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An easy synthesis of lepidopterene from 9-chloromethyl anthracene. Evidence for a free radical mechanism

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Abstract—This communication reports a novel and efficient synthesis of lepidopterene from 9-(chloromethyl)anthracene. Furthermore, the radical nature of the process is unambiguously established through the obtention of several 9-anthracenemethyl derivatives, which are formed via a common 9-anthracenemethyl radical intermediate, derived from 9-(iodomethyl)anthracene.

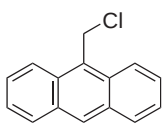
Lepidopterene **2**, a tetrabenzotetracyclotetradecatetraene, was first synthesized by reaction of 9-(chloromethyl)anthracene (**1**) with methylmagnesium iodide.[1] Through this methodology, lepidopterene **2** and 1,2-bis(9-anthracenyl)ethane (**3**) were obtained in 35% and 30% yield, respectively.

The authors proposed a free radical type process but no evidence was adduced. Afterwards, Becker et al.[2] described another synthesis of lepidopterene from 9-(halomethyl)anthracenes by reaction with stannous chloride dihydrate in dioxane at 70°C. The authors suggested an ionic mechanism with formation of a α,p-dimer by reaction of a 9-anthracenemethyl anion, generated from the (9-anthracenemethyl)tin trihalide, with 9-(halomethyl)anthracene.

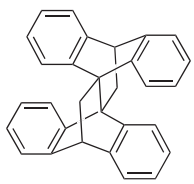
In addition, lepidopterene has also been prepared through oxidation of 9-methylanthracene with copper(II)/peroxydisulphate,[3] via photolysis and pyrolysis of 9-anthracenemethylsulphides and selenides[4] and as a product of photolysis from 9-(phenoxymethyl)-anthracene.[5] The fact that this compound can be obtained through a great variety of processes involving different mechanisms, along with its relevant photochemical properties,[6,7] have aroused considerable interest in the study of this compound and its derivatives.

In this communication an easy synthesis of lepidopterene from commercially available reagents and evidence for a free radical mechanism are reported. Thus, when a 0.08 M solution of 9-(chloromethyl)anthracene in dry acetone with 1.1 equiv. of sodium iodide was heated at reflux for 12 hours under an argon atmosphere, lepidopterene **2** was obtained in 75% yield[8] (Scheme 1), along with 1,2-bis(9-anthracenyl)ethane **3** in traces.

When this procedure was carried out at a higher concentration (0.5 M), 9-(chloromethyl) anthracene was quantitatively transformed into lepidopterene (59% yield) and 1,2-bis(9-anthracenyl)ethane (41% yield).



1



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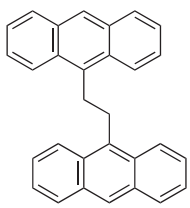

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Keywords: 9-(chloromethyl)anthracene; lepidopterene; 1,2-bis(9-anthracenyl)ethane; hydroquinone; TEMPO.
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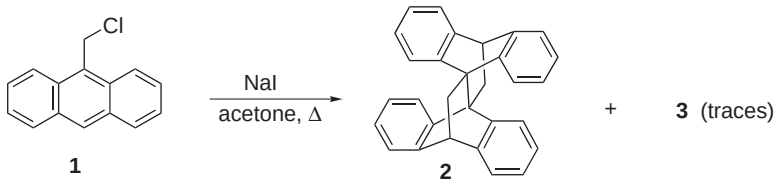
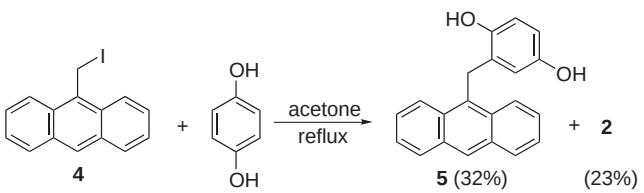


Scheme 1.

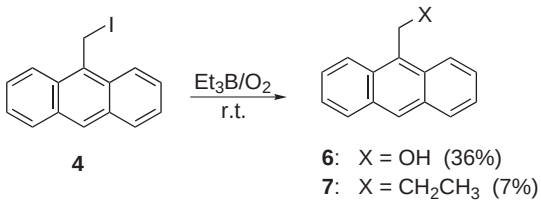
The reaction does not proceed without the addition of sodium iodide, which indicates that the formation of the previously undescribed 9-(iodomethyl)anthracene **4** is required. The latter can be obtained when 9-(chloromethyl)anthracene is treated with sodium iodide at room temperature for 1.5 hours.[9] Once this intermediate has been isolated, different products can be obtained depending on experimental conditions. On the one hand, heating at reflux a solution of 9-(iodomethyl)anthracene in dry acetone afforded lepidopterene (45% yield). On the other hand, when 9-(iodomethyl)anthracene was stirred in dry acetone at room temperature for 2 weeks, 1,2-bis(9-anthracenyl)ethane **3** was isolated in 24% yield.

