puterized program which measured the area under the GLC curves. A 10 ft, 10% SE-30 column, 70–300 °C, with a program rate of 6 °C/min using a thermal conductivity detector was used to analyze the phenols. A flame detector was used to determine methanol, dimethyl ether, and the anisoles with a 11 ft, 20% UCON 50 HB 5100 on 80–100 mesh HMDS-treated Chromosorb P column at 70 °C.

Reagents. The phenols were obtained from CONOCO Chemicals and were analyzed by GLC. Methanol and benzenemethanol were of analytical grade. CD_3OD was 99.5% isotopically pure. The $CDCl_3$ used as a solvent for NMR analysis was 99.96% isotopically pure.

3-Benzyl-2,6-dimethylphenol. Benzenemethanol was added dropwise to a stirred flask containing 2,6-xylenol at 190 °C. The water formed in the reaction was removed in a Dean-Stark trap. Analysis by NMR spectroscopy of the product indicated 84% of 3-benzyl-2,6-dimethylphenol and 16% of 4-benzyl-2,6-dimethylphenol.

Methanol-d_4 Experiment. CD_3OD (10 g) was added to 127 g of 2,6-xylenol, and the feed was pumped through the reactor at 350 °C, LHSV = 3, and 475 psig pressure. The product was collected after a 1-h run time and distilled to give a 2,6-xylenol cut and an enriched 2,3,6-TMP cut. A 2,6-xylenol sample was introduced via the direct inlet probe of a Consolidated Electrodynamics Corp. Model 21-110B mass spectrometer. A parent peak at mass 122 was observed at 100 °C, and the intensity of the mass 125 peak (CD_3 incorporation in 2,6-xylenol or ^{13}C contribution) was <0.1% that of the 122 mass parent peak intensity for $C_8H_{10}O$ (2,6-xylenol).

A 10 μL sample of the crude 2,3,6-TMP cut was injected onto the GLC column used to analyze the phenols. The component corresponding to 2,3,6-TMP was collected in a 2.0 × 125 mm tube at the exit port, and the capillary tube was sealed at one end and used as the NMR sample tube. $CDCl_3$ was added, and the NMR spectrum was obtained on a Bruker WP-80 Fourier transform NMR spectrometer with $CDCl_3$ as the lock solvent and Me_4Si as an internal standard. A total of 347 scans were used to generate the spectrum in Figure 1.

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Registry No.—2,6-Xylenol, 576-26-1; 2,3,6-TMP, 2416-94-6; 2,4,6-TMP, 527-60-6.

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Chemistry of the Sulfur–Nitrogen Bond. 13. A New Synthesis of *N*-Alkylidenearenesulfenamides (Sulfenimines): Alkylation of Sulfenamide Enolate Equivalents

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The alkylation of sulfenamide enolate equivalents (**2**), derived by treatment of **1** with LDA, represents a new and important source of sulfenimine derivatives. Not only does this procedure afford **1**, not available by other methods, but it avoids the limitation of the metal-assisted sulfenamide synthesis. These enolate equivalents are formed in excellent yield, with high stability and good regioselectivity. They are, however, highly reactive toward electrophiles such as halides, carbonyl compounds, and aryl disulfides without detectable polyalkylation or self-condensation. Elimination to form phenylthiolate ion and nitrile occurs on treatment of **1**, derived from aldehydes, with LDA.

N-Alkylidenearenesulfenamides (sulfenimines) (**1**) are an important class of reactive sulfur–nitrogen compounds[2] which have recently been shown to be useful intermediates in organic synthesis. These compounds are precursors of 2-arenesulfonyl-3-phenyloxaziridines,[3] a new class of stable oxaziridine derivative. The synthetic utility of **1** as "masked" imine derivatives of ammonia has recently been demonstrated in a convenient, one-step synthesis of secondary and tertiary carbinamines.[4]

Although **1** can generally be prepared in good yield from the corresponding aldehyde or ketone, disulfide, and ammonia using the metal-assisted procedure (eq 1),[1,5] this method has certain limitations.

$$\mathrm{ArSSAr} + \mathrm{MX} + \mathrm{R_1CR_2}\overset{\mathrm{NH_3}}{\longrightarrow} \underset{\mathbf{1}}{\mathrm{ArS}\!-\!\mathrm{N{=}CR_1R_2}} + \mathrm{ArSM} \quad (1)$$

$$\mathrm{MX} = \mathrm{AgNO_3},\ \mathrm{HgCl_2}$$

First is the inability to prepare **1** from aldehydes or ketones containing bulky and/or reactive functional groups.[1,5] Second, the excess of ammonia required by this method necessitates a correspondingly large excess of the carbonyl compound. From a synthetic point of view this becomes undesirable if the aldehyde or ketone is difficult to prepare.

