phosphino)ethane (dppe), and 200 mg (1.16 mmol) of 3-acetoxy-1-(trimethylsilyl)-1-propene in 2 mL of THF. After stirring overnight at room temperature, it was partitioned between 150 mL of ether and 30 mL of water. The water layer was washed with 3 × 20 mL of ether and the combined organic layers were dried. The solvent was removed by distillation and the residue subjected to PLC eluting with 15% ether in pentane to yield 124.4 mg (61%): ^{1}H NMR (270 MHz) δ 6.01 (1 H, ddd, J = 18.4, 7.4, 5.5 Hz), 5.50 (1 H dt, J = 18.4, 1.5 Hz), 2.57 (1 H, dtd, J = 14.0, 5.5, 1.5 Hz), 1.31-2.32 (8 H, m), -0.01 (9 H, s); ^{13}C NMR (50.1 MHz) δ 211.8, 144.2, 131.9, 50.2, 42.1, 36.8, 33.5, 28.0, 25.1, -1.0; calcd for $C_{12}H_{22}OSi$, 210.1439; found, 210.1441.

Spectral Data. 6a: ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.95 (1 H, ddd, J = 18.4, 7.7, 5.5 Hz), 5.59 (1 H, dt, J = 18.4, 1.4 Hz), 2.59 (1 H, dtd, J = 13.9, 5.5, 1.4 Hz), 1.3-2.4 (9 H, m), 0.86 (9 H, s), -0.01 (9 H, s); ^{13}C NMR (FX 200) δ 212.3, 144.7, 132.0, 49.2, 47.2, 41.6, 36.6, 34.7, 32.5, 28.7, 27.6, -1.2; calcd for $C_{16}H_{30}OSi$, 266.2058; found, 266.2065.

6b: ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.82 (1 H, ddd, J = 18.4, 7.4, 5.2 Hz), 5.56 (1 H, d, J = 18.4 Hz), 1.4-2.4 (10 H, m), 0.84 (9 H, s), -0.01 (9 H, s); ^{13}C NMR (FX 200) δ 214.6, 143.2, 133.4, 48.3, 41.9, 38.6, 38.3, 32.5, 30.0, 27.4, 26.6, -1.3; calcd for $C_{16}H_{30}OSi$, 266.2058; found, 266.2065.

7a: ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.94 (1 H, ddd, J = 18.4, 7.4, 5.5 Hz), 5.59 (1 H, dt, J = 18.4, 1.5 Hz), 2.60 (1 H, dtd, J = 14.3, 5.5, 1.5 Hz), 2.2-2.5 (9 H, m), 0.98 (3 H, d, J = 6.6 Hz), -0.00 (9 H, s); ^{13}C NMR (FX 200) δ 213.1, 144.9, 131.8, 50.3, 45.7, 37.4, 36.6, 34.7, 25.6, 14.5, -1.15; calcd for $C_{13}H_{24}OSi$, 224.1590; found, 224.1596.

7b: ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.84 (1 H, ddd, J = 18.8, 6.6, 5.5 Hz), 5.6 (1 H, d, J = 18.8 Hz), 2.45-1.46 (10 H, m), 1.01 (3 H, d, J = 7 Hz), -0.02 (9 H, s); ^{13}C NMR (FX 200) δ 215.3, 143.7, 132.5, 48.2, 42.9, 37.6, 34.9, 31.6, 20.4, 15.6, -1.3; calcd for $C_{13}H_{24}OSi$, 224.1590; found, 224.1596.

8 (n = 1): ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.91 (dd, J = 15.4, 10.1 Hz) and 6.8 (dd, J = 15.4, 11.4 Hz) total 1 H, 5.68 and 5.62 (total 1 H, each d, J = 15.4 Hz), 4.06 (2 H, m), 2.44 (1 H, dd, J = 11.4 and 3.2 Hz), 1.2-2.4 (11 H, m), 0.89 and 0.88 (total 3 H, each t, J = 8 Hz), 0.017 (9 H, s); ^{13}C NMR (50.1 MHz) δ 219.1, 218.3, 166.5, 149.8, 146.9, 120.7, 119.0, 63.9, 50.4, 48.9, 37.8, 37.6, 35.6, 33.7, 30.8, 29.8, 26.7, 20.7, 19.1, 13.6, -1.5, -2.3; calcd for $C_{16}H_{28}O_3Si$, 296.1806; found, 296.1806.

9 (n = 1): ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.04 (1 H, dd, J = 18.7, 7.4 Hz), 5.77 (1 H, dd, J = 18.7, 1.1 Hz), 4.04 (2 H, m), 3.61 (1 H, dd, J = 9.5, 5.5 Hz), 1.2-2.8 (11 H, m), 0.88 (3 H, t, J = 8 Hz), 0.01 (9 H, s); ^{13}C NMR (50.1 MHz) δ 217.9, 172.0, 141.0, 134.0, 64.6, 51.5, 50.6, 38.0, 32.5 30.7, 26.2, 20.7, 19.1, 13.6, -1.4.

8 and 9 (n = 2): (270 MHz, $CDCl_3$) δ 7.02 (dd, J = 15.8, 10.7 Hz), 6.81 (dd, J = 15.4, 11.4 Hz), 5.83 (d, J = 18 Hz), 5.73 (dd, J = 18, 7.7 Hz), 5.67 (d, J = 15.4 Hz), 5.56 (d, J = 15.8, Hz) [total 2 H], 4.05 (2 H, m), 3.10 (dd, J = 9.5, 5.5 Hz), 2.81 (m), 2.56 (m), 1.25-2.45 (m) [14 H], 0.88 (3 H, m), -0.01 (s) and -0.04 (s) [9 H]; ^{13}C NMR (50.1 MHz) δ 212.2, 211.5, 167.5, 151.3, 150.6, 141.7, 137.3, 119.5, 118.7, 63.9, 51.6, 42.0, 36.1, 34.1, 30.8, 28.0, 25.2, 25.0, 19.2, 13.7, -1.2, -1.8.

