A Novel Synthetic Method for Crown Ethers by a Redox Reaction Utilizing the Intermediate from Diphenyldiazomethane and 2,3-Dichloro-5,6-dicyanobenzoquinone

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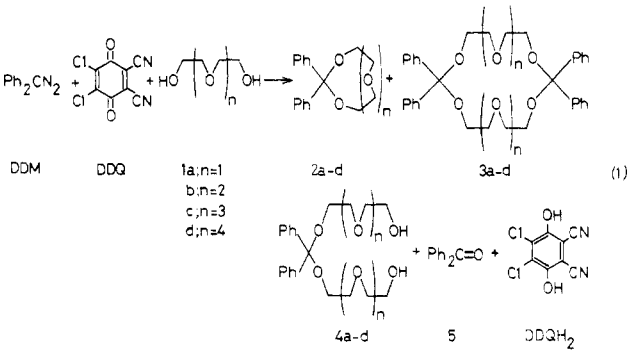
A synthetic method for the new crown ethers possessing a diphenylmethylene moiety by the reaction of diphenyldiazomethane (DDM) and 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) under the influence of oligoethylene glycols is described. The two types of crown ethers with 1:1 and 2:2 composition of diphenylmethylene/oligoethylene glycol moiety were obtained together with the noncyclic 1:2 compositional diols. The product distributions were dependent on the relative quantities and the manner of addition of the oligoethylene glycols.

Since the pioneering work of Pedersen on the preparation and properties of macrocyclic polyethers (crown ethers),[1] there have been numerous reports of syntheses of a wide variety of crowns.[2] The general methods proposed for the synthesis of crown compounds are a modified Williamson ether synthesis by the reactions of oligoethylene glycols with oligoethylene glycol dichlorides or ditosylates[1a,2,3] and of oligoethylene glycols with arenesulfonyl or alkanesulfonyl chlorides,[4] in the presence of suitable template metal cations.

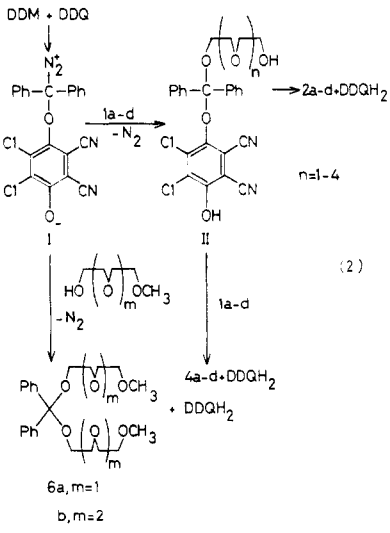
Recently, we reported the synthesis of various cyclic and noncyclic benzophenone acetals and thioacetals in high yields by means of the reaction of diphenyldiazomethane (DDM) with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) under the influence of the corresponding alcohols and thiols.[5] The preliminary experiment showed that these redox reactions were also applicable for di- and triethylene glycols to afford so-called crown ethers incorporated with a diphenylmethylene subunit. Thus, we attempted to extend these simple synthetic methods for preparing crown compounds to the higher series of oligoethylene glycols. In this paper, the preparation of the desired ethereal macrocycles **2** and **3** derived from di-, tri-, tetra-, penta-, and hexaethylene glycols (**1**) is described and the effects of the relative amount of glycols used on the product distributions are also discussed.

Results and Discussion

Reaction of DDM with DDQ in the Presence of Oligoethylene Glycols (Method A). Reaction of DDM with DDQ in the presence of 1, 3, and 5 equiv of di-, tri-, tetra-, and pentaethylene glycols (**1**) in dry benzene at 20–25 °C gave three macroethereal products, **2**, **3**, and **4**, incorporated with diphenylmethylene moiety together with benzophenone (10–20%) and an almost quantitative amount of 2,3-dichloro-5,6-dicyanohydroquinone ($DDQH_2$; eq 1). The reaction conditions and the product distributions are seen in Table I. The two macrocyclic products **2** and **3** have structures formally made by the dehydrocyclization of oligoethylene glycols toward diphenylmethylene with the aid of DDQ; compounds **3** have a dimeric formula of **2**. The noncyclic macroethers **4** possess diol structures of two molecules of glycols linked at the central carbon atom of diphenylmethylene.



