REGIOSELECTIVE CLEAVAGE REACTION OF THE METHYLENEDIOXY RING IN AROMATIC COMPOUNDS CONTAINING ELECTRON-WITHDRAWING GROUPS WITH SODIUM ALKOXIDES-ALCOHOLS IN DIMETHYL SULFOXIDE

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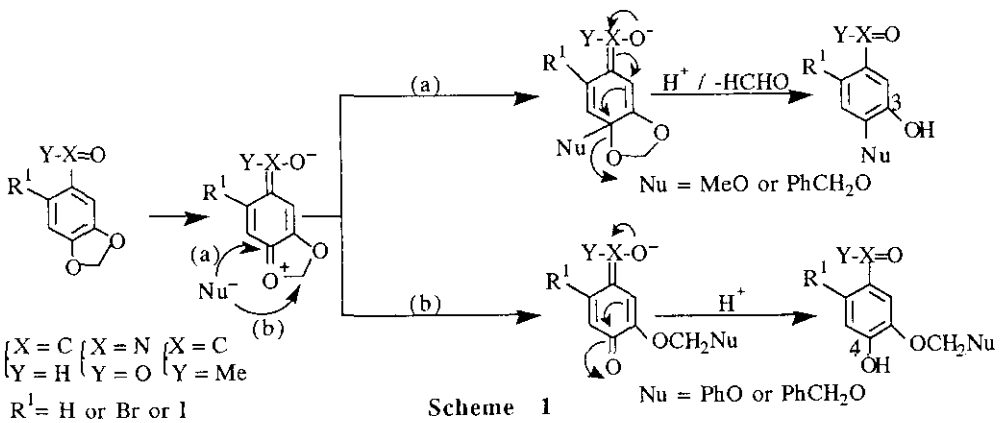
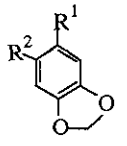
Abstract ----The reaction of 6-bromopiperonal (**1**) with sodium alkoxides (MeONa or $PhCH_2ONa$)-alcohols (MeOH or $PhCH_2OH$), and sodium alkoxides (MeONa, $PhCH_2ONa$ or PhONa)-phenol (PhOH) in dimethyl sulfoxide gave 3-hydroxybenzene derivatives (**3**, **5** and **6**) and 4-hydroxybenzene derivative (**4**), respectively. The reactivity and formational mechanism of various nucleophilic reagents (alkoxide anions) formed from the alcohols and phenol by sodium alkoxides in the regioselective cleavage reactions are discussed.

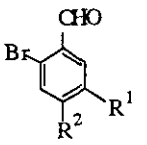
We have previously reported[2] the regioselective cleavage reaction of methylenedioxy ring on various kinds of aromatic compounds containing electron-withdrawing groups such as nitro (NO_2), formyl (CHO), and acetyl (MeCO) group with sodium alkoxides (RONa)-alcohols (ROH) or sodium phenoxide (PhONa)-phenol (PhOH) in dimethyl sulfoxide (DMSO) as shown in Scheme 1.



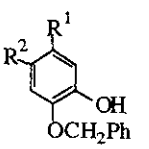
Scheme 1



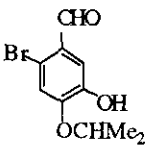
1 R^1 = CHO, R^2= Br
9 R^1 = NO_2, R^2= H



2 R^1 = OH, R^2 = OCD_3
3 R^1 = OH, R^2 = OMe
4 R^1 = OCH_2OPh, R^2 = OH
5 R^1 = OH, R^2 = OCH_2Ph
7 R^1 = OCH_2Ph, R^2 = OH
8 R^1 = OCH_2Ph, R^2 = OMe
14 R^1 = OCH_2O(4-MeO)Ph
R^2 = OH



6 R^1= CH_2OH, R^2= Br



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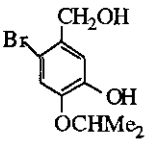

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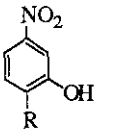

12 R = $OCHMe_2$
13 R = OMe

This paper describes the reactivity and formational mechanism of nucleophilic reagents (alkoxide anions) and the effect of DMSO for cleavage reaction of the methylenedioxy ring. The reaction of 6-bromopiperonal (1, 0.43 mmol) with sodium methoxide (MeONa, 0.45 mmol) in deuterated methyl alcohol [CD_3OD (0.5 ml, without DMSO)] at 150°C for 70 sec gave only 3-hydroxybenzene derivative (2) in 9.4 % yield by the regioselective attack of deuterated methoxide anion (CD_3O^-) formed from CD_3OD on the methylenedioxy ring.

