Preparation of Anthraquinones from 10-Hydroxy-9-anthracenecarbonitriles Obtained from a Novel Aryne Annulation Reaction

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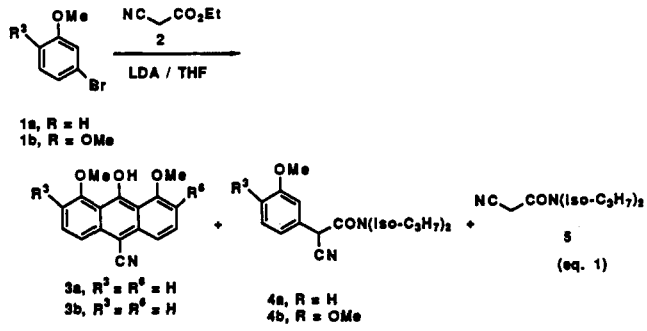
A new method for brief regioselective synthesis of anthraquinones via the reaction of anions of ethyl cyanoacetate or the anions of 2-(carbethoxyaryl)acetonitriles with arynes is described.

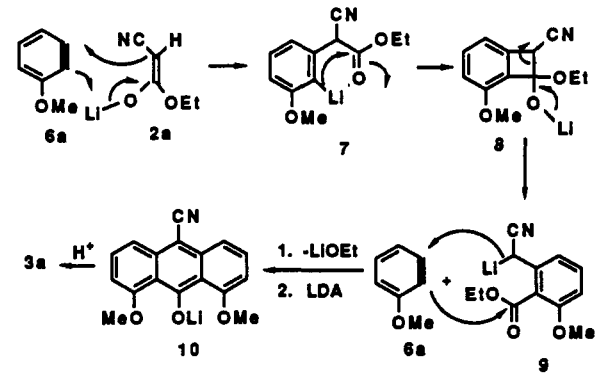
While studying the use of arynes in synthesis,[1] we have discovered a quick regioselective synthesis of methyl ethers of natural and unnatural anthraquinones,[2] which involves the oxidation of 10-hydroxy-9-anthracenecarbonitriles[3] obtained via a novel aryne annulation reaction as the key step. Thus the reaction of 3-bromoanisole (**1a**) with ethyl cyanoacetate (**2**) and lithium diisopropylamide (LDA) gave none of the expected α-arylated nitrile product but supplied instead 10-hydroxy-4,5-dimethoxy-9-anthracenecarbonitrile (**3a**) in 36% yield (eq 1). Similarly, 10-



hydroxy-3,4,5,6-tetramethoxy-9-anthracenecarbonitrile (**3b**) was produced in 38% yield from the reaction of 4-bromo-1,2-dimethoxybenzene (**1b**) and **2**. *N,N*-Diisopropylacetamide (**5**) and the *N,N*-diisopropylamide of the corresponding α-arylated nitrile **4** were also obtained in both reactions. It is noteworthy that **3a** and **3b** could be obtained only when the respective aryne intermediates were generated by the addition of LDA to the bromoarene (**1a** and **1b**) in the presence of **2a**. In this way the pathway for the conversion of the initially formed nitrile–aryne adduct to the anthracene (vide infra) could compete with the amidation of both that adduct and **2** by LDA. Attempts to prepare 10-hydroxy-9-anthracenecarbonitriles from the reaction of 2-bromo-1,4-dimethylbenzene, 2-bromo-4-methylanisole, and 2-bromo-1,4-dimethoxybenzene with **2** and LDA failed; only amidated nitriles **4** and **5** were obtained.

The structures of **3a** and **3b** are supported by IR, ^{13}C NMR, ^{1}H NMR, and mass spectroscopy. Of particular importance are the 10-hydroxy proton chemical shifts between δ 10.7 and 11.6, which are in the range of those previously reported for 10-hydroxy-9-anthracenecarbonitriles possessing a 4-methoxy group,[4] and the IR stretching frequencies between 3150 and 3250 cm^{-1}, which are indicative of intramolecular hydrogen bonding between the 10-hydroxy and 4-methoxy groups. Furthermore, the

Scheme I



^{13}C NMR spectra of these compounds lack the usual carbonyl absorbance signal in the δ 180–190 region.[5] That **3a** and **3b** exist preferentially as 10-hydroxyanthracenes rather than as the more commonly observed 10-anthrones[6] most likely reflects the intramolecular hydrogen bonding just mentioned and the mutual stabilizing resonance interaction between the 10-hydroxy and 9-cyano groups. The structure of **3a** including the intramolecular hydrogen bonding of the 10-hydroxy and 4-methoxy group was confirmed by X-ray analysis.[7] The ORTEP plot of **3b** is shown in Figure 1.

