**Table II. Chromium Atom Deoxygenation of Epoxides**

| Starting material | Product ratios |
|---|---|
| Cyclohexene oxide | Cyclohexene (86)<br>Benzene (3)<br>1,3-Cyclohexadiene (11)<br>Cyclohexane (0) |
| *cis*-Stilbene oxide | *cis*-Stilbene (40)<br>*trans*-Stilbene (60) |
| Allylbenzene oxide | Allylbenzene (100) |
| *cis*-4-Decene oxide | *cis*-4-Decene (36)<br>*trans*-4-Decene (64) |
| 1-Methylcyclopentene oxide | 1-Methylcyclopentene (100) |

by cocondensation with chromium (no olefin dismutation); hence the deoxygenation itself may well be stereospecific. Total conversion to products ranged from 3 to 10%.

Cyclohexene yields were decreased by over an order of magnitude when cyclohexene oxide was condensed onto a preformed chromium surface. When products were pumped off a chromium–cyclohexene oxide matrix without the customary 1-h warmup, yields were unaffected. These results are consistent with initial reaction at the atomic chromium stage. Consequently, the data in Table I likely reflect both the rate of metal reaction with epoxide *and* the rate of metal aggregation.[2]

Skell and Shevlin have observed epoxide reductions with arc[6] and chemically[7] generated carbon atoms. Deoxygenation can in principle occur by either concerted or stepwise mechanisms; intermediates formed via oxygen complexation and/or carbon–oxygen bond insertion are possible. Interestingly, molecular orbital calculations suggest that the deoxygenation of ethylene oxide by carbon atoms is a direct, concerted reaction with no local energy minima on the way to carbon monoxide and ethylene.[8]

Chromium also effects oxygen abstraction from heteroatom oxides. 2,6-Dimethylpyridine was obtained from 2,6-dimethylpyridine *N*-oxide, without formation of any stable $\pi$ complexes.[9] Dimethyl sulfoxide afforded dimethyl sulfide via a red matrix, and triethylphosphine oxide was converted (green matrix) to triethylphosphine. Yields (1–5%) were significantly lower when a preformed chromium surface was employed. Reactions of other oxygenated organic compounds are currently under study.[4]

Large-scale deoxygenations of organic compounds, including epoxides, are often executed with ill-defined low valent transition metal reagents.[10] We believe metal atoms offer an obviousadvantage. While the metal atom reactor is a rapid and definitive means for assaying the relative reactivities of atomic metals, it requires the utilization of excess organic reactant,[2] limiting product yields. Hence, results such as ours should be used as guidelines for the development of reagents which release a slow steady state of metal atoms into solution. Work toward this end is underway in this laboratory[5] and others.[11]

**Acknowledgment.** We thank the Research Corporation for financial support.

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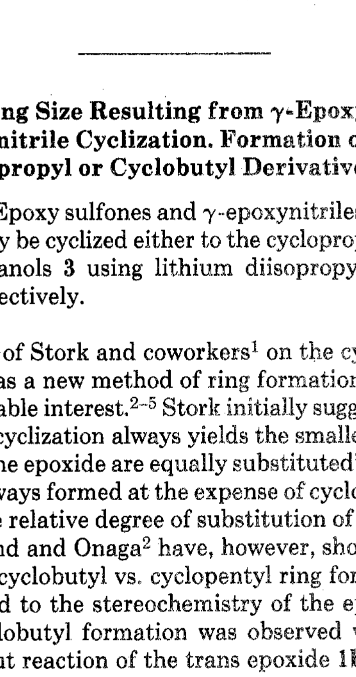
## Control of Ring Size Resulting from γ-Epoxy Sulfone and γ-Epoxynitrile Cyclization. Formation of Either Cyclopropyl or Cyclobutyl Derivatives

*Summary:* γ-Epoxy sulfones and γ-epoxynitriles of the type 1 ($R_3$ = H) may be cyclized either to the cyclopropylcarbinols 2 or cyclobutanols 3 using lithium diisopropylamide and $CH_3MgI$, respectively.

