. Calcd for $C_{19}H_{18}$: C, 92.64; H, 7.36. Found: C, 92.71; H, 7.32%.

7-(2-propyl)-16,17-dihydro-15*H*-cyclopenta[*a*]-phenanthrene 6d: IR (KBr): 1520, 1620 (aromatic C=C str.) cm^{-1}; ^1H NMR: δ 1.25 (6H, d, J = 7, $(CH_3)_2C$), 2.33 (2H, m, H16), 3.15-3.40 [5H, m, H15, H17 and $C\underline{H}(CH_3)_2$], 7.48-8.00 (5H, m, Ar-H), 8.37-8.62 (2H, m, H1 and H11); Anal. Calcd for $C_{20}H_{20}$: C, 92.26; H, 7.74. Found: C, 92.34; H, 7.69%.

5-Chloro-16,17-dihydro-15*H*-cyclopenta[*a*]phenanthrene 6e: IR (KBr): 1450, 1500, 1600 (aromatic C=C str.) cm^{-1}; ^1H NMR: δ 2.29 (2H, m, H16), 3.20-3.42 (4H, m, H15, H17), 7.42-7.95 (5H, m, Ar-H), 8.38-8.70 (2H, m, H1 and H11); MS (EI, m/z): 254 (35%, M+2), 252 (100%; M^+), 251 (17), 217 (50), 216 (42), 189 (20), 215 (60), 202 (25), 108 (32), 107 (25); Anal. Calcd for $C_{17}H_{13}Cl$: C, 80.79; H, 5.18; Cl, 14.03. Found: C, 80.70; H, 5.13; Cl, 14.08%.

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