On the other hand, the reaction of **1** (0.43 mmol) with MeONa (0.45 mmol) and CD_3OD (0.5 ml) in DMSO (0.5 ml) at 150°C for 70 sec gave an approximately 30:1 mixture of 3-hydroxybenzene derivatives (2 and 3) in 74.5 % yield. The following conception was revealed from the above experimental results: 1) Cleavage of the methylenedioxy ring with MeONa-CD_3OD system is achieved by the attack of CD_3O^- formed from CD_3OD with MeONa. 2) The presence of DMSO accelerates[3] the formation of CD_3O^- and increases the yield of the cleavage product due to the specific solvation effect of the transition state (A),[4] as observed in the nucleophilic substitution reactions of aromatic compounds.

To clarify further the formational mechanism of the cleavage of methylenedioxy ring, the reaction of 1 with a variety of sodium alkoxides (RONa)-alcohols (R'OH, R=R') systems in DMSO were studied as shown in Table 1.

The reaction of **1** with MeONa-PhOH or MeONa-benzyl alcohol ($PhCH_2OH$), and sodium benzyloxide ($PhCH_2ONa$)-methyl alcohol (MeOH) or $PhCH_2ONa$-PhOH systems in DMSO gave phenolic products (**4**),[2b] or (**5**[2c] and **6**), and (**3**)[2a] or (**4**),[2b] respectively, by the regioselective attack of alkoxide anions (MeO^-, $PhCH_2O^-$, and PhO^-) formed from the protic solvents (MeOH, $PhCH_2OH$, and PhOH) with MeONa or $PhCH_2ONa$ to the methylenedioxy ring. The structure of a new phenolic product (6) was established as 4-benzyloxy-6-bromo-3-hydroxybenzyl alcohol by oxidation of 6 to known

compound (5)[2c] with pyridinium dichromate (see Experimental). Compound (6)[2b] seems to be formed by the Cannizzaro-type reaction of 5 with base.

Table 1. Cleavage of Methylenedioxy Ring of 6-Bromopiperonal (1) with RONa and R'OH in DMSO

Compound (mmol)	R in RONa (mmol)	R' in R'OH (ml)	DMSO (ml)	Conditions time °C	Product	Yield (%) *a*	Yield (%) *b*
	methyl	methyl					
2.6[c]	2.7	2.7	3.0	70 sec, 150	3	72.3	67.5
	benzyl	methyl					
1.0	1.0	1.0	1.5	9 min, 150	3	41.5	36.5
	phenyl	methyl					
0.44	0.69	0.7	0.7	20 min, 170	3	42.7	35.7
					4	6.7	2.8
	benzyl	benzyl					
1.0[c]	1.0	1.0	1.2	9 min, 150	5	53.4	25.0
	methyl	benzyl					
1.0	1.0	1.0	1.5	70 sec, 150	5	5.5	5.2
					6	28.3	27.0
	phenyl	benzyl					
1.0	1.0	1.0	1.5	20 min, 170	4	10.7	10.2
					5	9.8	9.3
					7	9.7	9.3
	phenyl	phenyl					
2.2[c]	3.0	3.0	2.4	20 min, 170	4	78.7	55.7
	methyl	phenyl					
1.0	1.0	1.0	1.5	20 min, 170	4	22.8	12.6
	benzyl	phenyl					
1.0	1.0	1.0	1.5	20 min, 170	4	42.8	22.9
	methyl	isopropyl					
1.0	1.0	1.0	1.5	4.min, 150	3	13.4	10.0
					10	27.4	18.4
					11	9.0	6.0
	methyl	isopropyl					
1.0[d]	2.0	2.0	1.5	4 min, 150	12	66.1	44.3
					13	22.3	14.0

a) Based on the amount of 1 consumed. *b*) Based on the initial amount of 1. *c*) Data in Ref. 1. *d*) Compound (9) was used.

