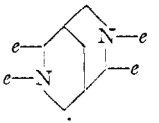
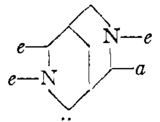
The moments of these compounds are, to a first approximation, the resultant of two group moments located at the $\mathrm{N} < \mathrm{C}_3$ portions of the respective molecule. The two group moments are parallel to each other in the conformation a, whereas they make a tetrahedral angle α with each other in the three other conformations b, c and d. The $\mathrm{N} < \mathrm{C}_3$ group moment μ_0 can be approximated with the moment of quinolizidine 0.74 D. or that of hexahydrojulolidine 0.76 D. rather than with that of trimethylamine 0.86 D.[11] Allomatridine having a moment nearly twice as great as that of quinolizidine must therefore be represented by the conformation a, while matridine having a moment nearer to $2\mu_0 \cos {}^1/_2\alpha = 1.15\mu_0$ than to $2\mu_0$ must correspond to one of the conformations b, c and d. One of the present authors[3] already has advanced an argument that compounds of allomatrine series have the structure a and those of matrine series the structure d from the considerations on the relative stability of matridine and its isomer as well as on the reactions of matrine and allomatrine with cyanogen bromide, of matridine and allomatridine with methyl iodide, and also of potassium matrinate and potassium allomatrinate with methyl iodide. The present results afford a definite evidence in favor of this conclusion. Quite recently, Bohlmann and collaborators[12] published a paper, in which they reported that they arrived at the same conclusion. Their argument is founded on other reactions than those studied by one of the present authors[3] and on the infrared absorptions of matrine and $\Delta^{5(\text{or } 6)}$-dehydromatridine in the wave number range 2700–2800 cm.$^{-1}$ showing features characteristic of a *trans*-fused quinolizine ring. The moment of 2-methylperhydropyrido[3,4,5-i,j]quinolizine is close to that of allomatridine, indicating that the molecule of the former compound, like that of the latter, assumes a stable extended structure.

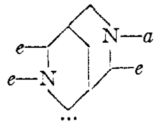
The conceivable conformations for sparteine and α-isosparteine[13] are the following six, of which iii, v and vi can be ruled out from the considerations of steric hindrance.



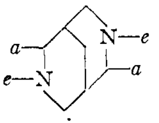
i



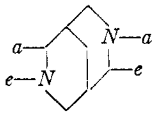
ii



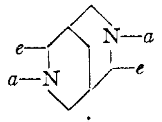
iii



iv



v



vi

Like the skeletons of matridine and allomatridine, the frameworks of sparteine and α-isosparteine can be accommodated in the diamond lattice and it is easy to see that the two $\mathrm{N} < \mathrm{C}_3$ group moments make a tetrahedral angle with each other in conformations i, ii and iv. The observed moments for the two compounds agree with any of the three possible conformations. The X-ray crystal analysis carried out by Przybylska and Barnes[14] on α-isosparteine monohydrate has shown that α-isosparteine has the structure shown by i. Accordingly sparteine must have either the conformation ii or iv. Although dipole moment data alone are unable to make a choice between these two alternatives, one may tentatively assign the conformation ii to sparteine, leaving iv for β-isosparteine.

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(11) R. J. W. Le Fèvre and P. Russel, *Trans. Faraday Soc.*, **43**, 374 (1947).

(12) F. Bohlmann, W. Weise and D. Rahtz, *Angew. Chem.*, **69**, 642 (1957).

(13) Reference 4, p. 156.

(14) M. Przybylska and W. H. Barnes, *Acta Cryst.*, **6**, 377 (1953).

CHIKUSA, NAGOYA, JAPAN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

The Stereochemistry of Base-catalyzed Epoxidation

BY HERBERT O. HOUSE AND ROLLAND S. RO[1]

RECEIVED NOVEMBER 30, 1957

The *cis* and *trans* isomers of 3-methyl-3-penten-2-one have been prepared. Each isomer, when allowed to react with alkaline hydrogen peroxide, yielded 3-methyl-*trans*-3,4-epoxy-2-pentanone thereby demonstrating that the epoxidation is not stereospecific. Appropriate experiments in a deuterium-containing medium demonstrated that the base-catalyzed epimerization of β-methyl-*trans*-benzalacetophenone oxide to the *cis* isomer and the reverse process involved a carbanionic intermediate.

The epoxidation of olefins with peracids is known to proceed stereospecifically, the configuration of the epoxide produced being the same as the configuration of the starting olefin.[2-4] However, this method of epoxidation is usually not applicable to α,β-unsaturated ketones since the reaction of such olefins with peracids either yields enol esters, the products of a Baeyer–Villiger reaction, rather than α,β-epoxy ketones[2,5] or occurs very slowly if at all.[6,7] For this reason the general procedure for the epoxidation of α,β-unsaturated ketones con-

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(1) Alfred P. Sloan Postdoctoral Fellow, 1957–1958.

(2) S. Winstein and R. B. Henderson in R. C. Elderfield, "Heterocyclic Compounds," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1950, p. 1.

(3) D. Swern, *Chem. Revs.*, **45**, 1 (1949).

(4) D. Swern, *Org. Reactions*, **7**, 378 (1953).

(5) C. H. Hassall, *ibid.*, **9**, 73 (1957).

(6) Although certain α,β-unsaturated esters have been epoxidized by the use of peroxytrifluoroacetic acid [W. D. Emmons and A. S. Pagano, THIS JOURNAL, **77**, 89 (1955)], we are unaware of any instances where this reagent has been employed successfully with α,β-unsaturated ketones. In one instance [P. L. Julian, E. W. Meyer and I. Ryden, *ibid.*, **72**, 367 (1950)] a steroidal α,β-unsaturated ketone was reported to yield an epoxide when treated with perbenzoic acid. The suggestion was made [E. Wenkert and M. Rubin, *Nature*, **170**, 708 (1952)] that this type of epoxidation might be general but no experimental evidence has been provided to support this suggestion.

