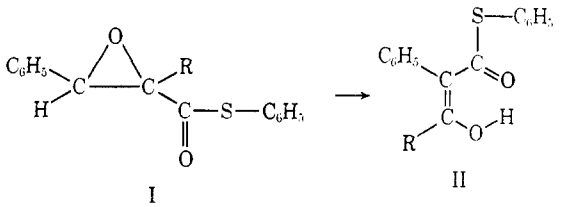
The Synthesis and Rearrangement of Glycidic Thiol Esters. An Example of Thiol Ester Group Migration

Sir:

Recently there has been interest in the synthesis of oxiranes substituted with electron-withdrawing groups. Thus preparations of α,β-epoxysulfones,[1] α-nitroepoxides,[2] and α,β-epoxyphosphonates[3] have been reported in the literature and α,β-epoxy esters, ketones, aldehydes, amides, and nitriles are well known. We have obtained the previously unreported glycidic thiol esters employing the sodium salt of the corresponding glycidic acid.[4] Thus thionyl chloride (1.1 equiv) was added to sodium *trans*-β-phenylglycidate (1.0 equiv) at $-80°$ in carbon tetrachloride and the mixture allowed to warm to room temperature where it was maintained for several minutes. Pyridine (1.5 equiv) and benzenethiol (1.0 equiv) were added to the mixture at $-80°$ and the reaction was again allowed to warm to room temperature where it was maintained for 30 min before work-up. The phenyl *trans*-β-phenylthiolglycidate (I, R = H) was purified on a silica gel column with benzene eluent and recrystallized from benzene–petroleum ether (mp 81°, ir[5] (halocarbon oil) 1695 (thiol ester) + 1700 cm^{-1} (shoulder, thiol ester). *Anal.* Calcd for $C_{15}H_{12}O_2S$: C, 70.30; H, 4.72; S, 12.49. Found: C, 70.50; H, 4.61; S, 12.63). The 60-MHz nmr spectrum in deuteriochloroform (δ_{TMS} 7.29 (C_6H_5, 5 H), 7.39 (C_6H_5S, 5 H), 3.70 (d, 1 H), 4.17 (d, 1 H), $J_{HH} = -1.5$ Hz) compares favorably with data reported for glycidic aldehydes, acids, and esters.[6] The mass spectrum[7] gave a molecular ion of 256.066 ($C_{15}H_{12}O_2S$ = 256.056) and a peak at *m/e* 199.057 ($C_6H_5CHSC_6H_5$ = 199.058) which corresponds to the interesting fragmentation pattern involving rearrangement previously reported for β-phenylglycidic amides.[8] The phenyl *trans*-β-phenylthiolglycidate could be converted cleanly to sodium *trans*-β-phenylglycidate and benzenethiol with sodium hydroxide in ethanol.

The rearrangement of α,β-epoxy ketones and glycidic esters has been studied extensively by House[9] and recently carbethoxy migration has been observed with α- or β-substituted β-phenylglycidic esters[10] although the unsubstituted ethyl β-phenylglycidate rearranges with proton migration to give ethyl phenylpyruvate. We have therefore studied the reaction of phenyl *trans*-β-phenylthiolglycidate with boron trifluoride etherate under anhydrous conditions. Thus phenyl *trans*-β-phenylthiolglycidate (1 equiv) was allowed to react with boron trifluoride etherate (4 equiv) in ether solvent at 25°. After 10 min the ether is removed under reduced pressure and the product is purified on a silica gel column with benzene eluent to give predominantly the enol tautomer of phenyl α-formylphenylthiolacetate [II, R = H; ir (neat) 1625 (s) and 1700 cm^{-1} (w); nmr δ_{TMS} (CCl_4) 7.20 (C_6H_5 + C_6H_5S, 10 H), 6.82 (d, 1 H), 12.45 (d, 1 H, J_{HH} = 12.5 Hz)] obtained in 60% yield. The spectral data agreed with those reported for the enol tautomer of ethyl α-formylphenylacetate which also displays a coupling constant of 12.5 Hz for the enolic and "aldehydic" protons.[11] The structure of the rearrangement product was confirmed by conversion to 4-phenylpyrazolone (mp 225°,[12] lit.[13] 226°) with hydrazine in ethanol.