These overall redox reactions can be explained to proceed via diazonium betaine (I; or carbonium betaine derived from it by the loss of N_2) intermediate as previously demonstrated.[5,6] The nucleophilic attack of the oligoethylene glycols to this intermidiate is expected to provide a relatively unstable product (II) which leads to cyclic **2** via an internal S_N2 displacement in competition with an external S_N2 attack of another glycol to afford noncyclic **4** (eq 2). In accordance with the schematic diagram,



reaction with di- and triethylene glycol monomethyl ethers has been found to give only noncyclic macroethers **6**. On

(1) (a) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017. (b) *Ibid.* **1970**, *92*, 386, 391.

(2) (a) Christensen, J. J.; Eatough, D. J.; Izatt, R. M. *Chem. Rev.* **1974**, *74*, 351. (b) Izatt, R. M.; Christensen, J. J. "Synthetic Multidentate Macrocyclic Compounds"; Academic Press; New York, 1978.

(3) (a) Cook, F. L.; Caruson, T. C.; Byrne, M. P.; Browers, C. W.; Speck, D. H.; Liotta, C. L. *Tetrahedron Lett.* **1974**, 4029. (b) Jones, G.; Ranson, C. R.; Reese, C. B. *Synthesis* **1976**, 515.

(4) (a) Kuo, P.-L.; Miki, M.; Okahara, M. *J. Chem. Soc., Chem. Commun.* **1978**, 504. (b) Kuo, P.-L.; Miki, M.; Ikeda, I.; Okahara, M. *Tetrahedron Lett.* **1978**, 4273.

(5) Oshima, T.; Nishioka, R.; Nagai, T. *Tetrahedron Lett.* **1980**, 3919.

(6) Oshima, T.; Nagai, T. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 2039.

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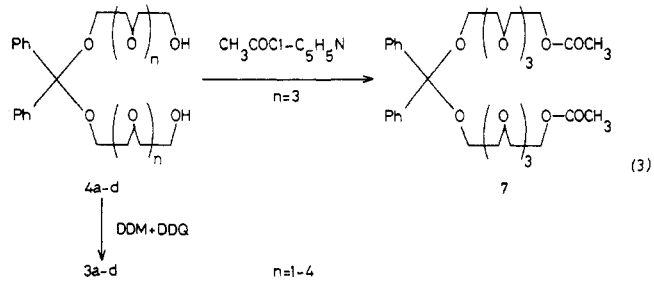
Table I. Reaction Conditions and Product Distribution

run	glycols[a] (rel equiv)	method	rctn time, h	products,[b] % yield 2	3	4	5
1	1a (1)	A	2	45	5	18	9
2	1a (3)	A	2	38	3	37	9
3	1a (5)	A	2	10	tr	43	3
4	1a (0.5)	B	2	84[c]	0	0	25
5	1b (1)	A	2	27	13	21	16
6	1b (3)	A	2	12	5	52	16
7	1b (5)	A	2	8	tr	68	14
8	1b (0.5)	B	2	79[c]	0	0	27
9	1b (1)	B	2	47	5	6	15
10	1b (3)	B	2	23	8	18	17
11	1c (1)	A	2	38	5	18	18
12	1c (1)	A	4	41	6	15	16
13	1c (3)	A	2	15	2	36	21
14	1c (5)	A	2	7	tr	44	18
15	1c (0.5)	B	2	70[c]	0	0	23
16	1d (1)	A	2	48	tr	19	16
17	1d (0.5)	B	2	89[c]	0	0	22
18	1e (0.5)	B	2	70[c]	0	0	16

[a] 1a; di-, 1b; tri, 1c; tetra-, 1d; penta-, and 1e; hexaethylene glycol. [b] Unless otherwise noted, based on DDM used. [c] Based on glycols.

the other hand, the formation of 3 may be attributed to the nucleophilic attack of the resulting 4 toward the betaine intermediate and the follow-up internal S_N2 displacement as well as the case of 2. The evidence of such an intermediary 4 was realized by the observation that 4 were easily transformed into 3 when treated with DDM and DDQ (see below). As was previously exemplified,[6] the present reaction system is very sensitive to water, so the reagents and the equipment must be carefully dried before use. Thus, the unfortunate occurrence of benzophenone can be ascribed to the residual water.

