

## The Aluminum Alkoxide Rearrangement of Epoxides. II.<sup>1</sup> Rearrangement of 3,4-Epoxy-*cis*- and -*trans*-*p*-menthane

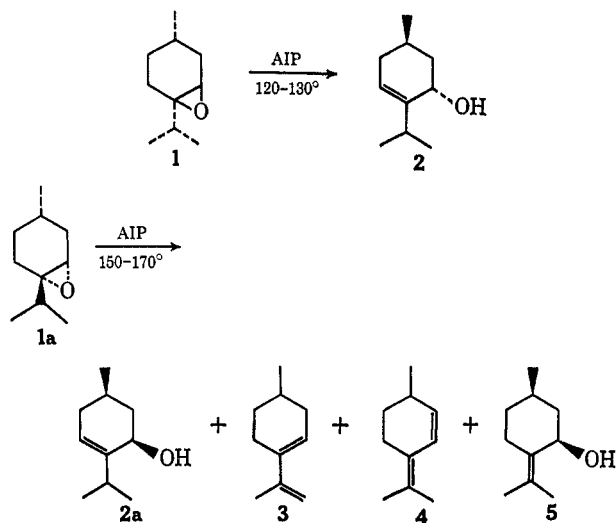
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The aluminum isopropoxide (AIP) catalytic rearrangement of 3,4-epoxy-*cis*-*p*-menthane (1) at *ca.* 120° affords *trans*-3-*p*-menthen-5-ol (2) in almost quantitative yield, whereas the rearrangement of 3,4-epoxy-*trans*-*p*-menthane (1a) requires more drastic conditions and 1a is only partially converted into a mixture of *cis*-3-*p*-menthen-5-ol (2a), traces of *cis*-pulegol (5), and substantial amounts of 3,8- and 2,4(8)-*p*-menthadiene (3 and 4). The last three components were among the typical products reported by us in the AIP reduction of pulegone. A mechanism accounting for the facile AIP rearrangement of 3,4-epoxy-*cis*-*p*-menthane (1) is suggested.

A review of the stereoselectivity of the AIP rearrangement of 3,4-epoxy-*p*-menthanes, reported by us,<sup>1</sup> has disclosed that the *cis* isomer (1) reacts rapidly at *ca.* 120–130° to yield, almost exclusively, the predicted *trans*-3-*p*-menthen-5-ol (2). The cleavage of the epoxide occurs at the site of the most substituted  $\alpha$  carbon of the oxirane oxygen accompanied by  $\beta$ -proton elimination from the least substituted carbon at C<sub>5</sub>. Under the same conditions, 3,4-epoxy-*trans*-*p*-menthane (1a) was recovered almost unchanged. At higher temperature (150–170°), however, 1a afforded as the major product *cis*-3-*p*-menthen-5-ol (2a), traces of *cis*-pulegol (5), and substantial amounts of 3,8- and 2,4(8)-*p*-menthadiene (3 and 4, respectively).



The presence of 3 and 4 could be rationalized as the dehydration products of *cis*-pulegol (5), which was shown to allylomerize to 3-*p*-menthen-8-ol (6) in the presence of AIP above 100°.<sup>2</sup>

The hydrogenation of *cis*-3-*p*-menthen-5-ol (2a) in the presence of Pd-C catalyst afforded almost exclusively menthol, whereas that of *trans*-3-*p*-menthen-5-ol (2) afforded isomenthol as the major product. Both 2 and 2a were identified with the reduction products of 3-*p*-menthen-5-one with lithium aluminum hydride and AIP, respectively.