On the other hand, the reaction of 1 with PhONa-MeOH or PhONa-$PhCH_2OH$ system in DMSO gave 4-hydroxybenzene derivatives (4) [prepared by attack of the phenoxide anion (PhO^-)] and (7), besides the usual 3-hydroxybenzene derivatives (3 and 5) [prepared by attack of MeO^- or $PhCH_2O^-$]. The structure of a new phenolic product (7)[5] was established as 3-benzyloxy-6-bromo-4-hydroxybenzaldehyde by conversion of 7 to compound (8), which was prepared by benzylation (see Experimental) of known compound (3).[2a] The formational mechanism of 4 might be considered as follows. A small amount of PhOH is formed when the usual alkoxide anions (MeO^- or $PhCH_2O^-$) are prepared from the MeOH or the $PhCH_2OH$ with the PhONa in PhONa-MeOH

or PhONa-$PhCH_2OH$ system. Since the PhOH in PhOH (pKa 9.97),[6] MeOH (pKa 15.1),[6] and $PhCH_2OH$ (pKa 15.4)[6] is a most strong proton donor for base, the PhOH yielded from the above reaction systems seems to be formed PhO^- readily to give **4** besides the usual cleavage products (**3** and **5**). This assignment was further proved by the following experiments. Since the MeOH in MeOH (pKa *15.1) and isopropyl alcohol [Me_2CHOH (pKa 17.0)] is more proton donor than* Me_2CHOH *for* base, the reaction of **1** with MeONa-Me_2CHOH in DMSO gave **3** (prepared by attack of MeO^-) besides the usual 3-hydroxybenzene derivatives (**10** and **11**) [prepared by attack of the isopropoxide anion (Me_2CHO^-)]. Similarly, the reaction of 3,4-methylenedioxynitrobenzene (**9**) with MeONa-Me_2CHOH in DMSO gave **13** (prepared by attack of MeO^-) besides the usual 3-hydroxybenzene derivative (**12**) [prepared by attack of Me_2CHO^-]. The structures of two new phenolic products (**10** and **12**) were established as 6-bromo-3-hydroxy-4-isopropoxybenzaldehyde and 3-hydroxy-4-isopropoxynitrobenzene, respectively, by the observation of the nuclear Overhauser effect (nOe) of 15.0 and 14.2 %, respectively, between 5-H (**10**: δ 7.03; **12**: δ 6.88) and the methine proton ($Me_2C\underline{H}O$-) (**10**: δ 4.71; **12**: δ 4.97) of isopropoxy group in their ^{1}H-nmr spectra.

Table 2. Cleavage of Methylenedioxy Ring of 6-Bromopiperonal (**1**) with RONa, R'OH, and R"OH in DMSO[a]

Entry	R in RONa (mmol)	R' in R'OH (mmol)	R" in R"OH (mmol)	Conditions time	°C	Product	Yield(%) *b*	*c*
(1)	methyl	methyl	benzyl					
		11.1	4.9	20 min,	150	**3**	60.4	49.1
						5	14.9	10.8
(2)	methyl	methyl	benzyl					
		11.1	11.1	20 min,	150	**3**	24.4	17.5
						5	8.3	5.0
(3)	benzyl	methyl	benzyl					
		11.1	4.9	120 min,	150	**3**	22.3	9.5
						5	6.3	2.7
(4)	methyl	methyl	phenyl					
		11.1	5.0	20 min,	170	**3**	16.1	15.5
						4	63.0	60.7
(5)	phenyl	methyl	phenyl					
		11.1	5.0	20 min,	170	**3**	13.1	7.7
						4	55.9	32.5
(6)	methyl	4-methoxy-phenyl	phenyl					
		5.0	5.0	20 min,	170	**4**	37.3	19.4
						14	31.5	17.4
(7)	methyl	benzyl	phenyl					
		4.9	5.0	20 min,	170	**4**	62.4	59.5
						5	3.9	3.7

a) Reaction of **1** (1 mmol) with RONa (1 mmol) in DMSO (1.5 ml). *b*) Based on the amount of **1** consumed. *c*) Based on the initial amount of **1**.

To confirm the reactivity of protic solvents [MeOH, $PhCH_2OH$, PhOH, and 4-methoxyphenol (4-$MeOC_6H_4OH$)] acted as nucleophilic reagents in the cleavage reaction, the reactions of **1** with MeONa, PhONa or $PhCH_2ONa$ and the mixture of protic solvents such as $PhCH_2OH$-MeOH, PhOH-MeOH, PhOH-4-$MeOC_6H_4OH$ or $PhCH_2OH$-PhOH in DMSO were studied as shown in Table 2.