10: ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.82 (1 H, d, J = 18.7 Hz), 5.71 (1 H, dd, J = 18.7, 7.5 Hz), 4.03 (2 H, m), 3.16 (1 H, dd, J = 10.3, 7.5 Hz), 2.93 (1 H, dt, J = 10.3, 5.2), 2.55 (1 H, m), 1.25-1.99 (10 H, m), 1.12 (3 H, d, J = 7 Hz), 0.87 (3 H, t, J = 7 Hz), 0.12 (9 H, s); ^{13}C NMR (50.1 MHz) δ 214.3, 172.9, 140.8, 136.2, 64.4, 53.6, 48.6, 44.2, 34.0, 30.6 (2C), 20.1, 19.1, 16.1, 13.6, -1.32; calcd for $C_{18}H_{32}O_3Si$, 324.2119; found, 324.2120.

12: ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.92 (2 H, m), 7.50 (3 H, m), 7.02 (1 H, dd, J = 15.4, 8.7 Hz), 5.60 (1 H, dd, J = 15.4, 1.2 Hz), 4.05 (2 H, t, J = 6.3 Hz), 3.22 (1 H, dd, J = 17.3, 9.6 Hz), 3.08 (1 H, dd, J = 17.3, 4.4 Hz), 2.59 (1 H, m), 1.28-1.61 (4 H, m), 0.89 (3 H, t, J = 6.3 Hz), 0.06 (9 H, s); ^{13}C NMR (50.1 MHz) δ 197.9, 166.5, 150.8, 136.6, 132.8, 129.1, 128.4, 128.1, 127.8, 117.6, 63.9, 37.2, 30.8, 29.6, 26.5, 19.3, 13.7, -2.8; calcd for $C_{19}H_{28}O_3Si$, 332.1806; found, 332.1807.

13: ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.83 (dd, J = 15.5, 11.2 Hz) and 6.72 (dd, J = 15.2, 10.5 Hz) [total 1 H], 5.64 (3 H, m), 4.08 (2 H, m), 1.18-3.22 (12 H, m), 0.89 (3 H, t, J = 6 Hz), 0.08 (9 H, s); calcd for $C_{19}H_{30}O_3Si$, 334.1962; found, 334.1963.

14: ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.10 (dd, J = 15.6, 10.8 Hz), 6.85 (dd, J = 15.4, 11.4 Hz) and 6.723 (dd, J = 15.4, 11.0 Hz) [total 1 H]; 5.70 (d, J = 15.4 Hz) and 5.57 (d, J = 15.4 Hz) [total 1 H]; 4.07 (2 H, t, J = 5.9 Hz), 1.36-2.68 (13 H, m), 0.895 (3 H, t, J = 5.9 Hz); 0.894 (s), 0.87 (s), 0.80 (s) [total 9 H], 0.005 (s), -0.016 (s), -0.024 (s) [total 9 H]; calcd for $C_{21}H_{38}O_3Si$, 366.2588; found, 366.2589.

15: ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.99 (dd, J = 15.4, 11 Hz), 6.82 (dd, J = 15.4, 11.2 Hz) [total 1 H]; 5.69 (d J = 15.4 Hz), 5.54 (d, J = 15.4 Hz) [total 1 H]; 4.04 (2 H, m), 2.60 (1 H, m), 2.45 (1 H, dd, J = 11.4, 4.4 Hz), 2.22 (1 H, m), 0.60-1.98 (50 H, m) with methyl peaks at δ 0.61, 0.79, 0.81, 0.83, 0.85; -0.02 (s) and -0.04 (s) [9 H]; ^{13}C NMR (50.1 Hz) δ 210.2, 210.0, 166.6, 150.5, 149.1, 119.6, 118.7, 63.7, 56.2, 53.9, 47.5, 46.5, 44.7, 44.3, 42.6, 39.9, 39.5, 36.6, 36.2, 35.7, 35.2, 33.3, 31.7, 30.8, 28.7, 28.2, 27.9, 24.2, 23.8, 22.7, 22.5, 21.5, 19.1, 18.6, 13.6, 12.3, 12.0, -1.24, -1.71; calcd for $C_{38}H_{66}O_3Si$, 598.4778; found, 598.4778.

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Registry No. **1**, 80401-14-5; **2**, 86970-26-5; **3**, 7299-28-7; **6a**, 87729-60-0; **6b**, 87729-61-1; **7a**, 87729-62-2; **7b**, 87729-63-3; **8** (n = 1), 87729-64-4; **8** (n = 2), 87729-65-5; **9** (n = 1), 87729-66-6; **9** (n = 2), 87729-67-7; **10**, 87729-68-8; **11**, 87729-69-9; **12**, 87729-70-2; **13**, 87729-71-3; **14**, 87729-72-4; **15**, 87729-73-5; $Me_3SnO_2CCF_3$, 6430-48-4; 4-*tert*-butylcyclohexanone, 98-53-3; cyclohexanone, 108-94-1; 2-methylcyclohexanone, 583-60-8; cyclopentanone, 120-92-3; acetophenone, 98-86-2; bicyclo[3.3.0]oct-7-en-2-one, 56138-05-7; 5α-cholestanone, 566-88-1; lithium hexamethyldisilazide, 4039-32-1; 1,2-bis(diphenylphosphino)ethane, 1663-45-2; tetrakis(triphenylphosphine)palladium, 14221-01-3.

Strong Base Induced Cycloaddition of Homophthalic Anhydrides Leading to *peri*-Hydroxy Polycyclic Compounds

Yasumitsu Tamura,* Manabu Sasho, Kiyomi Nakagawa, Teruhisa Tsugoshi, and Yasuyuki Kita

Faculty of Pharmaceutical Sciences, Osaka University, 1-6 Yamada-oka, Suita, Osaka, Japan

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A new and exceptionally facile cycloaddition of the alkaline metal salt of homophthalic anhydrides (**1a,b**) is described. The anions of the anhydrides **1a,b** undergo cycloadditions with various dienophiles (**5-14**) to give the corresponding *peri*-hydroxy polycyclic compounds (**15-26**) in good yields under extremely mild conditions, whereas thermal cycloaddition of **1a,b** requires high temperatures.

