Small-Ring Epoxides. III. Further Studies on 2,2,5,5-Tetramethyl-4-isopropylidene-1-oxaspiro[2.2]pentane[1a]

J. K. CRANDALL*[1b] AND D. R. PAULSON[1c]

Contribution No. 1881 from the Department of Chemistry, Indiana University, Bloomington, Indiana 47401

Received August 5, 1970

Solvolysis of 2,2,5,5-tetramethyl-4-isopropylidene-1-oxaspiro[2.2]pentane (1) in acetic acid–methanol leads initially to 2,5-dimethyl-3-(1-methyl-1-methoxyethyl)hexa-3,4-dien-2-ol (3). Further reaction gives 2,5-dimethyl-3,5-dimethoxy-4-isopropylidenehex-2-ene (5) and 2,5-dimethyl-4-(1-methyl-1-methoxyethyl)-5-methoxyhexa-2,3-diene (4) and subsequently 2,5-dimethyl-3-isopropenyl-2-methoxyhexa-3,4-diene (6), 2,5-dimethyl-4-isopropenyl-3-methoxyhexa-2,4-diene (7), and 2,5-dimethyl-4-isopropylidenehex-5-en-3-one (8). Treatment of 1 with sodium methoxide produces 2,5-dimethyl-4-isopropylhex-1,4-dien-3-one (16), 2,5-dimethyl-2-methoxy-4-isopropylhex-4-en-3-one (17), and 2-isopropylidene-3,3,4,4-tetramethylcyclobutanone (2). The use of either potassium *tert*-butoxide or lithium diethylamide transforms 1 into a mixture of 1-isopropenyl-2-(1-methyl-1-hydroxyethyl)-3,3-dimethylcyclopropene (19) and 8. Reaction of 19 with sulfuric acid in acetic acid also leads to 8. The mechanistic details of these transformations are discussed.

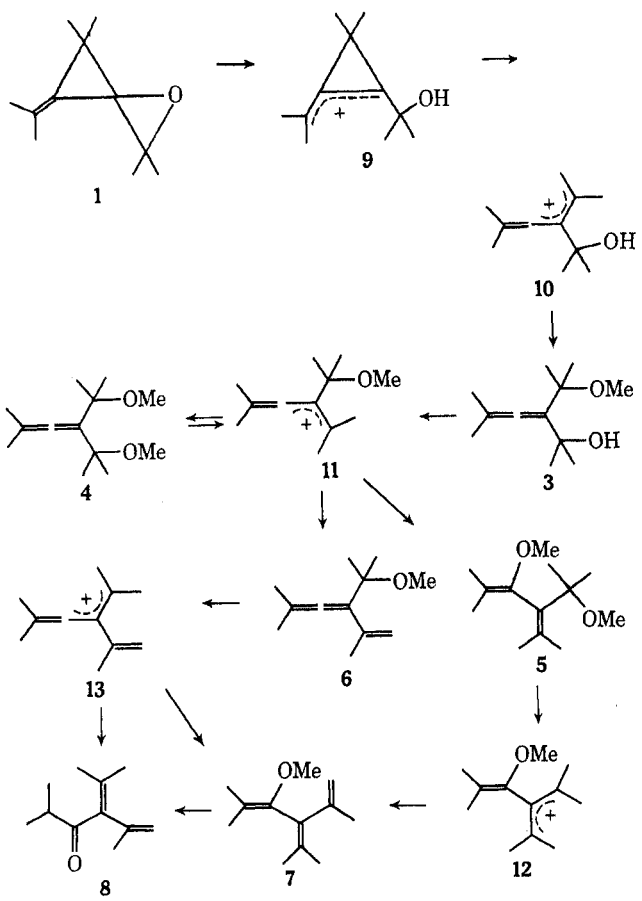
In connection with our interests in highly strained epoxides[2] and in the reactions of epoxides with strong bases,[3] we have further examined the chemistry of oxaspiropentane 1.[4] Experimental complications associated with facile solvolysis reactions of 1 in methanol prompted an examination of these processes prior to study of base-promoted reactions.