The nucleophile (MeO^- and $PhCH_2O^-$) formed in RONa-MeOH-$PhCH_2OH$ (Entries 1-3) attacked the carbon atom (abbreviated as aryl carbon) at C-4 in **1** to give 3-hydroxybenzene derivatives (**3** and **5**), and the ratio of **3** and **5** was about 3-4:1. The nucleophile (MeO^- and PhO^-) formed from RONa (R=Me, Ph)-MeOH-PhOH (Entries 4 and 5) attacked the aryl carbon at C-4 and the carbon atom (abbreviated as alkyl carbon) of methylenedioxy group in **1** to afford **3** and **4**, and the ratio of **3** and **4** was about 1:4. The nucleophile [4-methoxyphenoxide anion (4-$MeOC_6H_4O^-$) and PhO^-] formed in MeONa-4-$MeOC_6H_4OH$-PhOH (Entry 6) attacked the alkyl carbon of methylenedioxy ring in **1** to afford 4-hydroxybenzene derivatives (**4** and **14**), and the ratio of **4** and **14** was about 1:1. The structure of a new phenolic product (**14**) was established as 6-bromo-3-(4-methoxyphenoxymethoxy)-4-hydroxybenzaldehyde by the observation of nOe (13.0 %) between 2-H [δ 7.61(s)] and the methylene protons (4-$MeOC_6H_4OC\underline{H}_2O$) [δ 5.61(s)] of 4-methoxyphenoxymethoxy group in the ^{1}H-nmr spectrum. The nucleophile ($PhCH_2O^-$ and PhO^-) formed in MeONa-$PhCH_2OH$-PhOH (Entry 7) attacked the aryl carbon at C-4 and the alkyl carbon of methylenedioxy ring in **1** to afford **4** and **5**, and the ratio of **4** and **5** was about 16:1.

The following conclusions can be drawned from the above experimental results: I) The formational mechanism of this cleavage reaction can be classified into two types; i) when the alcohols (ROH) formed from sodium alkoxides (RONa, R = Me, $PhCH_2$, and Ph) have larger pKa value than the protic solvents (R'OH, R' = Me, $PhCH_2$, and Ph) used in the reaction, the protic solvents act preferentially as nucleophilic reagents to the methylenedioxy ring, and ii) when the alcohols (ROH) formed from sodium alkoxides (RONa) show smaller pKa values than the protic solvents (R'OH) used in the reaction, both the alcohols formed from sodium alkoxide and protic solvents act as nucleophilic reagents to the methylenedioxy ring.

II) The order of reactivity of the protic solvents used in the reactions was PhOH > 4-$MeOC_6H_4OH$ > MeOH > $PhCH_2OH$, which were inverse proportion to the order ($PhCH_2OH$ > MeOH > 4-$MeOC_6H_4OH$ > PhOH) of basicity of the protic solvents. Consequently, the reactivity of the protic solvents is thought to be controled by the polarizability[7] rather than basicity of the performed alkoxide anions.

This work represents a generally applicable method for a cleavage of the methylenedioxy ring on aromatic compounds containing electron-withdrawing groups with the regioselective introduction of the nucleophilic reagents (alkoxide anions) formed from the protic solvents (R'OH) by sodium alkoxides (RONa) in DMSO. We are investigating further the regioselective cleavage reaction of a

methylenedioxy ring on aromatic compounds with a varity of nucleophilic reagents to clarify the more deteiled mechanism and the regioselectivity.

EXPERIMENTAL

All melting points are uncorrected. Ir and ms spectra were measured with Hitachi IR-215 spectrophotometer and JEOL JMS-D-300 spectrometer, respectively. ^{1}H-Nmr spectra were taken with JEOL PS-100 and JEOL JNM-FX-200 spectrometers using tetramethylsilane (TMS) as an internal standard. Thin-layer chromatography (tlc) and preparative thin layer chromatography (ptlc) were performed with Merck Kieselgel GF_{254} and PF_{254}, respectively. Spots were detected under uv light or by spraying with 1% $Ce(SO_4)_2$-H_2SO_4 and then heating. Solvents were purified and dried by the standard methods.

Reaction of 6-Bromopiperonal (1) with Sodium Methoxide and Deuterated methyl Alcohol

In no DMSO.---A mixture of **1** (100 mg, 0.43 mmol), MeONa (24.4 mg, 0.45 mmol), and CD_3OD (0.5 ml, 11.1 mmol) was stirred at 150°C for 70 sec, and then poured into cold water (20 ml). Then sodium hydroxide (NaOH, 30 mg) was added, and the mixture was filtered to give the starting material **1** (75 mg, 75 %) and 6-bromopiperonyl alcohol (3.5 mg, 3.5 %), which were purified by ptlc (benzene). The filtrate was acidified (pH 5) with *conc.* hydrochloric acid (*conc.* HCl) and extracted with ether. The extract was washed with water, dried ($MgSO_4$), and evaporated. The residue was purified by ptlc (benzene-acetone, 4:1) to give a 6-bromo-4-deuterium-methoxy-3-hydroxybenzene **2** (9.4 mg, 9.4 %). ^{1}H-Nmr ($CDCl_3$) δ: 7.01(1H, s, 5-H), 7.45(1H, s, 2-H), and 10.13(1H, s, CHO). Ms Calcd for $C_8H_4D_3O_3Br$ *m/z*: 232.9767, 234.9747 (M^+). Found *m/z* 232.9760, 234.9743 (M^+).

