

### Experimental<sup>11</sup>

*Trans-* and *cis*-4-*t*-Butyl-1-ethynylcyclohexanols (I and II).—A mixture<sup>12</sup> of I and II was separated into pure *trans*-4-*t*-butyl-1-ethynylcyclohexanol (I), m.p. 101.3–102.3°, and pure II, m.p. 63.0–64.0°, essentially as described.<sup>3</sup> During the separation, a sample of 4-*t*-butylcyclohexanone<sup>4</sup> was obtained and converted into its 2,4-dinitrophenylhydrazone, m.p. 151.9–153.2°.

*Anal.* Calcd. for C<sub>16</sub>H<sub>22</sub>N<sub>4</sub>O<sub>4</sub>: N, 16.8. Found: N, 16.7.

**Rearrangements of I and II into 1-Acetyl-4-*t*-butylcyclohexene (III).**—A solution of 1.06 g. of *trans*-alcohol I in 4.6 ml. of 90% formic acid was heated at reflux for 45 minutes, then cooled and poured on ice. By extraction with ether-benzene and washing this extract with alkali, there was isolated 1.03 g. of a pale yellow oil. This oil was estimated to have between 4 and 8% of acetylenic hydrogen by testing as follows. A small amount of pure I was dissolved in 1:1 alcohol-water and a portion was treated with 2.5% silver nitrate solution. The resulting solution was tested with universal type indicator paper, a change in color from orange to orange-red indicating acidity. The original solution was then diluted before testing as above until the color change no longer occurred. Then, a solution of the same amount of unknown (yellow oil) was tested similarly and diluted until the test was no longer positive. This test does not distinguish starting ethynyl alcohol I from 4-*t*-butyl-1-ethynylcyclohexene (IV), but is fairly sensitive for showing the presence of acetylenic hydrogen.

A portion of the above pale yellow oil yielded the red 2,4-dinitrophenyl-hydrazone of 1-acetyl-4-*t*-butylcyclohexene in 72–78% yield. The pure derivative, purified by chromatography over alumina using benzene, melted at 178.2–179.0°.

*Anal.* Calcd. for C<sub>15</sub>H<sub>24</sub>N<sub>4</sub>O<sub>4</sub>: C, 60.0; H, 6.7. Found: C, 60.3; H, 6.7.

When 0.33 g. of *cis*-alcohol II in 1.45 ml. of 90% formic acid was heated at reflux for 45 minutes, a workup similar to that above provided 0.32 g. of pale yellow oil. This oil gave no test for acetylenic hydrogen when tested as described above and the yield of 2,4-dinitrophenylhydrazone indicated about a 95% yield of III. The purified derivative, m.p. 177.0–178.0°, was identical to that prepared above.

(11) All melting points are uncorrected. Analyses by Galbraith Laboratories, Knoxville, Tenn.

(12) We thank the Air Reduction Chemical Co., Murray Hill, N. J., for a supply of the mixed isomers, and Miss C. Gedeist for aid in separation of the isomers.

An examination by n.m.r. of the entire crude pale yellow oil obtained from another run with *trans*-I indicated that no aldehydic hydrogen was present.<sup>5</sup>

**1-Acetyl-4-*t*-butylcyclohexene (III).**—A solution of 10 g. of I in 46 ml. of 90% formic acid was held at reflux for 1.5 hours. Dilution with water followed by extraction with ether afforded the crude product in almost quantitative yield. The analytical sample, b.p. 135–137° at 14 mm., was obtained in 75% yield.

*Anal.* Calcd. for C<sub>12</sub>H<sub>20</sub>O: C, 80.0; H, 11.2. Found: C, 80.2, 80.4; H, 10.7, 10.9.

**1-Ethynyl-4-*t*-butylcyclohexene (IV).**—To a solution of 5.6 g. of I in 6 ml. of dry pyridine was added a solution of 2.4 ml. of phosphorus oxychloride in 2.4 ml. of pyridine. After warming to 65° for 20 minutes the product was isolated by ether extraction and distilled to yield 0.9 g. (18%) of IV, b.p. 64–67° at 9 mm. Redistillation yielded an analytical sample as a colorless oil, *n*<sub>D</sub><sup>20</sup> 1.4850.

*Anal.* Calcd. for C<sub>12</sub>H<sub>18</sub>: C, 88.8; H, 11.2. Found: C, 88.3; H, 11.6.

