Notes

A Simple Ring Annulation Method Using Homophthalic Anhydride

Young S. Rho*, Si Ho Park, Yoon Ja Kwon,
Jin Ho Yoo, and In Ho Cho

Department of Chemistry,
Chonbuk National University,
Chonju 561-756, Korea

Received February 2, 1996

Synthesis of anthraquinones[1a] has been the object of considerable interest because of the important antileukemic activity[1b] of the structurally related anthracycline antibiotics. In numerous synthetic methods, we have been particularly interested in Michael addition of the 3-phenylsulfonyl-1(3*H*)-isobenzofuranones developed by Hauser[2] and prepared various anthracycline derivatives[3] using this method. Recently, Kita *et al.*[4] reported that homophthalic anhydride underwent thermal cycloaddition to symmetrical carbon-carbon multiple bonds to afford biologically important *peri*-hydroxyanthraquinones in a single step and developed new ring annulation methods[5] by that. Khanapure[6] also reported that the annulation occurred with the lithiated 3-cyano-1(3*H*)-isobenzofuranones, which were developed by Kraus,[7] regardless of symmetry of the aryne intermediates. In contrast, Jung[8] observed that only 3-bromoanisole underwent the aryne reaction with 3- and 2-bromoanisoles.

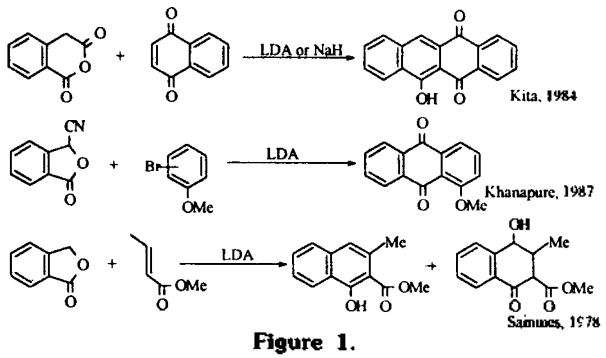
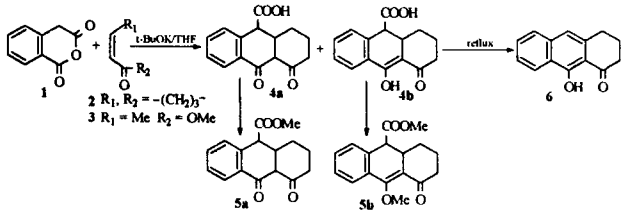


Figure 1.

On the basis of reference data,[4,6,8] we were interested in the way of the reaction of homophthalic anhydride (**1**) with α,β-unsaturated carbonyl systems **2-3** and haloarenes **7a-c** proceeds. We perceived that **1** showed different reaction type from those Kita and Khanapure reported. So in this paper, we would like to describe the new synthetic method toward anthracenone derivatives by those reactions.

Results and Discussion

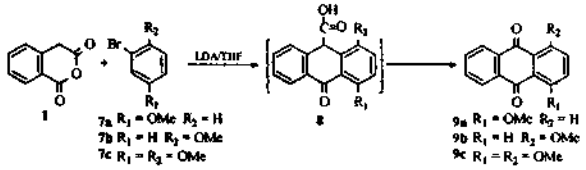
When compound **1** was reacted with **3** and **2** following the Kita's method (LDA/THF or NaH/THF) and modifications (MeONa/MeOH, *t*-BuOLi/THF), no reaction occurred as expected[4a] because the acceptors **2** and **3** were both unsymmetric. In the presence of *t*-BuOK in THF,[9] however, a clean reaction was realized with **2**, but again no reaction was observed with **3**. Carboxyanthracenone **4a** (liquid) and its tautomer **4b** (solid) were obtained in the ratio of 1 : 2 as shown in Scheme 1. Methylation of these tautomeric mixture with dimethyl sulfate furnished a chromatographically separable mixture of **5a** and **5b** in 63% overall yield. When the mixture of **4a** and **4b** was refluxed for 3 hr without isolation, decarboxylated product **6** was obtained below 40% yield as Kita's results,[4c] but refluxing in 1,2-dichlorobenzene for 3 hr after usual workup improved the yield to 89%.



Scheme 1.

According to Jung,[8] 3-phenylsulfonylphthalide[2,3] and 3-cyanophthalide[7] give condensation products with bromoanisoles **7a** and **7c**, but not with **7b**. Thus we turned our attention to the reactions of **1** with haloarenes (Scheme 2).