Enolate equivalents of imines have received relatively little study and have generally not been used to prepare new imine derivatives.[6] They are primarily used as protecting functionalities to avoid self-condensation and polyalkylation reactions observed for the corresponding carbonyl enolates.[7] Corey and Enders have recently reported high regioselectivity for the alkylation of enolate equivalents derived from *N,N*-dimethylhydrazones.[8]

Alkylation of sulfenamide enolate equivalents, **2**, would provide an alternative source of sulfenimine derivatives (eq 2) which would avoid the limitations of the metal-assisted synthesis.[1,5] These enolate equivalents, **2**, are conveniently

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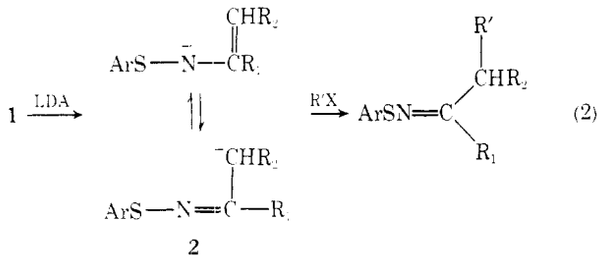
Table I. Synthesis of *N*-Alkylidenearenesulfenamides from Sulfenamide Enolate Equivalents

Entry	Sulfenamide	Registry no.	R–X	Registry no.	Product (% yield)[a]	Registry no.
1	$PhSN{=}CMe_2$	38206-14-3	MeI	74-88-4	$PhSN{=}C(Me)Et$ (95)	50314-94-8
2			$PhCH_2Br$	100-39-0	$PhSN{=}C(Me)CH_2CH_2Ph$ (92)	65276-64-4
3			Ph_2CO	119-61-9	$PhSN{=}C(Me)CH_2C(OH)Ph_2$ (92)	65276-65-5
4			$4\text{-}ClC_6H_4CHO$	104-88-1	$PhSN{=}C(Me)CH_2C(OH)HC_6H_4\text{-}4\text{-}Cl$ (78)	65276-66-6
5			PhS–SPh	882-33-7	$PhSN{=}C(Me)CH_2SPh$ (44)	65276-67-7
6			$(4\text{-}ClC_6H_4S)_2$	1142-19-4	$PhSN{=}C(Me)CH_2SC_6H_4\text{-}4\text{-}Cl$ (66)	65276-68-8
7	$PhSN{=}CEt_2$	65276-63-3	Ph_2CO		$PhSN{=}C(CH_2CH_3)CH(Me)C(OH)Ph_2$ (81)	65276-69-9
8	PhSN=CHMe	61501-00-6	MeI[b]		PhSMe (60), Ph_2S_2 (14), PhSN=CHEt (4)	100-68-5, 65276-70-2
9	PhSN=CHPh	52777-99-8	MeI[b]		PhSMe (87), PhCN (79)	100-47-0

[a] Isolated yields unless otherwise noted. [b] Determined by GLC.



2

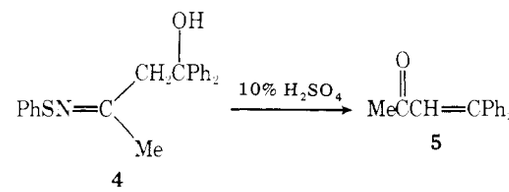
prepared by α-metallation of **1** with 1 equiv (0.5 M) of lithium diisopropylamide (LDA) in dry ether at 0 °C. Alkylation of **2** with halides, carbonyl compounds, and aryl disulfides affords new sulfenamide derivatives in good to excellent yields and in high isolated purity (as judged by TLC, GLC, and NMR). These results are summarized in Table I.

