Synthesis of Substituted Crown Ether Acetals

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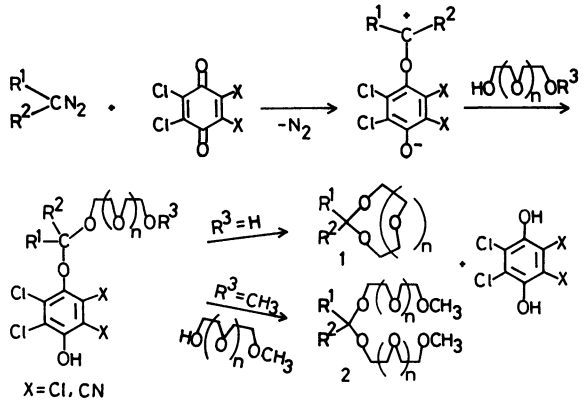
Synopsis. Reactions of phenyldiazomethane with chloranil and of 1-phenyldiazoethane and 9-diazofluorene with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone in the presence of oligoethylene glycols and its monomethyl ethers gave the corresponding substituted crown ether acetals and open-chain analogues.

Crown ether acetals (**1**) which involve one (or more) $-OCR^1R^2O-$ function in the crown rings, are interesting compounds as they exhibit cation-binding properties[1] and also undergo polymerization[2] and hydrolysis.[1b,3] A few varieties in which R^1 and/or R^2 are hydrogen were hitherto available by conventional methods using acid catalysts[2a,4] ion-exchange resins[5] from aldehydes and oligoethylene glycols. However, the formation of disubstituted acetals is noticeably difficult by the traditional methods.[6] Therefore, a new type of method is required to synthesize various disubstituted acetals.

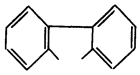
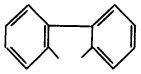
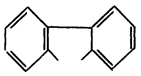
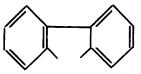
We have recently reported a new method for the synthesis of diphenyl-substituted crown ether acetals ($Ph_2C(OCH_2CH_2)_nO$, n=1—6) by way of the redoxical acetalization caused by three reactants, i.e., diphenyldiazomethane (DDM), 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ), and oligoethylene glycols.[7]

We have found that this technique is conveniently applicable for the preparation of several new substituted crown ether acetals (**1a—c**, **e**, and **f**) and open-chain analogues (**2a**, **b**) when adapted to other diazoalkanes like phenyldiazomethane (**3**), 1-phenyldiazoethane (**4**), and 9-diazofluorene (**5**). In a reaction with **3**, DDQ provided significant amounts of bicyclic dione derivatives[8] formed from the dipolar addition to the C=C bond, so that chloranil was utilized for this diazoalkane as an alternative quinone. As previously described,[7] this promising acetalization proceeds via a reaction sequence involving the formation of 1:1 betaines from diazoalkanes and quinones, subsequent nucleophilic attack of glycols, and final splitting into acetals and hydroquinones (Scheme).



The present diazoalkanes provided only about half yields of acetals compared to DDM as tested for the fourteen-membered crown acetals (Table). The drop in the yields may be due to two reasons. First, diazoalkanes, **3** and **4**, tended to thermally decompose to azines and further reacted with the generated hydroquinones giving hydroquinone diethers. However, stable **5** provided 9,9′-bifluorenylidene and oxirane[9] as

Table 1. Crown Ether Acetals (**1a—f**) or Open Acetals (**2a**, **b**) from Reactions of Diazoalkanes, Quinones, and Oligoethylene Glycols or Its Monomethyl Ethers

Diazoalkanes	Quinones	Reaction times/h[a]	Acetal **1**(n) and **2**(n)	Substituents R^1	Substituents R^2	Yield[b] %
Phenyldiazomethane (**3**)	Chloranil	0.5	**1a**(3)	Ph	H	21
1-Phenyldiazoethane (**4**)	DDQ	1	**1b**(1)	Ph	CH_3	30
4	DDQ	1	**1c**(3)	Ph	CH_3	16
Diphenyldiazomethane (DDM)	DDQ	2	**1d**(3)	Ph	Ph	38[c]
9-Diazofluorene (**5**)	DDQ	6	**1e**(3)			19
5	DDQ	6	**1f**(4)			16
5	DDQ	3	**2a**(1)			33
5	DDQ	3	**2b**(2)			27

a) Chosen depending on the relative reactivities of diazoalkanes. b) Isolated yields by chromatography on alumina. c) Cited from Ref. 7.

by-products. Second, newly prepared crown acetals are appreciably sensitive to water as is evidenced by their complete degradation into carbonyl components and alcohols even after standing one week in a stoppered NMR tube(in $CDCl_3$). This observation, combined with the presence of fairly amounts of benzaldehyde, acetophenone, and 9-fluorenone in the crude reaction mixtures, implies that some parts of acetals were lost during such work-up treatments as washing with aqueous alkaline solution and separation by column chromatography.