The purified 2 and 3 were all colorless prisms except for oily 3d, and the structures of these ethereal macrocyclic compounds were ascertained by the IR, NMR, mass spectra, and elemental analyses. A preliminary experiment showed that 2c remains unchanged on standing overnight in methanol solution containing excess water and CH_3ONa but completely degrades into benzophenone and tetraethylene glycol even when stirred for 5 h in methanol with a small amount of hydrochloric acid. The IR spectra of oily 4 showed the strong hydroxyl absorption at 3450–3470 cm^{-1} and several characteristic bands assignable to the ethereal bonds at 1020–1140 cm^{-1}. Mass spectra of 4 revealed $m/e = M^+ - (OCH_2CH_2)_nOH$ as the base peaks. Compounds 4 were separated by high-performance liquid chromatography (HPLC), but their elemental analyses deviated due to the hygroscopic property. Therefore, we confirmed the diol structures by acetylation into 7. Further evidence was offered by the cyclization into 3 when treated with DDM and DDQ (eq 3).



(3)

As is seen in Table I, increase of oligoethylene glycols used in method A brings about considerable decrease in the yields of cyclic 2 and 3. But the yields of noncyclic 4 reversely increased with such an increment of glycols. These results mean that the intramolecular cyclization giving 2 was highly disturbed by the growing intermolecular reaction giving 4 with the increasing amounts of glycols.

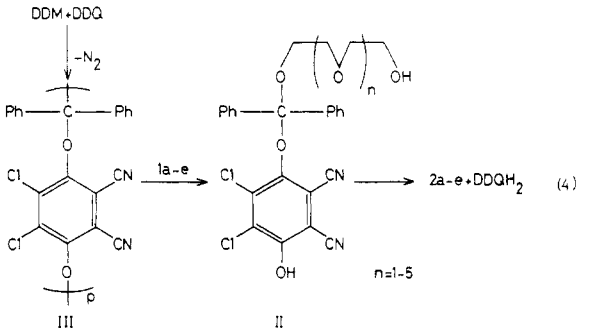
Being markedly different from the conventional synthetic methods of macrocyclic compounds,[7] the present reactions can be made under mild conditions without any special template cation, high dilution technique, or elevated temperature. Also relatively short reaction times (2 h) are sufficient to complete the reactions. Extended reaction times (4 h) did not greatly affect the product distributions; essentially similar percentages of 2, 3, and 4 were obtained in the case of triethylene glycol (runs 11 and 12). The facile preparation of these macrocyclic compounds can be essentially ascribed to the property of DDQ as a good oxidizing agent[8] in addition to the easy formation of diazonium betaine. Indeed, the precipitate of reduced $DDQH_2$ begins to appear at the early stage of the reactions.

Reaction of DDM with DDQ Followed by the Addition of Oligoethylene Glycols (Method B). The rapid reaction of DDM and DDQ is found to give a resinous poly(2,3-dichloro-5,6-dicyanohydroquinone benzhydryl ether) (III) generated by the successive combination of diazonium betaine, if any hydrolytic or solvolytic additive is absent.[6] Since the polyether undergoes rapid hydrolysis and methanolysis to give the same products as those obtained from the method A treatment,[6] we attempted to utilize its solvolytic property in the cyclization of oligoethylene glycols.

Dropwise addition of 0.5 equiv of glycols into the reaction solution of DDM and DDQ gave 2 in 70–90% yields (based on glycols used) without any detectable formation of 3 and 4. The selective and convenient formation of the desired 2 may be performed by both the slow addition and the small amounts of glycols. Under these conditions, most of the glycols exclusively attack the diphenylmethylene moieties in the polyether linkage so that the resulting II has an enough time to undergo internal S_N2 displacement, because free glycols are rarely present in the reaction solutions (eq 4). As represented in the case of triethylene

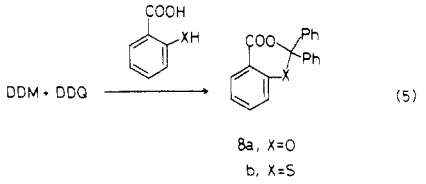
(7) (a) Kawamura, N.; Miki, M.; Ikeda, I.; M. Okahara, *Tetrahedron Lett.* **1979**, 535. (b) Newkom, G. R.; Khoshboo, F. D.; Nayak, A.; Benton, W. H. *J. Org. Chem.* **1978**, *43*, 2685. (c) Greene, R. N. *Tetrahedron Lett.* **1972**, 1973.

