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Synthesis of phenanthrene-9-carboxylic esters by the iron-catalyzed reaction of phenanthrene with CCl_4 and alcohols

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Alkyl phenanthrene-9-carboxylates were synthesized in 74–96% yields by the iron-catalyzed reaction of phenanthrene with tetrachloromethane and alkanols.

The phenanthrene moiety is a part of phenanthroindolizidine alkaloids (tylophorine, deoxytylophorine, tylocrebrine, antofine) known for their high cytotoxic activity.[1,2] Phenanthrene-9-carboxylic acid and its methyl ester are used in the synthesis of antimalarial agents[3] and compounds active against the tobacco mosaic virus.[4] Phenanthrene derivatives are applied to devise photoconducting, photochemical, electroluminescent and fluorescent materials.[5–7] Direct synthesis of phenanthrene-9-carboxylic acid by carboxylation of phenanthrene with carbon dioxide (3 MPa) in the presence of Lewis acids, $AlBr_3$, and R_3SiX is known.[8,9]

In this study, we found that phenanthrene-9-carboxylic esters **1a–d** can be accessed by the reaction of phenanthrene (phen) with CCl_4 and alkanols in the presence of iron catalysts such as $FeBr_2$, $FeCl_3·6H_2O$ and $Fe(acac)_3$. Among these, iron(III) acetylacetonate $Fe(acac)_3$ is the catalyst of choice. The conversion of phenanthrene in the cases of $FeBr_2$ or $FeCl_3·6H_2O$ does not exceed 48%.

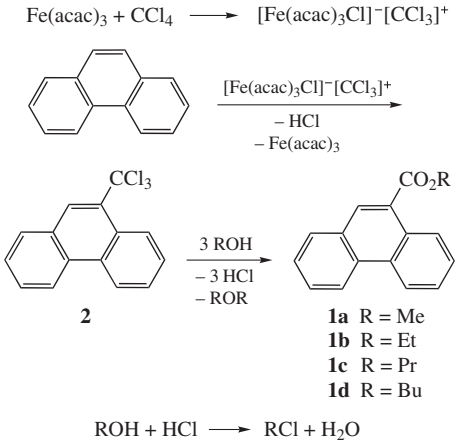
The optimization was carried out on the example of phenanthrene, *n*-propanol, CCl_4 and $Fe(acac)_3$. The reaction was carried out at the following catalyst and reactant molar ratios: $[Fe(acac)_3]$: [phen] : [PrOH] : $[CCl_4]$ = 1–15 : 100 : 500–1000 : 100–1000, at 130–140 °C, and over a period of 6 h. The highest yield of product **1c** (96%) was achieved under the following conditions: 130 °C, 6 h, $[Fe(acac)_3]$: [phen] : [PrOH] : $[CCl_4]$ = 1 : 10 : 100 : 100 (Table 1, entry 3).†

Table 1 Synthesis of alkyl phenanthrene-9-carboxylates by the reaction of phenanthrene with CCl_4 and alcohols in the presence of $Fe(acac)_3$.[a]

Entry	ROH	Product	Yield (%)
1	Methanol	**1a**	74
2	Ethanol	**1b**	80
3	*n*-Propanol	**1c**	96
4	*n*-Butanol	**1d**	85

[a] Reaction conditions: 130 °C, 6 h, $[Fe(acac)_3]$: [phen] : [ROH] : $[CCl_4]$ = = 1 : 10 : 100 : 100.

The reaction is general (Scheme 1): under the optimal conditions, it can proceed, apart from *n*-propanol, with methanol, ethanol and *n*-butanol (Table 1).



Scheme 1

† *Synthesis of compounds* **1a–d** *(general procedure).* The reactions were carried out in a 10-ml glass tube placed in a stainless-steel 17 ml micro autoclave with continuous stirring and controlled heating. The tube was charged under argon with $Fe(acac)_3$ (0.059 mmol), phenanthrene (0.59 mmol), tetrachloromethane (5.9 mmol), and appropriate alkanol (5.9 mmol). The sealed tube was placed into an autoclave, the autoclave was tightly closed and heated at 130 °C for 6 h with continuous stirring. After completion of the reaction, the autoclave was cooled to room temperature, the tube was opened, and the reaction mixture was filtered through a paper filter and refluxed with absorbent carbon. The volatiles were distilled off. The target ester **1** was separated from remaining phenanthrene by column chromatography on silica gel using a light petroleum : ethyl acetate (5 : 1) mixture as the eluent (column, l = 21 cm, d = 1.2 cm). The physicochemical and spectral characteristics of compounds **1a**,**b** correspond to published data.[10–13]