We recently reported[1] that homophthalic anhydrides (**1a,b**) undergo thermal cycloaddition to carbon-carbon multiple bonds to afford biologically important *peri*-hydroxyanthraquinones[2] in a single step. The cyclo-

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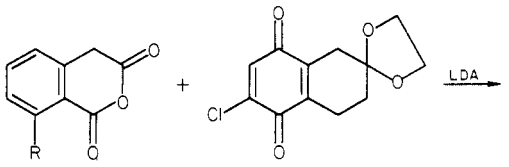
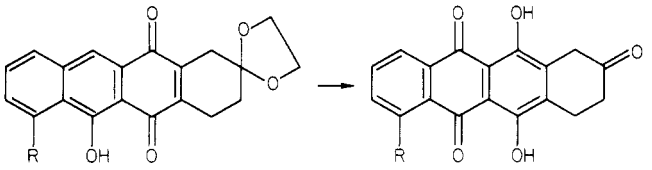
addition using **1a,b** and the appropriately functionalized



1a, R = H
b, R = OMe

2



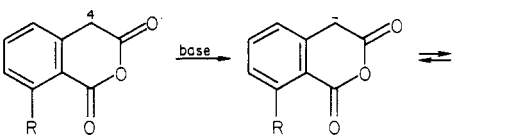
3a, R = H
b, R = OMe

4a, R = H
b, R = OMe

quinone (**2**) was successfully applied to a facile regiocontrolled synthesis of the anthracyclinone precursors (**4a,b**).[3] In this reaction, the use of the alkaline metal salt of **1a,b** dramatically improved the yield of the cycloadducts (**3a,b**) under remarkably mild conditions. It is of interest to explore the generality, scope, and mechanism of this novel base-induced cycloaddition of **1a,b**. We describe here the full details of the cycloadditions of **1a,b** to various dienophiles (**5–14**) and compare these results with the previously reported[1] thermal cycloaddition of **1a,b**.

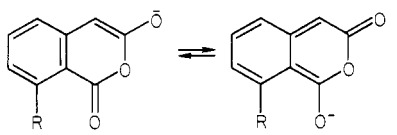
Results

The new method for the cycloadditions of **1a,b** in the present study is based on the following three assumptions: (i) Deprotonation of the benzyl proton (C-4 proton) of **1a,b** may occur readily because of the stabilization by the neighboring carbonyl group to produce the active species such as **1A**, **1B**, and/or **1C**. (ii) Orientation of the cycloaddition would be controlled so that the nucleophilic end (C-4 position) of **1a,b** reacts at the electrophilic site of the dienophiles. (iii) Simultaneous extrusion of carbon dioxide from the initially formed cycloadducts may occur smoothly under the mild conditions. The deprotonation of **1a,b**, however, proved to be an initial obstacle. Several weak bases, such as pyridine, triethylamine, potassium carbonate, and potassium hydroxide, were ineffective. Deprotonation was efficiently effected by strong bases such as lithium diisopropylamide (LDA) or sodium hydride (NaH) under mild conditions to give the corresponding alkaline salts, which reacted smoothly with various types of carbon–carbon multiple bonds (**5–14**) to give high yields of the linearly condensed *peri*-hydroxy polycyclic compounds (**15–26**) in a single step. Two typical experimental procedures using the lithium and sodium salts of **1a,b** are illustrated in the reaction of **1a** with 1,4-naphthoquinone (**5**). Treatment of the lithium salt generated from **1a** and an equivalent amount of LDA with **5** at −78 °C for 20 min under nitrogen gave the hydroxynaphthacenedione (**15**) in 76% yield (method A). A more general and practical preparation of **15** was performed by the reaction of **5** with the sodium salt generated from **1a** and an equivalent amount of NaH in dry tetrahydrofuran (THF) at 0 °C for a short period (method B). 8-Methoxyhomophthalic anhydride (**1b**) similarly reacted with these dienophiles (**5** and **8**) to give the corresponding regiocontrolled cycloadducts (**25** and **26**), the latter of which has been used as an intermediate for the synthesis of β-sorigenin (**27**).[4]

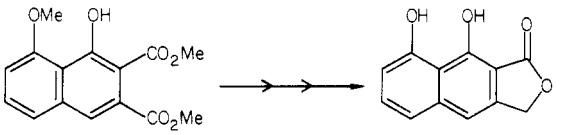


R = H, OMe
1a,b

1A



1B 1C



26 27

An attractive feature of these cycloadditions is that the *peri*-hydroxy polycyclic compounds were obtained regioselectively in a single step in high yields. The anhydrides **1a,b** were treated with alkyl propiolates (**6** and **7**) and bromojuglone methyl ethers (**12** and **13**) to give respectively **16**, **17**, **22**, and **23** as the sole regioisomers of reaction. The products **15–19** and **22–26** were identified by comparison with authentic samples.[5-8] The structures of compounds **20** and **21** were assigned on the basis of their spectral data. The reaction conditions, products, and yields are summarized in Table I and are compared with the results obtained from thermal-induced cycloadditions.