When *t*-BuOK, NaH, *t*-BuOLi or MeONa was used as base, no reaction was observed in all three cases. However, when LDA (3.0 equiv.) was used, **7a** and **7b** failed to react with **1** in contrast to the results of Khanapure[6] and Jung.[8] In the case of **7c**, an unexpected quinone **9c** was obtained as the sole product in 65% yield. In the expected product a carboxy group would be present[10] as **4** or be removed[4] as **6** at C-10 position. The symmetric structure was proven unambiguously by various spectroscopic analyses. Khanapure[6] reported that the arynes, generated *in situ* from bromoarenes with LDA react with lithiated 1(3*H*)-isobenzofuranones to yield lithium salt of 10-hydroxyanthrone, that subsequently undergo air oxidation slowly to the appropriate anthraquinone. Thus, the formation of carbonyl group of **9c** might be rationalized by the formation of lithiated anthrone **8** *via* decarboxylation of carboxylate, and subsequent air oxidation. Condensation of homophthalic anhydride with bromodimethoxybenzene, therefore, offers a novel approach to the synthesis of anthracycline derivatives containing quinone moiety at C-ring.



Scheme 2.

In conclusion, the condensation of homophthalic anhydride with unsymmetrical 2-cyclohexen-1-one in the presence of *t*-BuOK gives two kinds of carboxyanthracenones **4a-b**, and with 1-bromo-2,5-dimethoxybenzene (**7c**) in the presence of LDA affords anthraquinone **9c** in one-step procedure.

Experimental

All reagents and solvents were dried and purified according to the conventional procedures immediately before use. Melting points were determined on a Buchi 510 Apparatus and are uncorrected. GC/MS spectra were taken with a Nermag model R10-10C spectrometer. ^1H and ^{13}C NMR spectra were obtained on a JEOL JMN-EX 400 MHz apparatus with TMS as the internal standard.

Condensation of 1 with 2. To a solution of *t*-BuOK (3.1 mL, 3.05 mmol, 1.0 M solution in THF) in THF (20 mL) at 0 ℃ was added dropwise a solution of homophthalic anhydride **1** (0.49 g, 3.05 mmol) in THF (5 mL) over 15 min, and stirred for 30 min. A solution of 2-cyclohexen-1-one **2** (0.3 mL, 3.05 mmol) in 5 mL of THF was added dropwise over 15 min, and stirred for 1 hr, and warmed to room temperature for 3 hr. The reaction mixture was quenched with ammonium chloride. The product was isolated by successive extractions with EtOAc (4×30 mL) to give crude **4a-b** as a pale yellow oil. The mixture of **4a** and **4b** were methylated with dimethyl sulfate in acetone. Workup followed by column chromatography (EtOAc : Hexane, 1 : 4) afforded **5a** and **5b** (1 : 2, 63% overall yield): **5a**: White powder; mp 134-135 ℃; ^1H NMR ($CDCl_3$) δ 7.89 (dd, 1H, J=8.06, 1.47 Hz, ArH), 7.35 (ddd, 1H, J=8.06, 7.33, 1.46 Hz, ArH), 6.91 (d, 2H, J=7.32 Hz, ArH), 3.77 (s, 3H, OCH_3), 3.54 (d, 1H, J=13.19 Hz), 3.00 (ddd, 1H, J=13.18, 8.79, 4.39 Hz), 2.38 (ddd, 2H, J=12.45, 8.79, 3.66 Hz), 1.87-1.84 (m, 2H), 1.60-1.50 (m, 2H), 1.33-1.24 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 188.61, 181.72, 173.76, 138.29, 132.90, 131.04, 127.87, 126.77, 125.68, 106.18, 52.33, 52.08, 35.95, 32.39, 28.26, 20.55. **5b**: light yellow syrup; ^1H NMR ($CDCl_3$) δ 7.73 (dd, 1H, J=7.33, 5.13 Hz, ArH), 7.36-7.33 (m, 2H, ArH), 6.98 (dd, 1H, J=7.33, 5.13 Hz, ArH), 3.88 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 3.72 (d, 1H, J=14.66 Hz), 3.22 (dddd, 1H, J=13.92, 11.72, 4.40, 2.20 Hz), 2.58 (dddd, 1H, J=14.65, 11.72, 4.40, 2.20 Hz), 2.42 (ddd, 1H, J=12.46, 6.60, 5.76 Hz), 2.03-1.95 (m, 2H), 1.78-1.73 (m, 1H), 1.51-1.44 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 198.46, 174.09, 160.47, 135.50, 131.18, 130.47, 127.73, 125.49, 125.33, 117.15, 61.77, 52.33, 52.14, 40.90, 38.82, 28.81, 21.34. The Mixture of **4a** and **4b** was refluxed in 1,2-dichlorobenzene for 3 hr to give **6** (89%) as a light yellow powder: mp 77-78 ℃; ^1H NMR ($CDCl_3$) δ 14.00 (s, 1H, OH), 8.10 (d, 1H, J=7.81 Hz), 7.44 (d, 1H, J=7.81 Hz), 7.39 (dd, 1H, J=7.81, 6.83 Hz), 7.25 (t, 1H, J=6.84 Hz), 6.84 (s, 1H), 2.82 (dd, 2H, J=6.84, 5.86 Hz), 2.56 (dd, 2H, J=6.84, 5.86 Hz), 1.93 (ddd, 2H, J=12.69, 6.84, 5.86 Hz); ^{13}C NMR ($CDCl_3$) δ 205.1, 163.3, 138.3, 137.4, 130.3, 126.8, 124.4, 123.9, 116.3, 111.5, 39.0, 30.2, 23.0.