In DMSO.---To a solution of **1** (100 mg, 0.43 mmol) in DMSO (0.5 ml) were added MeONa (24.4 mg, 0.45 mmol) and CD_3OD (0.5 ml, 11.1 mmol), and the mixture was stirred at 150° C for 70 sec, and then poured into cold water (20 ml). Then NaOH (30 mg) was added, and the mixture was washed with ether. The ethereal washing solution was washed with water, dried ($MgSO_4$), and evaporated. Purification of the residue by ptlc (benzene) afforded the starting material **1** (12.2 mg, 12.2 %) and 6-bromopiperonyl alcohol (3.5 mg, 3.5 %). On the other hand, the alkaline solution was acidified (pH 5) with *conc.* HCl and extracted with ether. The extract was washed with water, dried ($MgSO_4$), and evaporated. The residue was purified by ptlc (benzene-acetone, 4:1) to give a mixture (75.1 mg, 74.5 %) of **2** and 6-bromo-3-hydroxy-4-methoxybenzaldehyde (**3**) in an approximate ratio of 30:1, as determined from the ^{1}H-nmr spectrum ($CDCl_3$): δ 3.93(0.1 H, s, OMe), 7.02(1.03H, s, 5-H), and 7.45(1.03 H, s, CHO).

2: [ms Calcd for $C_8H_4D_3O_3Br$ *m/z* 232.9767, 234.9747 (M^+). Found *m/z* 232.9742, 234.9739 (M^+)].
3: [ms Calcd for $C_8H_7O_3Br$ *m/z* 229.9577, 231.9559 (M^+), Found *m/z* 229.9547, 231.9646 (M^+)].

Cleavage of 1 with RONa-R'OH in DMSO

With $PhCH_2ONa$ and MeOH in DMSO.---To a solution of **1** (229 mg, 1 mmol) and MeOH (1.5 ml) in DMSO (1.5 ml) was added $PhCH_2ONa$ (130 mg, 1 mmol), and the mixture was stirred at 150 °C for 9 min. The reaction mixture was poured into cold water (20 ml), 10 % NaOH (10 ml) was added, and the mixture was extracted with ether. The starting material **1** (162.4 mg, 70.9 %) was recovered from the extract. The mother liquor was acidified (pH 4-5) with *conc.* HCl and extracted with ether. The extract was washed with water, dried ($MgSO_4$), and evaporated. The residue was purified by ptlc (benzene-acetone, 4:1) to give **3** (84.2 mg, 36.5 %), mp 104-108 °C (from ether-petr. ether).[2a]

With PhONa and MeOH in DMSO.---A mixture of **1** (100 mg, 0.44 mmol), PhONa (80 mg, 0.69 mmol), and MeOH (0.7 ml) in DMSO (0.7 ml) was stirred at 170 °C for 20 min. Work-up in the usual way gave **3** (36.0 mg, 35.4 %), mp 107-108 °C,[2a] 6-bromo-4-hydroxy-3-phenoxymethoxy-benzaldehyde (**4**, 4.0 mg, 2.8 %), mp 119-121 °C,[2b] and the starting material **1** (2.5 mg, 2.5 %).

With MeONa and $PhCH_2OH$ in DMSO.---A mixture of **1** (229 mg, 1.0 mmol), $PhCH_2OH$ (1.0 ml), MeONa (54 mg, 1.0 mmol), and DMSO (1.5 ml) was stirred at 150 °C for 70 sec. Work-up in the usual way gave a 4-benzyloxy-6-bromo-3-hydroxybenzaldehyde **5** (83.4 mg, 27.0 %), mp 127-128 °C(from $CHCl_3$-CCl_4), which was identical in all respect with authentic **5**,[2c] together with 4-benzyloxy-6-bromo-3-hydroxybenzyl alcohol (**6**, 16.0 mg, 5.2 %), 6-bromopiperonyl alcohol (39.7 mg, 17.2 %),[2b] and the starting material **1** (10.4 mg, 4.5 %).