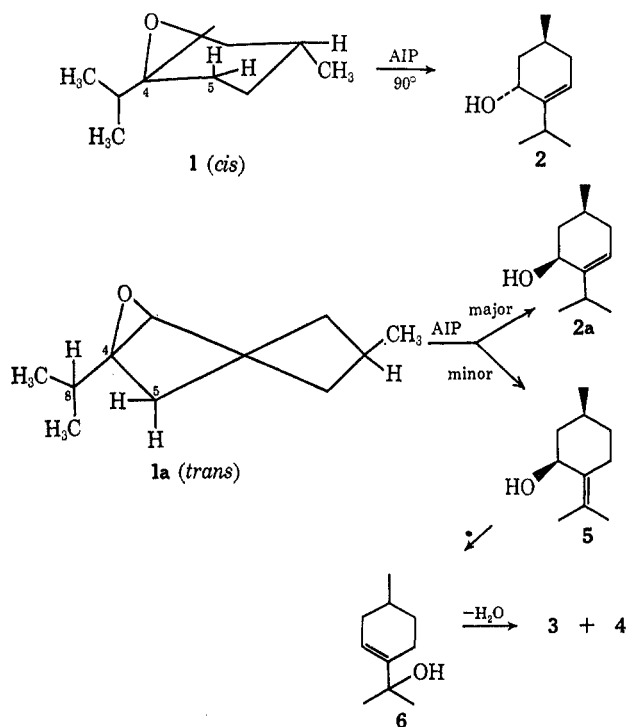
### Results and Discussion

The electrophilic attack of AIP on 3,4-epoxy-*cis*-*p*-menthane (1) results, as predicted,<sup>1</sup> in a cleavage of the

oxirane oxygen bond at the most substituted  $\alpha$  carbon accompanied by  $\beta$ -proton elimination from the least substituted carbon to yield *trans*-3-*p*-menthen-5-ol (2).

An examination of the molecular model of the *cis* isomer 1, which is best represented by a twisted chair, shows that one of the C<sub>5</sub>-H bonds in an  $\alpha$  position to the oxirane oxygen lies parallel to the C<sub>4</sub>-O bond of the oxirane, thus favoring  $\beta$ -proton elimination leading to the concerted formation of *trans*-3-*p*-menthen-5-ol (2).

Such a favorable conformation is not prevalent in the *trans* isomer 1a, and more drastic conditions are required for the formation of *cis*-3-*p*-menthen-5-ol (2a). Under these conditions, a small amount of  $\beta$  deprotonation from the C<sub>8</sub>-H bond affords, as an alternative, minor amounts of *cis*-pulegol (5), which was shown<sup>2</sup> to allylomerize to 3-*p*-menthen-8-ol (6) and dehydrate to 3 and 4.



Steric factors may also account for the facile rearrangement of 1, since the latter is rapidly converted into isomenthol by hydrogenation in the presence of Raney nickel catalyst, while the *trans* isomer 1a is recovered unchanged.<sup>3</sup>

(1) Part I: E. H. Eschinasi, *Israel J. Chem.*, **6**, 713 (1968).(2) E. H. Eschinasi, *J. Org. Chem.*, in press.

(3) E. H. Eschinasi, U. S. Patent 3,052,729 (1962).

TABLE I

Temp, °C	3, %	4, %	1, <sup>a</sup> %	1a <sup>a</sup> %	X, <sup>b</sup> %	2, %	2a, %	5, %
25			48%	52				
100-125				46		49	>2	
155-165	7	4		15	4	53	17	
170	9	5		7	9	53	12	1
Cut 1	10	6		9	10	53	12	
Cut 2					3	55	39	3

<sup>a</sup> Vpc analysis of epoxide made on 10% 2,4-xylenyl phosphate, 4 m × 0.125 in. column, accuracy ±5%. <sup>b</sup> X, 3-*p*-menthen-5-one.

AIP rearrangement product (15 g) corresponding to the composition of the 1st step was distilled at a reflux ratio of 200:1 and the following cuts were obtained: (1) 3,4-epoxy-*trans*-*p*-menthane (1a), yield 5 g, bp 86° (22 mm),  $n_D^{20}$  1.4445, purity (vpc) 98 ± 5% (2,4-xylenyl phosphate column at 80°) (for nmr and ir spectral data see Table I); (2) pure *trans*-3-*p*-menthen-5-ol (2), yield 6 g, bp 73° (2 mm),  $n_D^{20}$  1.4730, which was identified by vpc (20M column at 175°) and ir with the main isomer of the Meerwein-Ponndorf-Verley reduction of 3-*p*-menthen-5-one (see Table I). Upon hydrogenation with Pd-C catalyst it afforded a mixture of 25% neomenthol, 60% isomenthol, and, a minor amount of menthol.