Lower temperatures and/or THF as the solvent resulted in lower yields. With iodomethane, product yields were maximized when 3 equiv were used. Even with a large excess of iodomethane, i.e. >5 equiv, no evidence for polyalkylation was observed. *N*-2(Butylidene)benzenesulfenamide (**3**), the only sulfenimine that could be prepared by both alkylation of **2** (Table I, entry 1) and the metal-assisted procedure, gave only a 50% yield of this compound via the latter method.[4]

Starting material was recovered when **2** was treated with dimethyl disulfide. Enolates derived from *N,N*-dimethylhydrazones[9] and carbonyl compounds[10] react with dimethyl disulfide to afford good yields of the corresponding methyl sulfides. The greater stability and hence lower reactivity of sulfenamide enolates, **2**, is consistent with the known ability of sulfur to stabilize carbanions.[11]

New sulfenimines prepared by alkylation of sulfenamide enolate equivalents (Table I) had IR, NMR, and elemental analysis consistent with the proposed structures. With the exception of **3** (Table I, entry 1) which was isolated as a 26:74 mixture of *Z* and *E* isomers all other sulfenamides were isolated as a single isomer, presumably *E*.[5] Additional evidence for the proposed structures is the acid hydrolysis of **4** to **5**[12] in 75% yield.

Attempts to prepare enolate equivalents of **1** derived from aldehydes (ArSN=CHR) failed. Treatment of *N*-ethylidenebenzenesulfenamide (**6a**)[4] with LDA followed by alkylation with iodomethane gave thioanisole as the major product with only a trace of the desired alkylated sulfenimine (Table I, entry 8).



4 5

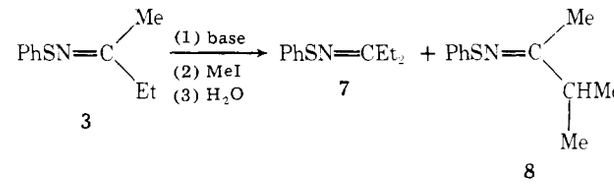
$$\text{Ph-S-N=CHR} \xrightarrow[(2)\ \text{MeI}]{(1)\ \text{LDA}} \text{Ph-S-Me} + \text{R-CN}$$

6a, R = Me
b, R = Ph

Apparently elimination, giving the phenylthiolate ion and acetonitrile, is favored over formation of **2**. Consistent with these results is the isolation of thioanisole and benzonitrile in 87 and 79% yield, respectively, on treatment of **6b** with LDA–iodomethane (Table I, entry 9).

One of the main problems which limits the use of enolates derived from ketones is their regioselective formation since mixtures of alkylated products result.[13] Base, temperature, reaction medium, and geometry of the carbonyl derivative all have an influence on the regioselectivity.[7-9,13,14]

Treatment of the sulfenimine derived from 2-butanone, **3**,[4] with base followed by alkylation of the enolate equivalents with iodomethane affords **7** and **8**. The influence of reaction



3 7 8

conditions on the yields of these products is summarized in Table II. As observed for other enolate equivalents[7-9,13,14] there is a similar preference for alkylation of the primary

Table II. Regioselectivity of Sulfenamide Enolate Equivalents; Alkylation with Iodomethane of the Enolate Equivalents Derived from Sulfenimine 3

Entry	Base concn, M (equiv)	Temp, C°	Solvent	Time,[a] h	Products[b] (% yield)
1	LDA 1.0 (1)	0	Ether	1.0	**7** (73), **8** (9)
2	LDA 0.65 (1)	0	Ether	1.0	**7** (73), **8** (9)
3	LDA 0.65 (2)	0	Ether	1.0	**7** (78),[c] **8** (5)
4	LDA 0.65 (3)	0	Ether	1.0	**7** (75),[c] **8** (8)
5	LDA 0.85 (1)	−78	Ether	2.5	**3** (95)
6	LDA 0.65 (1)	0	THF	1.0	**3** (37), **7** (40), **8** (4)
7	LDA 0.5 (1)	0	THF	2.0	**3** (30), **7** (55), **8** (5)
8	LDA 0.5 (1)	0	THF	3.0	**3** (15), **7** (45), **8** (3)
9	LDA 0.5 (3)	0	THF	1.0	**7** (45), **8** (5)
10	LiTMP 0.5 (1)	0	Ether	1.0	**7** (67), **8** (16)
11	LiTMP 0.65 (1)	0	Ether	1.0	**7** (71), **8** (16)
12	LiTMP 1.0 (1)	0	Ether	1.0	**7** (67), **8** (14)