n-*Propyl phenanthrene-9-carboxylate* **1c**. White crystals, yield 96%, mp 46–47 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.96 (d, 1H, C^1H, *J* 8 Hz), 7.71 (m, 1H, C^2H), 7.63 (t, 1H, C^3H, *J* 8 Hz), 8.65 (d, 1H, C^4H, *J* 8Hz), 8.71 (m, 1H, C^5H), 7.71 (m, 1H, C^6H), 7.71 (m, 1H, C^7H), 8.98 (m, 1H, C^8H), 8.48 (s, 1H, C^{10}H), 4.45 (t, 2H, CH_2), 1.93 (m, 2H, CH_2), 1.15 (t, 3H, Me). ^{13}C NMR (100.62 MHz, $CDCl_3$) δ: 129.91 (C^1), 128.81 (C^2), 126.98 (C^3), 122.64 (C^4), 130.10 (C^{4a}), 130.70 (C^{4b}), 122.83 (C^5), 126.87 (C^6), 127.37 (C^7), 126.67 (C^8), 126.60 (C^{8a}), 132.10 (C^9), 132.13 (C^{10}), 129.12 (C^{10a}), 167.74 (COO), 66.84 (CH_2Et), 22.26 (CH_2Me), 10.73 (Me). MS (EI, 70 eV), *m*/*z* (%): 264 $[M]^+$ (93), 222 (90), 205 (100), 177 (70), 151 (20), 88 (35). Found (%): C, 81.68; H, 6.16; O, 12.16. Calc. for $C_{18}H_{16}O_2$ (%): C, 81.79; H, 6.10; O, 12.11.

n-*Butyl phenanthrene-9-carboxylate* **1d**. White crystals, yield 85%, mp 56–57 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.99 (d, 1H, C^1H, *J* 8 Hz), 7.69 (t, 1H, C^2H, *J* 8 Hz), 7.76 (t, 1H, C^3H, *J* 8 Hz), 8.70 (d, 1H, C^4H, *J* 8 Hz), 8.74 (m, 1H, C^5H), 7.71 (m, 1H, C^6H), 7.71 (m, 1H, C^7H), 8.94 (m, 1H, C^8H), 8.47 (s, 1H, C^{10}H), 4.49 (t, 2H, CH_2), 1.89 (m, 2H, CH_2), 1.57 (m, 2H, CH_2), 1.06 (t, 3H, Me). ^{13}C NMR (100.62 MHz, $CDCl_3$) δ: 129.92 (C^1), 127.82 (C^2), 126.99 (C^3), 122.64 (C^4), 130.12 (C^{4a}), 130.70 (C^{4b}), 122.81 (C^5), 127.36 (C^6), 126.88 (C^7), 126.65 (C^8), 126.69 (C^{8a}), 134.42 (C^9), 132.08 (C^{10}), 129.10 (C^{10a}), 167.77 (COO), 65.12 (CH_2Pr), 30.89 (CH_2Et), 19.41 (CH_2Me), 13.83 (Me). MS (EI, 70 eV), *m*/*z* (%): 278 $[M]^+$ (60), 222 (100), 205 (65), 177 (70), 151 (20), 88 (10). Found (%): C, 81.89; H, 6.66; O, 11.45. Calc. for $C_{19}H_{18}O_2$ (%): C, 81.98; H, 6.52; O, 11.50.

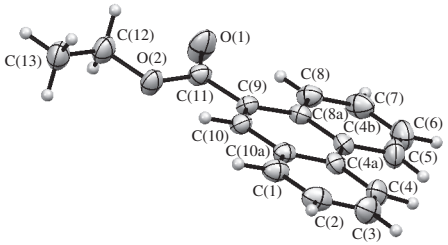


Figure 1 Molecular projection of **1b** showing the numbering scheme. Atomic displacement ellipsoids have been drawn at the 50% probability level.

The structures of compounds **1a–d** were proved by NMR data. The structure of *n*-propyl phenanthrene-9-carboxylate **1c** was studied more thorougly by 1D (^{1}H, ^{13}C) and 2D (COSY, HSQC, HMBC) NMR spectroscopy. The structure of ethyl ester **1b** was also proved by X-ray diffraction (Figure 1).‡

Compound **1b** crystallizes in the monoclinic system, the unit cell comprising four molecules. The phenanthrene moiety of the molecule is nearly planar. The dihedral angles between the central and peripheral rings are 0.81° and 0.98°, while the dihedral angle between the peripheral rings is 0.753°. The torsion angle C(8a)–C(9)–C(11)–O(1) is –15.07°, which is indicative of a minor deviation of the carbonyl group from the phenanthrene plane. The carbonyl and ethoxy groups occur in the *syn*-conformation [the torsion angle O(1)–C(11)–O(2)–C(12) is –3.77°].

Relying on the analysis of experimental data and taking into account the formation of HCl, dialkyl ether, and RCl as by-products, the following possible reaction pathway can be proposed (see Scheme 1). The reaction starts with the $Fe(acac)_3$-catalyzed Friedel–Crafts alkylation of phenanthrene with CCl_4. The next step is alcoholysis of 9-trichloromethylphenanthrene **2** to give products **1**.

