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# Deprotection of Acetals and Silyl Ethers Using Some $\pi$-Acceptors

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**Synopsis.** Hydrolysis of dodecanal dimethyl acetal and dodecyl silyl ethers in MeCN–$H_2O$ was examined using a catalytic amount of $\pi$-acceptors such as 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ), tetracyanoethylene (TCNE), 7,7,8,8-tetracyanoquinodimethane (TCNQ), 2,3,5,6-tetrafluoro-7,7,8,8-tetracyanoquinodimethane ($TCNQF_4$), and chloranil (CA). Cleavage of dodecyl triethylsilyl ether with TCNQ and CA was caused by room light. By application of DDQ-catalyzed deprotection of acetals to hydrolysis of tetrahydropyranyl ethers, the corresponding alcohols were obtained in quantitative yields.

We have reported that acetals(1) and silyl ethers(2) were deprotected by a catalytic amount of 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) in MeCN–$H_2O$ via a single electron transfer (SET) mechanism under neutral conditions. On the other hand, Oku et al.(3) reported the similar hydrolysis of acetals and silyl ethers in wet EtOAc and proposed that DDQ produced acidic materials in a wet organic solvent and acted as a Lewis acid by itself. We reexamined whether the reaction under our conditions proceeded via an SET or a protic (Lewis acid) mechanism. In this paper, we report the results of the deprotection catalyzed by various $\pi$-acceptors together with that by DDQ and discuss the mechanism. Synthetic application of this method to deprotection of tetrahydropyranyl (THP) ethers is also described.

First, deprotection of dodecanal dimethyl acetal and dodecyl silyl ethers in MeCN–$H_2O$ (9 : 1) were explored using some $\pi$-acceptors such as 2,3,5,6-tetrafluoro-7,7,8,8-tetracyanoquinodimethane ($TCNQF_4$), 7,7,8,8-tetracyanoquinodimethane (TCNQ), tetracyanoethylene (TCNE), and chloranil (CA) as well as DDQ. The results are shown in Table 1. Dodecanal dimethyl acetal and dodecyl *t*-butyldimethylsilyl (TBDMS) ether were hydrolyzed when DDQ, $TCNQF_4$, and TCNE were used as a catalyst. The reaction was not catalyzed by TCNQ and CA. Dodecyl triethylsilyl (TES) ether was treated with these acceptors to afford 1-dodecanol in all cases. DDQ, $TCNQF_4$, and TCNE cause a much faster reaction than TCNQ and CA. None of acceptors catalyzed the cleavage of dodecyl *t*-butyldiphenylsilyl (TBDPS) ether. For deprotection of acetals and silyl ethers by DDQ in wet MeCN, autodecomposition of DDQ(4) must be taken into consideration as indicated by Oku et al. DDQ is unstable in MeCN–$H_2O$ (9 : 1) and most of DDQ was decomposed in 6 h at room temperature. The resulting solution was acidic enough for an acetal cleavage reaction: Dodecanal dimethyl acetal was hydrolyzed for 2 h to give dodecanal in 69% yield. We measured the pH of an aqueous solution of DDQ with the same concentration as the reaction mixture using a pH meter (pH 2.2 in $1.43\times10^{-2}$ M aqueous solution) (1 M=1 mol dm$^{-3}$). # TCNE, which has a lower reduction potential among these acceptors, has high activity. Most of TCNE was decomposed in 6 h in MeCN–$H_2O$ (9 : 1) and yielded acidic materials. The pH of an aqueous solution of TCNE was measured (pH 2.2 in $1.43\times10^{-2}$ M aqueous solution). Also 35% of $TCNQF_4$ was decomposed in 6 h in MeCN–$H_2O$ (9 : 1). Because of the insolubility of $TCNQF_4$ in water, we measured the pH of an aqueous solution of the decomposed products (pH 2.1 in $1.43\times10^{-2}$ M aqueous solution). TCNQ was hardly decomposed in MeCN–$H_2O$ (9 : 1) in 6 h (<1%) and CA was not decomposed at all.

Interestingly, the reactions of the TES ether with TCNQ and CA were caused by room light. In the dark, the reaction did not proceed at all. With irradiation by a fluorescent lamp, the reaction was accelerated (Table 2). Under aerobic conditions, the reactions were not disturbed. Thus, photochemical cleavage of TES ethers occurred with much ease. Under these reaction conditions, a trace of acidic materials was formed by the photochemical reaction of TCNQ or CA with water and caused the deprotection in the dark.## Albini et al. have reported that acetals are hydrolyzed via a photochemical SET mechanism in the presence of CA and some acidic materials are formed under their conditions.(5) Deprotection of the TES ether with TCNQ and CA are considered to proceed via a photochemical SET route and a protic one as shown in Scheme 1.

