Aromatization of Highly Alkyl-substituted Dihydroanthracenes Using *n*-BuLi/TMEDA/MeI

Masanori Kitamura, Baojian Shen, Yanjun Liu, Hegen Zheng, and Tamotsu Takahashi*
Catalysis Research Center and Graduate School of Pharmaceutical Sciences, Hokkaido University and CREST, Science and Technology Corporation (JST), Sapporo 060-0811

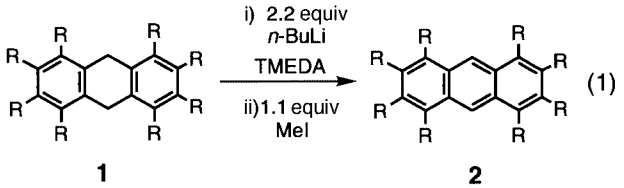
(Received, March 26, 2001; CL-010276)

Aromatization of highly alkyl-substituted dihydroanthracene was performed with the *n*-BuLi/TMEDA/MeI. Treatment of 1,2,3,4,5,6,7,8-octapropyl-9,10-dihydroanthracene with 2.2 equiv of *n*-BuLi, TMEDA at 50 °C in hexane for 3 h, followed by 1.1 equiv of MeI at room temperature for 1 h gave the corresponding anthracene in 98% yield.

Recently, we have reported novel method for the synthesis of highly substituted naphthacenes or pentacenes by homologation[1] and highly alkyl-substituted benzene derivatives,[2] naphthalenes or anthracenes.[3] Introduction of substituents in polycyclic compounds has been important to improve their solubility and change their properties.[4] During the course of our study, we found novel aromatization reaction using *n*-BuLi (2.2 equiv)/TMEDA/MeI(1.1 equiv) for the highly alkyl-substituted dihydroanthracenes.

Harvey and his coworkers reported that the treatment of 9, 10-dihydrophenanthrene with 3 equiv of RLi, TMEDA, and MeBr afforded 94% of phenanthrene as a sole product and they reported that this aromatization proceeded via electron transfer.[5] To the contrary, it was reported that treatment of dihydroanthracene with n-BuLi/TMEDA/MeBr gave a methylation product, 9-methyl-9,10-dihydroanthracene,[5] but not the aromatization product. In addition, it is also known that a reaction of 9-isopropyl-9,10-dihydroanthracene with n-BuLi/TMEDA/excess MeI afforded only the methylation product.[5a]

In this paper, we would like to report that highly alkyl substituted dihydroanthracene reacted with *n*-BuLi (2.2 equiv)/TMEDA/MeI (1.1 equiv) in this order to give anthracenes in high yields as shown in eq 1. In particular, only 1.1 equiv of MeI was required in this aromatization which is in sharp contrast to the method via electron transfer.[5]

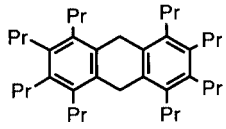
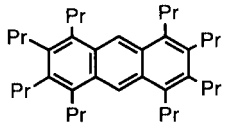
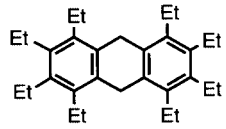
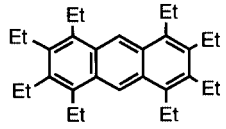
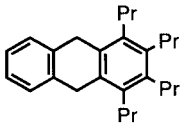
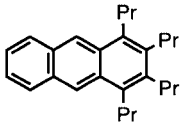
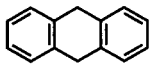
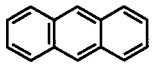
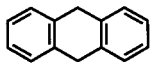
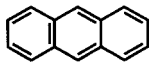


(1)

Typical procedure is as follows. To a hexane solution of 1,2,3,4,5,6,7,8-octapropyl-9,10-dihydroanthracene **1** (R = Pr) were added 2.2 equiv of *n*-BuLi and 2.2 equiv of TMEDA at room temperature and the mixture was stirred at 50 °C for 3 h under N_2. Treatment of the mixture with 1.1 equiv of MeI at room temperature for 1 h afforded **2** in 98% NMR yield.[6] The mixture was washed with 3M HCl. Its organic layer was dried and evaporated to remove all volatile compounds. Pure compound **2** was obtained in 96% yield. Purification using column chromatography was not necessary in this case.

