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C-C Bond Cleavage in O-Centered Mono- and Dianions Derived from α-Dicarbonyl Compounds

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Abstract: The reaction of organolithium compounds with oxalyl derivatives and cyclic 1,2-dicarbonyl compounds leads to pinacols or ketones derived from homolytic C-C bond cleavage of the intermediate O,O-centered pinacol dianions depending on the ability of the substituents for the stabilisation of the resulting radical anion. The homolysis is induced by electrostatic repulsion of the negatively charged oxygen atoms.

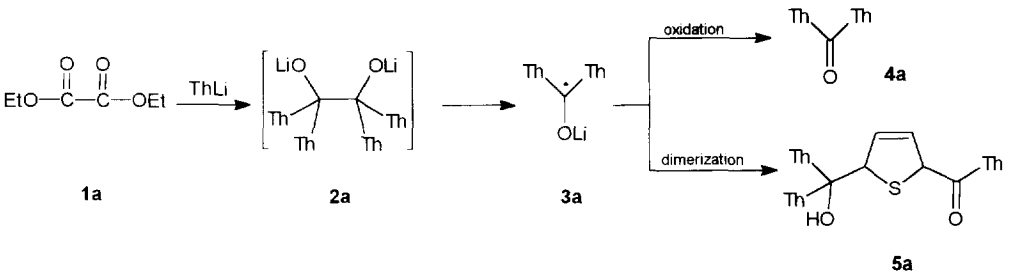
Benzopinacols undergo base-induced ionic and radical C-C bond cleavage depending on the reaction conditions.[1] For this reason, the addition of aromatic organolithium or Grignard reagents to α-dicarbonyl derivatives addressed to the synthesis of pinacols has been unsuccessful. It seems that in some cases this reaction does not follow a fully predictable path based on classical carbanion chemistry, and it leads to mixtures of products derived from the involvement of single electron transfer reactions.[2] Related findings were reported by Whitesides *et al.*[3] in a study on the mechanism of the addition of phenyllithium to carbon monoxide. On the other hand, only the recent development of new 1,2-dicarbonyl equivalents[4] has allowed the preparation of α-diketones by this approach.

The fragmentation of pinacols has been described under different conditions including the dismutation in basic medium,[5] the anodic oxidation,[5] the chemical oxidation by DDQ and Fe(III) complexes,[6] or Tl(III) salts,[7] and the photochemical oxidation to ketones.[8] On the other hand, it has been shown that benzopinacol dicarboxylates[9] and O,O'-disubstituted tin, germanium and silicon derivatives[10] experience thermally induced fragmentation reactions.

RESULTS AND DISCUSSION

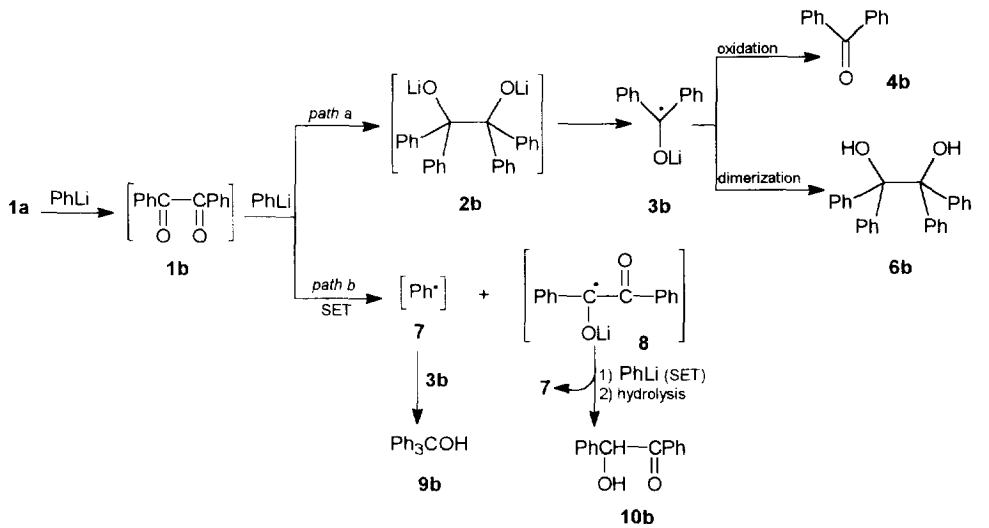
In this paper we wish to report on the course of the reaction of alkyl, aryl, and heteroaryllithium derivatives with linear and cyclic α-dicarbonyl compounds **1a-e**. The reaction of four equivalents of 2-thienyllithium with diethyl oxalate (**1a**) in ether at room temperature gives a dark green solution of the ketyl-type radical anion **3a** formed by homolytic C-C bond cleavage of the pinacol dianion precursor **2a**. The fate of **3a** depends on the work-up procedure. Oxidation by dry air or an oxygen stream leads to the formation of the

corresponding ketone **4a** in nearly quantitative yield. Variable amounts of the dimer **5a** were also obtained when the radical-anion solution was stored for a time before oxidation or hydrolysis (see Scheme 1).