Condensation of 1 with 7c. To a stirred solution of LDA at −78 ℃, prepared from diisopropylamine (0.78 mL, 5.99 mmol), dry THF (20 mL), and *n*-BuLi (4.6 mL, 5.99 mmol, 1.6 M solution in hexanes) under N_2 at 0 ℃, was added a slurry of homophthalic anhydride **1** (0.35 g, 2.19 mmol) in dry THF (5 mL), and the mixture was stirred 20 min. A solution of 1-bromo-2,5-dimethoxybenzene **7c** (0.3 mL, 1.99 mmol) in THF (5 mL) was added dropwise for 20 min at −40 ℃. The mixture was stirred further for 1 hr. and allowed to warm to room temperature slowly for 3 hr. The dark reddish brown solution was then quenched with saturated ammonium chloride solution. THF was evaporated at reduced pressure and the residue was extracted with EtOAc (3×20 mL). The combined extracts were washed with brine, dried (Na_2SO_4), and concentrated to provide crude products. Purification of the products was accomplished by flash column chromatography (EtOAc : Hexane, 7 : 3) to furnish **9c** (65%) as a yellow crystal: mp 160-162 ℃; ^1H NMR ($CDCl_3$) δ 8.16 (dd, 2H, J=8.0, 2.5 Hz, 1H, ArH), 7.71 (dd, 2H, J=8.0, 2.5 Hz, 1H, ArH), 7.33 (s, 2H, ArH), 3.99 (s, 6H, OCH_3×2); ^{13}C NMR δ 183.49, 154.14, 134.23, 133.33, 126.44, 123.05, 120.33, 57.02.

Acknowledgment. This work was supported by a 1995 grant from the Basic Science Research Institute Program, Korea Ministry of Education (BSRI-95-3431).