Solvolysis of carefully purified 1 in freshly distilled methanol proceeded smoothly to yield two products in a 77:19 ratio which were identified as cyclobutanone 2[4] and allene alcohol 3. Structure 3 follows from its ir (weak 5.1 μ allene absorption) and nmr spectra (three six-proton methyl singlets, a methoxy signal, and a hydroxyl proton at appropriate chemical shifts).

In the presence of added acetic acid up to five additional products could be isolated depending on the exact reaction conditions. These reactions were faster than those performed in the absence of acid and furthermore did not yield cyclobutanone 2. A reaction utilizing 12% acetic acid in methanol could be followed conveniently by glpc analysis. Starting epoxide was transformed extremely rapidly to alcohol 3 which was itself depleted by further reaction. Dimethoxyallene 4 accumulated and then decreased in quantity, whereas the isomeric dimethoxydiene 5 was formed more slowly but continued to increase in amount. Finally, trienes 6 and 7 appeared and increased in quantity as long as the reaction was monitored. Prolonged reaction eventually led to ketone 8 in accord with the earlier work[4] on the isomerization of 1 in acetic acid containing small amounts of sulfuric acid. Alcohol 3 was also converted to 8 by these latter conditions. Reaction of diene 5 with methanol–acetic acid slowly produced triene 7.

The mecahnistic details of these solvolyses are complex in that a variety of processes are occurring concurrently, but a reasonable outline can be constructed as illustrated in Scheme I. Competitive isomerizations of 1 to cyclobutanone 2 and materials with the allene skeleton were observed in our earlier work.[4] At that time acid-catalyzed pathways were suggested for both types of reactions. The predominance of 2 under neutral conditions and its absence in the faster reactions catalyzed by acetic acid suggest that an acid-catalyzed

SCHEME I



mechanism is probably not operative (*vide infra*). However, the acid-catalyzed route to allene alcohol 3 *via* cations 9 and 10 remains attractive, as well as fully consistent with the data. (Direct rearrangement of 1 to 10 is an equally viable alternative.) The isomeric dimethoxy compounds 4 and 5 result from solvolysis of 3 *via* cation 11. The kinetically controlled product is the allene 4, but this material is gradually converted to its isomer 5 and monomethoxyallene 6, presumably through reversible formation of 11. The remaining monomethoxytriene 7 arises from 5 *via* cation 12 and possibly from 6 *via* cation 13. Ketone 8 arises from attack of water on 13 or by multistep hydrolysis of 7. Other possible interconversions can be visualized, but

(1) (a) Supported by a research grant from the National Science Foundation; (b) Alfred P. Sloan Fellow, 1968–1970; (c) NIH Predoctoral Fellow, 1966–1968.

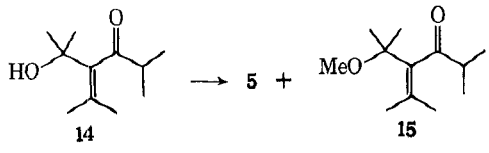
(2) J. K. Crandall and D. R. Paulson, *J. Org. Chem.*, **33**, 3291 (1968).

(3) J. K. Crandall and L. H. C. Lin, *ibid.*, **33**, 2375 (1968).

(4) J. K. Crandall and D. R. Paulson, *ibid.*, **33**, 991 (1968).

these do not change the essential features of the reaction course.

The characteristic spectral properties of the compounds discussed above define the assigned structures and are detailed in the Experimental Section. Noteworthy, however, is the nmr spectrum of **5** which displays eight distinct methyl resonances. This observation demands that the two CCH_3 groups of the $-C(CH_3)_2OMe$ moiety be magnetically nonequivalent. Hindered rotation of this group[5] or about the single bond of the conjugated diene function[6] can account for this result. The large steric perturbation of **5** is also indicated by its rather low wavelength ultraviolet maximum (212 nm).[7] Nonetheless, an alternate preparation of **5** was considered desirable to confirm the assigned structure. This was smoothly accomplished by reacting keto alcohol **14**[2] with triethyl orthoformate in methanol containing a trace of strong acid. A minor product of this reaction was methoxy ketone **15**.