Sir: The work of Stork and coworkers[1] on the cyclization of epoxynitriles as a new method of ring formation has stimulated considerable interest.[2–5] Stork initially suggested[1b] that "epoxynitrile cyclization always yields the smaller ring when both ends of the epoxide are equally substituted". Cyclopropanes were always formed at the expense of cyclobutanes regardless of the relative degree of substitution of the epoxide ring. Lallemand and Onaga[2] have, however, shown that the preference of cyclobutyl vs. cyclopentyl ring formation in 1 may be related to the stereochemistry of the epoxide ring. Exclusive cyclobutyl formation was observed with the cis epoxide **1a**, but reaction of the trans epoxide **1b** (R = $CH_3$, $C_4H_9$, $C_5H_{11}$) led to mixtures of the cyclobutyl and cyclopentyl derivatives in about a 35:65 ratio.



This type of cyclization has also been used to prepare 3-cyano-4-hydroxymethylpyrrolidines[3] and chrysanthemic acid.[4] Quite recently, Gaoni[5] has shown that γ-epoxy sulfones such as **4b** could be cyclized with *n*-BuLi in THF at −15 °C to the cyclopropyl derivative **5b.**

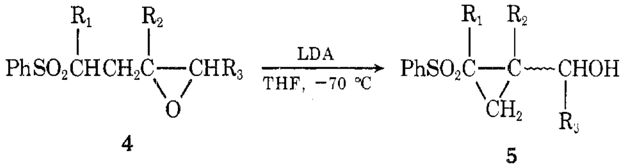
We have also been studying the reaction reported by Gaoni and found, in agreement with him, that epoxy sulfones of the type 4 react with $CH_3Li$ or lithium diisopropylamide (LDA) to give 1-phenylsulfonyl-2-hydroxymethylcyclopropanes (**5**).[6] With the exception of **4b**, in which a nucleophilic displacement at a tertiary center is required, the isolated yields of the cyclopropanes were in the 85–95% range (Table I).

In contrast to these results, we have found that treatment of the same epoxy sulfones 4 ($R_3$ = H) with ~2 equiv of a

**Table I. Reaction of γ-Epoxy Sulfones with Bases**

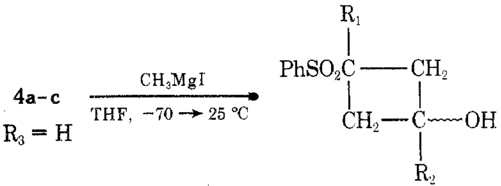
| Epoxy sulfone | Base | Products, % Cyclopropane | Products, % Cyclobutane |
|---|---|---|---|
| **4a** | LDA | 85 | |
| | $CH_3Li$ | 81 | |
| | $CH_3MgI$ | | 96 |
| | $CH_3CH_2MgBr$ | 14.5 | 71 |
| **4b** | LDA | 36 | |
| | $CH_3Li$ | 20 | |
| | $CH_3MgI$ | | 51 |
| **4c** | LDA | 95 | |
| | $CH_3MgI$ | | 98 |
| **4d** | LDA | 98 | |
| | $CH_3Li$ | 90 | |
| | $CH_3MgI$ | 70 | |
| **4e** | LDA | 71 | |
| | $CH_3MgI$ | 35 | |

Grignard reagent,[7] for example, $CH_3MgI$ or $CH_3CH_2MgBr$, at −70 °C, followed by warming to room temperature and stirring overnight, afforded 3-phenylsulfonylcyclobutanols **6** in fair to excellent yield. The cyclobutanol structures were confirmed by their NMR spectra[8] and oxidation to cyclobutanones (ir 1800 $cm^{-1}$). The cyclobutanol **6a** has also been obtained in 46% yield in a one-pot process by reaction of phenyl methyl sulfone with $CH_3MgI$ in THF containing 10% hexamethylphosphoramide, (HMPTA) followed by addition of *epi*-bromohydrin. Epoxy sulfones in which $R_3$ was either aryl or alkyl (**4d** and **4e**) continued to give cyclopropyl derivatives.