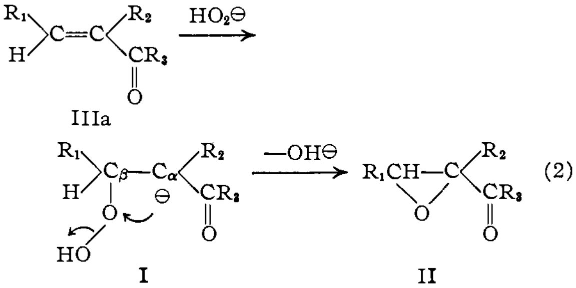
(7) H. O. House and D. J. Reif, THIS JOURNAL, **79**, 6491 (1957).

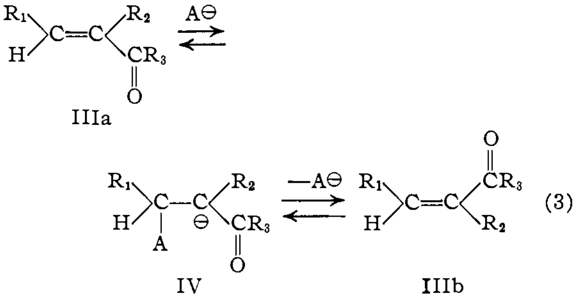
sists of the reaction of these compounds with hydrogen peroxide in alkaline solution.[8] The question of whether or not this base-catalyzed epoxidation proceeds with the same degree of stereospecificity which characterizes the peracid–olefin reaction cannot be answered unambiguously from the literature which is available. The present study was undertaken to answer this question.

A kinetic study[9] of the alkaline epoxidation reaction indicated that the reaction proceeds as shown in the accompanying equations (1 and 2). It will be noted that a reaction following this scheme would be stereospecific only if decomposition of the intermediate I to form the product II is very rapid or if structure I represents a transition state rather than an intermediate. Otherwise rotation about the bond C_α–C_β in intermediate I would lead to a mixture of diastereoisomer products II in which the more stable diastereoisomer predominates. An alternative process which would result in non-stereospecific epoxidation is the prior equilibration of the isomeric unsaturated ketones IIIa and IIIb *via* the reversible addition of an anion (*e.g.*, $A^\ominus = OH^\ominus$ or $O_2H^\ominus$ in equation 3) to form the enolate anion IV.

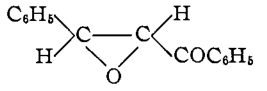
Previous reports of the stereochemical consequences of alkaline epoxidation have been based on the epoxidation of the *cis* and *trans* isomers of benzalacetophenone (V)[10,11] and β-methyl-*trans*-benzalacetophenone (VI) and derivatives.[12–14] In both of these studies the alkaline epoxidation was not stereospecific. Thus, both isomers of the ketone V yielded the *trans*-oxide VII, and the *trans*-ketone VI produced mixtures of the *cis*- and *trans*-oxides VIII. The interpretation which should be given these results is complicated by the possibility that both products VII and VIII might give enolate anions (*e.g.*, IX) in the basic reaction medium; hence, the results obtained may be explained in terms of a base-catalyzed epimerization of the product and do not necessarily provide information as to the stereochemistry of the alkaline epoxidation. Indeed, the base-catalyzed epimerization of the isomeric oxides VIII was shown to occur.[12,13]

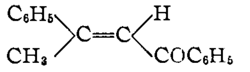
$$H_2O_2 + OH^\ominus \rightleftarrows HO_2^\ominus + H_2O \qquad (1)$$

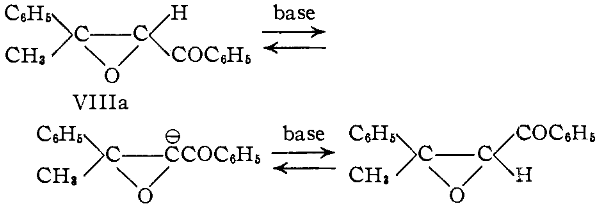

IIIa I II (2)


IIIa IV IIIb (3)

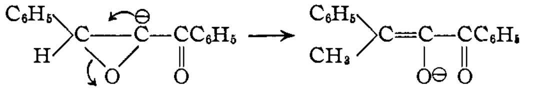
$C_6H_5CH{=}CHCOC_6H_5$
V

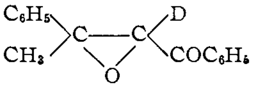

VII

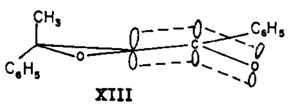

VI

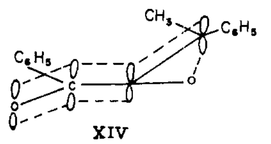

VIIIa IX VIIIb

In considering this problem it was of interest to demonstrate that the alkaline epimerization did involve an anionic intermediate such as IX since certain objections may be raised to this structure. For example, the formation of cyclopropyl carbanions has been shown to be relatively difficult although not impossible.[15,16] Also, it is necessary to question the existence of an anion such as IX since a pathway (*i.e.*, X) for the rapid rearrangement of this anion to form the enolate anion XI of an α-diketone is clearly present. In fact, the transformation of the oxide VIII to the enolate XI occurs very readily with concentrated alkali in boiling ethanol.[17] Such considerations have led to the suggestion[15] that an anion such as IX is not formed; rather, the initial proton abstraction and rearrangement represented by X were suggested to be concerted processes.


X XI


XII


XIII


XIV

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(8) This reaction was first described by E. Weitz and A. Scheffer, *Ber.*, **54**, 2327 (1921).