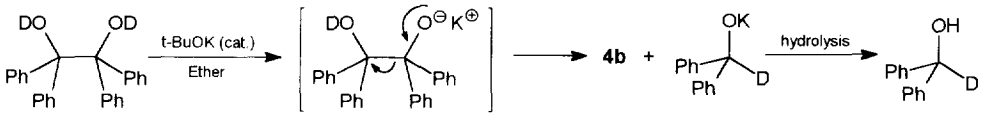
SCHEME 1

By contrast, the reaction of diethyl oxalate (**1a**) with an excess of phenyllithium in ether at room temperature gives rise to the formation of a complex mixture of compounds among which benzophenone (**4b**), benzopinacol (**6b**), triphenylcarbinol (**9b**), and benzoin (**10b**) were isolated. Similar results were obtained in the reaction of phenyllithium with benzil (**1b**). This suggests the simultaneous existence in this case of an alternative reaction path involving single electron transfer from phenyllithium to benzil from which the phenyl radical (**7**) and the radical anion **8** would be the intermediate species (see Scheme 2). Radical intermediates have been proposed in the literature[2] in the reaction of benzil with phenylmagnesium bromide and phenyllithium. Products derived from electron transfer were not observed in any case in the reactions of 2-thienyllithium. The fragmentation process above described only occurs when aryl or heteroaryl groups are present in the substrate. In this context, it has been reported that the addition of *n*-butyllithium to benzil[11] or diethyl oxalate[12] yields the corresponding pinacols which are stable under the reaction conditions.



SCHEME 2

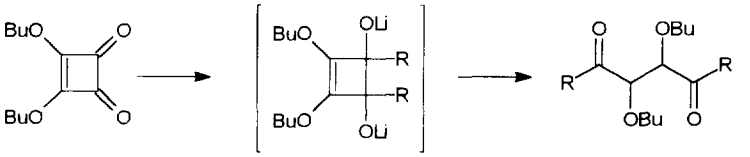
The treatment of benzopinacol (**6b**) in ether with the stoichiometric amount of *n*-butyllithium affords dianion **2b** from which a deep blue solution (λ=609 nm)[13] of radical anion **3b** is immediately formed. Oxidation with dry air gave benzophenone (**4b**). As expected, the products derived from the phenyl radical (**7**) are not observed in this case. Pinacol dianions **2a** and **2b** do not show under our aprotic conditions at room temperature the well documented dismutation of pinacols when they are treated with alkalis in protic solvents.[5] The dismutation of pinacols has been proposed to proceed through the pinacol monoanion **2b**-H.[1] To clarify this matter, a solution of pinacol **6b** in dry ether was treated with a catalytic amount of potassium *tert*-butoxide giving rise to the quantitative dismutation within a few seconds. The same process, when performed with **6b**-d_2, gave after hydrolysis C-deuterated benzhydrol **11b**-*d*. This result confirms the ionic mechanism of the dismutation of pinacol monoanions (see Scheme 3).



6b-d_2 **2b**-*d* **11b**-*d*

SCHEME 3

When the α-dicarbonyl moiety is a part of a cyclic framework, the ring size is an important factor in the C-C bond cleavage of the corresponding pinacol dianions. In the case of four membered rings such as squaric acid derivatives (**1c**) the ring cleavage occurs with great ease and it is promoted even by addition of alkyllithium reagents to give the corresponding 1,4-diketones (**12**) (see Scheme 4).[14] By contrast, the C-C