(8) Walker, D.; Hiebert, J. D. *Chem. Rev.* **1967**, *67*, 153.



glycol (runs 9 and 10), however, the increased addition (1 or 3 equiv) of glycol resulted in the production of **3** and **4** in addition to the major **2**. This phenomenon can be similarly ascribed to the further solvolysis of resulting II by the increased glycol as already demonstrated in method A. The present method B, of course, yields about twice as much cyclic **2** than the corresponding method A (runs 5 and 9), because the former method furnishes the reaction conditions with more II and less glycol especially at the early stage of the reaction.

Although a complete comparison has not been established for the other glycols, method B with 1 equiv of glycols appears to be preferable to method A for the more production of 1:1 macrocyclic **2**. Further advantage of method B is the possible extension to the acidic reagents which can decompose DDM.[9] For example, salicylic and thiosalicylic acids can be successfully cyclized in treatment according to method B (eq 5).



Experimental Section

All melting points were taken with a Laboratory Devices Mel-Temp instrument and are uncorrected. Infrared spectra were recorded on a Hitachi 260-10 spectrometer. Proton NMR spectra were taken at 90 MHz on a Varian EM-390 spectrometer. Mass spectral data were obtained with a Hitachi RMU-6E mass spectrometer at an ionization potential of 70 eV. High-performance liquid chromatography (HPLC) analyses were accomplished with use of naphthalene as an internal standard with a JASCO Trirotor high-pressure liquid chromatograph equipped with a 25 cm × 4 mm column packed with octadecylsilane on silica gel and with methanol–water (5:1) as an eluent.

Materials. DDM was prepared according to the procedure described by Smith and Howard[10]; mp 29–30 °C (from light petroleum). Oligoethylene glycols were distilled under reduced pressure. DDQ, salicylic and thiosalicylic acids, di- and triethylene glycol monomethyl ethers were of commercial origin and were used without further purification. Benzene was refluxed over lithium aluminum hydride and was fractionated.

Reaction of DDM with DDQ in the Presence of Oligoethylene Glycols (Method A). General procedure was described in the case of triethylene glycol. To a stirred suspension of DDQ (1.18 g, 5.2 mmol) in benzene (20 mL) was added dropwise over 1 h at 20–25 °C a benzene solution (10 mL) of DDM (1.0 g, 5.2 mmol) and 1 equiv of triethylene glycol (0.78 g, 5.2 mmol). After the mixture was stirred for 1 h, the precipitated $DDQH_2$ was filtered off and was washed with benzene (20 mL × 3). The washing and filtrate parts were combined, washed with 5% aqueous sodium carbonate (10 mL × 3) and then with NaCl saturated water (10 mL × 5), dried over anhydrous sodium sulfate, and concentrated in vacuo to give a pale-brown viscous oil. The oily products were column chromatographed on alumina. Careful successive elution gave benzophenone with light petroleum–benzene (1:1), 1:1 macrocyclic **2b** with benzene–ether (1:3), 2:2 macrocyclic **3b** with ether, and 1:2 noncyclic **4b** with benzene–methanol (20:1). In the case of diethylene glycol, 2:2 macrocyclic **3a** was eluted with benzene–ether (1:1) before 1:1 product **2a**. Column chromatographic separation of **3c** and **4c** or **3d** and **4d** was unsuccessful so that the yields of these compounds were determined by means of the HPLC, using naphthalene as an internal standard. As **4c** and **4d** isolated by the HPLC were colorless hygroscopic oils, structural evidence was demonstrated by conversion into **3c** and **3d** by treatment with DDM and DDQ and also by esterification with acetyl chloride. The structures of 1:1 and 2:2 macrocyclic compounds **2** and **3** were determined as follows.

Diphenyl-8-crown-3 (2a): mp 101–103 °C (from ether); IR (KBr) 2910, 1130, 1110 cm^{-1}; NMR ($CDCl_3$) δ 3.7–3.8 (m, OCH_2CH_2O, 8 H), 7.1–7.6 (m, Ph, 10 H); MS *m/e* 270 (M^+). Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.52; H, 6.71.

