A Simple Synthesis of 1,2,3,4-Tetrahydrophenanthrenone and 1,2,3,4-Tetrahydrochrysenone Derivatives

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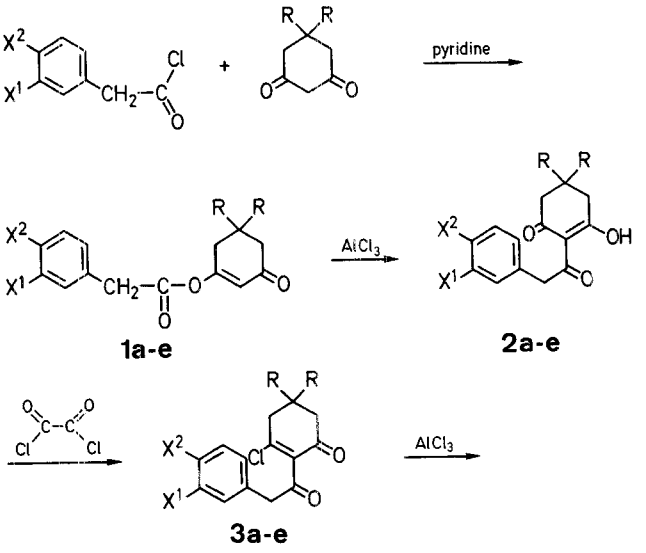
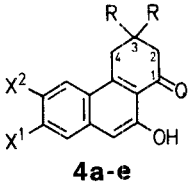
Many natural and synthetic polycyclic compounds (steroids, terpenes, alkaloids, and related compounds), having biological and therapeutic significance, possess as the major structural fragment partially or fully hydrogenated phenanthrene and chrysene nuclei[1]. Different phenanthrene and chrysene derivatives have been widely studied in view of the carcinogenic and mutant properties of polynuclear aromatic hydrocarbons[2,3].

The synthesis of the mentioned polycyclic compounds requires the formation of the phenanthrene (or the benzo-homologous chrysene) ring system[4]. The three main types of construction of the phenanthrene ring system involve as the key steps either a ring-enlargement reaction, an intramolecular cyclization, or an intermolecular cycloaddition[4].

We now report a new procedure for the synthesis of substituted 1,2,3,4-tetrahydrophenanthren-1-ones **(4)** and 1,2,3,4-tetrahydrochrysen-1-ones **(5)** which are useful synthons for the preparation of naturally occuring and related polycyclic compounds.

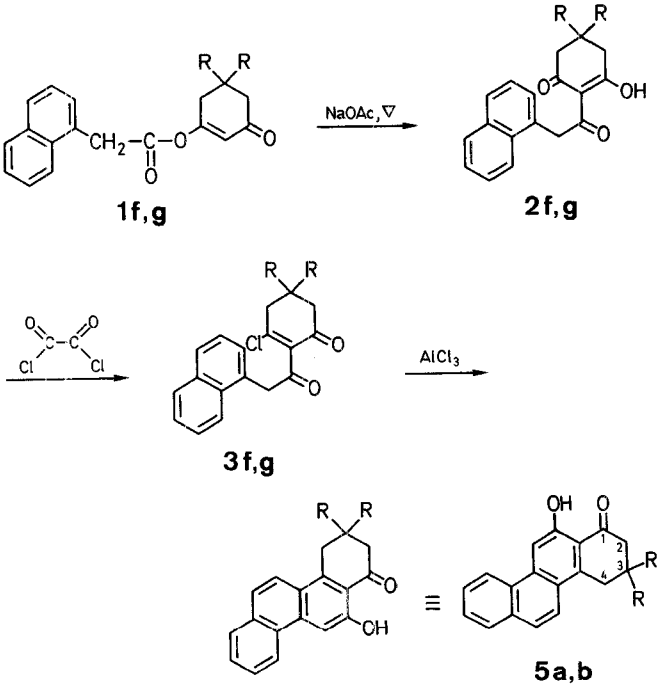
The reaction type used in our procedure is an intramolecular Friedel-Crafts reaction of a chlorovinyl benzyl ketone **(3)**. The whole sequence consists of the reaction of a phenylacetyl chloride with 1,3-cyclohexanedione (R = H) or dimedone (R = CH_3)[6], *O*-*C*-isomerization of the resultant enol esters **1** to give the 2-phenylacetyl-1,3-cyclohexanediones **2**[6], conversion of **2** into the chloro derivative **3** by reaction with oxalyl chloride, and cyclization of **3** in the presence of aluminum chloride.





1-4	R	X^1	X^2
a	H	H	H
b	CH_3	H	H
c	H	OCH_3	H
d	CH_3	OCH_3	H
e	CH_3	OCH_3	OCH_3

In the synthesis of the tetrahydrochrysenones **5a,b**, the isomerization step **1** → **2** does not proceed in the presence of aluminum chloride; the isomerization can be achieved, however, by heating the enol 1-naphthylacetates **1f,g** with anhydrous sodium acetate.