6: mp 147-148 °C (from $CHCl_3$-CCl_4); ir (KBr): 3480(OH) and 3150 cm^{-1}(OH); ^{1}H-nmr ($CDCl_3$) δ: 3.34 (1H, m, $PhCH_2O\underline{H}$), 4.56(2H, s, $PhC\underline{H}_2OH$), 5.15(2H, s, $PhC\underline{H}_2O$-). Irradiation at δ 5.15 showed 17 % nOe increase in the signal of 5-H. Anal. Calcd for $C_{14}H_{13}O_3Br$: C, 54.39; H, 4.24. Found: C, 54.28; H, 4.31.

Compound **6** (51.4 mg, 0.17 mmol) was added slowly to a stirred solution of the pyridinium dichromate (93.3 mg, 0.25 mmol) in DMF (1.5 ml) at 0 °C. After 2 h, the mixture was diluted with cold water (20 ml) and extracted with ether. The extract was washed with water, dried($MgSO_4$), and evaporated. The residue was purified by ptlc (benzene-acetone, 8:1) to give (**5**, 29.7 mg, 58.2 %), mp 127-128.5 °C,[2c] and the starting material **6** (13.1 mg, 25.5 %).

With PhONa and $PhCH_2OH$ in DMSO.---A mixture of **1** (229 mg, 1.0 mmol), PhONa (116 mg, 1.0 mmol), and $PhCH_2OH$ (1.0 ml) in DMSO (1.5 ml) was stirred at 170 °C for 20 min. Work-up in the usual way gave **4** (33.1 mg, 10.2 %), mp 120-121 °C,[2b] **5** (28.3 mg, 9.3 %), mp 128-129 °C,[2b] the starting material **1** (10.8 mg, 4.7 %), and 3-benzyloxy-6-bromo-4-hydroxybenz-aldehyde **7** (28.5 mg, 9.3 %).

7: mp 148-151 °C (from ether-acetone); ir (KBr): 3320(OH) and 1665 cm^{-1}(C=O); ^{1}H-nmr ($CDCl_3$-CD_3OD) δ : 5.08(2H, s, $PhC\underline{H}_2O$), 7.12(1H, s, 5-H), 7.37(5H, s, $\underline{Ph}CH_2O$), 7.45(1H, s, 2-H), and 10.12(1H, s, CHO); Anal. Calcd for $C_{14}H_{11}O_3Br$: C, 54.74; H, 3.58. Found: C, 54.68; H, 3.62.

Dimethyl sulfate (1 ml) and 2 % NaOH (2 ml) were added to a stirred solution of **7** (14.3 mg, 0.47 mmol) and 2 % NaOH (2 ml) at 85 °C. After 1 h, work-up in the usual way gave **8** (22.9 mg, 82.6 %), mp 139-140 °C, which was identical with **8** prepared by benzylation of **3** as follow.

A mixture of **3** (46.2 mg, 0.2 mmol), DMF (0.4 ml), benzyl chloride (0.5 ml), and potassium carbonate (15.2 mg) was stirred at 100 °C for 6 h. Work-up in the usual way gave **8** (56.2 mg, 87.9 %), mp 141-142 °C(from ether-acetone); ir (KBr): 1665 cm^{-1}(C=O); ^{1}H-nmr ($CDCl_3$) δ : 3.89(3H, s, 4-OMe), 5.09(2H, s, $PhC\underline{H}_2O$), 7.00(1H, s, 5-H), 7.33(5H, s, $\underline{Ph}CH_2O$), 7.44(1H, s, 2-H), and 10.10(1H, S).

With MeONa and PhOH in DMSO.---A mixture of **1** (22 mg, 1.0 mmol), MeONa (54 mg, 1.0 mmol), PhOH (1.0 ml), and DMSO (1.5 ml) was stirred at 170 °C for 20 min. Work-up in the usual way gave **4** (17.9 mg, 12.6 %), mp 119-119.5 °C, which was identical with an authentic sample (4),[2b] together with the starting material **1** (102.6 mg, 44.8 %).

With $PhCH_2ONa$ and PhOH in DMSO.---A mixture of **1** (229 mg, 1.0 mmol), $PhCH_2ONa$ (130 mg, 1.0 mmol), and PhOH (1.0 ml) in DMSO (1.5 ml) was stirred at 170 °C for 20 min. Work-up in the usual way gave **4** (73.8 mg, 22.8 %), mp 120-121 °C,[2b] benzoic acid (89.3 mg), and the starting material **1** (106.5 mg, 46.5 %).