TABLE II

NMR<sup>a</sup> AND IR DATA

Compd	Vinylc protons	Protons geminal to OH, etc.	General protons, including allylic, methyl, etc.	Characteristic ir absorption, $\mu$
	5.48 (br d, 1, $J = 4$ Hz)	4.06-4.25 (br m, 1)	1.4-2.70 (br m, 7, includes OH) 0.85-1.16 (five-peak m, 9, with <i>gem</i> -dimethyl) 0.99-1.10 (d, $J = 2$ Hz)	8.5, 9.3, 10.3, 10.7, 13
	5.48-5.6 (br, 1)	4.36 (br t, 1, $J = 6$ Hz)	1.35-2.99 (br m, 7, includes OH) 0.86-1.28 (m, 9, with <i>gem</i> -dimethyl) 0.99-1.10 ( $J = 1$ Hz)	7.7, 8.85, 9.65, 10.45, 11.05, 11.7
		4.72 (br t, 1, $J = 5$ Hz)	1.33-1.85 (m, 12, with <i>gem</i> -dimethyl) 1.70-1.80 (s)	6.85, 7.9, 9.5, 9.8, 10, 10.25, 12, 13.1, 13.55
	5.61-5.86 (br, 1)	In deuterated DMSO, 4.24 (s, tertiary OH proton)	1.12-2.41 (m, 14, with <i>gem</i> -dimethyl) 1.31 (s) 0.97 (d, $J = 5$ Hz, CH <sub>2</sub> CH)	6.91, 7.3, 7.4, 8.2, 8.5, 8.7, 8.9, 9, 9.05, 9.15, 11.2, 11.85, 12.32
			2.93 (d, 1, $J = 5$ Hz, epoxide) 1.13-2.3 (m, 8) 0.72-1.1 (m, 9, methyls) 2.95 (t, 1, $J = 1.5$ Hz, epoxide) 1.19-2.32 (m, 8) 0.73-1.12 (m, 9, methyl)	7.5, 8.65, 9.6, 10.1, 10.2, 10.55, 11.3, 11.7, 12.3, 13.2

<sup>a</sup> In  $\delta$  units on a Varian A-60A spectrometer with TMS as internal standard.

## Experimental Section

**AIP Rearrangement of *cis-trans*-3,4-Epoxy-*p*-menthane (1).**—3,4-Epoxy-*p*-menthane (10 g, 90% pure) consisting of a 1:1 mixture of 3,4-epoxy-*cis*- and -*trans*-*p*-menthane (as determined by vpc on a 4 m × 0.125 in. 2,4-xylenyl phosphate column at 80°) was added to a clear solution of 2.5 g of AIP in 10 g of dry isopropyl alcohol (IPA). The clear solution was heated in a small (50 ml) Vigreux flask at 85-90° for 5 min, and 11 g of IPA was collected. Heating was resumed and the pot temperature was gradually raised in three steps to 100 → 125°, 155 → 165°, and 170°. At each step the heating was maintained for 2 min while traces of IPA were distilled off 85-90° vapor temperature). Samples of the reaction mixture were quenched in 3 volumes of 30% NaOH and heated to 50-60° until all the aluminum salt dissolved, and the top organic layer was analyzed by vpc (20M column, 4 m × 0.125 in. at 175°). Finally, the reaction was cooled to 80° and high vacuum was applied to distil off a main cut (1), yield 6 g, bp 60-90° (2 mm),  $n_D^{20}$  1.4715. The viscous residue was treated with 20 ml of 30% NaOH heated to 60° under agitation until a clear solution was obtained. The top layer was separated and distilled, yielding a second minor cut (2), yield 1.5 g, bp 80-90° (2 mm),  $n_D^{20}$  1.4690.

The course of the reaction is given in Table I (vpc 20M at 175°).

**Distillation in Nester-Faust Teflon Spinning-Band Column of AIP Rearrangement Products of 3,4-Epoxy-*cis-p*-menthane (1).**—

**Reaction of 3,4-Epoxy-*trans-p*-menthane (1a) with AIP.**—3,4-Epoxy-*trans-p*-menthane (1a), yield 2.5 g, 95% pure, as recovered by Nester-Faust distillation from previous reaction, and 1 g of AIP were gradually heated to 100-155° and 170° within 5 min in a Claisen-Vigreux flask. Vacuum was gradually applied until it reached 2 mm, and 1.7 g, consisting mostly of unreacted epoxide 1a, was collected and showed no evidence of alcohols (by vpc and ir). The residue in the flask was decomposed with 30% NaOH and distilled to yield a second cut of 0.4 g. Vpc analysis of the two cuts showed the following composition: cut 1 (1.7 g), 3% 3, 5% 4, 92% 1a; cut 2 (0.4 g), 2% 3, 3% 4, 37% 1a, 15% 2, 28% 2a, >1% 6, 4% 5.