(9) C. A. Bunton and G. J. Minkoff, *J. Chem. Soc.*, 665 (1949).

(10) W. B. Black and R. E. Lutz, THIS JOURNAL, **75**, 5990 (1953).

(11) R. E. Lutz and J. O. Weiss, *ibid.*, **77**, 1814 (1955).

(12) H. H. Wasserman, N. E. Aubrey and H. E. Zimmerman, *ibid.*, **75**, 96 (1953).

(13) H. H. Wasserman and N. E. Aubrey, *ibid.*, **77**, 590 (1955).

(14) I. N. Nazarov and A. A. Akhrem [*Izvest. Akad. Nauk S. S. S. R. Otdel. Khim. Nauk*, 1457 (1956); *C. A.*, **51**, 8660 (1957)] have suggested that alkaline epoxidation yields an epoxy ketone having a configuration which is the reverse of the configuration of the α,β-unsaturated ketone precursor. The published evidence, cited elsewhere in this report, is ample to disprove this contention.

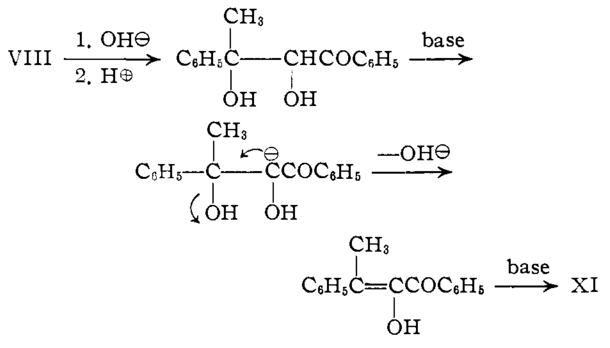
(15) F. J. Piehl and W. G. Brown, THIS JOURNAL, **75**, 5023 (1953).

(16) H. M. Walborsky and F. M. Hornyak, *ibid.*, **77**, 6026 (1955); **78**, 872 (1956).

(17) H. O. House and D. J. Reif, *ibid.*, **77**, 6525 (1955).

In order to elucidate the nature of the alkaline epimerization each of the isomeric oxides VIII was dissolved in a dilute solution of sodium ethoxide in ethanol-*d*. The *cis* and *trans* isomers of the keto oxide VIII were isolated from each reaction mixture and analyzed for deuterium content. The results of these experiments, summarized in Table I, indicate that each oxide incorporated one atom of deuterium during alkaline epimerization. Furthermore, comparison of the nuclear magnetic resonance spectra of deuterated and non-deuterated samples of the oxide VIIIa demonstrated that the deuterium atom occupied the position shown in structure XII. These observations leave little doubt that the anion IX was involved in the alkaline epimerizations studied.

Thus, the protonation of the anion IX to form the keto oxides VIII may represent a rapid process, whereas the apparent conversion of the anion IX to the α-diketone enolate XI is slower but thermodynamically favored. Presumably, the relatively slow conversion of the anion IX to the α-diketone enolate XI is attributable to the existence of the anion IX in a geometric arrangement which is unfavorable for subsequent reaction. Thus, the more stable conformations of the anion IX would be expected to be those in which the oxirane ring and the enolate anion are coplanar (*e.g.*, XIII). The rearrangement represented by structure X, which closely resembles a bimolecular elimination reaction, would be expected to require a transition state having a geometric arrangement such as XIV in which the former π-orbital of the enolate anion occupies a position behind the carbon–oxygen bond of the oxirane ring which is to be displaced. Since the energy required to attain a relatively strained transition state such as XIV in which the oxirane ring is not coplanar should be substantially higher than the activation energy for protonation of the anion IX, it is not surprising that the rearrangement represented by structure X is slow and proceeds readily only at higher temperature and higher base concentration. Alternatively, it is possible that the rearrangement represented by structure X never occurs; rather, the formation of the α-diketone enolate XI occurs *via* opening of the oxirane ring with hydroxide ion (which is present in the experiment cited[17]) followed by elimination as shown in the accompanying equations.



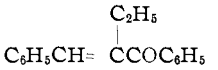
$$\mathrm{VIII} \xrightarrow[2.\ H^{\oplus}]{1.\ OH^{\ominus}} C_6H_5\overset{CH_3}{\underset{OH}{C}}-\underset{OH}{C}HCOC_6H_5 \xrightarrow{\text{base}} C_6H_5-\overset{CH_3}{\underset{OH}{C}}-\overset{\ominus}{\underset{OH}{C}}COC_6H_5 \xrightarrow{-OH^{\ominus}} C_6H_5\overset{CH_3}{C}=\underset{OH}{C}COC_6H_5 \xrightarrow{\text{base}} \mathrm{XI}$$

TABLE I

Compound epimerized	Reaction temp., °C	Reaction time, hr.	Recovered VIIIb		Recovered VIIIa	
			%	g./atom D/mole	%	g.-atom D/mole
VIIIa	25–30	48	25	0.905	30	0.267
VIIIb	78[a]	30	50	.985	15	.925

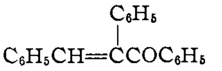
[a] A higher reaction temperature was required because of the insolubility of the *cis*-oxide VIIIb.

From the foregoing discussion, it is apparent that the alkaline epoxidation of α-substituted α,β-unsaturated ketones (*i.e.*, III, $R_2 \neq H$) should be studied if information concerning the stereochemistry of the reaction is to be obtained. The products (*i.e.*, II, $R_2 \neq H$) obtained from these reactions would not be capable of the base-catalyzed epimerization previously discussed. In previous work[7,17] epoxidations of *cis* and *trans* isomers of the ketones XV and XVI were studied. In both cases the derivatives of *trans*-benzalacetophenone yielded the derivatives of *trans*-benzalacetophenone oxide but the *cis* isomer failed to react. The lack of reactivity of the *cis* isomers was judged to reflect steric interference with the coplanar configuration required for conjugation of the carbon–carbon double bond and the carbonyl group. For this reason, we directed our attention to the synthesis and epoxidation of the geometrical isomers of 3-methyl-3-penten-2-one (XVII), an α,β-unsaturated ketone in which steric interactions were minimized.