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Thiol ester group migration is clearly demonstrated in the case of phenyl α-methyl-*trans*-β-phenylthiolglycidate (I, R = CH_3; ir (neat) 1695 and 1700 cm^{-1} (shoulder); nmr δ_{TMS} (CCl_4) 1.29 (CH_3, 3 H), 4.27 (epoxide proton), 7.25 (C_6H_5, 5 H), and 7.35 (C_6H_5S, 5 H); mass spectrum *m/e* 270.081 ($C_{16}H_{14}O_2S$ = 270.071) and 199 ($C_6H_5CHSC_6H_5$)) prepared from sodium α-methyl-*trans*-β-phenylglycidate. The phenyl α-methyl-*trans*-β-phenylthiolglycidate was allowed to react with boron trifluoride etherate in ether to give as the major rearrangement product the enol tautomer of phenyl α-phenylacetothiolacetate (II, R = CH_3; nmr δ_{TMS} (CCl_4) 1 71 (CH_3, 3), 7.28 (C_6H_5, 10 H), and 13.4 (OH, 1 H)) obtained in 45% yield. The structure was established by conversion to 4-phenyl-5-methylpyrazolone (mp, 211°,[14] lit.[15] 211°).

In addition, the rearrangement product, phenyl α-formylphenylthiolacetate, obtained from phenyl *trans*-β-phenylthiolglycidate was converted to the ethyl ester of tropic acid by transesterification to ethyl α-formylphenylacetate[16] followed by reduction[17] with sodium borohydride which provides a biochemically patterned synthesis of tropic acid esters assuming thiol ester group migration in preference to phenyl migration during the rearrangement of phenyl *trans*-β-phenylthiolglycidate. Thiol ester group migration during the rearrangement

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(5) Obtained with a Beckman IR 12 spectrophotometer. Glycidic esters are reported to have two bands in the carbonyl region: H. O. House and J. W. Blaker, *J. Amer. Chem. Soc.*, **80**, 6389 (1958).

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(12) Shown to be identical (mixture melting point and ir spectrum) with an authentic sample prepared from ethyl α-formylphenylacetate and hydrazine hydrate in ethanol.

(13) H. A. Offe, W. Siefken, and G. Domagk, *Z. Naturforsch. B*, 7, 446 (1952).

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(16) The transesterification is accomplished by initial formation of the diethylacetal of phenyl α-formylphenylthiolacetate with sulfuric acid in ethanol followed by conversion to the diethylacetal of ethyl α-formylphenylacetate with sodium ethoxide in ethanol followed by dilute acid hydrolysis to ethyl α-formylphenylacetate.

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of phenyl *trans*-β-phenylthiolglycidate is supported by the clear example of thiol ester group migration during the rearrangement of phenyl α-methyl-*trans*-β-phenylthiolglycidate where substitution of a methyl group at the α carbon atom would be expected to assist phenyl migration in preference to thiol ester group migration during the rearrangement.[9,10] The biosynthesis of tropic acid in *Datura stramonium* has been extensively studied by Leete,[18] who has demonstrated carbonyl group migration in the transformation of phenylalanine to tropic acid *via* some as yet unknown intermediate.

We are presently investigating other synthetic methods for the preparation of thiolglycidic esters and exploring their chemistry and biogenetic significance.

Acknowledgment. We wish to thank Professor Edward Leete of the University of Minnesota for inspiration and helpful discussions during the course of this work.

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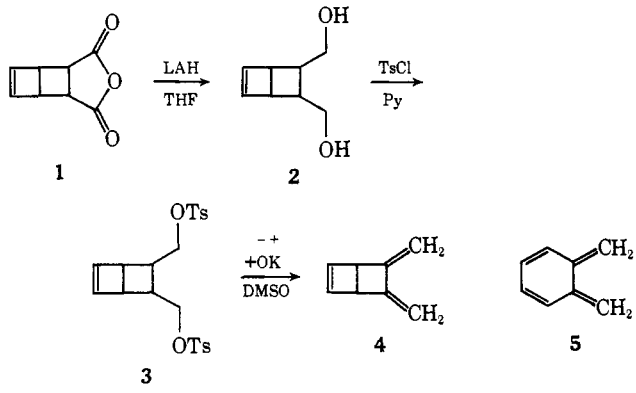
Synthesis and Reactions of 5,6-Dimethylenebicyclo[2.2.0]hexene-2. "Dewar *o*-Xylylene"

Sir:

o-Xylylene has never been isolated nor even characterized except by Diels–Alder trapping experiments.[1-5] We wish to report that its "Dewar" analog, the highly strained molecule **4**, is not nearly so elusive, as the success of the synthesis formulated in Scheme I demonstrates.