A first evidence of a free radical mechanism was found when a mixture of 9-(iodomethyl)anthracene **4** and hydroquinone was heated at reflux in dry acetone, affording 2-(9-anthracenemethyl)-benzene-1,4-diol[10] **5** in a 32% yield (Scheme 2), along with lepidopterene (23% yield).



Scheme 2.

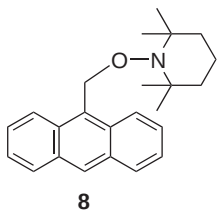
Triethylborane, a reagent widely used in synthetic radical reactions, has proved to be an efficient radical initiator.[11] In order to assess the intervention of a free radical, the reaction of 9-(iodomethyl)anthracene with triethylborane was performed. As a result, a mixture of 9-(hydroxymethyl)anthracene **6** and 9-propylanthracene **7** was obtained (Scheme 3).



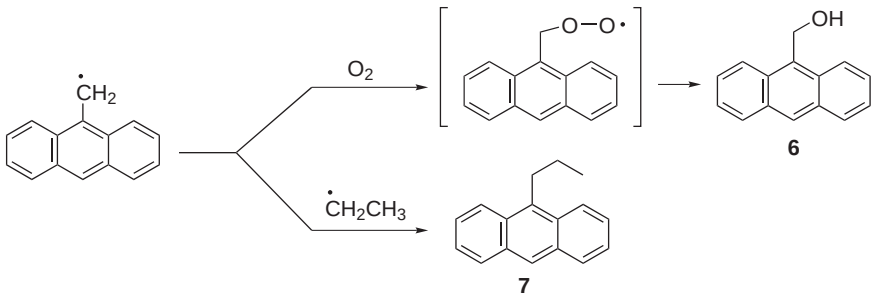
Scheme 3.

The formation of anthracene derivatives **6** and **7** can be explained through the process depicted in Scheme 4.

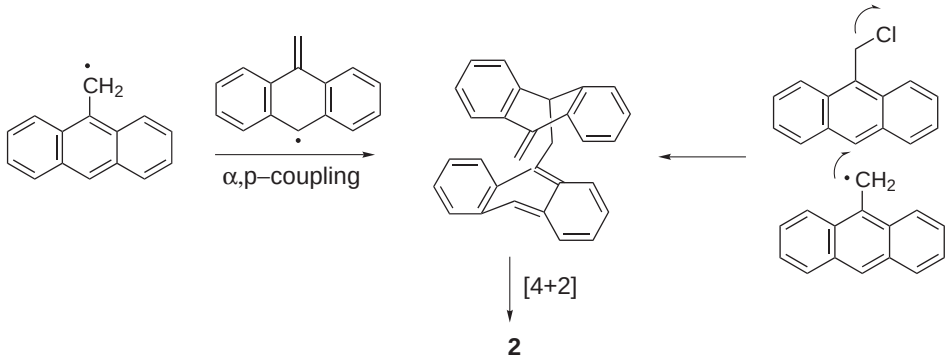
A free radical mechanism was definitely confirmed when a 0.01 M solution of 9-(iodomethyl)anthracene was heated at reflux with three equivalents of the 2,2,6,6-tetramethyl-1-piperidinyloxy free radical (TEMPO) for 15 hours, giving rise to 9-(2,2,6,6-tetramethyl-1-piperidinyloxymethyl)anthracene **8** in high yield (87%).[12]



From the results described so far, we conclude that the reaction occurs through formation of 9-(iodomethyl)-anthracene, which undergoes a homolytic cleavage leading to the 9-anthracenemethyl radical, which by dimerization produces 1,2-bis(9-anthracenyl)ethane **3**. Formation of lepidopterene can be explained considering two different pathways (Scheme 5). Hence, a α,p radical coupling, or a radical addition at 10 position of 9-(chloromethyl) anthracene, with a chloro radical act-



Scheme 4.



Scheme 5.

ing as a leaving group. In both mechanisms, the same intermediate is generated that, after a [4+2] cycloaddition, yields lepidopterene **2**.