In the case of DDQ, deprotection of acetals and silyl ethers are considered to proceed via a protic mechanism. Hydrolysis of dodecanal dimethyl acetal in the dark and with irradiation by a fluorescent lamp was examined in MeCN–$H_2O$ (97 : 3), but a difference in reactivity was not observed.

Next, we attempted the synthetic application of this reaction to removal of THP ether, a typical protecting group of alcohols.(6) The results are summarized in Ta-

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# Oku et al. measured the p$K_a$ of DDQ in water as 3.42, approximately. DDQ in wet EtOAc, being comparably acidic to *p*-nitrobenzoic acid, is more reactive than *p*-nitrobenzoic acid in the hydrolysis of acetals and silyl ethers (Ref. 3).

## To a solution of CA (0.1 mmol) in MeCN–$H_2O$ (9 : 1) (7.0 ml) which was irradiated by a fluorescent lamp for 2 h, was added dodecyl TES ether (1.0 mmol) and stirred for 2 h in the dark. 1-Dodecanol was obtained in 32% yield. In the case of TCNQ, the alcohol was obtained in 90% yield.

Table 1. Product Yield Data for Deprotection of Dodecanal Dimethyl Acetal and Dodecyl Silyl Ethers by Various Acceptors[a,b)]

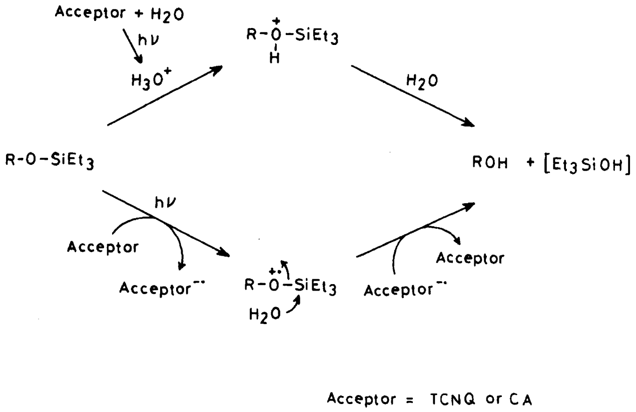
| Acceptor | $E_1$/V[c)] | Substrate | | | |
|---|---|---|---|---|---|
| | | $C_{11}H_{23}CH(OMe)_2$ | $C_{12}H_{25}OTES$ | $C_{12}H_{25}OTBDMS$ | $C_{12}H_{25}OTBDPS$ |
| DDQ | 0.59 | 2 h 81% | 1 h 93% | 2 h 69% | 6 h 0% |
| $TCNQF_4$ | 0.53 | 3 h 89% | 2 h 89% | 4 h 69% | 6 h 0% |
| TCNQ | 0.17 | 5 h 0% | 5 h 100% | 8 h 0% | 6 h 0% |
| TCNE | 0.15 | 1 h 63% | 1 h 93% | 2 h 67% | 6 h 0% |
| CA | 0.05 | 5 h 0% | 5 h 98% | 8 h 0% | 6 h 0% |

a) Acceptor (0.1 mmol) was added to a solution of substrate (1.0 mmol) in $MeCN-H_2O$ (9 : 1) (7.0 ml) at room temperature. b) Isolated yields. c) V vs. SCE in MeCN (Ref. 10).

Table 2. Deprotection of Dodecyl TES Ether by TCNQ and CA in the Dark and under Irradiation by a Fluorescent Lamp[a)]

| Acceptor | Yield[b)] | |
|---|---|---|
| | Dark | Irradiated |
| TCNQ | 5 h 0% | 2.5 h 90% |
| CA | 5 h 0% | 2 h 86% |

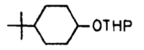
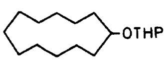
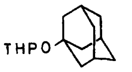
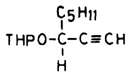
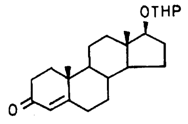
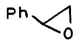
a) Acceptor (0.1 mmol) was added to a solution of TES ether (1.0 mmol) in $MeCN-H_2O$ (9 : 1) (7.0 ml) at room temperature under $N_2$. b) Isolated yields.