**4** **5**

a, $R_1 = R_2 = R_3 = H$
b, $R_1 = R_3 = H$; $R_2 = CH_3$
c, $R_1 = Ph$; $R_2 = R_3 = H$
d, $R_1 = R_2 = H$; $R_3 = Ph$
e, $R_1 = R_2 = H$; $R_3 = CH_3$

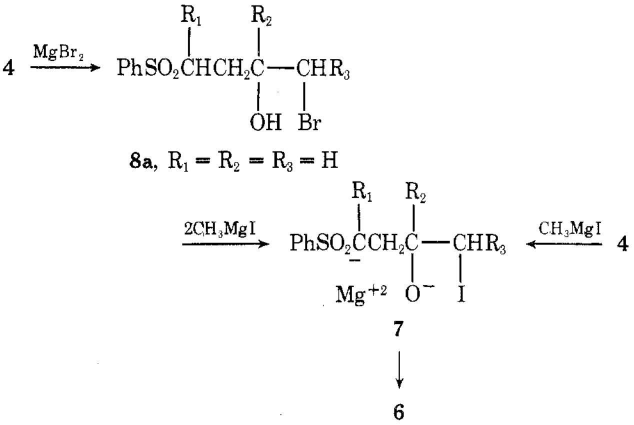


**6a-c**

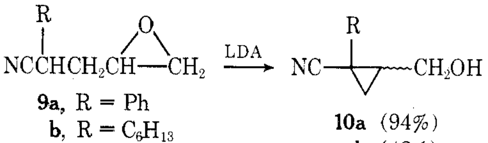
$$\mathbf{4d}, \mathbf{4e} \xrightarrow[\text{THF, } -70 \to 25\ °C]{CH_3MgI} \mathbf{5d}, \mathbf{5e}$$

Mechanistically, we have shown that the cyclobutanol formation is the result of an initial opening of the epoxide ring, most probably preceding proton abstraction α to sulfur, to form an iodo alkoxide, possibly best represented as **7**, which subsequently cyclizes. Both the halo alkoxide[9] and the α-sulfonyl carbanion formation[10] upon reaction of Grignard reagents with epoxides and sulfones respectively, have ample literature precedent. The above sequence of reactions is in agreement with the isolation of the iodohydrin corresponding to **7a**, 30% monodeuterated α to sulfur, and the cyclobutanol **6a**, in a 75:25 ratio when the reaction between **4a** and $2CH_3MgI$ was quenched with $D_2O$ after warming from −78 to +10 °C over a period of 1 h. The incomplete monodeuteration in the iodohydrin does not agree with the alternate possibility in which proton abstraction α to sulfur preceeds the epoxide opening,[11] but does indicate that the rates of formation of the α-sulfonyl Grignard reagent and its cyclization to the cyclobutanol **6a** are of comparable magnitude. Also supporting the above mechanistic suggestion is the observation that reaction of the bromohydrin **8a**, generated from **4a** and $MgBr_2$, with excess methylmagnesium bromide furnished **6a** in 60% yield. Interestingly, treatment of **8a** with 2 equiv of $CH_3Li$ in THF gave a 55% yield of a 1:1 mixture of **5a** and **6a.** It appears that there is a close balance between cyclobutanol formation and epoxide regeneration (leading eventually to the cyclopropyl derivatives **5**) in the reaction of the bromohydrins **8** with bases, and either a change in counterion from magnesium to lithium or substitution ($R_3 \neq H$) favor epoxide and thence cyclopropane formation (Scheme I).

**Scheme I. Formation of Cyclobutanols from γ-Epoxy Sulfones and $CH_3MgI$**

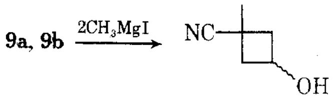


The above results suggest considerable potential for the synthesis of substituted cyclobutanols, and possible larger ring alcohols, some of which we have begun to explore. For example, the epoxynitriles **9** can be transformed into *either* cyclopropyl **10**[1b] or cyclobutyl derivatives **11**, using LDA or $CH_3MgI$, respectively. In the case of the epoxynitriles, the amount of Grignard reagent employed is more crucial than for the epoxy sulfones. For example, **9a** when reacted with 1 equiv of $CH_3MgI$ gave a mixture of cyclopropyl vs. cyclobutyl derivatives in a 1:3 ratio; 2 equiv gave 67% cyclobutylnitrile **11a**[12] and 17% cyclobutyl methyl ketone **12**,[13] while the use of ~4 equiv gave **12** in 62% isolated yield. The preferred method for the formation of **11a** from **9a** appears to involve