14 15

The reaction of epoxide **1** with sodium methoxide in refluxing methanol led gradually to cyclobutanone **2**, acyclic ketone **16**, and methoxy ketone **17** in a 48:36:8 ratio. The spectroscopic data for **16** define the structural units clearly, hydrogenation leads to the known compound **18**, and alternate structure **8** has already been given to a nonidentical ketone. These data secure the above assignment. Likewise, the spectral data for **17** and its nonidentity with isomer **15** ensure the structure portrayed. Methoxy ketone **17** was found to be stable to the reaction conditions, thereby ruling out its intermediacy in the formation of **16**.

Use of the stronger, more sterically hindered base, potassium *tert*-butoxide, in refluxing benzene resulted in the production of cyclopropenylcarbinol **19** and minor amounts of the ubiquitous ketone **8**. When the basic medium was lithium diethylamide in ether, the same two products were found; however, despite some variance from experiment to experiment, the predominant component was always **8**.

The structural assignment for **19** is derived from its nmr spectrum (two identical pairs of saturated methyl groups, an isopropenyl moiety, and a hydroxyl proton), a cyclopropene band[8] at 5.47 μ in the ir, and a conjugated diene chromophore in the uv. Treatment of **19** with sulfuric acid in acetic acid resulted in facile isomerization to ketone **8**, presumably *via* an initial cyclopropenylcarbinyl–allenylcarbinyl cationic rearrangement.[4,9] One possible pathway is **19** → **9** → **10** → **8**. (An alternate but essentially equivalent series of steps can be envisaged following ionization of the hydroxyl group.) Analogy for this type of rearrangement can be found in the work of Closs and Böll.[9] Of course, the reactions of **1** are proposed to generate the same allylic cation from an alternate source.[4] In the minimum, these results are fully consistent with the intervention of cation **9** in both processes.

It is possible to rationalize the transformations of **1** effected by methoxide in terms of simple nucleophilic displacement to yield cyclopropanol anion **20** and β elimination[10] to related intermediate **21**. Further isomerization of these species to **17** and **16**, respectively, is anticipated from the available information on the chemistry of cyclopropanols.[11] In this light, it is a little puzzling that *tert*-butoxide promotes elimination in an entirely different manner to yield **19**. Reservations may also be expressed with regard to the likelihood of nucleophilic displacement resulting from attack of methoxide at the tertiary epoxide center. Therefore, the consideration of more obscure pathways to these materials may not be altogether without justification. The absence of allene alcohol **3** in basic media supports the proposed scheme for the formation of this material under neutral and acidic conditions.

The isomerization of **1** to cyclobutanone **2** occurs with roughly equal facility in both neutral and strongly basic methanol, but other processes are more effective under acidic conditions. This seems to implicate some type of purely thermal isomerization for the **1** → **2** transformation. In fact, this same conversion has been shown to result from the gas-phase pyrolysis of **1**.[4] However, it must be noted that relatively high temperatures were utilized to effect this thermal reaction, which was considered to take place by a biradical mechanism. It is possible that in solution an alternate process obtains, for example, reaction *via* zwitterion **22**. This species should be generated more readily in polar solvents and, in addition to being a logical precursor of **2**, reaction of **22** with methoxide provides rational alternate pathways to ketones **16** and **17**. On the other hand, it is not easy to see why epoxide **1** would prefer to open in one fashion when protonated (to **9**) but in a rather different way (to **22**) when unassisted by acid. The peculiar response of the transformations of **1** to the reaction medium thus remains incompletely understood. See Scheme II.

The formation of cyclopropene alcohol **19** was unexpected owing to the highly strained nature of this compound, but a 1,4-elimination mechanism is apparent *a posteriori*. The absence of ketone **16** among the products of the reaction of **1** with *tert*-butoxide or diethylamide is conspicuous, particularly since this compound is an important product with methoxide. This ketone was expressly shown to be absent from the product mixture of the lithium diethylamide reaction and, furthermore, it was demonstrated to be stable to these conditions.