Cleavage of 1 with Sodium Methoxide and Isopropyl Alcohol in DMSO

A mixture of **1** (229 mg, 1.0 mmol), MeONa (54 mg, 1.0 mmol), and Me_2CHOH (1.0 ml) in DMSO (1.5 ml) was stirred at 150 °C for 8 min. Work-up in the usual way gave **3** (20.8 mg, 10.0 %), 6-bromo-3-hydroxy-4-isopropoxybenzaldehyde **10** (47.5 mg, 18.4 %), 6-bromo-3-hydroxy-4-isopropoxybenzylalcohol **11** (15.7 mg, 6 %), and the starting material **1** (95 mg, 41.3 %).

10: mp 76-79 °C ($CHCl_3$-n-hexane); ir (KBr): 3320(OH) and 1667cm^{-1}(C=O); ^{1}H-nmr ($CDCl_3$) δ : 1.38(6H, d, *J*= 6.0, $OCH\underline{Me}_2$), 4.71(1H, seventet, *J*= 6.0, $OC\underline{H}Me_2$), 7.03(s, 5-H), and 7.49(s, 2-H); Anal. Calcd for $C_{10}H_{11}O_3Br$: C, 46.36; H, 4.28. Found: C, 46.15; H, 4.21 . Irradiation at δ 4.71 showed 15 % nOe in the signal of 5-H.

11: oil; ^{1}H-nmr ($CDCl_3$): δ 1.33(6H, d, *J*=6.0, $OCH\underline{Me}_2$), 4.07(1H, seventet, *J*= 6.0, $OC\underline{H}Me_2$), 4.63(2H, s, $C\underline{H}_2OH$), and 7.00 (2H, s); [Ms Calcd for $C_{10}H_9O_3Br$ *m/z* 255.9720, 257.9712 (M^+). Found *m/z* 255.9728, 257.9712 (M^+)]. **11** was converted to **10** by pyridinium dichromate in DMF.

Cleavage of 3,4-Methylenedioxynitrobenzene (9) with Sodium Methoxide and Isopropyl Alcohol in DMSO

With MeONa and Me_2CHOH in DMSO.---A mixture of **9** (167 mg, 1.0 mmol), MeONa (108 mg, 2.0 mmol), and Me_2CHOH (2 ml) in DMSO (1.5 ml) was stirred at 150 C for 4 min. Wok-up in the

usual way gave 3-hydroxy-4-isopropoxynitrobenzene **12** (87.3 mg, 44.3 %), 3-hydroxy-4-methoxynitrobenzene **13** (23.7 mg, 14 %), and the starting material **9** (55.0 mg, 32.9 %).

12: mp 51-54 °C ($CHCl_3$-n-hexane); ir (KBr): 3400(OH), 1608 and 1347 cm^{-1}(NO_2); ^{1}H-nmr ($CDCl_3$) δ : 1.42(6H, d, *J*= 6.0, $OCHMe_2$), 4.97(1H, seventet, *J*= 6.0, $OCHMe_2$), 6.88(1H, d, *J*= 8.0, 5-H), 7.87(1H, d, *J*= 2.0, 8.0, 6-H); Anal. Calcd for $C_9H_{11}NO_4$: C, 54.82; H, 5.62; N, 32.46. Found: C, 54.75; H, 5.65; N, 32.21. Irradiation at δ 4.97 showed 14.2 % nOe in the signal of 5-H.

Cleavage of 1 with RONa-R'OH-R"OH in DMSO

(1) *With MeONa, MeOH, and $PhCH_2OH$ in DMSO* .---A mixture of **1** (229 mg, 1 mmol), MeOH (0.5 ml, 11. 1 mmol), $PhCH_2OH$ (0.5 ml, 4.9 mmol), and MeONa (54 mg, 1 mmol) in DMSO (1.5 ml) was stirred at 150 °C for 20 min. Work-up in the usual way gave **3** (113.4 mg, 49.1 %), mp 107-108 °C,[2a] and **5** (33.2 mg, 10.8 %), mp 128-129°C,[2c] together with the starting material **1** (42.8 mg, 18.7 %).

(2) *With MeONa, MeOH, and $PhCH_2OH$ in DMSO.*---A mixture of **1** (229 mg, 1 mmol), MeOH (0.5 ml, 11.1 mmol), $PhCH_2OH$ (1.1 ml, 11.1 mmol), and MeONa (54 mg, 1 mmol) in DMSO (1.5 ml) was stirred at 150°C for 20 min. Work-up in the usual way gave **3** (40.3 mg, 17.5.%), mp 107-108 °C,[2a] and **5** (15.3 mg, 5.0 %), mp 127-129 °C,[2c] together with the starting material **1** (30.5 mg, 13.3 %).