[a] Time at which iodomethane was added. [b] Analyzed by GLC. [c] Polyalkylation occurring.

carbanion, leading to **7**. The highest regioselectivity observed for the enolates derived from **3** was with 1–2 equiv of LDA in ether (Table II). However, as the concentration of base increased polyalkylation became a serious problem (Table II, entries 3 and 4). Although the polyalkylated product could not be successfully separated from the reaction mixture it appears to be **9** ($PhSN{=}C(Et)CHMe_2$) as judged by NMR. The use of lithium 2,2,6,6-tetramethylpiperidine (LiTMP), lower temperatures, or THF as the solvent resulted in reduced yields and lower regioselectivity (Table II).

The lower regioselectivity observed for sulfenamide enolate equivalents as compared with *N,N*-dimethylhydrazones may be a result of the geometry of **3**. The barriers to syn-anti isomerization in sulfenimines, **1**, are on the order of 20 kcal/mol[15] and **3** exists as a 26:74 mixture of the *Z* and *E* forms. Jung and Shaw have reported a preference for anti deprotonation in symmetrically substituted hydrazones.[15] Anti deprotonation in **3**, as a result of the bulky S-phenyl group, may therefore lead to the enolate equivalent favoring **8**.

The alkylation of sulfenamide enolate equivalents, derived from readily available **1**,[1,5] represents a new and important source of sulfenimine derivatives. Not only does this procedure afford **1**, not available by other methods, but it avoids the limitations of the metal-assisted sulfenamide synthesis. Sulfenamide enolate equivalents are formed in excellent yield, with high stability and good regioselectivity. These enolate equivalents are, however, highly reactive toward electrophiles such as halides, carbonyl compounds, and aryl disulfides without detectable polyalkylation or self-condensation.

Experimental Section

Melting points were obtained on a Mel-Temp apparatus and are uncorrected. IR spectra were obtained on a Perkin-Elmer 457 spectrometer and NMR spectra on a Varian A60 A spectrometer. Chemical shifts are expressed in ppm downfield from Me_4Si. Solvents were purified by standard procedures. Gas chromatography was performed on a Perkin-Elmer 900 gas chromatograph, FID, using a 6 ft. 6% OV-17 on 60/80 mesh Chromosorb W (regular) column by comparison of peak areas with standard solutions of reaction products. Analyses were performed at least twice and the results averaged.

General Procedure for Alkylation of Sulfenamide Enolate Equivalents. In a 100-mL three-necked flask equipped with magnetic stirrer, condenser, dropping funnel, nitrogen, and syringe inlets was placed 2.2 mmol of a 0.5 M solution of freshly prepared lithium diisopropylamide (LDA) in 4.4 mL of dry ether in an atmosphere of nitrogen. The reaction mixture was cooled to 0 °C and 2 mmol of the appropriate sulfenimine, **1**, in 2 mL of ether was added dropwise over 0.5 h. After being stirred for an additional 0.5 h at 0 °C, the reaction mixture was refluxed for 0.5 h and cooled to 0 °C and 6.0 mmol of iodomethane or 2.0 mmol of the other alkylating agents in 2 mL of ether was added dropwise. After stirring for 2 h in the case of iodomethane and benzyl bromide and 15 h for the carbonyl compounds and disulfides the reaction was quenched with 30 mL of water and the ether solution was dried over anhydrous $MgSO_4$. New sulfenimines were purified by crystallization from ether–pentane or preparative TLC on silica gel.

***N*-2(4-Phenylbutylidene)benzenesulfenamide:** mp 57–58 °C; NMR ($CDCl_3$) δ 2.1 (s, 3 H, Me), 2.6–3.2 (m, 4 H, CH_2CH_2), 7.0–7.5 (m, 5 H). Anal. Calcd for $C_{16}H_{17}NS$: C, 75.39; H, 6.67. Found: C, 75.30; H, 6.80.

***N*-2(4,4-Diphenyl-4-hydroxybutylidene)benzenesulfenamide (4):** mp 98–98 °C; IR (KBr) 3390 cm^{-1} (s, OH); NMR ($CDCl_3$) δ 2.0 (s, 3 H, Me), 3.3 (s, 2 H, CH_2), 5.5 (s, 1 H, OH, exchange D_2O), 7.0–7.4 (m, 15 H). Anal. Calcd for $C_{22}H_{21}NOS$: C, 76.05; H, 6.09. Found: C, 76.28, H, 6.11.