References

1. (a) Preebe, W. *Anthracycline Antibiotics*; ACS Symposium Series 574, American Chemical Society, Washington, DC, 1995. (b) Thomson, R. H. *Naturally Occurring Quinones*; 2nd ed.; Academic Press: NY. 1971. (c) Kupchan, S. M.; Karim, A. *Lloydia* **1976**, *39*, 223.
2. Hauser, F. M.; Rhee, R. P. *J. Org. Chem.* **1978**, *43*, 178.
3. (a) Hauser, F. M.; Hewawasam, P.; Rho, Y. S. *J. Org. Chem.* **1989**, *54*, 5110. (b) Rho, Y. S.; Park, S. H.; Kwon, Y. J.; Kang, H. S.; Cho, I. H. *J. Kor. Chem. Soc.* **1995**, *39*, 218. (c) Rho, Y. S.; Park, S. H.; Kim, S. Y.; Yun, Y. K.; Cho, I. H.; Kang, H. S. *Bull. Kor. Chem. Soc.* **1994**, *15*, 360.
4. (a) Tamura, Y.; Sasho, M.; Nakagawa, K.; Tsugoshi, T.; Kita, Y. *J. Org. Chem.* **1984**, *49*, 473. (b) Tamura, Y.; Wada, A.; Sasho, M.; Kita, Y. *Tetrahedron Lett.* **1981**, *22*, 4283. (c) Tamura, Y.; Wada, A.; Sasho, M.; Fukunaga, K.; Maeda, H.; Kita, Y. *J. Org. Chem.* **1982**, *47*, 4376.
5. (a) Tamura, A.; Kirihara, M.; Sekihachi, J.; Okunaka, R.; Morhri,S.; Tsugoshi, T.; Kita, Y. *Tetrahedron Lett.* **1987**, *28*, 3971. (b) Tamura, Y.; Fukata, F.; Sasho, M.; Tsugoshi, T.; Kita, Y. *J. Org. Chem.* **1985**, *50*, 2273. (c) Tamura, Y.; Kita, Y. *Yugi Gosei Kagaku Kyokaishi* **1988**, *46*, 205. (d) Kita, Y.; Akai, S.; Yoshigi, M.; Nakajima, Y.; Yasuda, H.; Tamura, Y. *Tetrahedron Lett.* **1984**, *25*, 6027. (e) Tamura, Y.; Wada, A.; Sasho, M.; Kita, Y. *Chem. Pharm. Bull.* **1983**, *31*, 2691. (f) Kita, Y.; Okunaka, R.; Sasho, M.; Taniguchi, M.; Honda, T.; Tamura, Y. *Tetrahedron Lett.* **1988**, *29*, 5943. (g) Kita, Y.; Mohri, S.; Tsugoshi, T.; Maeda, H.; Tamura, Y. *Chem. Pharm. Bull.* **1985**, *33*, 4723. (h) Kita, Y.; Okunaka, R.; Honda, T.; Shindo, M.; Taniguchi, M.; Kondo, M.; Sasho, M. *J. Org. Chem.* **1991**, *56*, 119. (i) Grummitt, O.; Egan, R.; Buck, A. *Org. Syn. Coll III*, **1955**, 449. (j) Sammes, P. G. *J. Chem. Soc., Chem. Commun.* **1979**, 33. (k) Broom, N. J. P.; Sammes, P. G. *J. Chem. Soc., Chem. Commun.* **1978**, 162.
6. (a) Khanapure, S. P.; Reddy, R. T.; Biehl, E. R. *J. Org. Chem.* **1987**, *52*, 5685. (b) Khanapure, S. P.; Reddy, R. T.; Biehl, E. R. *J. Org. Chem.* **1988**, *53*, 4915.
7. Kraus, G. A.; Sugimoto, H. *Tetrahedron Lett.* **1978**, *19*, 2263.

8. Jung, M. E.; Lowen, G. T. *Tetrahedron Lett.* **1986**, *27*, 5319.
9. Kraus, G. A.; Cho, H.; Crowley, S.; Roth, B.; Sugimoto, H.; Prugh, S. *J. Org. Chem.* **1983**, *48*, 3439.
10. Nozawa, K.; Yamada, M.; Tsuda, Y.; Kawai, K.; Nakajima, S. *Chem. Pharm. Bull.* **1981**, *29*, 3486.

Aromatic Ring Annelation Using the 3-Carbomethoxy-1(3*H*)-isobenzofuranone and Methyl 2-carbomethoxybenzylcarboxylate

Young S. Rho*, Jin Ho Yoo, Bok Nam Baek, Chul Ju Kim, and In Ho Cho

Department of Chemistry, Chonbuk National University, Chonju 561-756, Korea

Received February 12, 1996

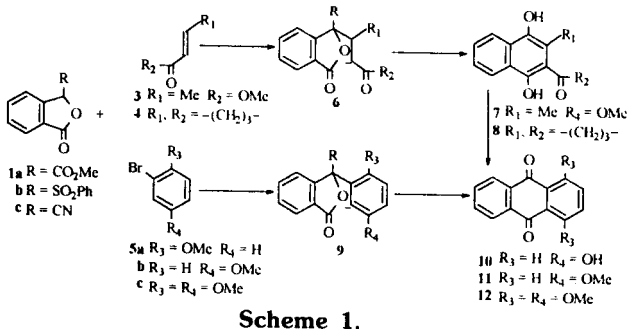
Phthalides are very useful in organic synthesis. Especially, by condensing their metallated intemediates with Michael acceptors such as α,β-unsaturated carbonyl compounds and arynes,[1] 3-phenylsulfonyl- and 3-cyano-1(3*H*)-isobenzofuranone have been widely used for the construction of anthraquinones, anthracyclines and other related compounds, which have biochemically important quinone moieties. These reactions are composed of Michael reaction followed by base-induced cyclization. Numerous phthalides which are cyclic form have been used as a Michael donor for the condensation with various α,β-unsaturated carbonyl compounds. For examples, 3-phenylsulfonyl-1(3*H*)-isobenzofuranone,[2] 3-cyano-1(3*H*)-isobenzofuranone,[3] and unvised phthalides[4] were employed. Various *o*-substituted benzyl derivatives which are open chained form have been also used as a Michael donor. For examples, methyl 2-carbomethoxybenzylcarboxylate,[5] 2-carboethoxybenzyl phenyl sulfoxide,[2] methyl 2-tosylmethylnicotinate[6] and 2-carbomethoxy toluene derivatives[7] were respectively utilized. Among those Michael donors, 3-cyano-1(3*H*)-isobenzofuranone was used to accomplish the quinone moiety with arynes by Khanapure.[8] Jung[9] explained the orientation of arynes generated *in situ* from haloarene with base. Besides, there are many examples to show the reactions of arynes with other donors.[10]