Diphenyl-11-crown-4 (2b): mp 105–106 °C (from ether); IR (KBr) 2900, 1128, 1107 cm^{-1}; NMR ($CDCl_3$) δ 3.7–3.8 (m, OCH_2CH_2O, 12 H), 7.1–7.6 (m, Ph, 10 H); MS *m/e* 314 (M^+). Anal. Calcd for $C_{19}H_{22}O_4$: C, 72.59; H, 7.05. Found: C, 72.58; H, 7.06.

Diphenyl-14-crown-5 (2c): mp 89–90 °C (from ether); IR (KBr) 2885, 1132, 1102 cm^{-1}; NMR ($CDCl_3$) δ 3.8–3.9 (m, OCH_2CH_2O, 16 H), 7.1–7.6 (m, Ph, 10 H); MS *m/e* 358 (M^+). Anal. Calcd for $C_{21}H_{26}O_5$: C, 70.37; H, 7.31. Found: C, 70.46; H, 7.28.

Diphenyl-17-crown-6 (2d): mp 61–62 °C (from ether); IR (KBr) 2880, 1138, 1105 cm^{-1}; NMR ($CDCl_3$) δ 3.5–3.8 (m, OCH_2CH_2O, 20 H), 7.1–7.5 (m, Ph, 10 H); MS *m/e* 402 (M^+). Anal. Calcd for $C_{23}H_{30}O_6$: C, 68.63; H, 7.51. Found: C, 68.78; H, 7.58.

Diphenyl-20-crown-7 (2e): mp 62–63 °C (from ether); IR (KBr) 2890, 1140, 1107 cm^{-1}; NMR ($CDCl_3$) δ 3.7–3.9 (m, OCH_2CH_2O, 24 H), 7.2–7.6 (m, Ph, 10 H); MS *m/e* 446 (M^+). Anal. Calcd for $C_{25}H_{34}O_7$: C, 67.24; H, 7.68. Found: C, 67.31; H, 7.78.

Tetraphenyl-16-crown-6 (3a): mp 182–183 °C (from ether); IR (KBr) 2876, 1090, 1018 cm^{-1}; NMR ($CDCl_3$) δ 3.3–3.8 (m, OCH_2CH_2O, 16 H), 7.1–7.6 (m, Ph, 20 H); MS *m/e* 540 (M^+). Anal. Calcd for $C_{34}H_{36}O_6$: C, 75.53; H, 6.71. Found: C, 75.57; H, 6.73.

Tetraphenyl-22-crown-8 (3b): mp 167–168 °C; IR (KBr) 2875, 1096, 1018 cm^{-1}; MS *m/e* 628 (M^+). Anal. Calcd for $C_{38}H_{44}O_8$: C, 72.59; H, 7.05. Found: C, 72.32; H, 6.90. NMR spectrum could not be obtained because of the insolubility in common solvents.

Tetraphenyl-28-crown-10 (3c): mp 89–91 °C (from ether); IR (KBr) 2875, 1090, 1015 cm^{-1}; NMR ($CDCl_3$) δ 3.4–3.8 (m, OCH_2CH_2O, 32 H), 7.2–7.7 (m, Ph, 20 H); MS *m/e* 716 (M^+). Anal. Calcd for $C_{42}H_{52}O_{10}$: C, 70.37; H, 7.31. Found: C, 70.35; H, 7.31.

Tetraphenyl-34-crown-12 (3d): colorless oil; IR (neat) 2880, 1098, 1025 cm^{-1}; NMR ($CDCl_3$) δ 3.3–3.7 (m, OCH_2CH_2O, 40 H), 7.1–7.6 (m, Ph, 20 H); MS *m/e* 804 (M^+). Anal. Calcd for $C_{46}H_{60}O_{12}$: C, 68.63; H, 7.51. Found: C, 68.69; H, 7.58.

Reaction with Di- and Triethylene Glycol Monomethyl Ethers. This reaction was carried out by use of 2 equiv of monomethyl ethers according to method A. Column chromatographic treatment (on alumina) of the reaction mixtures gave colorless oily **6a** and **6b** with benzene–methanol (20:1) as an eluent.

6a: 85% yield; IR (neat) 2870, 1095, 1020 cm^{-1}; NMR ($CDCl_3$) δ 3.35 (s, OCH_3, 6 H), 3.4–3.7 (m, OCH_2CH_2O, 16 H), 7.1–7.5 (m, Ph, 10 H); MS *m/e* 285 ($M - (OCH_2CH_2)_2OCH_3$). Anal. Calcd for $C^{23}H_{32}O_6$: C, 68.29; H, 7.97. Found: C, 68.00; H, 7.93.