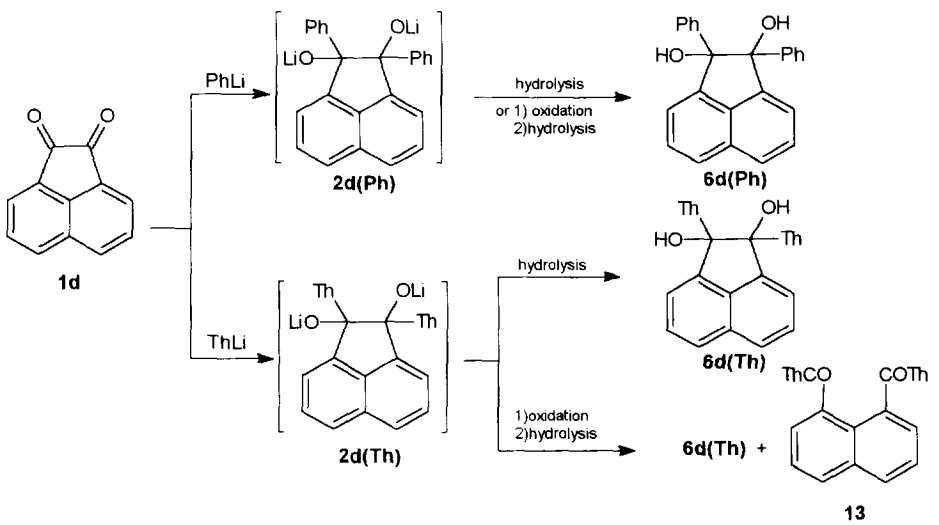
1c **12**

R = Me, Bu, Ph, Th

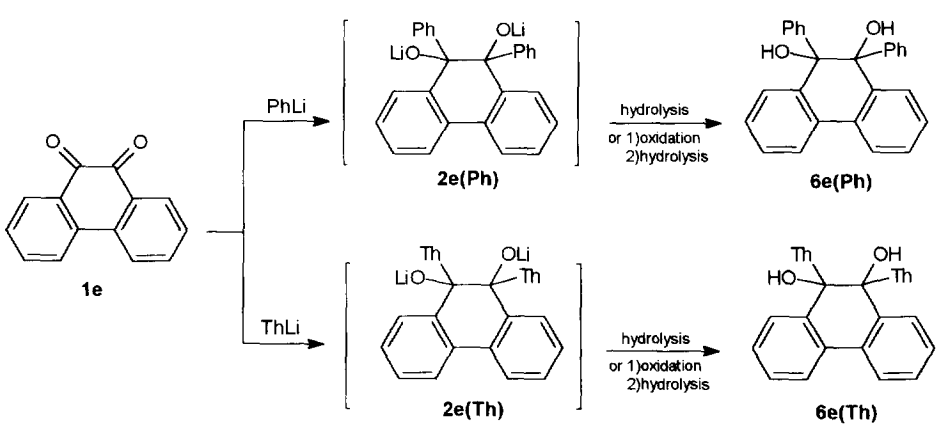
SCHEME 4

bond cleavage occurs with difficulty in the case of the cyclic five membered acenaphthenequinone (**1d**). The addition of phenyllithium to **1d** followed by hydrolysis gave the pinacol *trans*-**6d(Ph)**. The same result was obtained when a dry oxygen stream was bubbled through the reaction mixture before hydrolysis (see Scheme 5). This clearly suggests that the C-C bond does not suffer cleavage in dianion **2d(Ph)** or, eventually, that the diradical which would result from the cleavage of the C-C bond collapses faster than the oxidation can occur. Conversely a *ca.* 1:2 mixture of diol *trans*-**6d(Th)** and diketone **13** was obtained in the addition of thienyllithium to **1d** followed by oxygen or air oxidation. In absence of oxygen only diol *trans*-**6d(Th)** was obtained. The *trans*-configuration of diol **6d(Th)** could be ascertained by its sharp absorption maximum of free -OH at 3520 cm^{-1} in the IR spectrum.[15] A related study is due to Kasai and Tanaka,[11] which reported the

formation of 5,6-dibenzoylacenaphthene in the addition of 5,6-dilithiumacenaphthene to benzil. In this case, the configuration of the intermediate pinacol dianion is forced to be *cis* by the structure of the lithium reagent. Then, the formation of 5,6-dibenzoylacenaphthene is easily understood by considering the rupture of the intermediate *cis*-pinacol dianion and shows that steric and electrostatic repulsion play a determinant role in the cleavage of the C-C bond. The reaction in our usual conditions of phenanthrenequinone (**1e**) (see Scheme 6) with either phenyl- or thienylliihium gave only the corresponding diols *trans*-**6e(Ph)** and *trans*-**6e(Th)**. The total absence of the *cis* isomers in both cases suggests the formation of the biradicals from the *cis* pinacol dianions that collapse to afford the stable *trans*-pinacol dianions in a process faster than the oxidation. The formation of minor amounts of other products most probably derived from single electron transfer were always detected in reactions with phenyllithium.



