A Simple Route to Racemic Acenaphthene-1-carboxylic Acid via Hydroformylation of Acenaphthylene

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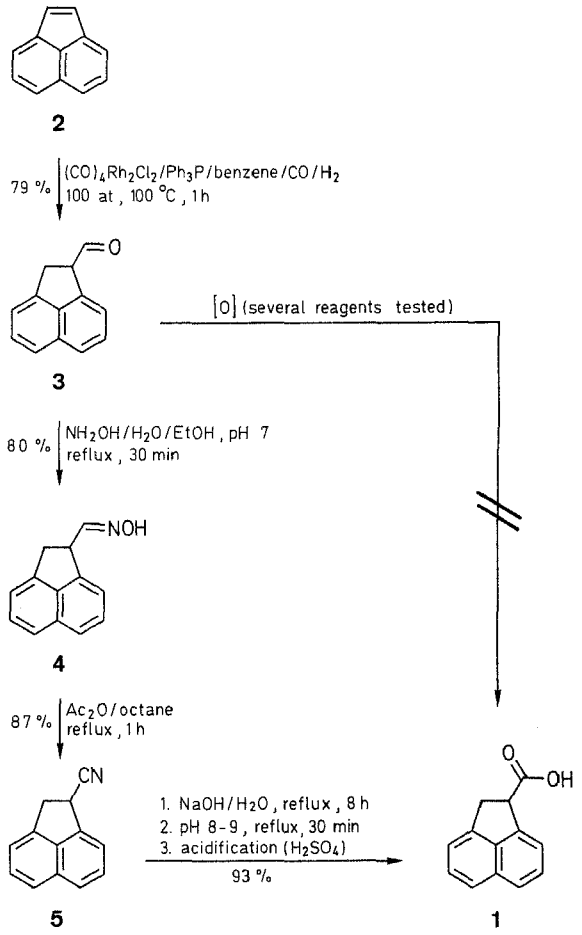
Hydroformylation of acenaphthylene using di-μ-chlorotetracarbonyldirhodium/triphenylphosphine as catalytic precursor affords acenaphthene-1-carboxaldehyde under mild conditions in 80% yield. This compound is easily transformed, via dehydration of the corresponding oxime followed by hydrolysis of the nitrile, into acenaphthene-1-carboxylic acid in an overall yield of $\approx 50\%$.

Several 1-monosubstituted acenaphthene derivatives show interesting biological properties. For instance, 1-methylaminoacenaphthenes are hypotensive agents[1] and acenaphthene-1-carboxylic acid (**1**) is a plant-growth controlling substance.[2] In addition, racemic **1** has been resolved[2] and it has been shown that the (−)-enantiomer is some 10 times more active than the (+)-enantiomer.

In spite of interest in new derivatives of type **1** and in the study of the relationship between their stereochemistry and activity, only three syntheses have been reported for racemic **1**. In one synthesis,[2] bromination of acenaphthene followed by reaction with diethyl sodiomalonate affords the diethyl acenapthenylmalonate, which is transformed into 1-cyanoacenaphthene by sequential treatment with butyl nitrite and acetic anhydride; alkaline hydrolysis of the cyano group then affords acid **1**. This method is quite laborious and requires the unconvenient use of butyl nitrite. The second route uses the reaction of acenaphthylene with sodium in diglyme at 100 °C affording the acenaphthenide anion which, by treatment with carbon dioxide in ether at 25 °C, is transformed into acid **1** (15–18% yield).[3] In the third synthesis, acenaphthylene is electrochemically carboxylated by carbon dioxide to give **1** (35–50% yield).[4] The major disadvantage of the second and the third method is that acid **1** is in both cases obtained as a by-product. In addition, the third route requires the use of a special, not usually available apparatus.

An alternative simplified route to acid **1**, using only conventional laboratory chemicals and equipment is outlined in the scheme.