(3) *With $PhCH_2ONa$, MeOH, and $PhCH_2OH$ in DMSO.*---A mixture of **1** (229 mg, 1 mmol), MeOH (0.5 ml, 11.1 mmol), $PhCH_2OH$ (0.5 ml, 4.9 mmol), and $PhCH_2ONa$ (130 mg, 1 mmol) in DMSO (1.5 ml) was stirred at 150°C for 2 h. Work-up in the usual way gave **3** (19.2 mg, 9.5.%), mp 106-107 °C,[2a] and **5** (7.3 mg, 2.7 %), mp 126-128 °C,[2c] together with the starting material **1** (114.9 mg, 57.2 %).

(4) *With MeONa, MeOH, and PhOH in DMSO.*---A mixture of **1** (229 mg, 1 mmol), MeOH (0.5 ml, 11.1 mmol), PhOH (470 mg, 5.0 mmol), and MeONa (54 mg, 1 mmol) in DMSO (1.5 ml) was stirred at 170°C for 20 min. Work-up in the usual way gave **3** (35.7 mg, 15.5.%), mp 106-107 °C,[2a] and **4** (196.0 mg, 60.7 %), mp 120-122°C,[2b] together with the starting material **1** (8.2 mg, 3.6 %).

(5) With PhONa, MeOH, and PhOH in DMSO ---A mixture of **1** (229 mg, 1 mmol), MeOH (0.5 ml, 11.1 mmol), PhOH (470 mg, 5.0 mmol), and PhONa (116 mg, 1 mmol) in DMSO (1.5 ml) was stirred at 170°C for 20 min. Work-up in the usual way gave **3** (17.7 mg, 7.7.%), mp 106-107 °C,[2a] and **4** (104.9 mg, 32.5 %), mp 120-121°C,[2b] together with the starting material **1** (41.7 mg, 18.2 %).

(6) *With MeONa, 4-$MeOC_6H_4OH$, and PhOH in DMSO.*---A mixture of **1** (229 mg, 1 mmol), 4-$MeOC_6H_4OH$ (625 mg, 5.0 mmol), PhOH (470 mg, 1 mmol), and MeONa (54 ml, 1 mmol), in DMSO (1.5 ml) was stirred at 170°C for 20 min. Work-up in the usual way gave **4** (62.7 mg, 19.4 %), mp 119-121 °C[2b] and 6-bromo-3-(4-methoxyphenoxymethoxy)-4-hydroxybenzaldehyde **14** (62.5 mg, 17.4 %), together with the starting material **1** (110 mg, 152.4 %).

14: mp 103-105 °C (from ether-n-hexane); ir (KBr): 3250(OH) and 1670(C=O) cm^{-1}; ^{1}H-nmr ($CDCl_3$-pyridine-d_5) δ : 3.66(3H, s, OMe), 5.61(2H, s, OCH_2O), 7.20(1H, s, 5-H), 7.61(1H, s, 2-H), and 10.12(1H, s, CHO); Anal. Calcd for $C_{15}H_{13}O_5Br$: C, 51.00; H, 3.72. Found: C, 51.30; H, 3.88.

(7) With MeONa, $PhCH_2OH$, and PhOH in DMSO.---A mixture of **1** (229 mg, 1 mmol), $PhCH_2OH$ (0.5 ml, 4.9 mmol), PhOH (470 mg, 5.0 mmol), and MeONa (54 mg, 1 mmol) in DMSO (1.5 ml) was stirred at 170°C for 20 min. Work-up in the usual way gave **4** (192.1 mg, 59.5.%), mp 121-122°C[2b] and **5** (11.3 mg, 3.7 %), mp 127-129 °C,[2c] together with the starting material **1** (15.1 mg, 6.6 %).

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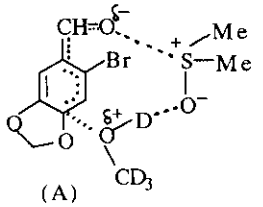
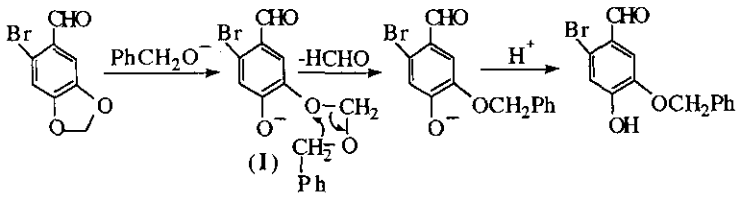


(A)

5. Compound (**7**) seems to be prepared via intermediate (**I**) as follow.



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