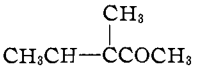
$C_6H_5CH=\overset{C_2H_5}{C}COC_6H_5$

XV



$C_6H_5CH=\overset{C_6H_5}{C}COC_6H_5$

XVI



$CH_3CH-\overset{CH_3}{C}COCH_3$

XVII

A sample of the ketone XVII, prepared *via* an acid-catalyzed aldol condensation as previously described,[18-20] was subsequently shown to be pure *trans* isomer XVIIa. Since attempts to convert the *trans*-ketone XVIIa, in part, into the *cis*-ketone XVIIb by irradiation with ultraviolet light (mercury-vapor arc) were unsuccessful, it was necessary to prepare the *cis* isomer XVIIb by a stereospecific chemical route. For this purpose, the isomeric 2-bromo-2-butenes XVIII were allowed to react with lithium metal[21] and the resultant organolithium compounds were added to acetaldehyde. The isomeric 3-methyl-3-penten-2-ols (XIX) so obtained were oxidized to the desired ketones XVII with activated manganese dioxide. The *cis*-alcohol XIXb was oxidized more slowly than the *trans* isomer XIXa, presumably because of the more hindered nature of the carbinol function in the *cis* isomer XIXb.

Each of the isomeric ketones XVIIa and XVIIb was allowed to react with a solution of sodium hydroxide and excess hydrogen peroxide in metha-

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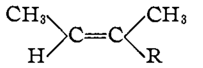
(18) L. E. Hinkel, E. E. Ayling, J. F. T. Dippy and T. H. Angel, *J. Chem. Soc.*, 814 (1931).

(19) L. P. Kyrides, THIS JOURNAL, **55**, 3431 (1933).

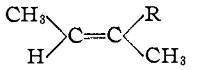
(20) R. B. Wagner, *ibid.*, **71**, 3214 (1949).

(21) See F. G. Bordwell and P. S. Landis [*ibid.*, **79**, 1593 (1957)] and ref. 7 and 17 for a discussion of the stereospecificity of this reaction with leading references. Our results are in agreement with the contention of Bordwell and Landis that the previously reported [A. S. Dreiding and R. J. Pratt, *ibid.*, **76**, 1902 (1954)] partial loss of configuration when the 2-bromo-2-butenes reacted with lithium is attributable to the presence of both isomeric 2-bromo-2-butenes in the starting material and not to a lack of stereospecificity in the metalation step.

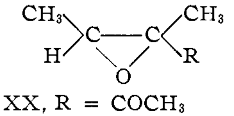
nol, the reactions being followed by measuring the optical densities in the ultraviolet region of the reaction mixtures. The rate of epoxidation of the *trans*-ketone XVIIa was about three times the rate of epoxidation of the *cis* isomer XVIIb. The liquid epoxy ketone XX samples obtained from the two reaction mixtures had identical infrared spectra and essentially identical boiling points and refractive indices; also, both separate products and a mixture of the two materials each gave a single peak in gas chromatograms on two different columns. Each product XX treated with an ethanolic solution of 2,4-dinitrophenylhydrazine containing a few drops of acid to yield the same crystalline derivative. Chromatography of the mother liquors from the dinitrophenylhydrazone preparations did not afford any additional derivative of the epoxy ketone. The composition and infrared and ultraviolet spectra of the 2,4-dinitrophenylhydrazone derivative are consistent with either structure XXI or XXII. The assignment of the *erythro* configuration to this derivative XXI or XXII is based on the reasonable assumption that the oxide ring (subsequently shown to have the *trans* configuration XX) was opened with inversion (*i.e.*, an S_N2 reaction) since the reaction medium was relatively non-polar and the acid concentration was low.[22]



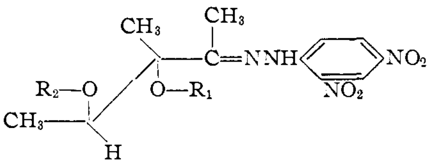
XVIIa. R = $COCH_3$
XVIIIa. R = Br
XIXa. R = $CHOHCH_3$



XVIIb, R = $COCH_3$
XVIIIb. R = Br
XIXb, R = $CHOHCH_3$



XX, R = $COCH_3$
XXIII, R = $CHOHCH_3$



XXI. R_1 = H, R_2 = C_2H_5
XXII. R_1 = C_2H_5, R_2 = H

The combined experimental data serve as compelling evidence that the epoxidation of either unsaturated ketone XVIIa or XVIIb yielded a single α,β-epoxy ketone and, consequently, that the reaction is not stereospecific. The results of previous studies[7,17] suggested that the epoxy ketone obtained had the *trans* configuration XX. This configuration was established by an independent synthesis of the *trans*-oxide XX consisting of epoxidation of the *trans*-alcohol XIXa with peracetic acid followed by oxidation of the resultant crude epoxy alcohol XXIII with chromium trioxide in pyridine.[23] The epoxy ketone XX so obtained was contaminated with pyridine; as a result the infrared spectrum of this product contained all of the bands present in the spectrum of the compound prepared by alkaline epoxidation plus additional bands attributable to pyridine. However, both samples gave the same peak on gas chromatography and the keto oxide sample prepared *via* the epoxy alcohol XXIII give the same 2,4-dinitrophenylhydrazone derivative XXI or XXII which was previously described.