Discussion

The mechanism of this base-induced cycloaddition of **1a,b** is not rigorously defined. There are two possible routes for the formation of the linearly condensed aromatic compounds from **1a,b** (Scheme I): the anhydrides **1a,b** reacted with carbon–carbon multiple bonds in what may be formulated as a Diels–Alder reaction (route A, involving a concerted cycloaddition of the intermediate **1c** to dienophiles) or Michael reaction (route B, involving a stepwise addition of the intermediates **1A–C** to dienophiles followed by intramolecular cyclization) accompanied by a simultaneous extrusion of carbon dioxide from the initial adducts.[9] We first examined the reaction of an alkaline metal salt

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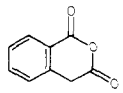
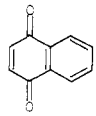
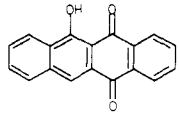
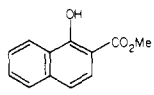
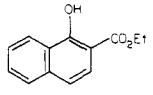
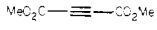
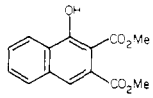
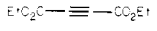
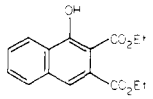
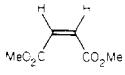
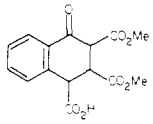
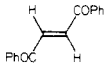
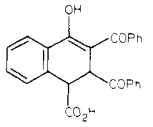
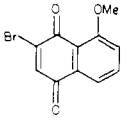
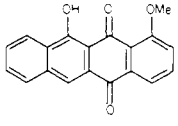
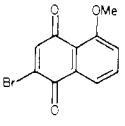
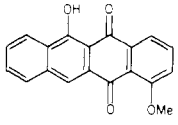
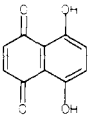
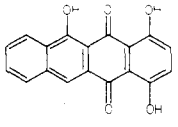
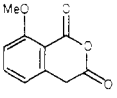
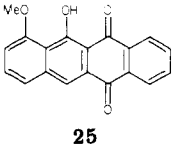
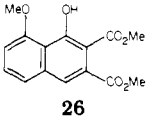
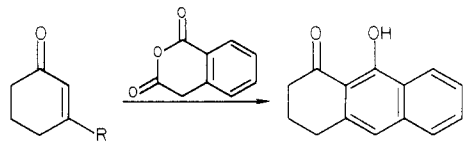
(9) An analogous mechanism involving a Diels–Alder or a Michael cascade reaction is postulated in the reaction of the lithiated cyclohexenones with some dienophiles, see: (a) Lee, R. A. *Tetrahedron Lett.* **1973**, 3333. (b) Cory, R. M.; Chan, D. M. T. *Ibid.* **1975**, 4441. (c) White, K. B.; Reusch, W. *Tetrahedron* **1978**, *34*, 2439. (d) Cory, R. M.; Renneboog, R. M. *J. Chem. Soc., Chem. Commun.* **1980**, 1081. (e) Spitzner, D. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 636.

Table I. Cycloaddition of 1a,b to Dienophiles

homophthalic anhydride 1	dienophile	product	method[a]	yield,[b] %	thermal conditions	yield,[b] %
 1a	 5	 15	method A method B	76 88	dichlorobenzene, 200 °C, 7 h	44
	 6	 16	method B	49	toluene, 150 °C, 24 h[c]	9
	 7	 17	method B	50	toluene, 150 °C, 24 h[c]	19
	 8	 18	method B	94	toluene, 150 °C, 24 h[c]	65
	 9	 19	method B	96	toluene, 150 °C, 24 h	63
	 10	 20[d]	method B[e]	46	toluene, 150 °C, 27 h	*f*
	 11	 21[d]	method B	83		
	 12	 22	method A method B	63 90	dichlorobenzene, 200 °C, 2 h	39
	 13	 23	method A method B	57 73		
	 14	 24	method B[g]	85	dichlorobenzene, 200 °C, 7 h	38
 1b	5	 25	method A method B	68	dichlorobenzene, 180 °C, 7 h	42
	8	 26	method B	79		

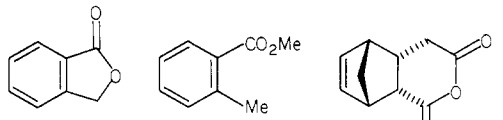
[a] Methods A and B are as follows: method A, LDA/THF, −78 °C, 30 min → room temperature; method B, NaH/THF, 0 °C, 20 min → 20 °C, 30 min. [b] Yields were based on homophthalic anhydride. No attempts to optimize yields were made. [c] The reaction was carried out in a sealed tube. [d] The stereochemistry has not been determined. [e] The reaction mixture was heated at 80 °C for 3 h. [f] The starting materials were recovered unchanged. [g] The reaction was carried out with 3 equiv of NaH.

of **1a** with known Michael acceptors. The lithium salt of **1a** did not react with various cyclohexenone derivatives (**28–31**) at −78 °C to room temperature. Next, we exam-



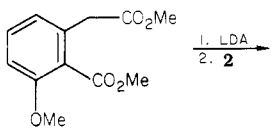
28, R = H
29, R = OEt
30, R = Cl
31, R = SO_2Ph

ined the reaction of the chloroquinone (**2**) with the lithium salts derived from phthalide (**32**) and methyl 2-methyl-

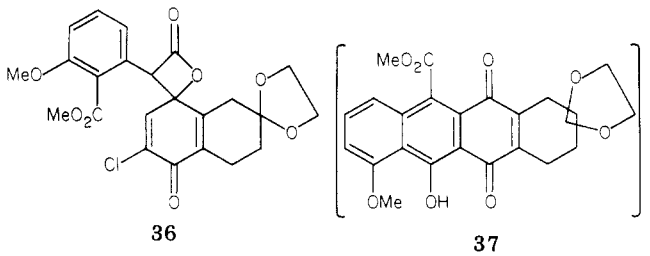


32 **33** **34**

benzoate (**33**), which are also known[10,11] to undergo Michael reactions. The former salt reacted with **2** to give only a small amount of the adduct (**3a**) (determined by TLC), and the latter salt was recovered unchanged. Another related sodium salt derived from 3-*endo*-carboxynorborn-5-en-2-*endo*-ylacetic anhydride (**34**),[12] which cannot exist in the *o*-xylylene form such as **1C**, did not react with **2** even under forcing conditions. To prove the effect of the anhydride ring participation, we have examined the reaction of **2** with the lithium salt of dimethyl 3-methoxylhomophthalate (**35**). This salt is expected[13] to undergo a Michael addition



35



36 **37**

followed by intramolecular cyclization. However, the major product obtained after chromatography is a [2 + 2] cycloadduct (**36**) probably from the ketene intermediate and the tetracyclic adduct (**37**) via a Michael addition followed by an intramolecular cyclization that could not be detected.