1,2,3f; 5a R = H
1,2,3g; 5b R = CH_3

Table 1. 3-Oxo-1-cyclohexenyl Arylacetates (**1**)

1	Yield[a] [%]	Molecular Formula	I.R. (film) ν_{max} [cm^{-1}]	^{1}H-N.M.R. (CCl_4/TMS_{int}) δ [ppm]
a	(93)[6]			
b	(94)[6]			
c	(93)[6]			
d	(94)[6]			
e	71	$C_{18}H_{22}O_5$ (318.4)	1770, 1675	
f	95	$C_{18}H_{16}O_3$ (280.3)	1760, 1675	1.7 (m, CH_2); 2.1 (m, CH_2); 3.9 (s, CH_2); 5.6 (s, CH); 6.9–7.6 (m, H_{arom})
g	96	$C_{20}H_{20}O_3$ (308.35)	1770, 1680	1.0 (s, $2CH_3$); 2.08 (s, CH_2); 2.2 (s, CH_2); 4.08 (s, CH_2); 5.7 (s, CH); 7.2–8.0 (m, H_{arom})

[a] All products **1** were obtained as oils.

Table 2. 2-Arylacetyl-1,3-cyclohexanediones (**2**)

2	Yield [%]	m.p. [°C]	Molecular Formula[a]	I.R. ν [cm^{-1}]	^{1}H-N.M.R. (solvent/TMS_{int}) Solvent	δ [ppm]
a	(93)[6]	(76–79°)[6]				
b	(89)[6]	(110–111°)[6]				
c	(82)[6]	(99–102°)[6]				
d	(87)[6]	(50–52°)[6]				
e	73	120–122°	$C_{18}H_{22}O_5$ (318.4)	1515, 1545, 1670 (KBr)	$CDCl_3$	1.08 (s, $2CH_3$); 2.36 (s, CH_2); 2.55 (s, CH_2); 3.88 (s, $2OCH_3$); 4.30 (s, CH_2); 6.88 (s, H_{arom}); 19.5 (s, OH)
f	85	133–136°	$C_{18}H_{16}O_3$ (280.3)	1560, 1595, 1665 (film)	CCl_4	1.7 (m, CH_2); 2.3 (m, CH_2); 4.7 (s, CH_2); 7.1–7.9 (m, H_{arom}); 17.5 (s, OH)
g	87	62–65°	$C_{20}H_{20}O_3$ (308.35)	1565, 1605, 1680 (KBr)	CCl_4	0.8 (s, $2CH_3$); 1.7 (s, CH_2); 2.28 (s, CH_2); 2.4 (s, CH_2); 4.75 (s, CH_2); 7.2–7.9 (m, H_{arom}); 17.54 (s, OH)

[a] The microanalyses were in satisfactory agreement with the calculated values: C ±0.31, H ±0.23, N ±0.29.

Table 3. 3-Chloro-2-arylacetyl-2-cyclohexenones (**3**)

3	Yield [%]	m.p. [°C]	Molecular Formula	I.R. ν [cm^{-1}]	^{1}N-M.R. Solvent	(solvent/TMS_{int}) δ [ppm]
a	94	81–84°	$C_{14}H_{13}ClO_2$ (248.5)	1620, 1675, 1725 (KBr)	CCl_4	1.92 (m, CH_2); 2.25 (m, CH_2); 2.6 (m, CH_2); 3.75 (s, CH_2); 7.11 (m, H_{arom})
b	96	64–68°	$C_{16}H_{17}ClO_2$ (276.5)	1630, 1670, 1720 (KBr)	$CDCl_3$	1.0 (s, $2CH_3$); 2.25 (s, CH_2); 2.52 (s, CH_2); 3.94 (s, CH_2); 7.2 (m, H_{arom})
c	97	oil	$C_{15}H_{15}ClO_3$ (278.5)	1620, 1670, 1720 (film)		
d	94	48–50°	$C_{17}H_{19}ClO_3$ (306.5)	1625, 1670, 1720 (KBr)		
e	82	70–73°	$C_{18}H_{21}ClO_4$ (336.5)	1625, 1670, 1715 (KBr)	$CDCl_3$	1.0 (s, CH_3); 2.20 (s, CH_2); 2.52 (s, CH_2); 3.82 (m, OCH_3, CH_2); 6.8 (m, H_{arom})
f	97	154–158°	$C_{18}H_{15}ClO_2$ (298.5)	1625, 1670, 1725 (KBr)	$CDCl_3$	1.92 (m, CH_2); 2.36 (m, CH_2); 2.62 (m, CH_2); 4.5 (s, CH_2); 7.4–8.3 (m, H_{arom})
g	91	133–136°	$C_{20}H_{19}ClO_2$ (326.5)	1625, 1670, 1720 (KBr)	$CDCl_3$	0.92 (s, CH_3); 2.2 (s, CH_2); 2.43 (s, CH_2); 4.42 (s, CH_2); 7.3–8.2 (m, H_{arom})

It is worthy of note that attempts to achieve the direct cyclocondensation of triketones **2** (which are vinylogous acids) to compounds **4** under the conditions described for the cyclization of 2-(2-arylethyl)-cyclohexane-1,3-diones[7,8] were unsuccessful. Only in the case of triketones **2c** and **2d** does cyclization take place to a minor extent in the presence of aluminum chloride so that traces of compounds **4c** or **4d**, respectively, are formed during the isomerization **1** → **2**.