Since the possibility remained that the *cis*-ketone XVIIb was reacting with hydroxide ion to form the *trans*-ketone XVIIa (*i.e.*, equation 3 where $A^{\ominus} = OH^{\ominus}$) prior to epoxidation, the stability of the *cis*-ketone XVIIb to hydroxide ion was investigated. A solution of the ketones XVII (*cis*/*trans* = 3.46) in methanol was treated with sufficient sodium hydroxide to yield a solution of about the same basicity ($pH = 11$) as the reaction mixture in the alkaline epoxidation. After six hours, the time required for epoxidation of the *cis*-ketone XVIIb, only a small amount (*cis*/*trans* = 2.65) of the *cis*-ketone had been isomerized to the *trans* isomer.[24] However, it was clear that substantial amounts of the *trans*-ketone XVIIa were being formed during the alkaline epoxidation of the *cis* isomer XVIIb since after reaction of the *cis*-ketone XVIIb (*cis*/*trans* > 99) with alkaline hydrogen peroxide for six hours (at which time about 90% of the unsaturated ketone had reacted) the proportion of the *trans* isomer XVIIa in the remaining unsaturated ketone XVII had increased markedly (*cis*/*trans* = 1.9). Since the *trans*-ketone XVIIa was epoxidized more rapidly than the *cis* isomer XVIIb, it follows that the *cis*-ketone XVIIb was being isomerized relatively rapidly to the *trans* isomer XVIIa in the reaction mixture required for alkaline epoxidation. These observations and the concurrent lack of stereospecificity in the base-catalyzed epoxidation are most easily rationalized if reaction of the highly nucleophilic[25] hydroperoxide anion with the unsaturated ketone is assumed to be reversible so that equilibration of the unsaturated ketones occurs as shown in equation 3 ($A^{\ominus} = O_2H^{\ominus}$). Thus, the intermediates for epoxidation (*i.e.*, I) and equilibration (*i.e.*, IV, A = O_2H) become identical

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[22] Even if the epoxide ring was opened after the formation of the 2,4-nitrophenylhydrazone, we regard the possibility of neighboring-group participation by the 2,4-dinitroanilino group as unlikely since the expected product from such participation would be a derivative of either pyrazoline or pyrazole. In an analogous case, the reaction of an α-ketoethylenimine with phenylhydrazine produced such compounds [N. H. Cromwell, N. G. Barker, R. A. Wankel, P. J. Vanderhorst, F. W. Olson and J. H. Anglin, Jr., THIS JOURNAL, **73**, 1044 (1951)]. Also each of the keto oxide samples obtained in this study was treated with phenylhydrazine in a mixture of ethanol and acetic acid. The crude products obtained had identical infrared spectra and exhibited the same behavior when heated. Several recrystallizations failed to yield a pure, sharp-melting sample. However, an elemental analysis of the partially purified material did establish that the products contained only carbon, hydrogen and nitrogen and, consequently, were not related to the derivative XXI or XXII obtained with 2,4-dinitrophenylhydrazine.

[23] The stereospecificity of this process was first demonstrated by Wasserman and Aubrey (ref. 13) and has been utilized in other cases (ref. 7 and 17).

[24] After this mixture had been allowed to stand for several days essentially no *cis*-ketone XVIIb remained; only the *trans*-ketone XVIIa and higher-boiling materials could be detected. As would be expected, an analogous experiment with the *trans*-ketone XVIIa did not result in the formation of the *cis*-ketone XVIIb.

[25] See K. B. Wiberg, THIS JOURNAL, **75**, 3961 (1953); **77**, 2519 (1955). The high order of nucleophilicity of this anion as compared with hydroxide ion readily accounts for the more rapid isomerization of the ketone XVIIb (*via* the reaction path represented by equation 3) in the reaction mixture than in the presence of only sodium hydroxide and methanol.

and must be judged to have a sufficient lifetime to permit rotation about the bond C_α–C_β.

Experimental[26]

Deuterium Exchange Experiments.—Solutions of 1.0 g. of each of the isomeric β-methylbenzalacetophenone oxides (VIII) in ethanol-*d* (20 ml. for the *trans* isomer and 50 ml. for the *cis* isomer) were treated with several drops of a dilute solution of sodium ethoxide in ethanol-*d* and subjected to the reaction conditions specified in Table I. The resultant solutions were diluted with successive amounts of deuterium oxide to permit isolation of the isomeric keto oxides VIII by fractional crystallization. The products so obtained were recrystallized from ordinary ethanol to obtain analytical samples.[27] The nuclear magnetic resonance spectrum[28,29] of a 20% solution of a non-deuterated sample of the *trans*-keto oxide VIIIa has the following peaks (expressed as cycles per second relative to the proton resonance of water. a positive shift denoting a shift in the direction of increasing resonance frequency at constant magnetic field strength): a series of peaks in the range +101 sec.$^{-1}$ to +108 sec.$^{-1}$ (protons bonded to aromatic rings); a singlet at −38 sec.$^{-1}$ (proton bond to the oxirane ring) and a second singlet, whose area is approximately three times the area of the first singlet, at −131 sec.$^{-1}$ (protons of a methyl group). The positions of the peaks were altered only very slightly when the concentration of the keto oxide solution was reduced to 5%. The nuclear magnetic resonance spectrum[28,29] of the deuterated *trans*-keto oxide XII differs from the spectrum of the non-deuterated sample only in the absence of the small peak attributable to the nuclear resonance of the proton bonded to the oxirane ring.