The source of ketone **8**, the second product in the strong base isomerizations of **1**, is not certain, but the most likely explanation for this material is that it results from a secondary transformation of **19**, probably in an acid-catalyzed process during work-up. Such a transformation under more acidic conditions is described

(5) J. W. Emsley, J. Feeney, and L. H. Sutcliff, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. 1, Pergamon Press, Oxford, 1965, pp 559–573; M. L. Martin and G. J. Martin, *Bull. Soc. Chim. Fr.*, 2117 (1966); B. Halpern, J. W. Westley, and B. Weinstein, *Chem. Commun.*, 160 (1967); M. Kajtar and L. Radics, *ibid.*, 784 (1967); P. D. Bartlett and T. T. Tidwell, *J. Amer. Chem. Soc.*, **90**, 4421 (1968).

(6) F. P. Boer, G. A. Doorakian, H. H. Freedman, and S. V. McKinley, *ibid.*, **92**, 1225 (1970).

(7) W. F. Forbes, R. Shilton, and A. Balasubramanian, *J. Org. Chem.*, **29**, 3527 (1964); R. Criegee, U. Zirngibl, H. Furrer, D. Seebach, and G. Freund, *Chem. Ber.*, **97**, 2942 (1964).

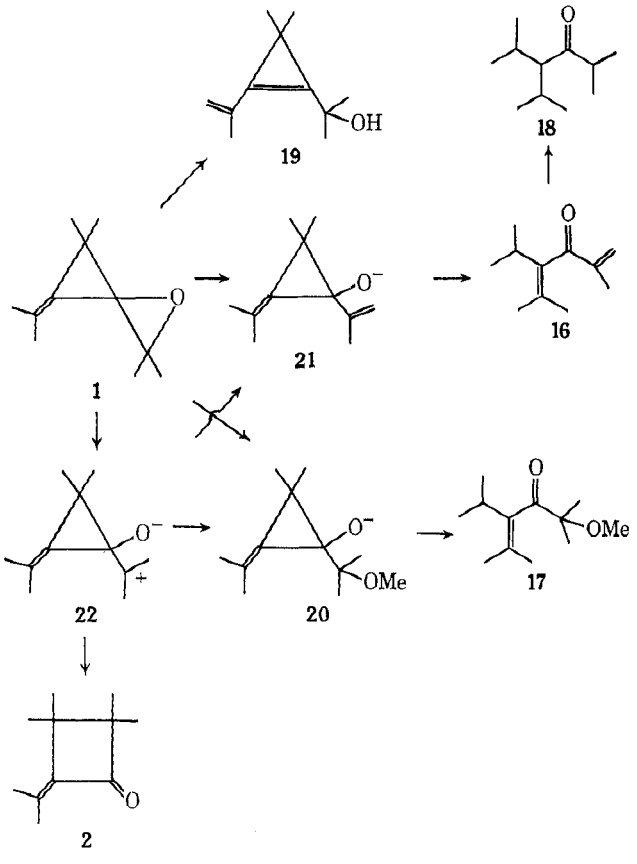
(8) G. L. Closs, L. E. Closs, and W. A. Böll, *J. Amer. Chem. Soc.*, **85**, 3796 (1963).

(9) Unpublished results cited in G. L. Closs, *Advan. Acyclic Chem.*, **1**, 98 (1966).

(10) B. Rickborn and R. P. Thummel, *J. Org. Chem.*, **34**, 3583 (1969).

(11) C. H. DePuy, *Accounts Chem. Res.*, **1**, 33 (1968).

SCHEME II



above, and support for this contention is found in the variability of the ratio of **19** to **8** in different experiments with lithium diethylamide. It was specifically shown that cyclobutanone **2** was recovered from the reaction conditions without transformation to **8**, thereby ruling out **2** as an intermediate in the formation of **8**. Consequently, the formation of cyclobutanone is not favored by strong, nonnucleophilic bases in aprotic solvents, in accordance with the ideas expressed above concerning the mode of conversion of **1** to **2**.