A possible mechanism, in which the formation of **3a** from aryne **6a** and ethyl α-lithiocyanoacetate (**2a**) is given as a typical example, is shown in Scheme I. For simplicity, the LDA-mediated generation of **6a** and **2a** from **1a** and **2**, respectively, has been omitted from the scheme. The suggested mechanism consists of two previously postulated pathways in aryne chemistry, i.e., the nonconcerted [2 + 2] cycloaddition involving a tandem-addition rearrangement (TARA)[8] and an aryne [4 + 2] cycloaddition.[9] We

(1) See: Biehl, E. R.; Khanapure, S. P. *Acc. Chem. Res.* **1989**, *22*, 275 and references therein.

(2) Thomson, R. H. *Naturally Occurring Quinones*, 2nd ed.; Academic: New York, 1971.

(3) Broadhurst, M. J.; Hassall, C. H.; Thomas, G. J. *J. Chem. Soc., Perkins Trans. 1* **1977**, 2502.

(4) Hassall, C. H.; Morgen, B. A. *J. Chem. Soc., Perkins Trans. 1* **1973**, 2853.

(5) For example, the carbonyl resonance of anthrone, itself, occurs at δ 183.7: Castelas, J. F.; Gottlieb, O. R.; De Lima, R. A.; Mesquita, A. L.; Gottlieb, H. E.; Wenkert, E. *Phytochemistry* **1977**, *16*, 735.

(6) For examples, see: House, H. O. *J. Org. Chem.* **1973**, *38*, 1167. Pirkle, W. H.; Finn, J. M. *J. Org. Chem.* **1983**, *48*, 2779. Field, K. W. *J. Org. Chem.* **1988**, *53*, 4000.

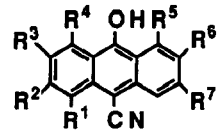
(7) Details of data collection and structure for **3B** are as follows: crystal data for $C_{17}H_{13}NO_3$, M_r 325.33, monoclinic space group $P2_{1/c}$, a = 9.142 (3) b = 18.426 (5), and c = 8.306 (2) Å, β = 109.00 (2)°, V = 1332.9 (7) Å^3, Z = 4, D_c = 1.400 g cm^{-1}, $R(F)$ = 0.040; Mo Kα, 293 K, 2θ(max) = 50.00°. Intensities were measured by the ω–2θ scan method. No absorption correction was applied to the data. Standard reflections (0,4,0) taken every 33 reflections indicate no loss of intensity. A total were used in the solution and refinement of the structure. With all non-hydrogen atoms anisotropic, and all hydrogen atoms found and isotropic with fixed u = 0.08 Å^2: $R(F)$ = 0.040, R(wF) = 0.049, GOF = 1.47, N_o/N_v = 6.9, D/s = 0.01, $D/(r)$ < 0.19 e Å^{-3}.

(8) Pansegrau, P. D.; Rieker, W. F.; Meyers, A. I. *J. Am. Chem. Soc.* **1988**, *110*, 7178. Khanapure, S. P.; Crenshaw, L.; Reddy, R. T.; Biehl, E. R. *J. Org. Chem.* **1988**, *53*, 4915.

(9) (a) Watanabe, M.; Kurosaki, A.; Furukawa, S. *Chem. Pharm. Bull.* **1984**, *32*, 1264. (b) Khanapure, S. P.; Biehl, E. R. *J. Nat. Prod.* **1989**, *52*, 1357. (c) Khanapure, S. P.; Biehl, E. R. *Synthesis* **1991**, 33. (d) Khanapure, S. P.; Biehl, E. R. *Heterocycles* **1988**, *27*, 2643. (e) Khanapure, S. P.; Reddy, T. R.; Biehl, E. R. *J. Org. Chem.* **1987**, *52*, 5685.