The 2-Bromo-2-butenes (XVIII).—The isomeric 2,3-dibromobutanes, prepared and characterized as previously described,[30] were converted to the isomeric 2-bromo-2-butenes by the procedure of Bordwell and Landis.[31] The 2-bromo-*cis*-2-butene (XVIIIa), b.p. 91–92°, $n^{29}\mathrm{D}$ 1.4575 (lit.[31] b.p. 91–92°, $n^{28}\mathrm{D}$ 1.4585), was shown by vapor-phase chromatographic analysis to contain 5% of the *trans* isomer. The crude 2-bromo-*trans*-2-butene (XVIIIb), containing 3% of the *cis* isomer, was dried and used without further purification since subsequent distillation was found to increase the amount of the *cis* isomer present.

3-Methyl-*cis*-3-penten-2-ol (XIXb).—A solution of 40 g. (0.296 mole) of 2-bromo-*trans*-2-butene in 100 ml. of ether was added, dropwise and with stirring, to a suspension of 4.2 g. (0.605 g.-atom) of lithium wire in 150 ml. of ether. The reaction mixture was maintained at 0–5° throughout the addition. A solution of 14 g. (0.318 mole) of acetaldehyde in 30 ml. of ether was added dropwise and the resulting mixture was stirred for 1 hr., poured into an ice–water mixture and extracted with ether. After the extract had been dried over potassium carbonate, the ether was removed and the residue distilled. The *cis*-alcohol,[32] b.p. 139–140°, $n^{29}\mathrm{D}$ 1.4374, amounted to 20 g. (67.5%). The infrared spectrum[28,33] of the product has a band at 3400 cm.$^{-1}$ (associated O–H); the spectrum differs from the spectrum of the *trans*-alcohol subsequently described only in the relative intensities of bands found in the 1000–1100 cm.$^{-1}$ region.

Reaction of the *cis*-alcohol with α-naphthyl isocyanate afforded an α-naphthylurethan which crystallized from petroleum ether as white needles, m.p. 93–94°.

Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.84; H, 7.34; N, 5.40.

3-Methyl-*trans*-3-penten-2-ol (XIXa). Procedure A.—The reaction of 90 g. (0.666 mole) of 2-bromo-*cis*-2-butene with 9.2 g. (1.32 g.-atoms) of lithium followed by the addition of 30 g. (0.68 mole) of acetaldehyde as previously described yielded 30 g. (45%) of the *trans*-alcohol,[32] b.p. 140.5–141°, $n^{29}\mathrm{D}$ 1.4376. The infrared spectrum[28,33] of the product has a band at 3400 cm.$^{-1}$ (associated O–H). Since the *cis*- and *trans*-alcohols were not resolved by vapor-phase chromatography, it was not possible to obtain an accurate estimate of the stereochemical purity of the two alcohols. However, an indirect measure of the purity of the two materials was available by considering the stereochemical purity of the two ketones obtained by oxidation of the alcohols as subsequently described.

The α-naphthylurethan of the *trans*-alcohol crystallized from petroleum ether as white prisms, m.p. 75.5–76°. A mixture of the urethans from the *cis*- and *trans*-alcohols melted over the range 75–85°.

Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.98; H, 7.36; N, 5.45.

Procedure B.—3-Methyl-*trans*-3-penten-2-one (11 g., 0.112 mole), prepared by an aldol condensation as subsequently described, was reduced with 2.2 g. (0.058 mole) of lithium aluminum hydride in 80 ml. of ether, a reaction time of 1.5 hr. being employed. After the reaction mixture had been decomposed with dilute, aqueous sulfuric acid, the product was isolated in the usual manner. The yield of the *trans*-alcohol, b.p. 139.5–140.5°, $n^{29}\mathrm{D}$ 1.4376, was 10.2 g. (91%). The product gave an α-naphthylurethan, m.p. 75.5–76°, which was shown by a mixed melting-point determination to be identical with the derivative previously described.

3-Methyl-*trans*-3-penten-2-one (XVIIa). Procedure A.—A solution of 15 g. (0.15 mole) of 3-methyl-*trans*-3-penten-2-ol in 50 ml. of pentane was stirred with 30 g. of activated manganese dioxide[34] at room temperature for 12 hr. Analysis of the reaction mixture by vapor-phase chromatography indicated that the oxidation was essentially complete and that the *trans*-ketone was contaminated with 6% of the *cis* isomer. Distillation of the mixture through an 18-in. spinning band column afforded 10.5 g. (71.5%) of the *trans*-ketone (stereochemical purity > 99%), b.p. 138–139°, $n^{28.4}\mathrm{D}$ 1.4451. The infrared spectrum[28] of the product has a band at 1675 cm.$^{-1}$ (conj. C═O); the ultraviolet spectrum has a maximum at 230 mμ (ε 12,800) [lit.[35] 229.5 mμ (ε 11,090)].

The *trans*-ketone yields a 2,4-dinitrophenylhydrazone which crystallized from ethanol as red prisms, m.p. 200–202°.[36] The infrared spectrum[37] of the product has a sharp band at 3350 cm.$^{-1}$, attributable to an N–H stretching vibration, which excludes the possibility that the product is a pyrazoline derivative. The ultraviolet spectrum of the product has a maximum at 375 mμ (ε 26,500); in chloroform solution the values are 380 mμ (ε 26,800).

Anal. Calcd. for $C_{12}H_{14}N_4O_4$: C, 51.79; H, 5.07; N, 20.14. Found: C, 52.01; H, 5.37; N, 20.18.

Procedure B.—The product obtained by the condensation of 2-butanone and acetaldehyde was prepared as described by Hinkel and co-workers.[18] The material, b.p. 139–

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[26] All melting points are corrected and all boiling points are uncorrected. The infrared spectra were determined with a Baird, model B, double beam infrared recording spectrophotometer fitted with a sodium chloride prism. The ultraviolet spectra were determined in 95% ethanol (except where noted) with a Cary recording spectrophotometer, model 11 MS. The microanalyses were performed by Dr. S. M. Nagy and his associates. The vapor-phase chromatographic analyses were obtained with an 8 mm. × 215 cm. column packed either with di-2-ethylhexyl sebacate, polyethylene glycol or ethyl N,N-dimethyloxamate suspended on 50–80 mesh firebrick. The fractions from the chromatogram, eluted with helium, were detected with a thermal-conductivity cell.