With the aim of establishing which is the predominant pathway, we carried out the reaction in dry acetone at reflux but using this time only 0.5 equiv. of sodium iodide. As a result, a total consumption of 9-(chloromethyl)anthracene was observed and lepidopterene and 1,2-bis(9-anthracenyl)ethane were obtained in 66 and 9% yield, respectively. This fact indicates that a total conversion of 9-(chloromethyl) anthracene into 9-(iodomethyl)anthracene is not required in the formation of lepidopterene and supports the second pathway. Moreover, a catalytic amount of sodium iodide was not enough to produce lepidopterene from 9-(chloromethyl)anthracene beyond a 2% yield, which invalidates the possibility of an autocatalytic process.

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8. Lepidopterene was isolated directly from the reaction mixture by removal of the solvent and precipitation with diethyl ether. Purification was carried out by crystallization from chloroform. Analytical data matched the reported structure.
9. Compound **4** is unstable and decomposes on standing. ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ 8.32 (s, 1H, H-10), 8.04 (d, $J=8.9$ Hz, 2H, H-4, H-5), 7.86 (d, $J=8.5$ Hz, 2H, H-1, H-8), 7.51 (app t, 2H, H-2, H-7), 7.30 (app t, 2H, H-3, H-6), 5.29 (s, 2H, CH_2); MS (EI, 70 eV) m/z 191 (M^+–I, 100), 127 (26).
10. Compound **5** has been recently synthesized by Sampath Kumar, H.M.; Subba Reddy, B.V.; Jagan Reddy, E.; Yadav, J.S. *Green Chem*., **1999**, 1, 141, but up to now characterization has not been reported. mp (petroleum ether/ethyl acetate) 150–152°C dec. ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ 8.45 (s, 1H, H-10), 8.15 (m, 2H, H-1, H-8), 8.04 (m, 2H, H-4, H-5), 7.46 (m, 4H, H-2, H-3, H-6, H-7), 6.74 (d, $J=8.6$ Hz, 1H, H-6′), 6.51 (dd, $J=8.6$, 3.0 Hz, 1H, H-5′), 5.85 (d, $J=3.0$ Hz, 1H, H-3′), 4.90 (s, 2H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ 149.50 (C-1′), 146.82 (C-4′), 131.63 (C-4a, C-5a or C-8a, C-9a), 131.23 (C-9), 130.68 (C-4a, C-5a or C-8a, C-9a), 129.08 (C-4, C-5), 128.45 (C-2′), 126.59 (C-10), 125.97 (C-3, C-6), 124.99 (C-2, C-7), 124.75 (C-1, C-8), 116.27 (C-3′), 115.66 (C-6′), 113.39 (C-5′), 27.09 (CH_2); MS (EI, 70 eV) m/z 300 (M^+, 15), 178 (100).
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12. Compound **8** was isolated by chromatography on silica gel with hexane:ethyl acetate (99:1) and purified by recrystallization from 2-propanol, mp 114–115°C. IR (KBr) 3049, 3001, 2971, 2928, 2867, 1624, 1525, 1479 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ 8.49 (d, $J=8.4$ Hz, 2H, H-1, H.8), 8.44 (s, 1H, H-10), 8.01 (dd, $J=8.2$ Hz, 1.5 Hz, 2H, H-4, H5), 7.43–7.55 (m, 4H, H-2, H-7, H-3, H-6), 5.82 (s, 2H, CH_2-O), 1.57 (m, 6H, CH_2), 1.36 (s, 6H, CH_3), 1.06 (s, 6H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ 131.42 (C-4a, C-5a or C-8a, C-9a), 130.58 (C-4a, C-5a or C-8a, C-9a), 130.31 (C-9), 128.73 (C-4, C-5), 127.71 (C-10), 125.57 (C-2, C-7 or C-3, C-6), 125.41 (C-2, C-7 or C-3, C-6), 124.73 (C-1, C-8), 72.59 (CH_2-O), 59.95 (2C-N), 39.98 (CH_2-CH_2-CH_2), 34.01 ($2CH_3$), 20.21 ($2CH_3$), 17.26 (CH_2-CH_2-CH_2); MS (CI) m/z 348 (M^++H, 5), 207 (23), 191 (81), 156 (100), 142 (81), 140 (18). Anal. calcd. for $C_{24}H_{22}NO$: C, 82.95; H, 8.41; N, 4.03. Found: C, 82.64; H, 8.39; N, 3.88.