0022-3263/91/1956-2846$02.50/0

Table I. 10-Hydroxyanthracene-9-carbonitriles 3 and Anthraquinones 11 (see eqs 1 and 2 and Scheme II)



3

11

method	3[a]	yield, %	R^1	R^2	R^3	R^4	R^5	R^6	R^7	11[a]	yield, %
A[b]	a	36	H	H	H	OMe	OMe	H	H	a	91
A	b	38	H	H	OMe	OMe	OMe	OMe	H	b	95
B[c]	c	70	H	H	H	OMe	H	H	H	c	90
B	d	46	H	H	OMe	OMe	H	H	H	d	91
B	e	42	H	OMe	OMe	OMe	H	H	H	e	91
B	f	54	OMe	H	H	OMe	H	H	H	f	93
B	g	59	H	H	H	OMe	H	H	OMe	g	98
B	h	57	H	H	OMe	OMe	H	H	OMe	h	97
B	i	45	H	OMe	OMe	OMe	H	H	OMe	i	88
B	j[d]		H	H	H	H	H	H	H	j	70
B	k	65	H	H	H	H	H	H	OMe	k	90

[a] Satisfactory analytical element analyses were obtained for all new compounds. [b] Method A: reaction of 1 and ethyl cyanoacetate with LDA. [c] Method B: reaction of 1 and 2-(carbethoxyaryl)acetonitriles **10** with LDA. [d] The parent anthracene (**3j**) was not detected; if formed, it was converted to anthraquinone (**10j**) during the reaction and/or reaction workup.

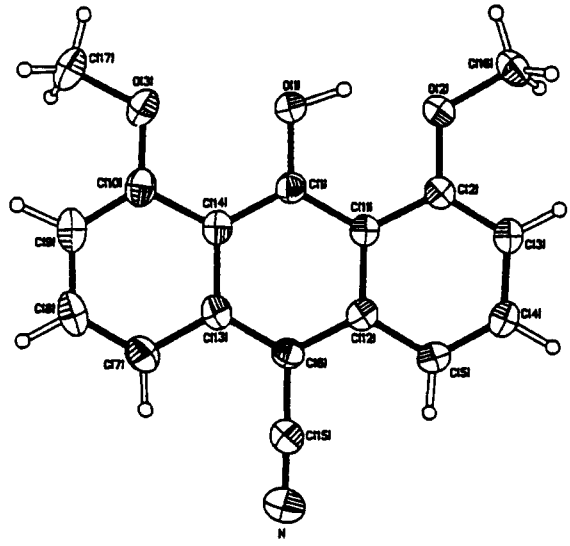
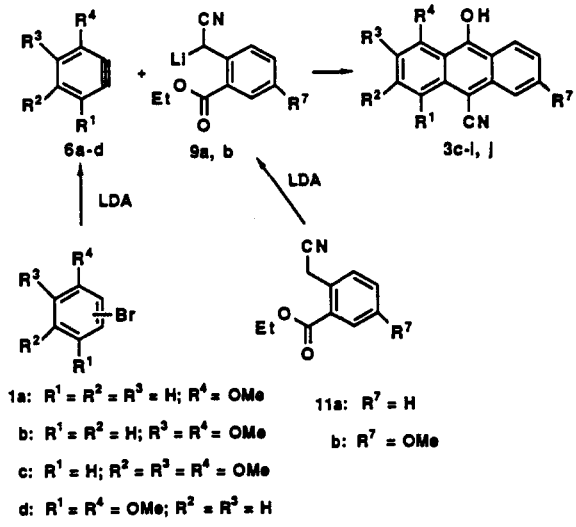


Figure 1. ORTEP of molecule **3a**.