Initially, we doubted that route A was the mechanism, since the Diels–Alder reaction through the most unstable intermediate, **1C**, should require high temperature. However, a survey of the literature reveals that some oxyanions have recently been shown to accelerate dramatically thermal pericyclic reactions such as [3,3] sigmatropic shifts,[14] [1,3] sigmatropic shift,[15] vinyl cyclopropane rearrangements,[16] and retro-Diels–Alder reactions.[17] On the basis of the results discussed in this paper together with the results obtained in the previous thermal cycloaddition of **1a,b**,[1] route A is reasonable for the mechanism;[18] however we do not know enough about the Michael receptor properties of **2** to rule out route B.

In summary, homophthalic anhydrides **1a,b** offer convenient diene equivalents through strong base induced deprotonations, which induce Diels–Alder type reactions with various dienophiles[19] under the remarkably mild conditions. Both the high yields and low reaction temperatures encountered in these strong base assisted cycloadditions imply that these modifications should significantly increase the synthetic utility of these and the related cycloadditions. Further mechanistic studies and applications to other analogues of homophthalic anhydrides are being explored currently.

Experimental Section

All melting points are uncorrected. ^1H NMR spectra were determined with a Hitachi R-22 (90 MHz) spectrometer with tetramethylsilane as an internal standard. IR absorption spectra were recorded on a JASCO IRA-1 spectrometer. Low- and high-resolution mass spectra were obtained with a JEOL JMS D-300 instrument, with a direct-inlet system at 70 eV. THF was distilled from the sodium benzophenone dianion under nitrogen. Column chromatography was carried out on Merck Silica gel 60.

General Procedures for the Cycloaddition of Homophthalic Anhydrides (1a,b). (i) Reaction of the Lithium Salt of 1 in THF with Dienophiles (Method A). A solution of *n*-BuLi (1.6 N, 0.68 mL, 1.1 mmol) was added dropwise under argon to a stirred solution of dry diisopropylamine (110 mg, 1.1

(10) (a) Kraus, G. A.; Sugimoto, H. *Tetrahedron Lett.* **1978**, 2263. (b) Hauser, F. M.; Rhee, R. P. *J. Org. Chem.* **1978**, *43*, 178. (c) Broom, N. J. P.; Sammes, P. G. *J. Chem. Soc., Chem. Commun.* **1978**, 162. (d) Sammes, P. G. *Ibid.* **1979**, 33. (e) Dodsworth, D. J.; Caliagno, M-P.; Ehrmann, U. E. *Tetrahedron Lett.* **1980**, *21*, 5075. (f) Broom, N. J. P.; Sammes, P. G. *J. Chem. Soc., Perkin Trans. 1* **1981**, 465. (g) Hauser, F. M.; Prasanna, S. *J. Am. Chem. Soc.* **1981**, *103*, 6378. (h) Hauser, F. M.; Prasanna, S.; Combs, D. W. *J. Org. Chem.* **1983**, *48*, 1328. (i) Marsden, R.; MacLean, D. B. *Tetrahedron Lett.* **1983**, *24*, 2063. (j) Swenton, J. S. *Acc. Chem. Res.* **1983**, *16*, 74 and references cited therein.

(11) (a) Evans, G. E.; Leeper, F. J.; Murphy, J. A.; Staunton, J. *J. Chem. Soc., Chem. Commun.* **1979**, 205. (b) Dodd, J. H.; Weinreb, S. M. *Tetrahedron Lett.* **1979**, 3593. (c) Dodd, J. H.; Garigipati, R. S.; Weinreb, S. M. *J. Org. Chem.* **1982**, *47*, 4045.

(12) Briggs, S. P.; Davies, D. I.; Newton, R. F.; Reynolds, D. P. *J. Chem. Soc. Perkin Trans. 1* **1981**, 146.

(13) Dimethyl homophthalate was reported to cause a Michael addition to benzoquinone dimethyl acetal, see: (a) Chenard, B. L.; Anderson, D. K.; Swenton, J. S. *J. Chem. Soc., Chem. Commun.* **1980**, 932. (b) Kozikowski, A. P.; Schmiesing, R. *Synth. Commun.* **1978**, *8*, 363.

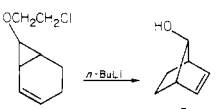
(14) (a) Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 4765. (b) Evans, D. A.; Baillargeon, D. J. *Tetrahedron Lett.* **1978**, 3319. (c) Evans, D. A.; Nelson, J. V. *J. Am. Chem. Soc.* **1980**, *102*, 774.

(15) (a) Thies, R. W.; Seitz, E. P. *J. Chem. Soc., Chem. Commun.* **1976**, 846. (b) Franzus, B.; Scheinbaum, M. L.; Waters, D. L.; Bowlin, H. B. *J. Am. Chem. Soc.* **1976**, *98*, 1241. (c) Wilson, S. R.; Mao, D. T.; Jernberg, K. M.; Ezmirly, S. T. *Tetrahedron Lett.* **1977**, 2559. (d) Thies, R. W.; Seitz, E. P. *J. Org. Chem.* **1978**, *43*, 1050.

(16) Danheiser, R. L.; Martinez-Davila, C.; Morin, J. M. Jr. *J. Org. Chem.* **1980**, *45*, 1340.

(17) RajauBabu, T. V.; Eaton, D. F.; Fukunaga, T. *J. Org. Chem.* **1983**, *48*, 652.