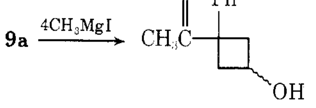


**9a**, R = Ph
**b**, R = $C_6H_{13}$
**c**, R = H

**10a** (94%)
**b** (43%)
**c** (59%)



**11a** (67%)
**b** (40%)



**12**, 62%

$$\mathbf{9a} \xrightarrow[2.\ CH_3MgI]{1.\ MgBr_2} \mathbf{11a}\ (80\%) + \mathbf{10a}\ (5\%)$$

sequential treatment of **9a** with $MgBr_2$ at room temperature followed by 1 equiv of $CH_3MgI$ at −70 °C; the isolated yield of **11a** in this case was 80%.

The present method of cyclobutanol formation from epoxides complements and significantly extends that described earlier by Stork and coworkers.[1] An important aspect of the results described herein is that either three- or four-membered rings can be obtained from the same starting materials. Preliminary results in the sulfone series indicate that our conditions, LDA or $CH_3MgI$, respectively, can be used to synthesize either four- or five-membered rings.[14]

**Acknowledgment.** Financial assistance from the National Research Council of Canada is gratefully acknowledged.

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(6) All new compounds gave NMR and ir spectra consistent with the assigned structures. Exact mass measurements and/or elemental analyses were also obtained.

(7) The concentration of the Grignard reagents was determined by the titration: M. S. Kharasch and O. Reinmuth in "Grignard Reactions of Nonmetallic Substances", Prentice Hall, New York, N.Y., 1954, p 3. When only 1 equiv was used, the reaction produced considerable amounts of iodohydrins in addition to **6**.

(8) Cyclobutanol **6a**, after exchange with $D_2O$, showed a multiplet from $\delta$ 2.3 to 3.0 (4 H) and two quintets showing additional fine structure at 3.39 (1 H) and 4.25 (1 H). In contrast, **5a** showed absorption for its nonaromatic protons at 1.0–1.3 (1 H), 1.4–1.6 (1 H), 1.9–2.7 (1 H), and 3.4–3.8 (3 H).

(9) W. R. Herr and C. R. Johnson, *J. Am. Chem. Soc.*, **92**, 4979 (1970), and references therein.

(10) Reference 7, p 1297.

(11) A competition between the proposed pathways could also account for the deuteration results. However, our results and those of the other workers[1,4,5] suggest that, if an anionic species in formed in the presence of the $\gamma$-epoxide, only cyclopropanes are obtained.

(12) NMR data after $D_2O$ exchange for **11a:** $\delta$ 2.4–3.5 (5 H), 3.3–3.9 (1 H), and 7.3–7.4 (5 H); ir 3350 and 2230 $cm^{-1}$. In contrast, **10a** showed NMR peaks at 1.4–2.1 (3 H), 3.4 (2 H), and 6.3 (5 H) after $D_2O$ exchange.

(13) Both diastereomers of the hydroxy NMR ketone **12** were isolated. The less polar isomer (16%) showed NMR peaks at $\delta$ 1.96 (3 H), 2.1–2.5 (2 H), 2.8–3.3 (2 H), 4.2 (quintet with fine splitting, 1 H), and 7.1–7.4 (5 H). The more polar isomer (44%) had peaks at 1.92 (3 H), 2.4–3.2 (4 H), 4.18 (quintet, 1 H), and 7.35 (5 H).

(14) J. M. Decesare, B. Corbel, and T. Durst, unpublished observations.

(15) Visitor, France-Canada (N.R.C.) Scientific Exchange Program.