However, our technique is expected to play a role in the preparation of many-membered disubstituted crown ether acetals for which no other efficient method has been found in a literature search.

Experimental

Infrared spectra were recorded on a Hitachi 260-10 and on a Perkin Elmer 983G spectrometer. ^1H 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.

Materials. DDQ was of commercial origin (98%, Aldrich Chemical Co. Inc.) and was used without further purification. Chloranil was recrystallized from benzene. Phenyldiazomethane (**3**),[10] 1-phenyldiazoethane (**4**),[11] and 9-diazofluorene (**5**)[12] were prepared according to the procedure described in the literatures. Oily **3** and **4** were contaminated with 10—30% azines, but were used without purification because of their thermal instability. The **5** was recrystallized from ether; mp 94—95 °C. Benzene was refluxed over lithium aluminum hydride and was fractionated.

General Procedure. To a stirred solution of DDQ (1.2 g, 5.0 mmol) in benzene (20 ml) was added dropwise over 10 min at 20—25 °C a benzene solution (10 ml) of an 1 equiv mixture of diazoalkane and oligoethylene glycol (3 equiv for oligoethylene glycol monomethyl ether). After the mixture was stirred for the requisite times, the precipitated hydroquinone was filtered off and was washed with benzene (10 ml×3). The filtrate and washing parts were combined and were treated according to the previous manner.[7] The crude acetals containing such by-products as azines, hydrolyzed carbonyl compounds, hydroquinone diethers, and 9,9′-bifluorenylidene were column chromatographed on alumina. After a complete elution of these by-products, the acetals were eluted with benzene (**1b**), ether (**1a, c**), ether-ethanol (50:1) (**2a, b**), and ether-methanol (4:1) (**1e, f**). The structures of these acetals were established by following analytical data.

2-Phenyl-1,3,6,9,12-pentaoxacyclotetradecane (1a): Colorless viscous oil; IR (film) 2867, 1116 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.6—3.9 (16H, m), 5.72 (1H, s), 7.2—7.6 (5H, m); MS m/z 282 (M^+). Found: C, 63.66; H, 7.76%. Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85%.

2-Methyl-2-phenyl-1,3,6-trioxacyclooctane (1b): Colorless viscous oil; IR(film) 2914, 1145 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.60 (3H, s), 3.5—4.0 (8H, m), 7.3—7.7 (5H, m); MS m/z 208 (M^+). Found: C, 69.27; H, 7.80%. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74%.

2-Methyl-2-phenyl-1,3,6,9,12-pentaoxacyclotetradecane (1c): Colorless viscous oil; IR (film) 2869, 1126 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.53 (3H, s), 3.4—3.7 (16H, m), 7.1—7.5 (5H, m); MS m/z 296 (M^+). Found: C, 64.79; H, 8.18%. Calcd for $C_{16}H_{24}O_5$: C, 64.84; H, 8.16%.

2,2-(Biphenyl-2,2′-diyl)-1,3,6,9,12-pentaoxacyclotetradecane (1e): Mp 128—129 °C, colorless prisms (from ether); IR (KBr) 2870, 1115 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.5—4.2 (16H, m), 7.2—7.7 (8H, m), MS m/z 356 (M^+). Found: C, 70.56; H, 6.81%. Calcd for $C_{21}H_{24}O_5$: C, 70.76; H, 6.79%.

2,2-(Biphenyl-2,2′-diyl)-1,3,6,9,12,15-hexaoxacycloheptadecane (1f): Mp 97—98 °C, colorless prisms (from ether); IR (KBr) 2860, 1072 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.5—4.0 (20H, m), 7.2—7.6 (8H, m), MS m/z 400 (M^+). Found: C, 69.88; H, 7.18%. Calcd for $C_{23}H_{28}O_6$: C, 69.98; H, 7.05%.

Fluorenone Bis(3,6-dioxaheptyl) Acetal (2a): Colorless viscous oil; IR (film) 2877, 1111 cm^{-1}; ^1H NMR($CDCl_3$) δ=3.30 (6H, s), 3.3—3.7 (16H, m), 7.2—7.7 (8H, m); MS m/z 402 (M^+). Found: C, 68.44; H, 7.47%. Calcd for $C_{23}H_{30}O_6$: C, 68.63; H, 7.51%.

Fluorenone Bis(3,6,9-trioxadecyl) Acetal (2b): Colorless viscous oil; IR (film) 2875, 1111 cm^{-1}; ^1H NMR δ=3.30 (6H, s), 3.4—3.7 (24H, m), 7.2—7.6 (8H, m); MS m/z 490 (M^+). Found: C, 66.40; H, 7.72%. Calcd for $C_{27}H_{38}O_8$: C, 66.10; H, 7.81%.

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