Scheme II



believe this to be the first example of an aryne reaction in which these two mechanism appear to be occurring consecutively. Thus **2a** adds regioselectively to **6a** to form adduct **7**, which cyclizes via a 4-*exo*-*trig*[10] ring closure to the bicyclic intermediate **8**. This overall nonconcerted [2 + 2] cycloaddition process may be facilitated by the geometric restraint imposed in **7** by chelation between the carbonyl oxygen atom and the aromatic lithium atom, which facilitates the ring-closure portion of the cycloaddition. The formation of **9** from the addition of **2a** to **6a** constitutes the TARA portion of the mechanism. Ring opening of **8** then affords the rearranged cyano ester **9**, which adds to aryne **6a** to give **10**, after the elimination of lithium ethoxide and the abstraction of the 9-hydrogen by LDA of the initially formed tricyclic cycloadduct. Proton quench of **10** then affords **3a**. We have shown the regiocontrol for the formation of **10** arising from a nonsynchronous [4 + 2] cycloaddition of **9** onto the polarized aryne (**6a**).[11] The regiocontrol could equally well arise by a nonconcerted *cine* substitution, which has precedent in the anisole system.[12] Proton quench of **10** then affords **3a**.

The cycloaddition reaction of arynes with 1,2-dipolar nucleophiles such as N-lithiated ethyl anthranilates, lithiated 3-cyanophthalides, and lithiated 3-cyanoazaphthalides has been used successfully for the synthesis of acridones,[9a] anthraquinones,[9b,e] anthracyclinones,[9c] and azaanthraquinones.[9d] This proposed mechanism suggests that the arylation of α-lithiated 2-(carbethoxyaryl)acetonitriles such as **9** with arynes might constitute another general approach to the synthesis of anthraquinones since the 10-hydroxy-9-anthracenecarbonitriles so formed can be readily oxidized to these tricyclic compounds.[4,13] Therefore 2-(carbethoxyphenyl)acetonitrile (**11a**) and its 4-methoxy derivative **11b** were prepared from readily available starting materials (see Experimental Section) and were made to react with **1a**, **1b**, 4-bromo-1,2,3-trimethoxybenzene (**1c**), 2-bromo-1,4-dimethoxybenzene (**1d**), and bromobenzene (**1e**) under the same reverse aryne-forming conditions previously described for the reaction of **1** with

(10) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.

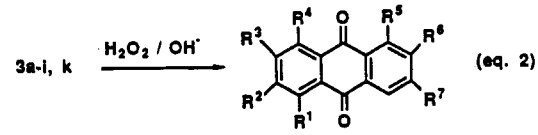
(11) Several workers have suggested a similar concerted, nonsynchronous [4 + 2] aryne cycloaddition. See, for example: Gribble, G. W.; Keavy, D. J.; Branz, S. E.; Kelly, W. J.; Pals, M. A. *Tetrahedron Lett.* **1988**, *29*, 6227. Pollart, D. J.; Rickborn, B. J. *J. Org. Chem.* **1987**, *52*, 792.

(12) Roberts, J. D.; Simmons, H. E.; Carlsmith, L. A.; Vaughan, C. W. *J. Am. Chem. Soc.* **1951**, *29*, 3290.

(13) Vedejs, E.; Miller, W. H.; Pribish, J. R. *J. Org. Chem.* **1988**, *53*, 1593; **1983**, *48*, 3611.

2 (Scheme II). With the exception of the reaction of **1e** and **11a**, the corresponding 10-hydroxy-9-anthracenecarbonitriles **3c-i,k** were obtained from these reactions in yields ranging from 42 to 70% (see Table I). The exceptional reaction gave the parent anthraquinone **12j** directly in 70% yield, indicating that the initially formed parent 10-hydroxy-9-anthracenecarbonitrile (**3j**) was presumably oxidized to **12j** during the reaction workup since the reaction was conducted under N_2.

For completion of the anthraquinone synthesis, the unsymmetrically substituted 10-hydroxy-9-anthracenecarbonitriles **3a–i,k** were readily oxidized with hydrogen peroxide in the presence of base[3] (eq 2) to the corresponding anthraquinones **12a–i,k** in excellent yields (89–98%). As shown in Table I, several of these anthraquinones are methyl ether derivatives of naturally occurring compounds, e.g., alizarin dimethyl ether (**12d**), quinizarin dimethyl ether (**12e**), and flavopurpurin trimethyl ether (**12h**), whereas 1,2,7,8-tetramethoxyanthraquinone (**12b**) and 1,2,6-trimethoxyanthraquinone (**12i**) are newly reported unnatural anthraquinones.