SCHEME 5



SCHEME 6

From these results it can be concluded that two aryl or heteroaryl groups attached to the same carbon atom must be present to allow the C-C bond cleavage in pinacol dianions except in the case of squaric acid derivatives. This suggest that the homolysis of the C-C bond can be induced not only by steric pressure[16] but also by electrostatic repulsion between the negatively charged oxygen atoms and it is controlled by the stability of the intermediate radical anions formed. Further studies should be conducted with cyclic diketones with a similar substitution pattern to determine the effect of the ring size on the C-C bond cleavage process.

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EXPERIMENTAL SECTION

General. Diethyl ether was dried by refluxing with sodium benzophenone ketyl under argon, and distilled prior to use. Commercially available chemicals (Aldrich) were used without further purification and only were degassed in vacuum before use. Organolithium compounds solutions were purchased (Aldrich) and were used as received. All reactions were made with precautions for rigorous exclusion of air and moisture and under inert argon atmosphere. Routine workup was conducted by addition of saturated aqueous NH_4Cl, extraction of the aqueous layer with ethyl acetate and drying ($MgSO_4$) followed by concentration in vacuum. Purifications by column chromatography were carried out using silica gel and different proportions of hexane-ethyl acetate as eluent. All yields are based on purified product except when otherwise specified. Melting points are uncorrected.

*Addition of Organolithium Compounds to Diethyl Oxalate (***1a***). General Procedure.* To a solution of the corresponding organolithium reagent (5 mmol) in anhydrous ether (10 ml) a solution of diethyl oxalate (1 mmol) in ether (20 ml) was added dropwise. The resulting mixture was stirred at room temperature for the time indicated in each case before oxidation or hydrolysis.

Reactions of **1a** *with 2-Thienyllithium.* When the reaction mixture was stirred for 10 min before hydrolysis, purification by column chromatography of the yellow oily residue obtained after usual workup afforded dithienylketone (**4a**) (mp: 88°C, lit.:88-89°C)[17] in 85% yield. Hydroxyketone dimer **5a** was also isolated (5% yield) : IR ($CHCl_3$): ν (cm^{-1}) 3300, 1650; ^{1}H-NMR (200 MHz, Acetone-d_6) δ 5.62 (m, 2H), 5.85 (m, 1H), 6.03 (m, 1H), 6.95 (m, 2H), 7.40-7.10 (m, 5H), 8.09 (dd, J = 5 and 1 Hz, 1H), 8.15 (dd, J =5 and 1 Hz,1H); ^{13}C-NMR (50 MHz, Acetone-d_6) δ 59.05 (d), 70.11 (d), 78.27 (s), 123.42 (d), 124.20 (d), 125.12 (d), 125.31 (d), 127.70 (dx2), 129.85 (s), 131.46 (d), 132.47 (d), 135.63 (d), 137.90 (d), 142.82 (s), 151.09 (s), 155.28 (s), 192.07 (s) ; MS (EI)(m/z): 372 (M^+-18, 10%), 195 (77%), 111(100%). By contrast, when the reaction mixture was stirred for 14 h before hydrolysis, yields were 20% (**4a**) and 45% (**5a**). Oxidation before hydrolysis of the reaction mixture (reaction time 5 min) with an air stream until disappearance of green color gave **4a** (90%) and

tris(2-thienyl)carbinol (10% based on NMR spectroscopy) identified by comparison with an authentic sample.[18]

Reaction of **1a** *with Phenyllithium.* After stirring for 5 min., hydrolysis of the reaction mixture and usual workup gave a complex mixture of products. Benzophenone (**4b**) (8%), benzopinacol (**6b**) (18%), triphenylcarbinol (**9b**) (31%), and benzoin (**10b**) (23%) were isolated and characterised by NMR after column chromatography.

Addition of Phenyllithium to Benzil (**1b**). To a solution of phenyllithium (2.4 mmol) in ether (5 ml) a solution of benzil (1 mmol, 0.2M) in ether was added dropwise and the mixture stirred for 5 min. Hydrolysis and usual workup gave a complex mixture as a yellow solid residue. Purification by column chromatography afforded in this case benzophenone (**4b**) (12%), benzopinacol (**6b**) (18%), triphenylcarbinol (**9b**) (32%), and benzoin (**10b**) (17%).