Referring to the series of those papers, we have been interested in whether phthalides and methyl 2-methylbenzoate substituted at the benzylic position with carbomethoxy group could serve as a Michael donor or not. The calculation of the withdrawing force of substituents[11] made us find out some differences in cyanides, phenyl sulfones, and recently reported dimethyl phthalide 3-phosphonate[12] (Table 1). Nevertheless, in the reaction of phthalide (**1a**) and methyl 2-methylbenzoate (**2a**) substituted at the benzylic position with carbomethoxy group, we obtain a similar reactivity that we did with various α,β-unsaturated carbonyl compounds and arynes. So herein we would like to report the results.

Results and Discussion

To synthesize the anthracycline derivatives, we have carried out the Michael reaction by three kinds of phthalide sulfone (7-methoxy, 4-methoxy- and unvised phthalide sulfone).[13] However, these three phthalides did not show any difference in their reactivities whether it had methoxy group on aromatic ring or not. So we tried the reaction with unvised phthalides **1a-c** and carboxylates **2a-c**. 3-Carbomethoxy-1(3*H*)-isobenzofuranone (**1a**), the new donor was obtained by the reaction of phthalide (1.0 g, 7.45 mmol) with methyl chloroformate (0.18 mL, 10.4 mmol) in the presence of *t*-BuOK (11.9 mL, 11.9 mmol, 1.0 M solution in THF) in 85% yield (mp 174-175 C) and **1b**, **1c** was prepared as reported[2,3] Methyl 2-carbomethoxybenzylcarboxylate (**2a**), 2-carbomethoxybenzyl phenyl sulfone (**2b**) and 2-carbomethoxy benzyl cyanide (**2c**) were prepared from methyl 2-methylbenzoate by the method 1. Schemes 1 and 2 show the reactions of two types of Michael donor (**1** and **2**) with two types of Michael acceptor (**3**, **4** and **5**).

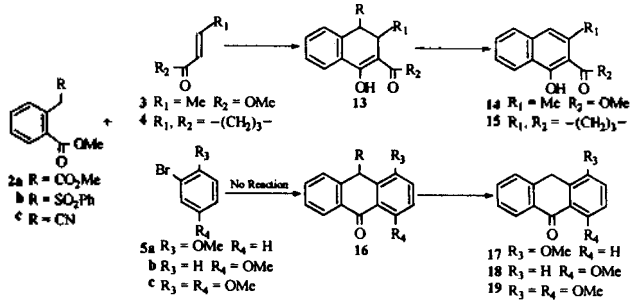
The reaction of **1a** with α,β-unsaturated carbonyl compounds (**3**, and **4**) was carried out under the method A (LDA/THF)[2,3] and the B (*t*-BuOLi/THF).[13] Consequently, the method B showed the better yield than the method A (Table 2). The other donors (**1b** and **1c**) were carried out under the same condition, and method B also showed the better



Scheme 1.

Table 1. Predicted Charge Densities for Benzylic Anions of the Donors **1**, **2** by PM3 and AM1

	R	HH	COOMe	SO_2Ph	CN	$PO(OMe)_2$	Tos	SOPh
Donor 1	AM1	−0.2865	−0.3256	−1.0601	−0.2257	−1.0682	−0.1022	−0.5073
	PM3	−0.3047	−0.3642	−0.7971	−0.2307	−0.7007	−0.0720	−0.4657
Donor 2	AM1	−0.3922	−0.4908	−1.0068	−0.3835	−1.3134	−0.3017	−0.6460
	PM3	−0.4602	−0.5666	−0.8217	−0.4185	−9522	−0.3604	−0.6267



Scheme 2.

yield than in LDA (Method A) or *t*-BuOK/DMSO.[14,15] However, three donors **1a-c** showed the almost same yield in the reaction with **3** and **4** under the method B.