Experimental Section

General.—Infrared spectra (ir) were obtained with Perkin-Elmer Model 137 and 137G Infracord spectrophotometers. Unless otherwise specified, these were taken in carbon tetrachloride solution. Nuclear magnetic resonance (nmr) spectra were obtained with Varian Associates A-60 and HR-100 spectrometers in carbon tetrachloride solution. Ultraviolet spectra (uv) were recorded on a Cary 14 spectrophotometer. Raman spectra were taken on a Cary 81 spectrophotometer. Mass spectra were obtained with an AEI MS-9 mass spectrometer at 70 eV. Gas chromatography (glpc) was performed on Aerograph Model 600, Model 1200 (analytical, hydrogen flame detector) chromatographs. The analytical column was 10 ft × 1/8 in. of 15% Carbowax 20M on 60–80 Chromosorb W; preparative columns were 10 ft × 3/8 in. of either 30% FFAP or 15% Carbowax 20M on 60–80 Chromosorb W. Percentage composition data were estimated by peak areas (uncorrected). Anhydrous magnesium sulfate was used for all drying operations. Microanalyses were performed by Midwest Microlabs, Inc., Indianapolis, Ind.

Solvolysis of 1 in Methanol.—A solution of 0.22 g of **1** in 50 ml of methanol was refluxed for 18 hr, diluted with 50 ml of water, and extracted with four 25-ml portions of pentane. The combined pentane extracts were washed with 25 ml of saturated sodium chloride solution and dried. Removal of the solvent by flash evaporation gave 0.20 g of crude product. Glpc analysis showed two major products as **19** and 77% of the volatile reaction products. The products were purified by glpc collection.

The minor product was identified as 2,5-dimethyl-3-(1-methyl-1-methoxyethyl)hexa-3,4-dien-2-ol (**3**): ir 2.9, 5.1 (weak), 9.4, and 10.4 μ; nmr τ 8.73 (s, 6), 8.63 (s, 6), 8.30 (s, 6), 6.77 (s, 3, OCH_3), and 5.9 (s, 1, OH).

Anal. Calcd for $C_{12}H_{22}O$: C, 72.68; H, 11.18. Found: C, 72.56; H, 11.08.

The major product was identified as ketone **2** by comparison with an authentic sample.[4]

Solvolysis of 1 in 12% Acetic Acid–Methanol.—To a solution of 7 ml of glacial acetic acid in 60 ml of methanol was added 0.79 g of **1**, and the resulting mixture was refluxed for 56 hr, poured into 100 ml of saturated sodium bicarbonate solution, and extracted with four 50-ml portions of pentane. The pentane extracts were combined and dried. Removal of the pentane by flash evaporation gave 0.83 g of a crude oil. Four compounds were isolated by preparative glpc as 58, 20, 16, and 6% of the volatile reaction mixture.

The major material was identified as 4-isopropylidene-3,5-dimethoxy-2,5-dimethylhex-2-ene (**5**): ir 5.95 (weak), 6.10, 8.35, 8.55, 8.92, 9.28, and 9.72 μ; nmr τ 8.82 (s, 3), 8.75 (s, 3), 8.52 (s, 3), 8.39 (s, 3), 8.35 (s, 3), 8.02 (s, 3), 6.95 (s, 3, OCH_3), and 6.75 (s, 3, OCH_3); uv max (hexane) 212 nm (ϵ 12,700); Raman (CCl_4) 1380, 1445 (very strong), 1635, and 1678 cm^{-1} (strong). The mass spectrum shows a weak molecular ion at m/e 2.12.

Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39. Found: C, 73.68; H, 11.41.

The second product was ketone **8** as established by glpc isolation and comparison with an authentic sample.

The third product is assigned as 4-isopropenyl-3-methoxy-2,5-dimethylhex-2,4-diene (**7**): ir 3.24, 6.0, 6.14, 8.35, 8.88, and 11.21 μ; nmr τ 8.53 (s, 3), 8.33 (s, broad, 9), 8.18 (m, 3, CH_2=CCH_3), 6.72 (s, 3, OCH_3), 5.31 (m, 1, C=CH_2), and 5.02 (m, 1, C=CH_2). The mass spectrum shows a molecular ion at m/e 180.1518 (calcd for $C_{12}H_{20}$, 180.1514).