(18) The following two reported results also strongly support route A for the mechanism: (i) Some recent reports on the formation of *o*-xylylene intermediates from 1,3-dihydro-1,1-dimethoxyisobenzofuran or methyl *o*-methylbenzyl ethers by treatment with strong base have some similarlities. See: (a) Makhlouf, M. A.; Rickborn, B. *J. Org. Chem.* **1981**, *46*, 2734. (b) Tuschka, T.; Naito, K.; Rickborn, B. *Ibid.* **1983**, *48*, 70. (ii) The exclusive formation of the anti isomer (I) from the cyclopropyl ether (II)

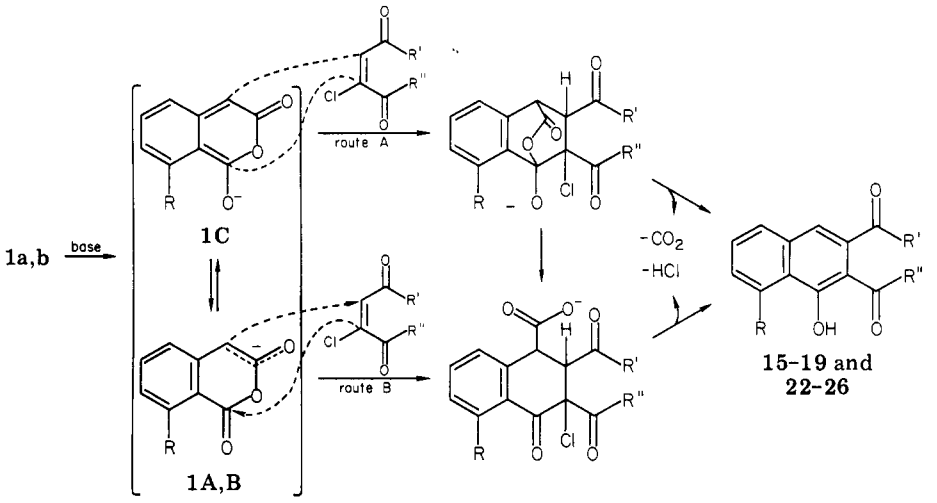


II I

is believed to undergo a concerted oxyanion-assisted [1,3] sigmatropic rearrangement controlled by orbital symmetry. See: (a) Day, A. C. *J. Am. Chem. Soc.* **1975**, *97*, 2431. (b) Silver, D. M. *Ibid.* **1974**, *96*, 5959.

(19) Readily proton exchangeable dienophiles, however, have some limitations. The lessened yields from acetylenic acceptors containing an acetylenic proton and the failure to achieve addition to cyclohexenones may be a consequence of proton exchange.

Scheme I



mmol) in anhydrous THF (4 mL) cooled to −78 °C. The mixture was stirred for 0.5 h under the same conditions and then used as a THF solution of LDA. A solution of homophthalic anhydride (1, 1 mmol) in anhydrous THF (4 mL) was added dropwise to the solution of LDA over a few minutes and a solution of dienophile (1 mmol) in anhydrous THF (5 mL) was then added to the mixture. The whole was stirred at −78 °C for 20 min, allowed to warm to room temperature, and stirred for 1 h. The reaction mixture was quenched with saturated aqueous NH_4Cl (5 mL) and then partitioned between 5% hydrochloric acid (5 mL) and methylene chloride (50 mL). The organic layer was washed with saturated aqueous NaCl (10 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was subjected to column chromatography on silica gel using benzene, chloroform, or benzene–ether as eluting solvents to give the corresponding adduct.

(ii) Reaction of the Sodium Salt of 1 in THF with Dienophile (Method B). A mixture of 1 (1 mmol) and NaH (60% in mineral oil, 1 mmol) in anhydrous THF (20 mL) was stirred at 0 °C for 3 min. A solution of dienophile (1 mmol) in anhydrous THF (2 mL) was added to the mixture. The whole was stirred at 0 °C for 20 min, allowed to warm to room temperature, and stirred for 30 min. The reaction mixture was worked up in the same manner as described above (method A) to give the corresponding adduct.

6-Hydroxynaphthacene-5,12-dione (15). (i) This was prepared from **1a** (163 mg, 1.0 mmol) and **5** (158 mg, 1.0 mmol) by method A. Recrystallization from chloroform gave pure **15**: mp 262–264 °C (lit.[20] mp 268–270 °C); IR ($CHCl_3$) 1665, 1620, 1610 cm^{-1}. Acetylation of **15** by a usual method gave the acetate, which was recrystallized from benzene to give a pure sample: mp 228–230 °C; IR ($CHCl_3$) 1760, 1700, 1665 cm^{-1}.

(ii) This was prepared from **1a** (41 mg, 0.25 mmol) and **5** (40 mg, 0.25 mmol) by method B. Recrystallization of the crude product gave pure **15**, which was identical with an authentic sample obtained from i in all respects.

Methyl 1-Hydroxy-2-naphthoate (16). This was prepared from **1a** (81 mg, 0.50 mmol) and **6** (63 mg, 0.75 mmol) by method B. Recrystallization from methanol gave pure **16**: mp 74.5–76 °C (lit.[5] 76–77 °C); IR ($CHCl_3$) 1660, 1635 cm^{-1}.

Ethyl 1-Hydroxy-2-naphthoate (17). This was prepared from **1a** (81 mg, 0.50 mmol) and **7** (74 mg, 0.75 mmol) by method B. Recrystallization from *n*-hexane gave pure **17**: mp 40.5–41 °C (lit.[6] 48–49 °C); IR ($CHCl_3$) 1640 cm^{-1}.

Dimethyl 1-Hydroxynaphthalene-2,3-dicarboxylate (18). This was prepared from **1a** (41 mg, 0.25 mmol) and **8** (36 mg, 0.25 mmol) by method B. Recrystallization from benzene-*n*-hexane gave pure **18**: mp 102–103.5 °C (lit.[5] 102–108 °C); IR ($CHCl_3$) 1715, 1655 cm^{-1}.