[27] The deuterium analyses, given in Table I, were performed by Mr. Jozsef Nemeth, Department of Chemistry, University of Illinois.

[28] Determined in carbon tetrachloride solution.

[29] Determined with a Varian Associates high-resolution nuclear magnetic resonance spectrometer, model V4300B. The radio signal used had a frequency of 40 mc.

[30] H. O. House and R. S. Ro, THIS JOURNAL, **80**, 182 (1958).

[31] F. G. Bordwell and P. S. Landis, *ibid.*, **79**, 1593 (1957).

[32] A. Guillemonat [*Compt. rend.*, **201**, 904 (1935); *Ann. chim.* (*Paris*), [11] **11**, 143 (1939)] has reported the preparation of this alcohol by the oxidation of 3-methyl-2-pentene. The stereochemistry of the product was not specified; the physical properties were b.p. 139–140°, $n^{21}\mathrm{D}$ 1.4400.

[33] Determined in carbon disulfide solution.

[34] The manganese dioxide, prepared by the reduction of potassium permanganate with sodium bisulfite, was dried in an oven at 120° for two days before use.

[35] L. K. Evans and A. E. Gillam, *J. Chem. Soc.*, 815 (1941).

[36] This 2,4-dinitrophenylhydrazone was reported by G. F. Hennion, R. B. Davis and D. E. Maloney [THIS JOURNAL, **71**, 2813 (1949)] to melt at 193–194°. Comparison of other melting points listed in this paper with literature values suggests that this melting point is low by about 8°. R. Heilmann, G. de Gaudemaris and P. Arnaud [*Compt. rend.*, **234**, 1177 (1952)] and R. Heilmann and R. Glenat [*ibid.*, **234**, 1557 (1952)] have reported a correct melting point of 198.5° for this derivative and also an ultraviolet maximum (in ethanol) at 377 mμ (ε 26,000).

[37] Determined as a suspension in a potassium bromide pellet.

139.5°, n^{30}_{D} 1.4448 (lit.[38] 138–140°, n^{25}_{D} 1.4465), was shown by vapor-phase chromatographic analysis to contain less than 1% of the *cis* isomer. The 2,4-dinitrophenylhydrazone of the product was shown by a mixed melting-point determination to be identical with the derivative described previously.

3-Methyl-*cis*-3-penten-2-one (XVIIb).—A solution of 11 g. (0.11 mole) of 3-methyl-*cis*-3-penten-2-ol in 50 ml. of pentane was stirred with 30 g. of activated manganese dioxide for 12 hr. Since a vapor-phase chromatogram of the reaction mixture showed that a substantial amount of unchanged alcohol remained, the pentane solution was stirred 12 hr. with each of two additional 20-g. portions of manganese dioxide. The product, isolated by distillation through a Holtzmann column, amounted to 8.0 g. (74%) and consisted of the desired *cis*-ketone contaminated with smaller amounts of the *trans*-ketone (12%) and the unchanged alcohol (21%). Fractional distillation of this product through an 18-in. spinning band column afforded the *cis*-ketone (stereochemical purity >99%), b.p. 78.5–80° (140–143 mm.), $n^{28.4}_{\mathrm{D}}$ 1.4345. The infrared spectrum of the product has a band at 1690 cm.$^{-1}$ (conj. C=O); the ultraviolet spectrum has a maximum at 235.5 mμ (ε 4,570).

The *cis*-ketone formed a 2,4-dinitrophenylhydrazone which crystallized from ethanol as orange needles, m.p. 140–142°. The infrared spectrum[37] of the product has a sharp band at 3350 cm.$^{-1}$ (N–H) which indicates that the compound is not a pyrazoline derivative. The ultraviolet spectrum of the product has a maximum at 367 mμ (ε 22,100); in chloroform solution the values are 370 mμ (ε 24,100).

Anal. Calcd. for $C_{12}H_{14}N_4O_4$: C, 51.79; H, 5 07; N, 20.14. Found: C, 51.91; H, 5.40; N, 19.95.

The Epoxidation of 3-Methyl-*trans*-3-penten-2-one (XVIIa).—To a solution of 10 g. (0.102 mole) of the *trans*-ketone and 30 ml. (0.31 mole) of 30% aqueous hydrogen peroxide in 100 ml. of methanol cooled to 10° was added, dropwise and with stirring, 8.5 ml. (0.051 mole) of 6 *N* aqueous sodium hydroxide. After 2.5 hr. the optical density of the reaction mixture at 230 mμ had fallen to 1% of its initial value. The reaction mixture was diluted with 200 ml. of water and extracted with ether. After the extract had been dried over magnesium sulfate and the ether removed, distillation of the residual liquid afforded 5.2 g. (45%) of 3-methyl-*trans*-2,3-epoxy-2-pentanone, b.p. 93–94.5° (120–125 mm.), n^{28}_{D} 1.4141. The infrared spectrum[28] of the product has a band at 1710 cm.$^{-1}$ (C=O); the ultraviolet spectrum exhibits only end absorption, the molecular extinction at 210 mμ being 251. The vapor-phase chromatogram of the product has one major peak accompanied by very small peaks corresponding to traces of the *cis*- and *trans*-unsaturated ketones.