(eq. 2)

12

In summary, an efficient approach to the synthesis of 10-hydroxy-9-anthracenecarbonitriles and their subsequent conversion to anthraquinones has been developed by using low-temperature aryne annulation methodology in the first step. This aryne methodology is especially useful for the synthesis of the initial cyanoanthracenes resulting from (a) condensation of arynes with unsubstituted or symmetrically substituted anions of 2-(carboxyaryl)acetonitriles, (b) condensation of symmetric arynes with these anions, and (c) regioselective condensation of these anions to arynes possessing strong directing groups, such as methoxy. However, the method is limited in scope since methylbenzynes cannot be used (anion addition to these arynes is not regioselective)[12] and certain isomers are not formed in regioselective arynic condensations. However, the low-temperature arynic preparation of 10-hydroxy-9-anthracenecarbonitriles should provide an alternative in many cases to the Hassall[4,13] condensation method, which involves the cyclization at elevated temperatures (ca. 140 °C) of benzophenone carbanions, during which a methoxy group on one of the benzene rings is sacrificed.

Experimental Section

Melting points, which are uncorrected, were determined on an electrothermal apparatus. High-field proton and carbon-13 spectra were taken at 200 MHz. All reactions were conducted under N_2 in thoroughly dried glassware. E. Merck silica gel 9385 (230–400 mesh) was used for flash chromatography. Tetrahydrofuran (THF) was obtained dry and peroxide free by distillation from sodium benzophenone ketyl. Diisopropylamine was distilled from $CaCl_2$ and the other organic reactants were distilled before use. 2-(Carbethoxyphenyl)- and 4-methoxy-2-(carbethoxyphenyl)-acetonitrile were prepared by treating ethyl toluate and ethyl 4-methoxytoluate successively with *N*-bromosuccinimide in CCl_4 and KCN in dimethyl sulfoxide.

General Procedure for the Synthesis of 10-Hydroxy-9-anthracenecarbonitriles 3a–i. To a cooled (−70 °C) solution of the ester (**2**, **11a**, or **11b**) (10 mmol in 10 mL THF) was added a cold solution of LDA (10 mmol in 20 mL in THF) over a period of 15 min, and the solution was stirred at that temperature for 10 min. Then bromoarene **1** (10 mmol in 40 mL of THF) was added rapidly, the solution was warmed to −40 °C, and then a cooled (−40 °C) solution of LDA (20 mmol in 40 mL of THF) was added slowly (ca. 20 min). After being stirred for an additional 10 min, the solution was allowed to warm to room temperature and quenched with saturated NH_4Cl, and the solvent was evaporated under reduced pressure. The remaining residue was dissolved in CH_2Cl_2 (100 mL) and the resulting solution was washed with dilute HCl then brine, dried ($NaSO_4$), and concentrated (rotary evaporator) to provide a crude mixture, which was purified by flash column chromatography using a mixture of hexane/acetone (19:1) as the eluent. The yields of **3a–i,k** and their characterizations follow.

10-Hydroxy-4,5-dimethoxy-9-anthracenecarbonitrile (3a): yield 1.0 g (36%); yellow crystals (EtOAc), mp 261–262 °C; IR ($CHCl_3$) 3279 (OH), 2207 (CN) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.11 (s, 6 H), 6.78 (d, J = 7.7 Hz, 2 H), 7.54 (dd, J = 7.7 and 8.6 Hz, 2 H), 7.90 (d, J = 8.6 Hz, 2 H), 11.63 (s, 1 H); MS(EI) m/z 279 (M^+). Anal. Calcd for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.01. Found: C, 73.25; H, 4.81; N, 5.12.