It is supposed that the mechanism in the reaction of **1a** with α,β-unsaturated carbonyl compound **3** and **4** would be almost the same as that of **1b**[2] or **1c**.[3] Through those procedures, **7** was obtained easily from the reaction of **1** with **3**. The reaction of **1** with **4** made **8**, which was readily oxidized to the corresponding anthraquinone **10** in the air.[13,14] For the reaction of **1c** and bromoarene **5**, Khanapure[8] reported that *o*- and *m*-haloanisole could be reacted with **1c** in LDA respectively and Jung[9] reported that only *m*-haloanisole could be performed. Nevertheless, in our experiment, the new donor **1a** which had carbomethoxy group reacted with **5b**, **5c** under the method A, but *o*-bromoanisole (**5a**) what is like Jung's result, and that **1b**, **1c** also showed the same result as **1a** in LDA. However, in the method B, the result was proved completely different from that of the method A. It seems that three kinds of donor **1a-c** were not proceeded with any bromoarene **5a-c** in the presence of *t*-BuOLi.

In the reaction with benzyl carboxylate derivatives which are open chained form, Schmid[5] first reported the condensation of **2a** with **3** in the NaOMe to yield compound **13** (53%). So, Two kinds of base (Method A, B) were applied to Scheme 2. Compound **14** was obtained from the reaction of **2a** with **3** in LDA followed by the acidification of **13** with no purification, and the reaction of **2a** with **4** made **15** by the same method. The other donors, **2b** and **2c** made the results as shown in Table 2 by the reaction with **3** and **4**. In the method B, almost the same result was obtained by the reaction of **2a-c** and **3**, **4** respectively. Hauser and co-workers[2] could not obtain the **15** from the reaction of 2-carboethoxy phenyl sulfoxide with **4** in LDA. In contrast, we were able to prepare **15** from **2b** and **4** by the two methods. In the respective reaction of **2a** and bromoarenes **5a-c**, all the anisoles which had halogen in any position did not proceed. Furthermore, **2b** and **2c** did not react with **5a-c** under the two conditions, either. These suggest that the reactivity of **1** in the reaction with **5** is better than that of **2** between **2** types of donor.

In conclusion, the new Michael donor **1a** can produce the same reaction with Michael acceptor like as **1b** and **1c**. **2a-c** can react with α,β-unsaturated carbonyl compound **3** and **4**, but not with haloarenes **5a-c**. The reactivity of donor **1** composed of lactone ring is better than that of the open chained type donor **2** in the reaction with all of the Michael acceptors.

Experimental

All reagents and solvents were dried and purified according to the conventional procedures immediately before use. Melting points were determined on a Büchi 510 Apparatus and are uncorrected. GC/MS spectra were taken with a Nermag model R10-10C spectrometer. ^{1}H and ^{13}C NMR spectra were obtained on a JEOL JMN-EX 400 MHz apparatus with TMS as the internal standard.

General Procedure for the Reaction of Michael Acceptors 3, 4 with Michael Donors 1, 2; (Method B).

Table 2. Yield(%) on Condensations of Michael Donors (**1a-c**, **2a-c**) with Michael Acceptors (**3**, **4**, **5a-c**) in Two Kinds of Base Condition

Donor	**1a**					**1b**					**1c**				
Acceptor	**3**	**4**	**5a**	**5b**	**5c**	**3**	**4**	**5a**	**5b**	**5c**	**3**	**4**	**5a**	**5b**	**5c**
Method A (LDA)[a,b]	78	74	–	35	70	72 (70)[e]	71 (69)[e]	–	40	70	76 (85)[b]	70 (42)[e]	– (35)[g]	43 (40)[g]	80 (75)[g]
Method B (*t*-BuOLi)[13]	93	90	–	–	–	92	91	–	–	–	85 (66)[f]	79 (60)[f]	–	–	–
Product	**7**	**10**	–	**11**	**12**	**7**	**10**	–	**11**	**12**	**7**	**10**	**11**	**11**	**12**
Donor	**2a**					**2b**					**2c**				
Acceptor	**3**	**4**	**5a**	**5b**	**5c**	**3**	**4**	**5a**	**5b**	**5c**	**3**	**4**	**5a**	**5b**	**5c**
Method A (LDA)[a,b]	62 (53)[e]	35	–	–	–	58 (44)[e]	31 (–)[e]	–	–	–	55	27	–	–	–
Method B (*t*-BuOLi)[13]	66	38	–	–	–	67	35	–	–	–	62	31	–	–	–
Product	**14**	**15**	–	–	–	**14**	**15**	–	–	–	**14**	**15**	–	–	–