Scheme I



1 2 3 4 5

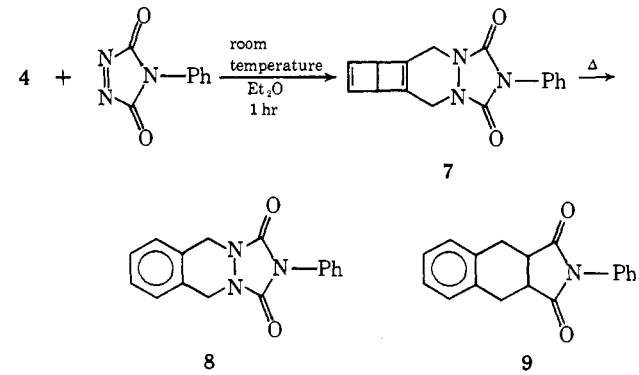
Anhydride **1**[6,7] was first converted to the diol **2** by LAH–THF reduction (inverse addition, 1.5-hr reflux). In our hands, better yields were obtained when the crude anhydride photolysate[6,7] was reduced directly and the diol partially purified by distillation or column chromatography: bp 90–105° (5 × 10^{-3} Torr); 20–27% composite yield of *ca.* 90% pure diol in the photolysis and reduction steps; nmr ($CDCl_3$) τ 3.66 (t, 2 H, J = 1 Hz), 5.36 (s, 2 H), 6.1–6.5 (m, 2 H), 7.20 (m, 2 H), 7.5–7.8 (m, 2 H). Several attempts to convert **2** to a dibromide (PBr_3) failed, but tosyl chloride–pyridine (0°, overnight) gave ditosylate **3**: mp 146–147° (MeOH); 18–34%; nmr ($CDCl_3$) τ 2.1–2.8 (q, J = 8.5), 3.73 (t, 2 H, J = 1 Hz), 5.8–6.0 (m, 4 H), 7.03 (m, 2 H), 7.56 (s, 8 H). Elimination by *tert*-butoxide–DMSO (ambient, 10^{-6} Torr) gave **4** isolated from the −78° trap: 40%, nmr (CCl_2=CCl_2, HA-100) τ 3.83 (t, 2 H, J = 1.0 Hz), 4.88 (d, 2 H, J = 1.0 Hz), 5.24 (s, 2 H), 6.27 (s, 2 H) ($J_{^{13}C-H}$ = 156 (bridgehead) and 169 (cyclobutene) Hz; uv (EtOH) λ_{max} 234 mμ (sh), 242 (ε 6100), 253 (sh); mass spectrum *m/e* 104, 103 (P, P − 1); ir (vapor) ν 3050, 3000, 1770, 1650, 883, 800, 730, 670 cm^{-1}.

Note that the uv spectrum of **4** is virtually identical with that of 1,2-dimethylenecyclobutane[8] (**6**, λ_{max} 237, 246, 255 mμ) suggesting no interaction between the ene and diene moieties, even in the excited state of **4**. The ^{13}C–H splittings are also in conformity with the structure assigned to **4**.

In sharp contrast to its fully conjugated counterpart (**5**), **4** is thermally stable at room temperature (evacuated sealed tube), although the decomposition rate is perceptible at 60°. As is the case with Dewar benzene,[6] the thermal disrotatory ring opening of **4** is symmetry forbidden, and it is, no doubt, at least partly to this circumstance that **4** owes its modicum of stability. However, because of the high exothermicity of the transformation **4** → **5**, one might suspect that it will nevertheless manage to transpire and, under mild conditions, furnish **5** in either its ground or, more interestingly, one of its excited states. Pertinent studies are underway.

Scheme II summarizes our results in reactions of **4** with dienophiles. The hyperreactive dienophile 2-phenyl-2,4,5-triazoline-1,3-dione converts **4** to a

Scheme II



7 8 9

Dewar benzene adduct (**7**), thus providing a new approach to this class of molecules. The crude **7** is nearly pure, but does contain a small amount of the benzenoid isomer (**8**). Brief warming of **7** in methanol, followed by recrystallization or column chromatography, yields pure **8**: **7** has nmr ($CDCl_3$) τ 2.4–2.8 (m, 5 H), 3.40 (s, 2 H), 5.8 (m, 4 H), 5.96 (s, 2 H); **8** has mp

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