Diethyl 1-Hydroxynaphthalene-2,3-dicarboxylate (19). This was prepared from **1a** (81 mg, 0.50 mmol) and **9** (85 mg, 0.50 mmol) by method B. Recrystallization from *n*-hexane gave pure **19**: mp 54–54.5 °C (lit.[8] bp 163–164 °C (0.05 torr)); IR ($CHCl_3$) 1715, 1650 cm^{-1}.

4-Carboxy-2,3-bis(methoxycarbonyl)tetralone (20). This was prepared from **1a** (324 mg, 2.0 mmol) and **10** (288 mg, 2.0 mmol) by the modification of method B. After the reaction mixture was stirred under the same conditions (method B), additional stirring was continued for 13 h under reflux. Purification of the crude solid by column chromatography on silica gel using chloroform–ether (5:1) as eluting solvent gave **20**. Recrystallization from ether–petroleum ether gave pure **20**: mp 182–184 °C; IR (KCl) 3300–2900, 2700–2500, 1740, 1710, 1675, 1595 cm^{-1}; NMR ($CDCl_3$) δ 3.73 (s, 3 H), 3.84 (s, 3 H), 3.5–4.1 (m, 3 H), 6.58 (br s, 1 H), 7.3–7.6 (m, 3 H), 7.9–8.1 (m, 1 H). Anal. Calcd for $C_{15}H_{14}O_7$: C, 58.82; H, 4.61. Found: C, 58.89; H, 4.66.

4-Carboxy-2,3-bis(benzoyloxy)-3,4-dihydro-1-naphthol (21). This was prepared from **1a** (162 mg, 1.0 mmol) and **11** (236 mg, 1.0 mmol) by method B. Purification of the crude solid by column chromatography on silica gel using benzene–ether (5:1) as eluting solvent gave pure **21**: mp 82–85 °C; IR (KCl) 3300–2800, 2700–2500, 1720, 1710, 1690–1670, 1595 cm^{-1}; NMR ($CDCl_3$) δ 4.0 (br s, 1 H), 5.26 (d, 1 H, J = 1.5 Hz), 6.9–8.5 (m, 16 H); exact mass calcd for $C_{25}H_{18}O_5$, 398.1152; found, 398.1137.

1-Methoxy-11-hydroxynaphthacene-5,12-dione (22). (i) This was prepared from **1a** (41 mg, 0.25 mmol) and **12** (67 mg, 0.25 mmol) by method A. Recrystallization from toluene gave pure **22**: mp 272–273 °C (lit.[8] 263–266 °C); IR ($CHCl_3$) 1670, 1620, 1585 cm^{-1}. Demethylation of **22** with BBr_3 in methylene chloride gave 1,11-dihydroxynaphthacene-5,12-dione, mp 280.5–281 °C, which was identical with an authentic sample (lit.[8] 281–283 °C).

(ii) This was prepared from **1a** (31 mg, 0.19 mmol) and **12** (50 mg, 0.19 mmol) by method B. Recrystallization of the crude product gave pure **12**, which was identical with a sample obtained from i in all respects.

1-Methoxy-6-hydroxynaphthacene-5,12-dione (23). (i) This was prepared from **1a** (67 mg, 0.41 mmol) and **13** (110 mg, 0.41 mmol) by method A. Recrystallization from chloroform gave pure **23**: mp 263–264 °C; IR ($CHCl_3$) 1660, 1615, 1580 cm^{-1}; NMR ($CDCl_3$) δ 4.03 (s, 3 H), 7.2–7.4 (m, 1 H), 7.5–7.8 (m, 2 H), 7.8–8.1 (m, 2 H), 8.19 (s, 1 H), 8.35–8.6 (m, 2 H), 14.43 (s, 1 H). Anal. Calcd for $C_{19}H_{12}O_4$: C, 74.99; H, 3.98. Found: C, 74.86; H, 3.87. Demethylation of **23** with BBr_3 in methylene chloride gave 1,6-dihydroxynaphthacene-5,12-dione, mp 274.5 °C, which was identical with an authentic sample (lit.[8] 270–271 °C).

(ii) This was prepared from **1a** (31 mg, 0.19 mmol) and **13** (50 mg, 0.19 mmol) by method B. Recrystallization of the crude product gave pure **23**, which was identical with an authentic sample obtained from i in all respects.

1,4,6-Trihydroxynaphthacene-5,12-dione (24). This was prepared from **1a** (41 mg, 0.25 mmol), **14** (47 mg, 0.25 mmol), and NaH (60% in mineral oil, 0.825 mmol) by method B. Recrystallization from chloroform gave pure **24**: mp 290–292 °C (lit.[21] 294 °C). Acetylation of **24** by a usual method gave the acetate, which was recrystallized from chloroform to give the pure tri-

(20) Barton, D. H. R.; Bateson, J. H.; Datta, S. C.; Magnus, P. D. *J. Chem. Soc. Perkin Trans. 1* **1976**, 503.

(21) Brockmann, H.; Müller, W. *Chem. Ber.* **1959**, *92*, 1164.

acetate of **24**: mp 269–272 °C; IR ($CHCl_3$) 1770, 1680, 1620, 1580 cm^{-1}.

7-Methoxy-6-hydroxynaphthacene-5,12-dione (25). This was prepared from **1b** (48 mg, 0.25 mmol) and **5** (40 mg, 0.25 mmol) by method A. Recrystallization from chloroform gave pure **25**: mp 260.5–261.5 °C (lit.[1] 260.5–261.5 °C); IR ($CHCl_3$) 1665, 1615, 1580 cm^{-1}.

Dimethyl 8-Methoxy-1-hydroxynaphthalene-2,3-dicarboxylate (26). This was prepared from **1b** (50 mg, 0.26 mmol) and **8** (37 mg, 0.26 mmol) by method B. Recrystallization from ethanol gave pure **26**: mp 144–145 °C (lit.[4] 145.5 °C); IR ($CHCl_3$) 3330, 1725, 1705 cm^{-1}.