[a] Acceptor (**3**) is ethylcrotonate, and Donor (**2b**) is 2-carboethoxybenzyl phenyl sulfoxide.[2] [b] Acceptor (**3**) is 3-penten-2-one or ethylcrotonate.[3] [c] Acceptor (**4**) is naphthalenone derivatives (two steps).[16] [d] Acceptor (**3**) is methyl vinyl ketone, base is *t*-BuOK/DMSO.[15] [e] Base is *t*-BuOK/DMSO[14] insted of *t*-BuOLi/THF. [f] Base is sodium methoxide.[5]

To a magnetically stirred cold (−78 ℃) solution of lithium *tert*-butoxide (3.0 mmol) prepared from *n*-butyllithium (1.87 mL, 3.0 mmol, 1.6 M solution in hexanes) and *tert*-butyl alcohol (0.28 mL, 3.0 mmol), Michael donor (1.0 mmol) was added as a slurry in THF (10 mL). The yellow anion solution, still at −78 ℃, was stirred 1 h and then Michael acceptor (1.0 mmol) in THF (5 mL) was added. The reaction was continued at −78 ℃ for 1 h at which point the cooling bath was removed and reaction was allowed to stand at rt overnight and was quenched by the addition of 3 N HCl. After standard assay work-up, the crude product was carried column chromatography (hexane : CH_2Cl_2, 1 : 9) to give **7**, **10**, **14**, **15** respectively.

Method A. All the procedures and conditions are the same as the method B except using LDA (3.0 mmol) instead of *t*-BuOLi.

Methyl 3-methyl-1,4-dihydroxy-2-naphthoate (7). light brown syrup; ^{1}H NMR ($CDCl_3$) δ 12.03 (s, 1H, OH), 8.01-8.10 (m, 2H), 7.59-7.63 (m, 2H), 3.99 (s, 3H, OCH_3), 2.50 (s, 3H, $PhCH_3$).

1-Hydroxyanthraquinone (10). **8** was prepared from **1** and **4**, and readily oxidized to **10**: yellow crystal; mp 177-8 ℃; ^{1}H NMR ($CDCl_3$) δ 12.62 (s, 1H, OH), 8.29-8.36 (m, 2H), 7.80-7.87 (m, 3H), 7.69 (t, 1H, J=8.06 Hz), 7.49-7.56 (m, 1H), 7.33 (dd, 1H, J=7.33, 1.47 Hz).

Methyl 1-hydroxy-3-methyl-2-naphthoate (14). light yellow syrup; ^{1}H NMR ($CDCl_3$) δ 11.90 (s, 1H, OH), 7.64-7.67 (m, 1H), 7.43-7.52 (m, 4H), 4.11 (s, 3H, $PhCH_3$), 3.84 (s, 3H, OCH_3); MS, m/z 216 (M^+).

10-Hydroxy-1,2,3,4-tetrahydroanthracen-1-one (15). orange crystal; mp 77-78 ℃; ^{1}H NMR ($CDCl_3$) δ 14.00 (s, 1H, OH), 8.10 (d, 1H, J=7.81 Hz), 7.44 (d, 1H, J=7.81 Hz), 7.39 (dd, 1H, J=7.81, 6.83 Hz), 7.25 (t, 1H, J=6.84 Hz), 2.82 (dd, 2H, J=5.86, 6.84 Hz), 2.56 (dd, 2H, J=5.86, 6.84 Hz), 1.93 (ddd, 2H, J=12.69, 6.84, 5.86 Hz); ^{13}C NMR δ 205.1, 163.3, 138.3, 137.4, 130.3, 126.8, 124.9, 124.4, 123.9, 116.3, 111.5, 39.0, 30.2, 23.0; Ms, m/z 212 (M^+).

General Procedure for the Reaction of bromoarenes 5a-c with Michael Donors 1, 2; (Method A). In a flame-dried flask flushed with nitrogen, LDA (3.0 mmol) was prepared by adding diisopropylamine (0.39 mL, 3.0 mmol) into a −78 ℃ solution of *n*-BuLi (1.87 mL, 3.0 mmol, 1.6 M solution in hexanes) in THF (10 mL) under a nitrogen atmosphere. After solution was stirred for 10 min, the appropriate Michael donor (1.0 mmol) in THF (10 mL) was added dropwise over 20 min. The reaction mixture was stirred at −78 ℃ for 10 min and then allowed to warm to −40 ℃. The reaction mixture was stirred further and allowed to warm to room temperature. The dark reddish brown solution was then quenched with saturated aqueous ammonium chloride solution, THF was evaporated under the reduced pressure, and the residue was extracted with methylene chloride. The combined extracts were washed with brine, dried ($MgSO_4$).