The epoxy ketone (200 mg., 0.00175 mole) was added to a warm solution of 400 mg. (0.0020 mole) of 2,4-dinitrophenylhydrazine in 20 ml. of ethanol containing several drops of sulfuric acid and the resulting mixture was cooled to room temperature. The crude derivative (510 mg. or 85%, m.p. 175–182°) was recrystallized from ethanol to give orange needles, m.p. 193–196°. Chromatography of the mother liquors from the derivative preparation on Merck acid-washed alumina afforded an additional crop of the same derivative, m.p. 192–195°, as the only crystalline product. Chromatography of the crystalline derivative on alumina (eluted with 10% ethyl acetate in ether) raised the melting point of the derivative to 196.5–198°; there was no indication that an appreciable amount of a second component was present. The infrared spectrum[37] of the derivative has strong, relatively sharp bands at 3550 (O–H) and 3400 cm.$^{-1}$ (N–H); the ultraviolet spectrum[38] has a maximum at 356 mμ (ε 25,200).

Anal. Calcd. for $C_{14}H_{20}N_4O_6$: C, 49.40: H, 5.92; N, 16.46. Found: C, 49.74; H, 5.75; N, 16.65.

Epoxidation of 3-Methyl-*cis*-3-penten-2-one (XVIIb).—The *cis*-ketone (5.0 g. or 0.051 mole) was epoxidized as described for the *trans* isomer. The optical density of the reaction mixture at 235 mμ had decreased to 10% of its initial value after 6 hr. The product, 3-methyl-*trans*-2,3-epoxy-2-pentanone, b.p. 92–93° (118–122 mm.), n^{28}_{D} 1.4142, amounted to 2.5 g. (43%). A vapor-phase chromatogram of the crude product before distillation indicated the presence of the epoxy ketone accompanied by 4.3% of the *trans*-unsaturated ketone and 8.2% of the *cis*-unsaturated ketone.

The infrared spectrum of the product is identical with the spectrum of the product obtained from the *trans*-unsaturated ketone. The ultraviolet spectrum has a maximum at 235 mμ (ε 204) attributable to the presence of small amounts of the *cis*- and *trans*-unsaturated ketones as impurities. The molecular extinction of the product at 210 mμ is 397. Reaction of 200 mg. of the product with 2,4-dinitrophenylhydrazine as previously described afforded the crude derivative, yield 500 mg. or 83%, m.p. 165–172°, which crystallized from ethanol as orange needles, m.p. 193–196°. The infrared[37] and ultraviolet[38] spectra of this sample are identical with the spectrum of the derivative described previously. Also, the melting point of a mixture of the two samples was not depressed. As before, chromatography of the mother liquors failed to isolate a second crystalline derivative.

3-Methyl-*trans*-2,3-epoxy-2-pentanone (XX).—To a cold (5°) solution of 10 g. (0.10 mole) of 3-methyl-*trans*-3-penten-2-ol in 150 ml. of methylene chloride was added 25 ml. of a 40% solution of peracetic acid in acetic acid in which had been dissolved 2.0 g. of sodium acetate trihydrate. Throughout the addition, which required 10 min., the reaction mixture was cooled in an ice-bath; the temperature of the mixture rose to 20° and then fell back to 5° after 15 min. After the reaction mixture had been stirred for 1.5 hr., it was washed with aqueous potassium carbonate and then dried over solid potassium carbonate and concentrated. Distillation of the residue afforded 8.0 g. (69%) of crude 3-methyl-*trans*-2,3-epoxy-2-pentanol, b.p. 79–82° (25 mm.). The infrared spectrum[28] of the crude product has a band at 3500 cm.$^{-1}$ (O–H), but no band in the 6 μ region attributable to a carbonyl function. However, the vapor-phase chromatogram of the crude product exhibited, in addition to a peak attributable to the epoxy alcohol, peaks corresponding to higher boiling contaminants. Since fractional distillation through a Holtzmann column failed to remove the contaminants (fractions b.p. 71–78° (16 mm.), n^{28}_{D} 1.4268–1.4282), a 1.5-g. (0.013 mole) portion of the crude product was oxidized with the complex obtained from 2.0 g. of chromium trioxide and 20 ml. of pyridine in the usual manner.[39] After the crude product had been extracted with ether, the extract was dried over magnesium sulfate and concentrated. Distillation of the residue in a short path still afforded 0.7 g. 47%) of crude 3-methyl-*trans*-2,3-epoxy-2-pentanone The vapor-phase chromatogram of the crude product exhibited a peak corresponding to the epoxy ketone as well as a peak corresponding to pyridine. The infrared spectrum[28] of the product exhibits all of the bands present in the spectrum of the *trans*-epoxy ketone previously described as well as additional bands attributable to pyridine. Reaction of the product with 2,4-dinitrophenylhydrazine as previously described afforded a 2,4-dinitrophenylhydrazone, m.p. 195–196.5°. The sample was shown to be identical with the derivative previously described both by a mixed melting-point determination and by comparison of the infrared spectra and ultraviolet spectra of the two samples.

Isomerization of 3-Methyl-*cis*-3-penten-2-one (XVIIb).—A solution of 0.5 g. of a mixture of the isomeric 3-methyl-3-penten-2-ones (77.6% *cis* isomer and 22.4% *trans* isomer) in 10 ml. of methanol was treated with sufficient dilute, aqueous sodium hydroxide to give a solution of *p*H 11 and the resulting solution was allowed to stand at room temperature. The proportions of the two ketones in the reaction mixture were determined by vapor-phase chromatographic analysis. After 6 hr. the composition of the ketone mixture was 72.6% of the *cis*-ketone and 27.4% of the *trans* isomer. After the solution had stood for three days, the chromatogram exhibited peaks corresponding to the *trans*-ketone accompanied by peaks attributable to higher-boiling components.

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[38] Determined in chloroform solution.

[39] G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, THIS JOURNAL, **75**, 422 (1953).