The fourth product is assigned as 3-isopropenyl-2,5-dimethyl-2-methoxyhex-3,4-diene (**6**): ir 5.10 (weak), 6.19, 8.56, 11.1, and 12.6 μ; nmr τ 8.72 (s, 6, $C(CH_3)_2OCH_3$), 8.26 (s, C=C=C-$(CH_3)_2$), 8.25 (m, 3, H_2C=CCH_3), 6.96 (s, 3, OCH_3), 5.10 (m, 1, C=CH_2), and 4.58 (m, 1, C=CH_2). The mass spectrum shows a molecular ion at m/e 180.1513 (calcd for $C_{12}H_{20}O$, 180.1514).

Solvolysis of 1 in 2% Acetic Acid–Methanol.—To a solution of 0.5 ml of glacial acetic acid in 25 ml of methanol was added 50 mg of **1**. The resulting solution was refluxed for 36 hr, poured into 100 ml of saturated sodium bicarbonate solution, and extracted with two 50-ml portions of pentane. The combined pentane extracts were dried. Glpc analysis showed formation of 70% **5** and 30% of a new compound identified as 2,5-dimethyl-4-(1-methyl-1-methoxyethyl)-5-methoxyhexa-2,3-diene (**4**): ir 5.1 (weak, allene), 8.2, 8.6, 8.9, and 9.4 μ (strong); nmr τ 8.74 (s, 12), 8.29 (s, 6, C=C=C$(CH_3)_2$), and 7.0 (s, 6, $(OCH_3)_2$).

Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.41. Found: C, 73.74; H, 11.28.

Solvolysis of 5 in Acetic Acid–Methanol.—To a 5-ml solution of 12% acetic acid–methanol was added 10 mg of **5**. After 24 hr of reflux, the reaction mixture was poured into 25 ml of water and extracted with four 25-ml portions of pentane. The combined pentane extracts were washed with 25 ml of saturated sodium bicarbonate solution and dried. Glpc analysis of the crude product showed 15% **8**, 18% **7**, and 67% unreacted **5**.

Acid-Catalyzed Rearrangment of 3.—A 15-mg sample of **3** was dissolved in 3 ml of methanol containing 5 mg of *p*-toluenesulfonic acid. The resulting solution was refluxed for 3 hr, cooled to room temperature, neutralized with solid potassium hydroxide, poured into 25 ml of water, and extracted with three 25-ml portions of pentane. The combined pentane extracts were dried and the pentane was removed by flash evaporation to give 12 mg of crude product. Glpc and spectral analysis showed this material to be essentially pure ketone **8**.

2,5-Dimethyl-3,5-dimethoxy-4-isopropylidenehex-2-ene (5).—A solution of 5 ml of methanol, 0.20 g of **14**, 0.10 g of trimethyl orthoformate, and 2 mg of *p*-toluenesulfonic acid was stirred at room temperature for 12 hr, poured into 50 ml of water, and extracted with four 50-ml portions of pentane. The combined pentane extracts were dried and the pentane was removed by flash evaporation to give 0.21 g of crude oil. Glpc analysis showed four components as 38, 50, 8, and 4% of the volatile reaction products. The two major components were purified by glpc collection. The major product was shown to be **5**, identical in every respect with that obtained from the acetic acid catalyzed

solvolysis of **1**. The minor product is assigned as 2,5-dimethyl-5-methoxy-4-isopropylidenehexan-3-one (**15**): ir 5.91, 6.10, 7.95, 8.55, 9.35 (strong), and 10.5 μ; nmr τ 8.93 (d, 6, J = 7 Hz), 8.71 (s, 6), 8.42 (s, 3), 8.12 (s, 3), 7.38 (septet, 1, J = 7 Hz), and 6.94 (s, 3).