10-Hydroxy-3,4,5,6-tetramethoxy-9-anthracenecarbonitrile (3b): yield 1.29 g (38%); yellow crystals (EtOAc), mp 171–173 °C; IR ($CHCl_3$) 3199 (OH), 2206 (CN) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.05 (s, 6 H), 4.11 (s, 6 H), 7.50 (d, J = 9.5 Hz, 2 H), 8.09 (d, J = 9.5 Hz, 2 H), 11.78 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 57.5, 62.2, 95.0, 114.7, 122.2, 131.0, 147.5, 155.6; MS(EI) m/z 339 (M^+). Anal. Calcd for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05; N, 4.13. Found: C, 67.54; H, 5.03; N, 4.12.

10-Hydroxy-4-methoxy-9-anthracenecarbonitrile (3c): yield 1.74 g (70%); yellow needles (EtOAc), mp 177–179 °C; IR ($CHCl_3$) 3326 (OH), 2207 (CN) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.14 (s, 3 H), 6.70 (d, J = 7.6 Hz, 1 H), 7.40–7.66 (m, 1 H), 7.70 (m, 1 H), 8.24 (d, J = 8.7 Hz, 1 H), 7.88 (d, J = 8.8 Hz, 1 H), 8.24 (d, J = 8.7 Hz, 1 H), 8.43 (d, J = 8.7 Hz, 1 H), 10.82 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 56.35, 102.17, 118.17, 118.26, 119.01, 123.55, 128.47, 129.78, 134.74, 155.15, 156.75, 156.89; MS(EI) m/z 249 (M^+). Anal. Calcd for $C_{16}H_{11}NO_2$: C, 77.10; H, 4.45; N, 5.62. Found: C, 77.34; H, 4.53; N, 5.75.

10-Hydroxy-3,4-dimethoxy-9-anthracenecarbonitrile (3d): yield 1.28 g (46%); brown crystals (EtOAc), mp 174–175 °C; IR ($CHCl_3$) 3253 (OH), 2206 (CN) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.05 (s, 3 H), 4.20 (s, 3 H), 7.47–7.50 (m, 2 H), 7.60–7.65 (m, 1 H), 8.11 (d, J = 9.4 Hz, 1 H), 8.22 (d, J = 8.5 Hz, 1 H), 8.42 (d, J = 8.5 Hz, 1 H), 11.26 (br s, 1 H); MS(EI) m/z 279 (M^+). Anal. Calcd for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.01. Found: C, 73.34; H, 4.53; N, 5.01.

10-Hydroxy-2,3,4-trimethoxy-9-anthracenecarbonitrile (3e): yield 1.30 g (42%); yellow crystals (EtOAc), mp 194–195 °C; IR ($CHCl_3$) 3271 (OH), 2204 (CN) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.00 (s, 3 H), 4.08 (s, 3 H), 4.27 (s, 3 H), 7.32 (s, 1 H), 7.44 (dd, J = 7.0 Hz, 1 H), 7.66 (t, J = 7.0 Hz, 1 H), 8.17 (d, J = 8.7 Hz, 1 H), 8.40 (d, J = 8.7 Hz, 1 H), 11.06 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 56.18, 61.36, 62.63, 99.70, 123.23, 124.02, 124.25, 129.55, 133.46, 134.63, 155.79; MS(EI) m/z 309 (M^+). Anal. Calcd for $C_{18}H_{15}NO_4$: C, 69.89; H, 4.89; N, 4.53. Found: C, 70.02; H, 4.73; N, 4.59.

10-Hydroxy-1,4-dimethoxy-9-anthracenecarbonitrile (3f): yield 1.50 g (50%); yellow crystals (EtOAc), mp 190–191 °C; IR ($CHCl_3$) 3294 (OH), 2203 (CN) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.03 (s, 3 H), 4.05 (s, 3 H), 6.53 (d, J = 8.5 Hz, 1 H), 6.66 (d, J = 8.5 Hz, 1 H), 7.54 (m, 1 H), 7.71 (m, 1 H), 8.44 (m, 2 H), 11.10 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 55.88, 56.45, 91.70, 101.72, 105.34, 110.37, 119.24, 120.34, 123.38, 124.83, 125.10, 128.32, 129.68, 135.57, 149.15, 150.60, 156.52; MS(EI) m/z 279 (M^+). Anal. Calcd for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.01. Found: C, 73.23; H, 4.65; N, 5.08.