6b: 90% yield; IR (neat) 2875, 1100, 1022 cm^{-1}; NMR ($CDCl_3$) δ 3.36 (s, OCH_3, 6 H), 3.4–3.8 (m, OCH_2CH_2O, 24 H), 7.2–7.6 (m, Ph, 10 H); MS *m/e* 329 ($M - (OCH_2CH_2)_3OCH_3$). Anal. Calcd for $C_{27}H_{40}O_8$: C, 65.83; H, 8.19. Found: C, 65.53; H, 8.28.

Reaction of DDM with DDQ Followed by Addition of Oligoethylene Glycols (Method B). General procedure was described in the case of triethylene glycol. To a stirred suspension of DDQ (1.18 g, 5.2 mmol) in benzene (20 mL) was added all at once a benzene solution (10 mL) of DDM (1.0 g, 5.2 mmol) at 20–25 °C. The reaction was very vigorous with the violent evo-

(9) Buckley, A.; Chapman, N. B.; Dack, M. R. J.; Shorter, J.; Wall, H. M. *J. Chem. Soc.* **1968**, 631.

(10) Smith, L. I.; Howard, K. L. "Organic Syntheses", Collect. Vol. III; Wiley: New York, 1955; p 351.

lution of N_2 and gave a resinous product. The 0.5 equiv of triethylene glycol (0.39 g, 2.6 mmol) in benzene (10 mL) was added dropwise over 1 h to the reaction solution. After the solution was stirred for 1 h followed by treatment with a small amount of water, the precipitated $DDQH_2$ was filtered off and washed with benzene (20 mL × 3). The same workup technique as for method A was adopted to give a pale-brown viscous oil. The oily products were column chromatographed (alumina) with light petroleum–benzene (1:1) as an eluent to afford benzophenone and then with benzene–ether (1:3) to afford 1:1 macrocyclic **2b**, but possible **3b** and **4b** were not detectable when 0.5 equiv of glycol was used. However, 1 or 3 equiv of triethylene glycol brought about the formation of **3b** and **4b** in addition to **2b**.

Conversion of 4 into 3. This reaction was made by employing 0.5 equiv of **4** with respect to DDM and DDQ according to method B. The converted products **3** were isolated by column chromatography on alumina with ether or ether–methanol (20:1) as an eluent. The yields were respectively 65% (**3a**), 74% (**3b**), 58% (**3c**), and 73% (**3d**).

Acetylation of 4b. To a benzene solution (10 mL) of **4b** (300 mg, 0.47 mmol) was added all at once a benzene solution (10 mL) of acetyl chloride (100 mg, 1.27 mmol) and pyridine (150 mg, 1.9 mmol). After the solution stood for 1 h, precipitated salt was filtered off and washed with benzene (10 mL × 3). The washing and filtrate were combined, washed with 5% aqueous sodium carbonate (5 mL × 3) and then with NaCl saturated water (5 mL × 3), dried over anhydrous sodium sulfate, and evaporated in vacuo at 50 °C to give a pale-yellow viscous oil. The oily products were gel chromatographed (Sephadex LH-20, Pharmacia), with methanol as an eluent, to afford **7**: colorless oil; 80% yield; IR (neat) 2780, 1735, 1235, 1105 cm^{-1}; NMR ($CDCl_3$) δ 2.0 (s, $COCH_3$, 6 H), 3.3–3.7 (m, OCH_2CH_2O, 28 H), 4.0–4.2 (m, CH_2OCO, 4 H), 7.1–7.5 (m, Ph, 10 H); MS *m/e* 401 (M – $(OCH_2CH_2)_4OCOCH_3$). Anal. Calcd for $C_{33}H_{48}O_{12}$: C, 62.24; H, 7.60. Found: C, 62.07; H, 7.60.

Reaction with Salicylic and Thiosalicylic Acids. To a stirred reaction solution of DDM (1.0 g, 5.2 mmol) and DDQ (1.18 g, 5.2 mmol) in benzene (20 mL) was added dropwise for 1 h a benzene solution (10 mL) of salicylic acid (0.72 g, 5.2 mmol) or thiosalicylic acid (0.80 g, 5.2 mmol). After the solution was stirred for 1 h, the precipitated $DDQH_2$ was filtered off and washed with benzene (20 mL × 3). The same workup technique as for method B was adopted to give a crude reaction mixture as a brown paste. **8a** and **8b** were isolated by alumina column chromatography with benzene–methanol (20:1) as an eluent.