Rearrangement of 1 with Sodium Methoxide.—To a solution of 1.9 g of metallic sodium in 50 ml of anhydrous methanol was added dropwise a solution of 0.50 g of **1** in 5 ml of methanol. After heating to reflux for 18 hr, the mixture was poured into 100 ml of water and extracted with four 25-ml portions of pentane. The combined pentane extracts were washed with saturated sodium chloride solution and dried. Removal of the solvent by flash evaporation gave 0.38 g of crude oil. Glpc analysis showed three major products as 36, 48, and 8% of the volatile reaction product. No other product amounted to more than 1%. The products were purified by glpc.

The first component (36%) was identified as 2,5-dimethyl-4-isopropyl-1,4-hexadien-3-one (**16**): ir (neat) 6.02, 6.14, and 10.69 μ; nmr τ 9.03 (d, 6, J = Hz, $CH(CH_3)_2$, 8.51 (s, 3), 8.26 (s, 3), 8.15 (m, 3, $H_2C{=}CCH_3$), 7.92 (septet, 1, $CH(CH_3)_2$), and 4.2 (m, 2, $C{=}CH_2$); uv max (hexane) 215 nm (ϵ 2050) and 255 (190). The mass spectrum of **16** shows a molecular ion at m/e 166.

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.43; H, 10.76.

The second product was identified as 2-isopropylidene-3,3,4,4-tetramethylcyclobutanone (**2**) by comparison with an authentic sample.[4]

The third product was identified as 2,5-dimethyl-4-isopropyl-2-methoxyhex-4-en-3-one (**17**): ir 5.94, 6.09, 8.35, 8.65, and 9.35 μ; nmr τ 8.71 (s, 6, $C(CH_3)_2$), 8.48 (s, 3), 8.29 (s, 3), 7.35 (septet, 1, J = 7.0 Hz, $CH(CH_3)_2$), 9.05 (d, 6, J = 7.0 Hz, $CH(CH_3)_2$), and 6.78 (s, 3, OCH_3). The mass spectrum of **17** shows a molecular ion at m/e 198.

Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.72; H, 11.07.

Rearrangement of 1 with *tert*-Butoxide in Benzene.—To a mixture of 1.2 g of potassium *tert*-butoxide and 70 ml of benzene was added a solution of 0.58 g of **1** in 10 ml of benzene. After heating to reflux for 6 hr, the mixture was shaken with 100 ml of water, the layers were separated, and the aqueous layer was extracted with 50 ml of benzene. The benzene layers were combined and dried. Removal of the solvent by flash evaporation gave 0.53 g of crude product. Glpc collection gave three compounds as 7, 10, and 83% of the volatile reaction product.

The first compounds was identified as starting material **1**; the second compound was shown to be ketone **8**. The major product was a new compound assigned as 1-isopropenyl-2-(1-methyl-1-hydroxyethyl)-3,3-dimethylcyclopropene (**19**): ir 2.71, 2.82, 3.20, 5.47, 6.20, and 11.20 μ; nmr τ 8.78 (s, 6, $C(CH_3)_2$), 8.60 (s, 6, $C(CH_3)_2OH$), 8.06 (m, 3, $H_2C{=}CCH_3$), 7.06 (s, 1, OH), 4.91 (m, 2, $C{=}CH_2$); uv max (hexane) 242 nm (ϵ 4475). The mass spectrum of **19** shows a molecular ion at 166.1358 (calcd for $C_{11}H_{18}O$, 166.1358). Similar results were obtained when *tert*-butyl alcohol was used as solvent in place of benzene.

Rearrangement of 1 with Lithium Diethylamide.—To a predried flask were added 50 ml of anhydrous ether, 0.16 g of anhydrous diethylamine, and 1.5 ml of 1.6 N n-butyllithium solution in hexane. The resulting solution was stirred for 30 min under a nitrogen atmosphere, 0.25 g of **1** in 5 ml of ether was added dropwise, and the resulting solution was refluxed for 18 hr. The reaction mixture was poured into 100 ml of water, the layers were separated, and the aqueous layer was washed with 25 ml of ether. The combined ethereal solutions were dried and the ether was removed by flash evaporation to give 0.22 g of crude product. Glpc analysis showed three major components as 11, 57, and 28% of the reaction product. Glpc collection and comparison with known samples showed these to be unreacted epoxide **1**, ketone **8**, and cyclopropenol **19**, respectively. This reaction was repeated under identical conditions on several occasions with varying percentages of **8** (57–90%) and **19** (39–10%) observed.