Scheme 1.

ble 3. In $MeCN-H_2O$ (9 : 1), dodecyl THP ether and testosterone THP ether were deprotected in the presence of a catalytic amount of DDQ to give the corresponding alcohols in moderate yields (Entries 4 and 14). In $MeOH-H_2O$ (9 : 1), the reaction proceeded smoothly and 1-dodecanol was isolated in quantitative yield (Entry 6). Similarly, other THP ethers were deprotected in excellent yields in $MeOH-H_2O$ (9 : 1) (Entries 8—13). In contrast, analogous methoxymethyl (MOM) and 2-methoxyethoxymethyl (MEM) ethers were recovered unchanged under similar conditions. Epoxides were converted to the corresponding diols, but yields were low because of polymerization (Entries 15 and 16). THP ethers and epoxides were hardly hydrolyzed in wet EtOAc[3)] and in $CH_2Cl_2-H_2O$.[7)] Alcoholysis of epoxides with a catalytic amount of DDQ is known.[8)]

Table 3. Hydrolysis of THP Ethers and Epoxides by DDQ[a)]

| Entry | Compound | Solvent | Time h | Yield %[b)] |
|---|---|---|---|---|
| 1 |  | $CH_2Cl_2-H_2O$ (19:1) | 7 | 18 |
| 2 | | $C_6H_6-H_2O$ (19:1) | 7 | 15 |
| 3 | | $THF-H_2O$ (9:1) | 7 | 20 |
| 4 | | $MeCN-H_2O$ (9:1) | 3 | 71 |
| 5 | | $MeCN-H_2O$ (19:1) | 5 | 26 |
| 6 | | $MeOH-H_2O$ (9:1) | 7 | 95 |
| 7 | | MeOH | 7 | 85 |
| 8 |  | $MeOH-H_2O$ (9:1) | 10 | 84 |
| 9 |  | $MeOH-H_2O$ (9:1) | 4 | 95 |
| 10 |  | $MeOH-H_2O$ (9:1) | 7 | 98 |
| 11 |  | $MeOH-H_2O$ (9:1) | 1 | 96 |
| 12 |  $THPO-\overset{C_5H_{11}}{\underset{H}{C}}-C\equiv CH$ | $MeOH-H_2O$ (9:1) | 10 | 81 |
| 13 |  | $MeOH-H_2O$ (9:1) | 7 | 87 |
| 14 | | $MeCN-H_2O$ (9:1) | 6 | 50 |
| 15 |  | $MeCN-H_2O$ (9:1) | 8 | 40 |
| 16 |  | $MeCN-H_2O$ (9:1) | 8 | 43 |

a) DDQ (0.1 mmol) was added to a solution of substrate (1.0 mmol) in solvent (7.0 ml) at room temperature. b) Isolated yields.

## Experimental

Melting points are uncorrected. IR spectra were recorded on a Hitachi I-3000 spectrophotometer. $^1H$ NMR spectra were measured on a Hitachi R-24B spectrometer using $Me_4Si$ as the internal standard. Column chromatography was done on Wakogel C-200 silica gel. DDQ was recrystallized from benzene–hexane. CA was recrystallized from benzene. TCNE, TCNQ, and $TCNQF_4$ were purified by sublimation. All products obtained in this study were completely characterized by comparison with authentic samples.

**Typical Procedure for Deprotection of THP Ethers by DDQ.** To a solution of dodecyl THP ether (270 mg, 1.0 mmol) in MeOH–$H_2O$ (9 : 1) (7.0 ml), was added DDQ (23 mg, 0.1 mmol). After the mixture was stirred for 7 h at room temperature, it was evaporated and the residue was chromatographed (benzene–ether=2 : 1) on silica gel to give 1-dodecanol (176 mg, 95%) as colorless crystalline solid; Mp 24 °C (from aqueous EtOH) (lit,[9] 24 °C); IR (Neat) 3336 $cm^{-1}$ (OH); $^1$H NMR ($CDCl_3$) $\delta$=0.92 (3H, t, $J$=6 Hz, $CH_3$), 1.10—1.78 (20H, br s, $CH_2$). 1.89 (1H, s, OH), and 3.67 (2H, t, $J$=6 Hz, $CH_2$).

**Typical Procedure for Deprotection of Dodecanal Dimethyl Acetal and Dodecyl Silyl Ethers by Various Acceptors.** To a solution of dodecyl TES ether (300 mg, 1.0 mmol) in MeCN–$H_2O$ (9 : 1) (7.0 ml), was added CA (25 mg, 0.1 mmol). The reaction mixture was stirred for 5 h at room temperature and then worked up as described above to give 1-dodecanol (182 mg, 98%).

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