This reaction pathway is supported by the fact that in the experiment involving phenanthrene and *n*-butanol, the reaction mixture was found to contain dibutyl ether ($[M]^+$ 130), chlorobutane ($[M]^+$ 92), and HCl (mercurimetric titration). The HCl concentration was 33.45 mg ml^{-1}, which was three times lower than the theoretical value as some of HCl was consumed for the formation of BuCl.

The formation of alkyl phenanthrene-9-carboxylates **1a–d** in the reaction between phenanthrene, CCl_4 and alkanol was unexpected. According to the literature,[15,16] the reaction of aromatic hydrocarbons with CCl_4 in the presence of Lewis acids do not stop at the stage of trichloromethyl derivative. The latter usually alkylated the next arene molecule to give diaryldichloromethane. In our case alkanol presenting in the reaction mixture would cause fast alcoholysis of the CCl_3 group.[17]

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References

1 E. Gellert, in *Alkaloids: Chemical and Biological Perspectives*, ed. S. W. Pelletier, Academic Press, New York, 1987, pp. 55–132.
2 M. Suffness and G. A. Cordell, in *The Alkaloids, Chemistry and Pharmacology*, ed. A. Brossi, Academic Press, New York, 1987, pp. 3–355.
3 W. T. Colwell, V. Brown, P. Christie, J. Lange, C. Reece, K. Yamamoto and D. W. Henry, *J. Med. Chem*., 1972, **15**, 771.
4 K. Wang, Y. Hu, Y. Liu, N. Mi, Z. Fan, Y. Liu and Q. Wang, *J. Agric. Food Chem*., 2010, **58**, 12337.
5 F. D. Lewis and E. L. Burch, *J. Photochem. Photobiol A: Chem*., 1996, **96**, 19.
6 A. M. Machado, M. Munano, T. D. Martis, L. Y. Davila, R. Giro, M. J. Caldas, T. D. Z. Atvars and L. C. Akcelrud, *Macromolecules*, 2006, **39**, 3398.
7 R. Liu, J. P. S. Farinha and M. A. Winnik, *Macromolecules*, 1999, **32**, 3957.
8 Y. Suzuki, T. Hattori, T. Okuzawa and S. Miyano, *Chem. Lett*., 2002, 102.
9 K. Nemoto, H. Yoshida, N. Egusa, N. Morohashi and T. Hattori, *J. Org. Chem*., 2010, **75**, 7855.
10 H. Sakuragi, K. Tokumaru, H. Itoh, K. Terakawa, K. Kikuchi, R. A. Caldwell and C. C. Hsu, *Bull. Chem. Soc. Jpn*., 1990, **63**, 1049.
11 H. Itoh, M. Takada, F. Asano, Y. Senda, H. Sakuragi and K. Tokumaru, *Bull. Chem. Soc. Jpn*., 1993, **66**, 224.
12 H. J. Bestmann, H. Häberlein and W. Eisele, *Chem. Ber.*, 1966, **99**, 28.
13 Y. H. Kim, H. Lee, Y. J. Kim, B. T. Kim and J.-N. Heo, *J. Org. Chem*., 2008, **73**, 495.
14 G. M. Sheldrick, *Acta Crystallogr., Sect. A*, 2008, **64**, 112.
15 L. I. Belen'kii, N. D. Chuvylkin and I. A. Suslov, *Russ. Chem. Bull., Int. Ed*., 2001, **50**, 2046 (*Izv. Akad. Nauk, Ser. Khim*., 2001, 1955).
16 L. I. Belen'kii, D. B. Brokhovetskii and M. M. Krayushkin, *Chem. Scripta*, 1989, **29**, 81.
17 G. M. Le Fave and P. G. Scheurer, *J. Am. Chem. Soc*., 1950, **72**, 2464.

‡ *Crystal data for* **1b**: $C_{17}H_{14}O$, M = 234.28, monoclinic, space group $P2_1/n$ (no. 14), at 200 K: a = 8.7674(4), b = 7.9374(6) and c = 18.321(2) Å, β = 99.657(6)°, V = 1256.86(19) Å^3, Z = 4, d_{calc} = 1.238 g cm^{-3}, 2925 reflections collected, 2213 independent reflections (R_{int} = 0.0113), final R indexes [$I > 2\sigma(I)$]: R_1 = 0.0463, wR_2 = 0.1016; R indexes (all data): R_1 = 0.0662, wR_2 = 0.1130, GOF = 1.146.

Single crystal of **1b** was grown from hexane at room temperature. The intensities of reflections were measured on an XCalibur Eos diffractometer (graphite monochromated MoKα radiation, λ = 0.71073 Å, ω-scan technique, $2\theta_{max}$ = 62°). Collection and processing of data were performed using the program CrysAlisPro Oxford Diffraction Ltd., Version 1.171.36.20. Structure solution and refinement were performed with SHELX97.[14] The structure was refined by a full-matrix least-square technique using anisotropic thermal parameters for non-hydrogen atoms and a riding model for hydrogen atoms.

CCDC 1002463 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

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