***N*-2(4-(4-Chlorophenyl)-4-hydroxybutylidene)benzenesulfenamide:** mp 65–7 °C; IR (KBr) 3490 cm^{-1} (s, OH); NMR ($CDCl_3$) δ 2.0 (s, 3 H, Me), 2.6 (d, 2 H, CH_2), 4.1 (bs, 1 H, OH), 5.1 (t, 2 H), and 7.0–7.5 (m, 9 H).

Anal. Calcd for $C_{16}H_{16}ClNOS$: C, 62.84; H, 5.27. Found: C, 62.69; H, 5.32.

***N*-2(3-Phenylthiopropylidene)benzenesulfenamide:** oil; NMR ($CDCl_3$) δ 2.15 (s, 3 H, Me), 3.75 (s, 3 H, CH_2), 7.1–7.6 (m, 10 H). A satisfactory elemental analysis could not be obtained.

***N*-2(3-(4-Chlorophenylthio)propylidene)benzenesulfenamide:** mp 33 °C; NMR ($CDCl_3$) δ 2.15 (s, 3 H, Me), 3.7 (s, 2 H, SCH_2), 7.3 (m, 9 H). Anal. Calcd for $C_{15}H_{14}ClNS_2$: C, 58.52; H, 4.58. Found: C, 58.56; H, 4.56.

***N*-3-(5,5-Diphenyl-5-hydroxy-4-methylpentylidene)benzenesulfenamide:** mp 71–3 °C; IR (KBr) 3400 cm^{-1} (s, OH); NMR ($CDCl_3$) δ 1.2 (d-t, 6 H, Me), 2.3 (q, 2 H), 3.7 (q, 1 H), 5.9 (s, 1 H, OH, exchange D_2O), 7.0–7.6 (m, 15 H). Anal. Calcd for $C_{24}H_{25}NOS$: C, 76.76; H, 6.71. Found: C, 76.93; H, 6.76.

Hydrolysis of 4. In a 50-mL single-necked flask was placed 0.1 g (0.37 mmol) of **4** in 10 mL of 2 N H_2SO_4. After refluxing for 2 h the solution was cooled and extracted with ether, 3 × 20 mL portions, and dried over anhydrous $MgSO_4$. Evaporation of the solvent gave an oil which was purified by preparative TLC on silica gel to give 0.045 g (75%) of a low-melting solid mp ~38 °C (lit.[13] mp 34–36 °C) identified as **5**.

Treatment of 6a and 6b with LDA–Iodomethane. Sulfenimines **6a** and **6b** were treated as described above for the alkylation of sulfenamide enolate equivalents. Thioanisole and benzonitrile were analyzed by gas chromatography.

Synthesis of *N*-3(Pentylidene)benzensulfenamide (7) and *N*-2(3-Methylbutylidene)benzenesulfenamide (8). Sulfenimines **7** and **8** were prepared from 10.0 g (0.64 mol) of phenyl disulfide and a fivefold excess of the corresponding ketone using the metal-assisted sulfenamide synthesis previously described.[1,5] Compound **7** was obtained in 53% yield: bp 75–78 °C (0.25 mm); NMR ($CDCl_3$) δ 1.1 (d-t, 6 H, Me), 2.3 (d-q, 4 H, CH_2), and 7.0–7.6 (m, 5 H). Anal. Calcd for $C_{11}H_{15}NS$: C, 68.34; H, 7.82. Found: C, 68.37; H, 7.75.

Compound **8** was obtained in 40% yield: bp 84–6 °C (0.35 mm); NMR ($CDCl_3$) δ 1.1 (d, 6 H, Me, J = 7 Hz), 1.95 (s, 3 H, Me), 2.5 (m, 1 H), and 7.0–7.6 (m, 5 H). Anal. Calcd for $C_{11}H_{15}NS$: C, 68.34; H, 7.82. Found: C, 68.41; H, 7.64.