The *n*-BuLi/TMEDA/MeI is effective for, in particular, highly alkyl-substituted dihydroanthracenes. As shown in Table 1, non-substituted 9,10-dihydroanthracenes gave only 47% and less than 5% of anthracene when treated in this system with MeI and MeBr, respectively. However, octapropyl- or octaethyl-dihydroanthracene, or even 1,2,3,4-tetrapropyl-9,10-dihydroanthracene was converted into the corresponding anthracenes in excellent yields using the *n*-BuLi/TMEDA/MeI system. It is obvious that alkyl substituents restrained the methylation with MeI but promoted aromatization by steric factor.

Table 1. Effect of the *n*-BuLi/TMEDA/MeI system for alkyl-substituted dihydroanthracenes

Dihydroanthracene	Anthracene	Yield/%[a]
		98 (96)
		94 (90)
		96 (92)
		47 (43)
		<5[b]

[a]NMR yield. Isolated yields are given in parentheses.
[b]MeBr was used instead of MeI.

Various kinds of combination of RM/R'X were investigated for the aromatization of **1**. The results were summarized in Table 2. As for R'X, MeI was the best. PrI or BuBr gave low yield of the product. As for RM, *sec*-BuLi, *tert*-BuLi, PhLi showed excellent yields of **2**. Grignard reagent did not give the product.

Table 2. Aromatization of **1** (R = Pr) using various combination of RM and R'X

RM	R'X	Time/h	Yield/%[a]
n-BuLi	MeI	1	98 (96)
	PrI	24	45 (40)
	BuBr	24	35 (31)
	MeBr	1	94
sec-BuLi	MeI	1	96 (92)
tert-BuLi	MeI	1	95 (92)
MeLi	MeI	1	40 (33)
PhLi	MeI	1	91 (86)
EtMgBr	MeI	1	N. R.

Otherwise noted, **1** was treated with 2.2 equiv of RM and 2.2 equiv of TMEDA in hexane at 50 °C for 3 h. Reaction with R'X was carried out at rt for 1 h. N.R.: no reaction. [a]NMR yields. Isolated yields are given in parentheses.

It is also noteworthy that only 1 equiv of MeI is required as shown in Figure 1. This clearly showed that this aromatization system is different from the conventional electron transfer reaction. A novel aromatization mechanism for our reaction is proposed in Scheme 1. It involves i) the formation of a dianion of the dihydroanthracene, ii) monoiodination of the dianion with one equiv of MeI, and iii) elimination of lithium iodide giving highly substituted anthracenes. Monoiodination with one equiv of MeI produces MeLi. In fact, addition of benzaldehyde to the reaction mixture gave 1-phenylethyl alcohol.

Compared with various conventional aromatization reagents[5c] such as Pd/C, *n*-BuLi/$CdCl_2$, and DDQ, our novel aromatization system has some advantage. Pd/C requires very high reaction temperature. $CdCl_2$ is not desirable from the point of view of circumstances. DDQ can be used under mild conditions. However, DDQ reacted with the aromatization product.[7] In fact, aromatization of **1** (R = Pr) using 1.1 equiv of DDQ at room temperature afforded a mixture of the desired compound **2** (R = Pr) and the Diels-Alder product[8] in 49% and 30% yields, respectively, after 1 h, although control of the amount of DDQ or reaction temperature can improve the yield of **2**.