2-(1-Naphthylacetyl)-1,3-cyclohexanediones (2f,g); General Procedure:

A mixture of the 3-naphthylacetyloxy-2-cyclohexenone **1f** or **1g** (5 mmol) and anhydrous sodium acetate (0.41 g, 5 mmol) is kept for 15 min at 160 °C under nitrogen. Then, the mixture is cooled and dissolved in ether (100 ml). This solution is washed with water (2 × 25 ml) and dried with magnesium sulfate. The solvent is evaporated to dryness in vacuo and the crude product is recrystallized from ether/hexane.

Table 4. 1-Oxo-1,2,3,4-tetrahydrophenanthrenes (**4**) and -chrysenes (**5**)

Compound	Yield [%]	m.p. [°C]	Molecular Formula[a]	I.R. (KBr) ν [cm^{-1}]	^{1}H-N.M.R. Solvent	(solvent/TMS$_{int}$) δ [ppm]
4a	84	103–106°	$C_{14}H_{14}O_2$ (212.25)	1620, 1655	CCl_4	2.19 (m, CH_2); 2.61 (t, CH_2); 3.22 (t, CH_2); 6.81–7.74 (m, H_{arom}); 11.32 (s, OH)
4b	83	88–91°	$C_{16}H_{16}O_2$ (240.3)	1630, 1655	CCl_4	1.20 (s, CH_3); 2.61 (s, CH_2); 3.21 (s, CH_2); 6.81–7.96 (m, H_{arom}); 11.65 (s, OH)
4c	80	114–117°	$C_{15}H_{14}O_3$ (242.3)	1620, 1650	CCl_4	2.16 (m, CH_2); 2.62 (t, CH_2); 3.20 (t, CH_2); 3.82 (s, OCH_3); 6.79 (m, H_{arom}); 7.66 (d, H_{arom}); 11.70 (s, OH)
4d	81	124–127°	$C_{17}H_{18}O_3$ (270.3)	1625, 1650	CCl_4	1.20 (s, CH_3); 2.58 (s, CH_2); 3.11 (s, CH_2); 3.90 (s, OCH_3); 6.89 (m, H_{arom}); 7.80 (d, H_{arom}); 11.71 (s, OH)
4e	89[b]	174–177°	$C_{18}H_{20}O_4$ (300.3)	1615, 1650	$CDCl_3$	1.20 (s, CH_3); 2.58 (s, CH_2); 3.08 (s, CH_2); 4.00 (s, OCH_3); 6.87 (s, H_{arom}); 6.96 (s, H_{arom}); 7.10 (s, H_{arom}); 11.60 (s, OH)
5a	91	182–187°	$C_{18}H_{14}O_2$ (262.3)	1570, 1640	$CDCl_3$	2.24 (m, CH_2); 2.74 (m, CH_2); 3.34 (m, CH_2); 7.56–8.96 (m, H_{arom}); 12.24 (s, OH)
5b	85	160–163°	$C_{20}H_{18}O_2$ (290.35)	1570, 1640	$CDCl_3$	1.20 (s, CH_3); 2.66 (s, CH_2); 3.30 (s, CH_2); 7.26–8.60 (m, H_{arom}); 12.30 (s, OH)

[a] The microanalyses were in satisfactory agreement with the calculated values: C ±0.29, H ±0.23, N ±0.32.

[b] Tetrahydrophenanthrenone **4e** is prepared by cyclization of **3d** followed by *O*-methylation of the resultant compound **4** (R = CH_3, X^1 = OH, X^2 = OCH_3) with diazomethane.

3-Chloro-2-arylacetyl-2-cyclohexenones (3); General Procedure:
Oxalyl chloride (5 ml) is added to the 2-arylcyclohexane-1,3-dione **2** (5 mmol) and the mixture is stirred at room temperature for 3 h. Then, excess oxalyl chloride is evaporated in vacuo. The residue is dissolved in ether (150 ml). This solution is washed with saturated aqueous sodium hydrogen carbonate (50 ml) and with water (25 ml) and is dried with magnesium sulfate. The solvent is evaporated and the residue recrystallized from hexane.

1,2,3,4-Tetrahydrophenanthren-1-ones (4a–e) 1,2,3,4-Tetrahydrochrysen-1-ones (5a,b); General Procedure:
A solution of the 3-chloro-2-arylacetyl-2-cyclohexenone **3** (5 mmol) in dry 1,2-dichloroethane (25 ml) is added to a stirred suspension of anhydrous aluminium chloride (5 mmol) in dry 1,2-dichloroethane (100 ml). Stirring is continued for 3 h at room temperature. The mixture is then stirred with ice (2 g) + conc. hydrochloric acid (2 ml) whereupon water (25 ml) is added. The organic layer is separated and the aqueous layer is extracted with chloroform (3 × 50 ml). The combined organic phases are washed with water (2 × 25 ml) and dried with magnesium sulfate. The solvent is evaporated in vacuo and the residue is recrystallized from hexane.

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