***cis*-3-*p*-Menthen-5-ol (2a) by Reduction of 3-*p*-Menthen-5-one with LiAlH<sub>4</sub>.**—3-*p*-Menthen-5-one (8 g) in 20 ml of dry ether were fed within 0.5 hr into 0.6 g of LiAlH<sub>4</sub> in 25 ml of dry ether. The reaction mixture was stirred for an additional 0.5 hr and decomposed first with 2 ml of ethanol followed by 20 ml of water. The ether layer was separated and distilled in a Vigreux flask,

(4) The amount of *trans*-3-*p*-menthen-5-ol (2) present is due to a small amount (5-10%) of *cis*-epoxide 1 present in the starting material which could not be evaluated accurately by vpc (2,4-xylenyl phosphate column).

(5) *cis*-3-*p*-Menthen-5-ol (2a) was separated from the mixture by distillation through a Nester-Faust column, bp 80° (2 mm),  $n_D^{20}$  1.4735. It was identical with the main reduction product of 3-*p*-menthen-5-one with LiAlH<sub>4</sub> (for nmr and ir data see Table II); it gave upon reduction with Pd-C 90% menthol.

yielding 6 g, bp 76–80° (2 mm),  $n_D^{20}$  1.4735. Vpc (20M column at 200°) showed the following composition: 6% *trans*-3-*p*-menthen-5-ol (2); 94% *cis*-3-*p*-menthen-5-ol (2a). For nmr and ir spectra see Table I.

*trans*-3-*p*-Menthen-5-ol (2) by Reduction of 3-*p*-Menthen-5-one with AIP (Meerwein-Ponndorf-Verley).<sup>6</sup>—3-*p*-Menthen-5-one (8 g) and 8 g of AIP were heated in a Claisen-Vigreux flask for 5 min at 130–140° while acetone distilled off. Analysis of the reaction product (vpc, 20M column at 200°) showed that 25% of the ketone was reduced, affording a mixture of 60% *trans*-3-*p*-menthen-5-ol (2) and 40% *cis*-3-*p*-menthen-5-ol (2a). The reaction mixture was quenched in 30% NaOH and separated. After boration with 1 g of B<sub>2</sub>O<sub>3</sub> at 120–130°, the unreacted ketone (5 g) was recovered by distillation at 95° (5 mm). The borate ester residue was then decomposed with 30% NaOH and afforded 1 g of distillate, bp 80–85° (2 mm),  $n_D^{20}$  1.4650, which consisted of a mixture of 2 and 2a in a ratio of 60:40, respectively. The components of the mixture were identified by vpc with those obtained from the LiAlH<sub>4</sub> reduction and with pure samples obtained by Nester-Faust distillation of the rearrangement products of 3,4-epoxy-*cis*- and -*trans*-*p*-menthane (1 and 1a).

(6) D. Malcolm and J. Read, *J. Chem. Soc.*, 1037 (1939).

Pure *trans*-3-*p*-menthen-5-ol (2), bp 102–108° (14 mm),  $n_D^{20}$  1.4712, has been previously described by Malcolm and Read.<sup>6</sup>

**Catalytic Reductions.**—The catalytic reductions of the various samples of the allylic alcohols were carried out in a 10% ethanolic solution using 2 g of substance and 0.5 g of catalyst. The hydrogenation was carried out in a Parr shaker at 50 psi hydrogen pressure at 30° and continued until the hydrogen absorption ceased. The results are given below.

*cis*-Pulegol (5) gave 3% neoisomenthol, 90% menthol, and 8% menthone.

*trans*-3-*p*-Menthen-5-ol (2) gave 25% neomenthol, 15% menthol, and 60% isomenthol.

*cis*-3-*p*-Menthen-5-ol (2a) gave 88% menthol and 12% menthones. 3-*p*-Menthen-5-ol (6) gave 60% *trans*-*p*-menthan-8-ol and 40% *cis*-*p*-menthan-8-ol.

$\alpha$ -Terpineol gave 60% *trans*-*p*-menthan-8-ol and 40% *cis*-*p*-menthan-8-ol.

**Registry No.**—1, 23602-11-1; 1a, 23602-12-2; 2, 22472-77-1; 2a, 22472-78-2; 5, 22472-80-6; 6, 18479-65-7.

## A New and Useful Sulfur Ylide. Thetin Anions

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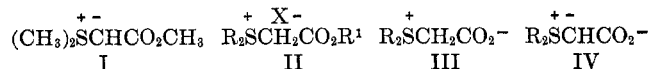
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A procedure for utilization of stabilized sulfur ylides in ketone condensations in good yields is described. The sodium salts of dimethylthetin anion and diphenylthetin anion condense with ketones to produce glycidic acids and with  $\alpha,\beta$ -unsaturated ketones to produce cyclopropanecarboxylic acids. With 4-*t*-butylcyclohexanone, the formed glycidic acid was almost exclusively the *trans* isomer. Thermal decomposition of glycidic acids is known to give aldehydes with loss of CO<sub>2</sub>. Thus this method allows easy chain extension by one or two carbon atoms.