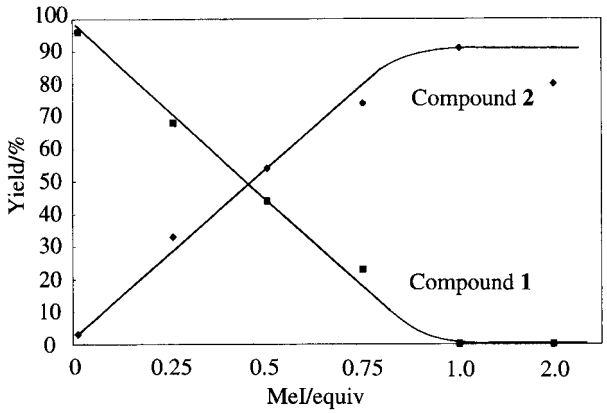
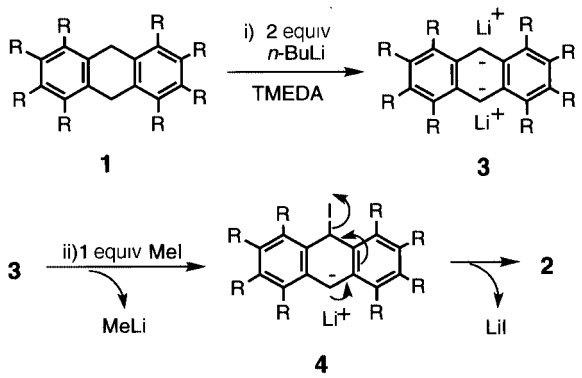


Figure 1. Correlation between the amount of MeI and yield. *n*-BuLi (2.0 equiv), TMEDA (2.0 equiv) and compound **1** (R = Pr, 1.0 equiv) were used.

Scheme 1



The novel aromatization system, *n*-BuLi/TMEDA/MeI, has the following advantage. (i) High reaction temperature is not required; (ii) excellent yield is achieved within several hours for highly alkyl substituted anthracenes; (iii) easy work-up affords very pure products.

Further investigation is in progress in the area of highly substituted aromatic compounds.

References and Notes

1 T. Takahashi, M. Kitamura, B. Shen, and K. Nakajima, *J. Am. Chem. Soc.*, **122**, 12876, (2000).

2 a) T. Takahashi, F.-Y. Tsai, Y. Li, K. Nakajima, and M. Kotora, *J. Am. Chem. Soc.*, **121**, 11093 (1999). b) T. Takahashi, Z. Xi, Yamazaki, A. Y. Liu, K. Nakajima, and M. Kotora, *J. Am. Chem. Soc.*, **120**, 1672 (1998). c)T. Takahashi, M. Kotora, and Z. Xi, *J. Chem. Soc., Chem. Commun.*, **1995**, 361.

3 T. Takahashi, R. Hara, Y.Nishihara, and M. Kotora, *J. Am. Chem. Soc.*, **118**, 5154 (1996).

4 For a review on alkylation of aromatic compounds, see a) F. M. Menger, *Top. Curr. Chem.*, **136**, 1 (1986). b) G. A. Olah, R. Krishnamurti, and G. K. S. Prakash in "Comprehensive Organic Synthesis," ed by B. M. Trost and I. Fleming, Pergamon Press Ltd., Oxford (1991), Vol. 3, p. 293.

5 a) R. G. Harvey, L. Nazareno, and H. Cho, *J. Am. Chem. Soc.*, **95**, 2377 (1973). b) R. G. Harvey and H. Cho, *J. Am. Chem. Soc.*, **96**, 2434 (1974). c) P. P. Fu and R. G. Harvey, *Chem. Rev.*, **78**, 317 (1978).

6 NMR yields were calculated using mesitylene as an internal standard.

7 A. Matsuura, T. Nishinaga, and K. Komatsu, *Tetrahedron Lett.*, **38**, 3427 (1997).

8 ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.02 (t, *J* = 7.2 Hz, 6H), 1.05 (t, *J* = 7.2 Hz, 6H), 1.13 (t, *J* = 7.2 Hz, 6H), 1.20 (t, *J* = 7.2 Hz, 6H), 1.26–1.54 (m, 14H), 1.85–1.96 (m, 2H), 2.35–2.63 (m, 12H), 2.66-2.87 (m, 4H), 5.46 (s, 2H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 14.88, 14.93, 15.13, 24.66, 24.83, 24.86, 25.02, 31.16, 31.63, 31.92, 49.55, 56.76, 114.77, 131.40, 132.58, 135.65, 135.90, 139.91, 140.51, 143.61, 179.43.