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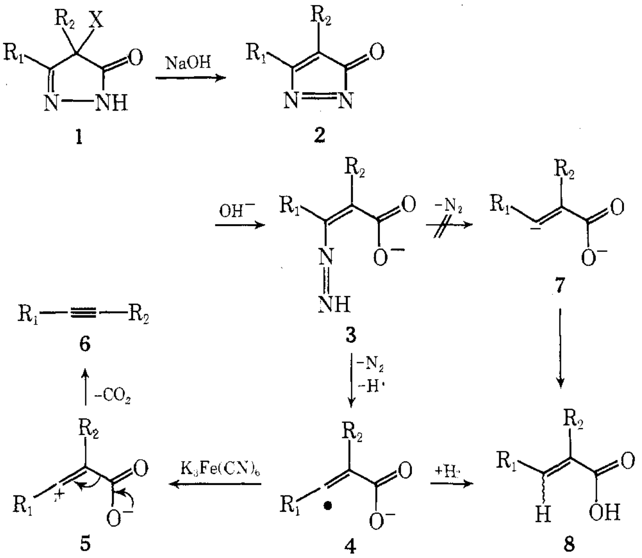
## A New Acetylene Synthesis. Junipal

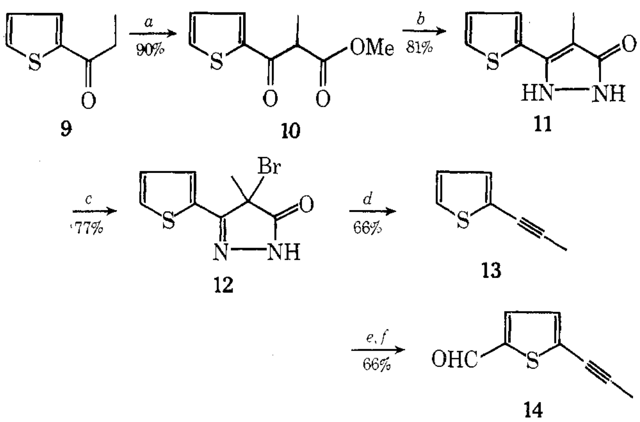
*Summary.* A new acetylene synthesis involving the reaction of 3,4-disubstituted 4-halo-2-pyrazolin-5-ones with aqueous NaOH in the presence of $K_3Fe(CN)_6$ was applied to the synthesis of junipal [5-(1-propynyl)-thiophene-2-carboxaldehyde].

*Sir:* The reaction of 3,4-disubstituted 4-halo-2-pyrazolin-5-ones **1** with aqueous NaOH affords a mixture of isomeric $\alpha,\beta$-unsaturated carboxylic acids **8** (Scheme I).[1] A previous investigation firmly established the intermediacy of the azacyclopentadienone **2** en route to the acids **8**;[2] however, the fact that an isomeric mixture was obtained in which the *Z* isomer (inversion at C-3) has thus far always predominated is inconsistent with the proposed vinyl carbanion intermediate **7**[2,3] since such an intermediate should protonate in a protic milieu much faster than invert and thereby give the *E* isomer (retention at C-3). We recently suggested the following alternate mechanism[3] to explain the lack of stereoselectivity: extrusion of nitrogen from the vinyl diimide **3** to give a configurationally unstable vinyl radical (e.g., **4**) which can then capture a hydrogen atom to give the isomeric acids **8**. We now report evidence in support of a radical mechanism for the conversion of **1** to **8**, and a modification of the reaction which provides a novel synthesis of disubstituted acetylenes under mild conditions.

Scheme I



Scheme II



[a] $(MeO)_2CO$, NaH, benzene. [b] $NH_2NH_2$/MeOH. [c] Pyr·$HBr_3$/HOAc. [d] NaOH, $K_3Fe(CN)_6/H_2O$. [e] *n*-BuLi, 0 °C. [f] DMF, −78 °C.

If an intermediate vinyl radical **4** were generated with a sufficient lifetime to permit electron abstraction by an appropriate oxidizing agent, then a vinyl carbonium ion **5** might result which could then suffer loss of $CO_2$ to afford an acetylene **6**. Indeed, the addition of the chloropyrazolinones **1a–e**

**Table I. Acetylenes from the Reaction of 4-Chloro-2-pyrazolin-5-ones with Aqueous NaOH–$K_3Fe(CN)_6$**

| | Chloropyrazolinone 1 | | |
|---|---|---|---|
| | $R_1$ | $R_2$ | % **6**[a,b] |
| a | Ph | Ph | 80 |
| b | Ph | Me | 60 |
| c | Me | Ph | 12 |
| d | c-$C_6H_{11}$ | Me | 25 |
| e | –$(CH_2)_{10}$– | | 18 |

[a] Yields represent pure, isolated products. [b] Identified by comparison with authentic samples.