Regioselectivity of Sulfenamide Enolate Equivalents. In a 100-mL three-necked flask equipped with magnetic stirrer, dropping funnel, nitrogen, and syringe inlets was placed a freshly prepared solution of the appropriate base in ether or THF (Table II) under an atmosphere of nitrogen. The reaction mixture was cooled to the pre-

scribed temperature and 2.0 mmol of *N*-(2-butylidene)benzenesulfenamide (3)[4] in 2.0 mL of the appropriate solvent was added dropwise over 0.5 h. After stirring for the required time, 6.0 mmol of iodomethane was added dropwise and the stirring was continued for an additional 2 h. The reaction was quenched with 30 mL of water and the ether solution was dried over anhydrous $MgSO_4$. Sulfenimines 7 and 8 were analyzed by gas chromatography.

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Registry No.—8, 65276-71-3.

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On the Mechanism of the Thermal Isomerization of 1,2-Diolates. Is the Pinacol Coupling Reaction Reversible?

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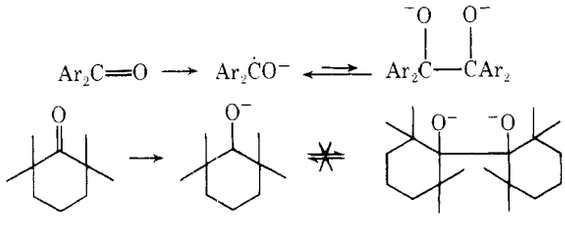
1,2-Diols containing at least one α proton will isomerize when heated to 155 °C as their dilithium salts. The mechanism of the isomerization is shown to be an oxidation–reduction rather than a reverse pinacol coupling as had been suggested by earlier workers. Evidence in support of the proposed mechanism is presented.

The pinacol coupling reaction is a potentially powerful method of carbon–carbon bond formation which has received little attention from synthesis chemists.[1] We have been interested for some time in the synthetic uses of the pinacol reaction,[2,3] and one of the questions which we wished to answer involved the reversibility (or lack thereof) of the reaction. Such information could be valuable if, for example, one wished to plan the stereospecific synthesis of a cyclic 1,2-diol by internal pinacol cyclization.[4]

It has long been known that *certain* pinacol couplings are readily reversible when, for some reason, the central carbon–carbon bond is unusually weak. Such, for example, is the case when diaryl ketones are reductively coupled to tetraarylethanediols.[5] Similarly, although for steric rather than electronic reasons, 2,2,6,6-tetramethylcyclohexanone cannot be reductively coupled to a pinacol because its ketyl will not dimerize.[6]



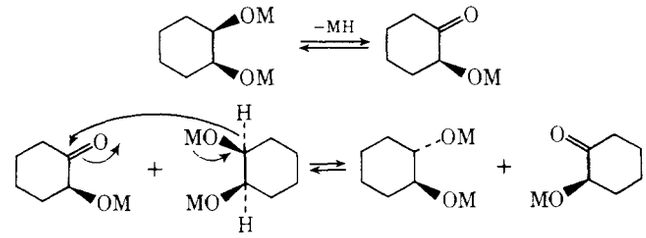
The situation for saturated, sterically uncrowded 1,2-diols is less clear, however. Schlosser, in a 1970 communication, reported the thermal isomerization of a series of dilithium 1,2-diolates and proposed a bond homolysis mechanism (reverse pinacol coupling) to account for his results.[7] *cis*-1,2-Dihydroxycyclohexane, for example, isomerized nearly completely (97%) to its trans isomer when heated as its dilithium salt for 17 h at 155 °C.

Yet a further example was reported sometime later by Sharpless.[8]

In considering the Schlosser report, we were struck by the fact that all of the cases examined were disecondary 1,2-diols and that an alternative oxidation–reduction mechanism, perhaps initiated by a trace amount of ketone, could also account for the observed results. We therefore investigated the isomerization of a selected 1,2-diol, *cis*-1,2-dihydroxycyclohexane (1), in more detail. Our results are summarized in Table I.

Runs 1–3 were carried out to establish the minimum condition necessary to achieve diol equilibration, and we verified the Schlosser report in this respect. In order to establish whether or not the observed equilibration was due to a catalytic amount of O_2 initiating a redox process, we next (runs 4 and 5) attempted equilibration using scrupulously oxygen-free conditions (freeze–thaw deoxygenation of solvents; sealed tube) under both nitrogen and argon atmospheres. Although the equilibration seemed qualitatively somewhat slower, and although higher yields of recovered products were obtained, it was nevertheless clear that diol equilibration still occurred readily in the absence of oxygen.

An alternative means of generating a trace amount of oxidized material necessary to start the catalytic redox cycle



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