The hydroformylation of acenaphthylene (**2**) to acenaphthene-1-carboxaldehyde (**3**) has been briefly reported[1] to occur under drastic conditions (100 °C, 700 atm, 54% yield) using 1,5-cyclooctadiene-μ-dichlorodirhodium as catalyst precursor. We have found that in the presence of di-μ-chlorotetracarbonyldirhodium/triphenylphosphine (mole ratio $\sim 1:4$, that is a Rh/P ratio of $\sim 1:2$) hydroformylation of **2** (mole ratio **2**/catalyst ~ 250) occurs rapidly (1 h) with almost complete conversion under mild conditions (100 atm, 100 °C). Reduced-pressure distillation of the crude product affords **3** as a viscous oil in 79% yield. Two more attempts were carried out: (1) asymmetric hydroformylation using DIOP in place of triphenylphosphine gave a lower yield ($\sim 45\%$) of **3** and an only insignificant enantiomeric excess; (2) the use of Rh/toluene solutions ("metal atoms" catalyst[5]) provided about the same yield of racemic aldehyde.

Unfortunately, all attempts to oxidize aldehyde **3** to acid **1** with standard reagents were unsuccessful. The use of Ag_2O/OH^-,[6] neutral $KMnO_4$,[7] CrO_3/acetone,[8] $Py_2Cr_2O_7$,[9] $Ca(OCl)_2$,[10] or O_3/KOH in methanol at −78 °C[11] led only to products formed via oxidative 1,2-cleavage to naphthalene-1,8-dicarboxylic acid. We therefore prepared acid **1** from **3** by the sequence described in the Scheme. Oxime **4** is easily obtained in 80% yield from **3** and hydroxylamine under standard conditions; it is then dehydrated by acetic anhydride in boiling octane to form the nitrile **5** (87% yield) which is hydrolysed in

boiling aqueous sodium hydroxide[2] to afford acid **1** in 93% yield (50% overall yield based on **2**).

Benzene was distilled from the potassium ketyl of benzophenone, octane from calcium hydride, acetic anhydride from quinoline. Acenaphthylene was recrystallized from pentane. Di-μ-chlorotetracarbonyldirhodium was prepared according to a known procedure.[12] All other reagents were used without purification.

Melting points were measured using a Kofler hot stage microscope. Microanalysis were performed at Laboratorio di Microanalisi, Istituto di Chimica Organica, Facoltà di Farmacia, Università di Pisa. IR spectra were recorded neat between KBr plates or solid in KBr discs using a Perkin-Elmer model 283B spectrophotometer. ^{1}H-NMR spectra were recorded with a VARIAN model T60 spectrometer at 60 MHz.

1-Formylacenaphthene (3):
Di-μ-chlorotetracarbonyldirhodium (100 mg, 0.26 mmol) and Ph_3P (270 mg, 1.03 mmol) are placed in a stainless-steel autoclave under N_2. Acenaphthylene (**2**; 10.0 g, 65.7 mmol) dissolved in benzene (50 mL) is then added. The vessel is charged with CO/H_2 (1:1) at 100 atm and rocked in an oil bath at 100 °C for 1 h. The mixture is recovered, and the solvent removed at reduced pressure. The residue is distilled under reduced pressure using a short-path distillation apparatus to give the aldehyde **3** as a viscous oil; yield: 9.5 g (52.1 mmol, 79%); bp 154 °C/0.1 Torr.

$C_{13}H_{10}O$	calc.	C 85.69	H 5.53	
(182.2)	found	85.78	5.42	

IR (neat): ν = 3040, 2920, 2820, 2720 (C–H); 1720 (C=O); 1600, 1500 cm^{-1} (ring).

^{1}H-NMR ($CDCl_3$/TMS): δ = 3.0–4.3 (m, 3H, H-1 + 2H-2); 7.1–7.6 (m, 6H_{arom}); 9.6 (d, 1H, CHO).