8a: mp 104–106 °C (from benzene); 55% yield; IR (KBr) 1742, 1301, 765 cm^{-1}; NMR ($CDCl_3$) δ 7.2–7.6 (m, aromatic H). Anal. Calcd for $C_{20}H_{14}O_3$: C, 79.46; H, 4.67. Found: C, 79.72; H, 4.67.

8b: mp 178–180 °C (from benzene); 62% yield; IR (KBr) 1721, 1275, 748 cm^{-1}; NMR ($CDCl_3$) δ 7.2–7.8 (m, aromatic H). Anal. Calcd for $C_{20}H_{14}O_2S$: C, 75.45; H, 4.43. Found: C, 75.76; H, 4.63.

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Registry No. 1a, 111-46-6; **1b**, 112-27-6; **1c**, 112-60-7; **1d**, 4792-15-8; **1e**, 2615-15-8; **2a**, 77130-21-3; **2b**, 77130-22-4; **2c**, 81194-61-8; **2d**, 81194-62-9; **2e**, 81194-63-0; **3a**, 81194-64-1; **3b**, 81194-65-2; **3c**, 81194-66-3; **3d**, 81194-67-4; **4a**, 81205-68-7; **4b**, 81205-69-8; **4c**, 81194-68-5; **4d**, 81194-69-6; **5**, 119-61-9; **6a**, 81194-70-9; **6b**, 81194-71-0; **7**, 81194-72-1; **8a**, 1433-60-9; **8b**, 19185-81-0; DDQ, 84-58-2; DDM, 883-40-9; $DDQH_2$, 4640-41-9; salicyclic acid, 69-72-7; thiosalicylic acid, 147-93-3.

Palladium-Catalyzed Cross-Coupling of (2-Ethoxyvinyl)boranes with Aryl and Benzyl Halides. A New Method for Conversion of Organic Halides into Aldehydes with Two More Carbon Atoms

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Vinyl ethers **3** can be synthesized in high yields by the cross-coupling of an aryl or benzyl halide with tris(2-ethoxyvinyl)borane (**1**) or (2-ethoxyvinyl)-1,3,2-benzodioxaborole (**2**) in the presence of 1 mol % of a palladium complex such as $PdCl_2(PPh_3)_2$, $Pd(OAc)_2(PPh_3)_2$, or $Pd(PPh_3)_4$ and a base while retaining the original configuration of the double bond in (2-ethoxyvinyl)boranes. No noticeable quantities of biaryls or conjugated dienes were found in this reaction. The reaction did not proceed in the absence of a base. This new vinyl ether synthesis was found to be applicable to aryl halides substituted with a variety of functional groups such as halogen, methoxy, carboethoxy, and acetyl groups. Electron-attracting substituents facilitate the coupling. Since vinyl ethers **3** thus obtained can readily be hydrolyzed to give aldehydes (eq 4), the sequence (eq 1–4) provides an efficient new method for converting an aryl halide into an aldehyde with two more carbon atoms.

It is becoming increasingly apparent that palladium-catalyzed reactions of organoboranes are useful in organic synthesis. We have thus shown that alkenylboranes react with a variety of organic halides in the presence of a catalytic amount of a palladium complex and a base to give the conjugated alkadienes due to cross-coupling while retaining the configurations of the starting alkenylboranes and the alkenyl halides.[1-3] The usefulness of this coupling reaction in synthesis arises from the fact that the alkenylboranes are readily available via monohydroboration of alkynes and are quite inert toward functional groups and the couplings can be carried out without protecting these groups. Thus, this cross-coupling reaction provides a versatile method for the synthesis of the conjugated alkadienes.

(1) (a) N. Miyaura, K. Yamada, and A. Suzuki, *Tetrahedron Lett.*, 3437 (1979). (b) N. Miyaura, H. Suginome, and A. Suzuki, *ibid.*, 127 (1981).

(2) N. Miyaura and A. Suzuki, *J. Chem. Soc., Chem. Commun.*, 867 (1979).

(3) N. Miyaura, T. Yano, and A. Suzuki, *Tetrahedron Lett.*, 2865 (1980).

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