The utilization of ylides in organic synthesis has exploded in the last few years. Although phosphorus ylides enjoy the most widespread use, interest into the applications of sulfur ylides to synthetic problems has been stimulated by the work of Corey and coworkers.<sup>3</sup> Utilization of all kinds of stabilized ylides has been hampered by the unreactivity of these synthetic intermediates. One solution to the problem with phosphorus ylides involves the use of a less electronegative phosphorus substituent. The decreased stabilization by phosphorus of the carbanionic center sufficiently enhanced the reactivity of the species to allow normal condensation with most carbonyl partners. A second approach involves reducing the ability of the substituent on carbon to stabilize an adjacent carbanionic center. We have explored this latter alternative to the solution of this problem in the area of sulfur ylides and wish to report our results at this time.

Dimethyl(carbomethoxymethylene)sulfuran (I) has been reported not to add to carbonyl groups of aldehydes and ketones, although its Michael condensation with  $\alpha,\beta$ -unsaturated systems to produce cyclopropanes is well documented.<sup>4,5</sup> Conversion of the carbo-



a, R = CH<sub>3</sub>

b, R = Ph

(1) NSF Undergraduate Research Participant, 1969.

(2) Alfred P. Sloan Foundation Fellow.

(3) E. J. Corey and M. Jautelat, *J. Amer. Chem. Soc.*, **89**, 3912 (1967), and references cited therein.

(4) (a) A. W. Johnson and R. T. Amel, *J. Org. Chem.*, **34**, 1240 (1969).

(b) Similar reactivity has been reported for very closely related sulfuranyl-

methoxy group into a carboxy anion may sufficiently reduce the stabilization of the ylide to allow normal carbonyl condensations. To examine this possibility, the requisite betaines, IIIa<sup>5a</sup> and IIIb, were prepared from the corresponding sulfonium salts, IIa and IIb. Dimethylthetin (IIIa) was obtained by treatment of an aqueous solution of the sulfonium bromide with silver oxide at room temperature;<sup>5a</sup> diphenylthetin (IIIb) was obtained by treatment of the sulfonium fluoroborate with Amberlite resin at 25°. Other attempts to prepare IIIb led only to decomposition products.

Reaction of dimethylsulfur with dimethylthetin generated a suspension of the anion in DMSO (see Scheme I). This suspension reacted with chalcone to produce two cyclopropanes in approximately equimolar amounts. Analysis of this mixture proceeded after conversion of the acids into their esters with diazomethane. Nmr allowed unambiguous assignment of stereochemistry to the two compounds. In cyclopropane V,<sup>6</sup> the cyclopropyl hydrogen adjacent to the benzoyl group had couplings to the adjacent protons of 5.0 and 10.0 Hz, the benzylic cyclopropyl hydrogen of 5.0 and 7.0 Hz, and the cyclopropyl hydrogen  $\alpha$  to the ester of 7.0 and 10.0 Hz. In cyclopropane

ideneacetates. See H. Nozaki, D. Tunemoto, S. Matubara, and K. Kondo, *Tetrahedron*, **23**, 545 (1967).

(5) For preparation and properties of very closely related sulfuranylidenacetates, see (a) K. W. Ratts and A. N. Yao, *J. Org. Chem.*, **31**, 1185 (1966); (b) J. J. Tufariello, L. T. C. Lee, and P. Wojtkowski, *J. Amer. Chem. Soc.*, **89**, 6804 (1967); (c) J. Casanova and D. A. Rutolo, *Chem. Commun.*, 1224 (1967); (d) G. B. Payne, *J. Org. Chem.*, **32**, 3351 (1967); (e) G. B. Payne, *ibid.*, **33**, 1284, 3517 (1968); (f) G. B. Payne and M. R. Johnson, *ibid.*, **33**, 1385 (1968); (g) H. Nozaki, M. Takaku, Y. Hayashi, and K. Kondo, *Tetrahedron*, **24**, 6536 (1968).

(6) In cyclopropanes, it has been established that *cis* couplings are larger than *trans*. See S. Sternhell, *Quart. Rev. (London)*, **23**, 236 (1969); J. D. Graham and M. T. Rogers, *J. Amer. Chem. Soc.*, **84**, 2249 (1962).