Reactions of Benzopinacol (**6b**). *General Procedure.* To 1 mmol of **6b** in ether (20 ml), the corresponding base was added in the amount specified in each case. After 5 min, the reaction mixture was hydrolysed, and the usual workup gave a residue which was analysed by NMR spectroscopy. Identification of products was made by comparison of the NMR data with those of authentic samples.

Reaction of **6b** *with Butyllithium.* 2.1 mmol of a 1.6M solution of BuLi in hexane were added in this case. The strong dark blue coloration of the reaction mixture only disappeared when saturated aqueous NH_4Cl (2 ml per mmol) was added with vigorous stirring. Benzophenone (**4b**) (53%) and benzopinacol (**6b**) (45%) were the only products isolated. When the reaction mixture was submitted to a dry air stream (5 min) before hydrolysis, only benzophenone (**4b**) (99%) was obtained.

Reaction of **6b** *with Potassium Tert-butoxide.* 0.3 mmol of solid K^{t}BuO was employed in this case. NMR analysis of the residue showed the presence of an equimolecular mixture of benzophenone (**4b**) and benzhydrol (**11b**).

Reaction of Potassium Tert-butoxide with Benzopinacol-d_2 (**6d**-d_2). Benzopinacol-d_2 was obtained by shaking an ethereal solution of **6b** with D_2O (5 times) and the deuteration degree checked by ^{1}H-NMR. 0.3 mmol of solid K^{t}BuO was added to a solution of **6b**-d_2 following the above described procedure. NMR analysis of the crude residue showed the presence of an equimolar mixture of benzophenone (**4b**) and benzhydrol-d_1 (**11b**-d): ^{13}C-NMR (62.9 MHz) δ 76.5 (t, J = 22 Hz, CDOH), 127.69 (d), 128.18 (d), 129.23 (d), 145.85 (s).

Addition of Phenyllithium to Acenaphthenequinone (**1d**). To a solution of phenyllithium (3 mmol) in THF (20 ml), acenaphthenequinone (1 mmol) was added in small portions with vigorous stirring. The reaction mixture was stirred at room temperature for 5 min and then hydrolysed with aqueous saturated NH_4Cl (2 ml).

The usual workup followed by purification of the crude residue by column chromatography (silica gel, hexane:ethyl acetate 9:1) afforded *trans*-1,2-diphenyl-1,2-acenaphthenediol (**6d(Ph)**) (68% yield): mp(CCl_4): 153°C (lit.: 155-156°C)[15b] IR (KBr): ν (cm^{-1}) 3524, 3452, 1445, 1160 ; ^{1}H-NMR (250 MHz, $CDCl_3$) δ 2.20 (bs, 2OH), 7.20 (m, 4H), 7.35 (m, 8H), 7.63 (dd, 2H, *J* = 8.3 and 7.0 Hz), 7.88 (d, 2H, *J* = 8.3 Hz); ^{13}C-NMR (62.9 MHz, $CDCl_3$) δ 89.90 (s), 121.73 (d), 125.22 (d), 127.67 (dx2), 127.89 (dx2), 127.98 (d), 128.85 (d), 130.93 (s), 137.13 (s), 140.61 (s), 145.37 (s); HRMS (FAB) Calcd.. for $C_{24}H_{18}O_2$: 338.1307, Obt.: 338.1303.