10-Hydroxy-2,5-dimethoxy-9-anthracenecarbonitrile (3g): yield 1.64 g (59%); yellow crystals (EtOAc), mp 203–204 °C; IR ($CHCl_3$) 3328 (OH), 2204 (CN) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.03 (s, 3 H), 4.15 (s, 3 H), 6.71 (d, J = 7.6 Hz, 1 H), 7.11 (dd, J = 2.4 and 9.3 Hz, 1 H), 7.42 (m, 2 H), 7.87 (d, J = 8.7 Hz, 1 H), 8.34 (d, J = 9.3 Hz, 1 H), 10.77 (s, 1 H). Anal. Calcd for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.01. Found: C, 73.13; H, 4.55; N; 5.06.

10-Hydroxy-2,5,6-trimethoxy-9-anthracenecarbonitrile (3h): yield 1.76 g (57%); yellow crystals (EtOAc), mp 184–185 °C; IR ($CHCl_3$) 3199 (OH), 2206 (CN) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.01 (s, 3 H), 4.06 (s, 3 H), 4.15 (s, 3 H), 7.11 (dd, J = 2.4 and 8.6 Hz, 1 H), 7.42 (d, J = 2.4 Hz, 1 H), 7.48 (d, J = 8.5 Hz, 1 H), 8.06 (d, J = 8.6 Hz, 1 H), 8.35 (d, J = 8.5 Hz, 1 H), 11.26 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 55.51, 57.32, 62.27, 92.62, 100.90, 111.76, 115.49, 118.73, 119.49, 119.58, 122.28, 125.04, 136.43, 145.32, 155.47.

Anal. Calcd for $C_{18}H_{15}NO_4$: C, 69.89; H, 4.89; N, 4.53. Found: C, 70.13; H, 4.75; N, 4.56.

10-Hydroxy-2,5,6,7-tetramethoxy-9-anthracenecarbonitrile (3i): yield 1.52 g (45%); yellow crystals (EtOAc), mp 186–187 °C; IR ($CHCl_3$) 3278 (OH), 2201 (CN) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.98 (s, 3 H), 4.03 (s, 3 H), 4.09 (s, 3 H), 4.26 (s, 3 H), 7.08 (dd, J = 2.1 and 9.4 Hz, 1 H), 7.33 (m, 2 H), 8.29 (d, J = 9.4 Hz, 1 H), 11.00 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 55.48, 56.15, 61.33, 62.58, 91.06, 99.68, 101.03, 106.87, 114.65, 118.33, 119.09, 125.19, 133.91, 137.06, 138.50, 148.83, 155.79, 155.88, 161.00. Anal. Calcd for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05; N, 4.13. Found: C, 67.37; H, 5.15; N, 4.26.

10-Hydroxy-2-methoxy-9-anthracenecarbonitrile (3k): yield 1.62 g (65%); yellow crystals (EtOAc), mp 233–235 °C; IR ($CHCl_3$) 3248 (OH), 2206 (CN) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.88 (s, 3 H), 6.96 (d, J = 2.3 Hz, 1 H), 7.3 (m, 2 H), 7.5 (m, 1 H), 8.09 (d, J = 8.5 Hz, 1 H), 8.35 (m, 2 H), 10.60 (br s, 1 H). Anal. Calcd for $C_{16}H_{11}NO_2$: C, 77.10; H, 4.45; N, 5.62. Found: C, 77.24; H, 4.39; N; 5.64.

General Procedure for the Preparation of Anthraquinones 12a–i,k. To a solution of the nitrile **3** (1 mmol), prepared in ethanol (60 mL) at 75 °C, was added in one portion an aqueous solution containing 10% NaOH (6 mL) and 30% H_2O_2 (10 mL), and the resulting solution was stirred for 5 h at 75 °C and then for 12 h at room temperature. Upon cooling the reaction mixture to 10–15 °C, the precipitated anthraquinone was filtered, washed with water, and dried to give an essentially pure product. Yields and the characterizations of anthraquinones **12a–k** follow.

1,8-Dimethoxyanthraquinone (12a): yield 224 mg (91%); yellow crystals (EtOH), mp 226–227 °C (lit.[14] mp 223–224 °C.