Treatment of **3** with an acidic solution of 2,4-dinitrophenylhydrazine in EtOH affords **3**-2,4-DNP as red-orange crystals; mp 245–250 °C.

$C_{19}H_{14}N_4O_4$	calc.	C 62.98	H 3.89	N 15.46
(362.3)	found	62.91	3.75	15.74

1-Oximinoacenaphthene (4):
A solution of $NH_2OH \cdot HCl$ (1.22 g, 17.6 mmol) in H_2O (20 mL) is brought to pH 7 by the addition of 10% NaOH solution (≈ 4 mL), aldehyde **3** (2.91 g, 15.9 mmol) in EtOH (50 mL) is added, the mixture is refluxed for 30 min, then allowed to cool. Water (150 mL) is added, and the oxime **4** is isolated by suction and recrystallized from benzene (~ 20 mL) to afford oxime **4** as light yellow needles; yield: 2.49 g (80%); mp 152 °C.

$C_{13}H_{11}NO$	calc.	C 79.17	H 5.62	N 7.10
(197.2)	found	79.65	5.64	6.98

IR (KBr): ν = 3500–2800 (OH); 1665 (C=N); 1600, 1500 cm^{-1} (ring).

^{1}H-NMR ($CDCl_3$/TMS): δ = 3.2–4.0 (m, 2H, CH_2); 5.2, 4.6 (2 m, 1H, C<u>H</u>–CH=NOH, two signals due to *syn* and *anti* stereoisomers); 6.8–8.2 (m, 8H, C<u>H</u>=NO<u>H</u> + 6H_{arom}).

1-Cyanoacenaphthene (5):
A stirred suspension of oxime **4** (2.38 g, 12.1 mmol), *n*-octane (25 mL), and Ac_2O (5 mL) is slowly heated until a vigorous reaction occurs. The mixture is then kept at refluxed temperature for ~ 1 h to complete dissolution of the oxime. After cooling, the mixture is poured with swirling into ice-cold H_2O (100 mL). The red-orange oil is extracted with Et_2O (3 × 15 mL), and the organic extract is dried (Na_2SO_4). The solvent is removed *in vacuo* and the remaining viscous red-brown oil is chromatographed on a silica gel (≈ 30 g) column using benzene as eluent to give the nitrile **5** as a pale-yellow solid; yield: 1.88 g (87%). An analytical sample is obtained by recrystallization from *n*-octane; colorless crystals, mp 66 °C (Lit.[13,14] mp 68 °C).

IR (KBr): ν = 3040, 2960, 2840 (CH); 2240 (C≡N); 1600, 1500 cm^{-1} (ring).

^{1}H-NMR ($CDCl_3$/TMS): δ = 3.7 (d, 2H, J = 7 Hz, CH_2); 4.5 (t, 1H, J = 7 Hz, CH); 7.8–8.1 (m, 6H_{arom}).

Acenaphthene-1-carboxylic Acid (1):
Nitrile **5** (1.79 g, 10.0 mmol) is heated in boiling aqueous 3N NaOH (50 mL) until no more ammonia is evolved (≈ 8 h). The pH is then lowered to 8–9 and the solution is extracted with Et_2O (2 × 20 mL). The aqueous phase is heated to boiling for 30 min, and acidified with excess 5% H_2SO_4. The crude product is isolated by suction and recrystallized from *n*-octane to give acid **1** as a pale-yellow solid; yield: 1.85 g (93%). An analytical sample is obtained by a second recrystallization from *n*-octane; colorless needles, mp 160 °C (Lit.[2,3,13,14] mp 162, 160, 161, 163–164 °C).

IR (KBr): ν = 3500–2500 (OH); 1700 (C=O); 1600, 1500 cm^{-1} (ring).

^{1}H-NMR ($CDCl_3$/TMS): δ = 3.4–3.9 (m, 2H, CH_2); 4.5 (dd, 1H, CH); 7.2–7.8 (m, 6H_{arom}); 11.2 (br s, 1H, CO_2H).

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