Method B. All the procedures and conditions are the same as the method A except using *t*-BuOLi (3.0 mmol) instead of LDA.

1-Methoxyanthraquinone (11). yellow crystal; mp 168-169 ℃; ^{1}H NMR ($CDCl_3$) δ 8.28 (dd, 1H, J=7.33, 1.47 Hz), 8.24 (d, 1H, J=8.06 Hz), 7.97 (d, 1H, J=7.32 Hz), 7.71-7.80 (m, 3H), 4.06 (s, 3H, OCH_3); MS, m/z 238 (M^+).

1,4-Dimethoxyanthraquinone (12). orange crystal; mp 160-162 ℃ (lit.[a] mp 165-166 ℃); ^{1}H NMR ($CDCl_3$) δ 8.17 (dd, 2H, J=5.86, 2.93 Hz), 7.71 (dd, 2H, J=5.86, 2.93 Hz), 7.35 (s, 2H), 4.00 (s, 6H, $OCH_3\times2$); ^{13}C NMR δ 183.5, 154.1, 134.2, 133.3, 126.4, 123.0, 120.2, 57.0; MS, m/z 268 (M^+).

Acknowledgment. This work was supported by a 1995 grant from the Basic Science Research Institute Program, Korea Ministry of Education (BSRI-95-3431).

References

1. (a) Snieckus, V. *Chem. Rev.* **1990**, *90*, 879. (b) Snieckus, V. *Heterocycles* **1980**, *14*, 1649. (c) Watanabe, M. *Yuki Gosei Kagaku Kyokai Shi* **1983**, *41*, 728.
2. Hauser, F. M.; Rhee, R. P. *J. Org. Chem.* **1978**, *43*, 178.
3. Kraus, G. A.; Sugimoto, H. *Tetrahedron Lett.* **1978**, *19*, 2263.
4. Broom, N. J. P.; Sammes, P. G. *J. Chem. Soc., Chem. Comm.* **1978**, 162.
5. Eisenhuth, W.; Renfroe, H. B.; Schmid, H. *Helvetica Chim. ACTA.* **1965**, *48*, 375.
6. VanLeusen, A. M.; Terpstra, J. W. *Tetrahedron Lett.* **1981**, *22*, 5097.
7. Dodd, J. H.; Weinreb, S. M. *Tetrahedron Lett.* **1979**, *20*, 3593.
8. Khanapure, S. P.; Reddy, R. T.; Biehl, E. R. *J. Org. Chem.* **1987**, *52*, 5685.
9. Jung, M. E.; Lowen, G. T. *Tetrahedron Lett.* **1986**, *27*, 5319.
10. (a) Sammes, P. G. *J. Chem. Soc., Chem. Comm.* **1979**, 33. (b) Tamura, Y.; Sasho, M.; Nakagawa, K.; Tsugoshi, T.; Kita, Y. *J. Org. Chem.* **1984**, *49*, 473.
11. (a) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902. (b) war, M. J. S.; Ford, G. P. *J. Am. Chem. Soc.* **1977**, *99*, 1685. (c) Rho, Y. S.; Park, S. H.; Kim, S. Y.; Yun, Y. K.; Cho, I. H.; Kang, H. S. *Bull. Kor. Chem. Soc.* **1994**, *15*, 360.
12. Watanabe, M.; Furukawa, S. *Synlett.* **1991**, 481.
13. (a) Hauser, F. M.; Hewawasam, P.; Rho, Y. S. *J. Org. Chem.* **1989**, *54*, 5110. (b) Rho, Y. S.; Park, S. H.; Kwon, Y. J.; Kang, H. S.; Cho, I. H. *J. Kor. Chem. Soc.* **1995**, *39*, 218.
14. Kraus, G. A.; Cho, H.; Crowley, S.; Roth, B.; Sugimoto, H.; Prugh, S. *J. Org. Chem.* **1983**, *48*, 3439.
15. Kraus, G. A.; Molina, M. T.; Walling, J. A. *J. Org. Chem.* **1987**, *52*, 1237.
16. (a) Li, T-S.; Wu, Y. L. *J. Am. Chem. Soc.* **1981**, *103*, 7007. (b) Li, T-S.; Walsgrove, T. C. *Tetrahedron Lett.* **1981**, *22*, 3741.