1,2,7,8-Tetramethoxyanthraquinone (12b): yield 311 mg (95%), yellow crystals (EtOH), mp 159–160 °C; IR ($CHCl_3$) 1679, 1574 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.98 (s, 1 H), 4.01 (s, 3 H), 7.20 (d, J = 8.6 Hz, 2 H), 8.05 (d, J = 8.6 Hz, 2 H); ^{13}C NMR ($CDCl_3$) 56.92, 62.35, 116.25, 124.72, 149.56, 159.32, 181.41, 182.30. Anal. Calcd for $C_{18}H_{16}O_6$: C, 65.85; H, 4.91. Found: C, 65.97; H, 4.98.

1-Methoxyanthraquinone (12c): yield 311 mg (95%); yellow crystals (EtOH), mp 173–175 °C (lit.[15] mp 170 °C).

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1,2-Dimethoxyanthraquinone (12d): yield 244 mg (91%); yellow crystals (EtOH), mp 215–217 °C (lit.[15] mp 211–212 °C).

1,2,3-Trimethoxyanthraquinone (12e): yield 280 mg (91%); yellow crystals (EtOH), mp 175–177 °C (lit.[16] mp 171–172 °C).

1,4-Dimethoxyanthraquinone (12f): yield 258 mg (93%); yellow crystals (EtOH), mp 175–176 °C (lit.[17] mp 171 °C).

1,7-Dimethoxyanthraquinone (12g): yield 292 mg (98%); yellow crystals (EtOH), mp 195–197 °C (lit.[18] mp 185 °C).

1,2,7-Trimethoxyanthraquinone (12h): yield 299 mg (97%); yellow crystals (EtOH), mp 232–235 °C (lit.[19] mp 225–226 °C).

2,5,6,7-Tetramethoxyanthraquinone (12i): yield 289 mg (88%); yellow crystals (EtOH), mp 199–200 °C; IR ($CHCl_3$) 1666, 1598 cm^{-1}; ^1H NMR δ 3.98 (s, 3 H), 4.01 (s, 6 H), 4.06 (s, 3 H), 7.27 (m, 1 H), 7.65 (d, J = 2.6 Hz, 1 H), 7.69 (s, 1 H), 8.21 (d, J = 8.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 55.81, 56.34, 61.27, 61.58, 105.65, 106.48, 109.34, 120.99, 121.25, 128.59, 129.50, 134.44, 157.17, 163.56, 181.52, 182.67. Anal. Calcd for $C_{18}H_{16}O_6$: C, 65.85; H, 4.91. Found: C, 65.90; H, 4.98.

Anthraquinone (12j): yield 1.53 g (70%); yellow crystals (EtOH), mp 282–283 °C (lit.[20] mp 283–285 °C).

2-Methoxyanthraquinone (12k): yield 223 mg (90%); yellow crystals (EtOH), mp 198–199 °C (lit.[21] mp 195–197 °C).

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Supplementary Material Available: X-ray data for 4,5-dimethoxy-10-hydroxy-9-anthracenecarbonitrile (**3a**) (9 pages); observed and calculated structure factors for **3a** (5 pages). Ordering information is given on any current masthead page.

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Tandem Radical Cyclization of Acyclic Homoallylic Xanthates: Cyclopentannulated γ-Thionolactone and γ-Lactones

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The first tandem radical cyclization of linear homoallylic xanthates was explored. Homoallylic xanthates prepared from α,β-unsaturated esters were easily cyclized by tin hydride with an radical initiator to give the corresponding thionolactone annulated cyclopentane skeleton in a high yield. The stereochemistry of cyclized products was also discussed. Thionolactones obtained were oxidized chemoselectivity with *m*-CPBA under neutral condition to afford γ-lactones in a high yield.

Radical chemistry has advanced rapidly through the discovery of novel radical species, the synthetic utility of radical chain reactions, and investigation of radical reaction mechanisms.[1] Intramolecular serial radical cyclizations provide a useful method for the synthesis of multifused compounds. Because of the mild reaction conditions, protection of functional groups may not be necessary.[2] Relatively few reports of successful tandem radical cyclizations of functionalized radical species have been published,[3] although many examples of radical cyclizations[4]

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