Addition of 2-Thienyllithium to Acenaphthenequinone (**1d**). The same procedure described for the reaction of **1d** with phenyllithium was used in this case. The usual workup afforded quantitatively (NMR) trans-1,2-bis(2-thienyl)-1,2-acenaphthenediol (**6d(Th)**): mp: 175-178°C (dec) (CCl_4); IR (KBr): ν (cm^{-1}) 3520, 1432; ^{1}H-NMR (250 MHz, $CDCl_3$) δ 3.37 (bs, 2 OH), 6.73 (dd, 2H, *J* = 3.4 and 1.1 Hz), 6.97 (dd, 2H, *J* = 5.0 and 3.4 Hz), 7.35 (dd, 2H, *J* = 5.0 and 1.1 Hz), 7.46 (d, 2H, *J* = 7.1 Hz), 7.61 (dd, 2H, *J* = 7.6 and 8.2 Hz); 7.86 (d, 2H, *J* = 8.2 Hz); ^{13}C-NMR (62.9 MHz, $CDCl_3$) δ 88.63 (s), 121.76 (d), 125.64 (d), 126.37 (d), 126.76 (d), 126.89 (d), 128.74 (d), 130.96 (s), 135.84 (s), 144.15 (s) 144.69 (s); HRMS (FAB) Calcd. for $C_{20}H_{14}O_2S_2$: 350.0435, Obt.: 350.0446. Oxidation before hydrolysis of the reaction mixture by an oxygen stream until disappearance of dark color followed by usual workup and purification by column chromatography (silica gel, hexanes:ethyl acetate 4:1) gave **6d(Th)** (32%) and the diketone **13** (66%): mp: 168-170°C (CCl_4); IR (KBr): ν (cm^{-1}) 1636, 1410; ^{1}H-NMR (250 MHz, $CDCl_3$) δ 6.94 (dd, 2H, *J* = 4.0 and 4.8 Hz), 7.44 (dd, 2H, *J* = 7.2 and 8.0 Hz), 7.46 (dd, 2H, *J* = 4.0 and 1.0 Hz), 7.52 (dd, 2H, *J* = 4.8 and 1.0 Hz), 7.65 (dd, 2H, *J* = 7.1 and 1.2 Hz); 7.92 (dd, 2H, *J* = 8.0 and 1.2Hz); ^{13}C-NMR (62.9 MHz, $CDCl_3$) δ 124.99 (d), 127.79 (d), 129.27 (d), 131.95 (d), 134.74 (d), 134.86 (s), 135.03 (d), 136.28 (s), 144.62 (s) 189.21 (s); HRMS (FAB) Calcd. for $C_{20}H_{13}O_2S_2$: 349.0357, Obt.: 349.0366.

Addition of 2-Thienyllithium to Phenanthrenequinone (**1e**). To a solution of 2-thienyllithium (3 mmol) in THF (20 ml), phenanthrenequinone (1 mmol) was added in small portions with vigorous stirring. The reaction mixture was stirred at room temperature for 5 min and then hydrolysed with 2 ml of saturated aqueous NH_4Cl. The usual workup afforded quantitatively (NMR) *trans*-9,10-dihydro-9,10-bis(2-thienyl)-9,10-phenanthrenediol (**6e(Th)**). The same product and yield was obtained when the reaction mixture was submitted to an oxygen stream before hydrolysis. **6e(Th)**: mp: 187-192°C (dec) (AcOEt, Hexane); IR (KBr): ν (cm^{-1}) 3490, 1450; ^{1}H-NMR (250 MHz, $CDCl_3$) δ 2.95 (bs, 2 OH), 6.68 (dd, 2H, *J* = 3.7 and 1.2 Hz), 6.77 (dd, 2H, *J* = 5.1 and 3.7 Hz), 7.13 (dd, 2H, *J* = 5.1 and 1.2 Hz), 7.35 (dt, 2H, *J* = 7.6 and 1.4 Hz), 7.45 (dt, 2H, *J* = 7.6 and 1.4 Hz), 7.70 (dd, 2H, *J* = 7.6 and 1.4 Hz); 7.85 (dd, 2H, *J* = 7.6 and 1.4 Hz); ^{13}C-NMR (62.9 MHz, $CDCl_3$) δ 80.53 (s), 123.80 (d), 125.53 (d), 125.84 (d), 125.96 (d), 126.59 (d), 128.84 (d), 128.92 (d), 132.56 (s), 140.59 (s), 144.94 (s); HRMS (EI) Calcd. for $C_{22}H_{16}O_2S_2$: 376.0591, Obt.: 376.0564.

Addition of Phenyllithium to Phenanthrenequinone (**1e**). The same procedure described for the reaction of **1e** with 2-thienyllithium was used in this case. Purification of the crude residue by column chromatography (silicagel, CH_2Cl_2:hexanes 6:4) afforded *trans*-9,10-dihydro-9,10-diphenyl-9,10-phenanthrenediol (**6e(Ph)**) (75% yield): mp (AcOEt, Hexane): 181-182°C (lit.: 182°C)[19]; IR (Kbr) ν (cm^{-1}) 3545, 1444; ^{1}H-NMR (250 MHz, $CDCl_3$) δ 2.27 (bs, 2 OH), 7.15-7.36 (m, 8H), 7.40-7.57 (m, 8H), 7.92 (d, 2H, J = 7.6 Hz); ^{13}C-NMR (62.9 MHz, $CDCl_3$) δ 80.73 (s), 123.04 (d), 126.52 (d), 127.58 (d), 127.84 (dx2), 128.04 (dx2), 128.55 (d), 128.94 (d), 133.55 (s), 139.94 (s), 141.21 (s); HRMS (FAB) Calcd. for $C_{26}H_{20}O_2$: 364.1463, Obt.: 364.1439.

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