3-(Phenylsulfonyl)-2-cyclohexen-1-one (31). This was prepared from 3-chloro-2-cyclohexen-1-one (**30**) by the modification of the reported method.[22] Purification of the crude oil by column chromatography on silica gel using benzene–ethyl acetate (15:1) as eluting solvent gave pure **31**: IR ($CHCl_3$) 1680, 1570, 1510, 1420, 1310, 1200 cm^{-1}.

3-*endo*-Carboxynorborn-5-en-2-*endo*-ylacetic Anhydride (34). This was obtained according to the reported method.[12]

Dimethyl 3-Methoxyhomophthalate (35). This was obtained from the known[23] dimethyl 3-hydroxyhomophthalate by methylation with diazomethane. To a stirred solution of dimethyl 3-hydroxyhomophthalate (500 mg, 2.23 mmol) in ether (3 mL) was added an ethereal solution of diazomethane at 0 °C. The mixture was stirred at room temperature overnight and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using benzene and benzene–ethyl acetate (15:1) as eluting solvent to give **35**: 61% yield; bp 110 °C (0.2 torr) (lit.[24] bp 116 °C (0.4 torr)); IR ($CHCl_3$) 1730, 1595, 1470, 1435 cm^{-1}; NMR ($CDCl_3$) δ 3.62 (s, 2 H), 3.64 (s, 3 H), 3.80 (s, 3 H), 3.87 (s, 3 H), 6.81 (br d, 2 H, J = 8 Hz), 7.24 (t, 1 H, J = 8 Hz).

Reaction of the Lithium Salt of Dimethyl 3-Methoxyhomophthalate (35) with 2-Chloro-6-oxo-5,6,7,8-tetrahydro-1,4-naphthoquinone 1,2-Ethanediyl Acetal (2). The lithium salt obtained from the homophthalate **35** (119 mg, 0.50 mmol) and LDA (0.50 mmol) in anhydrous THF was treated with **2** (127 mg, 0.50 mmol) in anhydrous THF was treated with **2** (127 mg, 0.50 mmol) at −78 °C for 1 h. Workup of the reaction mixture as described for the general procedures for the cycloaddition of **1a,b** gave the [2 + 2] cycloadduct **36**: 160 mg (69%). Recrystallization from benzene–ether gave pure sample: mp 195.5–196.5 °C; IR ($CHCl_3$) 1805, 1720 cm^{-1}; NMR ($CDCl_3$) δ 1.96 (t, 2 H, J = 6.5 Hz), 2.85–3.1 (m, 4 H), 5.10 (s, 1 H), 5.49 (br s, 1 H), 6.66 (d, 1 H, J = 8 Hz), 6.87 (d, 1 H, J = 8 Hz), 7.29 (t, 1 H, J = 8 Hz); exact mass calcd for $C_{23}H_{21}O_8Cl$, 460.0923; found, 460.0918.

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Registry No. **1a**, 703-59-3; **1b**, 74794-52-8; **2**, 83043-87-2; **5**, 130-15-4; **6**, 922-67-8; **7**, 623-47-2; **8**, 762-42-5; **9**, 762-21-0; **10**, 23055-10-9; **11**, 4070-75-1; **12**, 69833-10-9; **13**, 69833-09-6; **14**, 475-38-7; **15**, 6336-86-3; **15** acetate, 88036-06-0; **16**, 948-03-8; **17**, 33950-71-9; **18**, 36112-45-5; **19**, 68376-15-8; **20**, 88036-07-1; **21**, 88036-08-2; **22**, 19938-28-4; **23**, 88036-09-3; **24**, 3677-09-6; **24** triacetate, 73682-92-5; **25**, 88036-10-6; **26**, 88036-11-7; **30**, 5682-75-7; **31**, 88036-12-8; **34**, 77411-77-9; **35**, 1214-87-5; **36**, 88036-13-9; dimethyl 3-hydroxyhomophthalate, 43071-26-7.

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Regiospecific Synthesis of Aromatic Compounds via Organometallic Intermediates. 3. *n*-Alkyl-Substituted Benzene[1]

Kalathil C. Eapen,[2a] Sujan S. Dua,[2b] and Christ Tamborski*

Air Force Wright Aeronautical Laboratories, Materials Laboratory, Wright Patterson Air Force Base, Ohio 45433

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High molecular weight tri- and tetra-*n*-alkylbenzenes have been synthesized by the cross-coupling of the appropriate chlorinated benzenes with long-chain *n*-alkylmagnesium bromides using (1,2-bis(diphenylphosphino)ethane)nickel(II) chloride [$NiCl_2$(dppe)] as catalyst. The reactions proceeded without any positional scrambling or alkyl group isomerization. A new method is described for the preferential substitution of one chlorine atom by an *n*-alkyl group in 1,3,5-trichlorobenzene. The reaction between an *n*-alkylmagnesium bromide and 1,3,5-trichlorobenzene catalyzed by nickel acetylacetonate [$Ni(acac)_2$] at low temperature and in tetrahydrofuran solvent favors monosubstitution. The cross-coupling reactions of these *n*-alkyldichlorobenzenes with other *n*-alkylmagnesium bromides, in the presence of $NiCl_2$(dppe), proceeded at a much slower rate than those of 1,3,5-trichlorobenzene to yield the asymmetric 1,3,5-tri-*n*-alkylbenzenes.

Introduction

The formation of a carbon–carbon σ bond by the nickel–phosphine complex catalyzed cross-coupling of Grignard reagents with organic halides has received considerable attention since its discovery in 1972.[3,4] The reaction has been successfully extended to a variety of Grignard reagents and organic halides using different nickel–phosphine complexes. Besides Grignard reagents, other organometallic reagents have been employed for cross-coupling reactions, using in many cases, $Pd[PPh_3]_4$ as a suitable catalyst precursor. Such organometallic reagents include those of lithium, zinc, boron, aluminum, and zirconium.[5,6]

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