A second reaction was followed closely by removing aliquots and analyzing by glpc. All of the **1** was gone after 2 hr when the ratio of **8**:**19** was 59:41. Subsequent work-up gave a 75:25 ratio of these same two materials in good yield.

Acid-Catalyzed Rearrangement of 19.—To an 87-mg sample of **19**, in 75 ml of glacial acetic acid, was added 9 drops of concentrated sulfuric acid, and the resulting mixture was stirred for 4 hr, poured into 200 ml of water, and extracted with five 25-ml portions of pentane. The pentane extracts were washed with two 25-ml portions of saturated sodium bicarbonate solution and dried. The solvent was removed by flash evaporation to give 82 mg of crude product. Two products were isolated by preparative glpc as 66 and 34% of the volatile reaction product. The major material was shown to be ketone **18**, and the minor product was the enol acetate of ketone **8** as established by glpc isolation and comparison with authentic materials.[4]

Hydrogenation of 16.—A solution of 50 mg of **16** in 24 ml of methanol was hydrogenated at atmospheric pressure using 30% palladium on charcoal as catalyst. After the uptake of 2 mol of hydrogen, the resulting mixture was filtered to remove the catalyst and the filtrate was poured into 100 ml of water and extracted several times with 25-ml portions of pentane. The pentane extracts were combined and dried. After removal of the solvent, a single product was isolated in almost quantitative yield. Ketone **18** was shown to be 2,5-dimethyl-4-isopropylhex-3-one by comparison with an authentic sample.[4]

Registry No.—**1**, 15448-69-8; **3**, 28054-75-3; **4**, 28054-76-4; **5**, 28054-77-5; **6**, 28054-78-6; **7**, 28054-79-7; **15**, 28054-80-0; **16**, 28054-81-1; **17**, 28054-82-2; **19**, 28054-83-3.

Reductive Elimination of Epoxides to Olefins with Zinc–Copper Couple

S. MORRIS KUPCHAN* AND MASAO MARUYAMA

Department of Chemistry, University of Virginia, Charlottesville, Virginia 22901, and Department of Pharmaceutical Chemistry, University of Wisconsin, Madison, Wisconsin 53706

Received October 28, 1970

A new direct and single-step reductive elimination of epoxides to olefins by treatment with zinc–copper couple in ethanol is described. The scope and stereochemistry of the reaction have been studied with epoxides of sesquiterpenes, steroids, styrene, stilbenes, and octenes. The reaction has been compared with reductive elimination of epoxides with the Cr^{II}–ethylenediamine complex.

In the course of structural studies of sesquiterpene lactones from *Eupatorium rotundifolium*,[1] an attempt was made to dehydrochlorinate eupachloroxin (**1**) to eupatundin (**2**) with zinc–copper couple in boiling ethanol.[2] The desired product was not obtained, but treatment for 3 days resulted primarily in reductive elimination of the 3,4 epoxide to yield eupachlorin (**3**) as the principal isolable product. Treatment for 4 days resulted in reductive elimination of the epoxide *and* dehydrochlorination to give deoxyeuparotin (**4**) in 31% yield.

(1) S. M. Kupchan, J. E. Kelsey, M. Maruyama, and J. M. Cassady, *Tetrahedron Lett.*, 3517 (1968); S. M. Kupchan, J. E. Kelsey, M. Maruyama, J. M. Cassady, J. C. Hemingway, and J. R. Knox, *J. Org. Chem.*, **34**, 3876 (1969).

(2) J. Elks, G. H. Phillipps, T. Walker, and L. J. Wyman, *J. Chem. Soc.*, 3440 (1956).