**Rough Kinetic Measurements.**—The rates of reaction of I, II and IV with the same batch of approximately 90% formic acid at about 79° (b.p. of carbon tetrachloride) were estimated by following the change in absorption at 234 m $\mu$ . Aliquots, suitably diluted with alcohol containing sufficient piperidine to neutralize the formic acid, were taken after 20, 110, 255 and 450 minutes. The percentage of 4-*t*-butyl-1-acetylcyclohexene (III) was estimated by using the molar extinction coefficients obtained from the aliquots and comparing with that obtained after the 450-minute interval after which time no further change occurred. The molar extinction coefficient at 234 m $\mu$  of both final solutions was almost the same (10,600). The extinction coefficient of 4-*t*-butyl-1-ethynylcyclohexene (IV) at 234 m $\mu$  is 6100 and is maximal (8900) at 223 m $\mu$ . No corrections for possible variations from Beer's law were made. These experiments showed that the *cis*-isomer II reacts considerably more rapidly than the *trans* isomer I. For example, after 20 and 110 minutes, compound I had yielded 17 and 71% of III, whereas II had yielded 38 and 90% of III. Under similar conditions after 20 minutes 4-*t*-butyl-1-ethynylcyclohexene (IV) had almost completely reacted to form III.

The infrared absorption spectra of samples of crude product obtained by quenching reaction mixtures of both I and II with 90% formic acid at 50° after 15 minutes showed a band at 5.75 $\mu$  characteristic of formate esters,<sup>13</sup> in addition to hydroxyl bands.

(13) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen and Co., London, 1954, p. 179ff.

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

## The Reaction of Ketones with Diazomethane

BY HERBERT O. HOUSE, EDWARD J. GRUBBS<sup>1</sup> AND WALTER F. GANNON<sup>2</sup>

RECEIVED DECEMBER 23, 1959

The reactions of diazomethane with benzil, biacetyl, acetophenone, benzyl methyl ketone, 3,3-dimethyl-2-butanone, 3-methyl-2-butanone, 2-pentanone and 4-methyl-3-penten-2-one have been studied. Use of boron trifluoride as a catalyst for these reactions was found to accelerate markedly the reactions and to favor the formation of ketones rather than other products. The ratios of ketonic products obtained from these reactions suggest the order of migratory aptitudes: C<sub>6</sub>H<sub>5</sub> ~ (CH<sub>3</sub>)<sub>2</sub>C=CH > CH<sub>3</sub> ~ CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub> > (CH<sub>3</sub>)<sub>2</sub>CH ~ C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub> ~ (CH<sub>3</sub>)<sub>3</sub>C. Similar product ratios were obtained from the semipinacolic deamination of the appropriate 1,1-disubstituted-2-aminoethanols.

The reaction of diazomethane with ketones<sup>3,4</sup> is usually considered to follow the course illustrated

in the accompanying equations. The diazonium ion II, also a probable intermediate in the semipinacolic deamination of amino alcohols of the type V,<sup>5-7</sup> is believed to lose nitrogen with the si-

(1) Eastman Kodak Predoctoral Fellow, 1958–1959.

(2) Monsanto Chemical Co. Predoctoral Fellow, 1958–1959.

(3) C. D. Gutsche, *Org. Reactions*, **8**, 364 (1954).

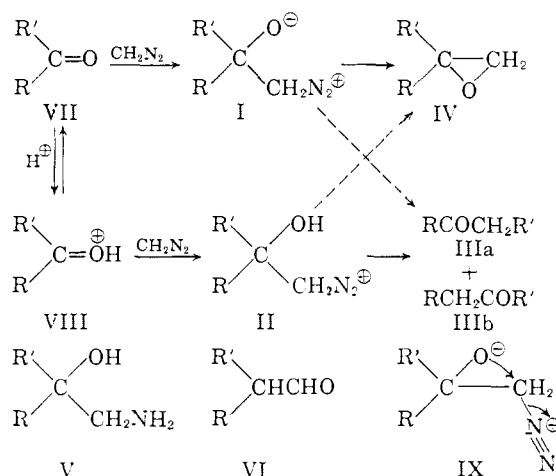
(4) B. Eistert in "Newer Methods of Preparative Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1948, pp. 513–570.

(5) M. Tiffeneau and H. Cahnmann, *Bull. soc. chim. France*, [5] **2**, 1876 (1935).

(6) D. Y. Curtin and M. C. Crew, *THIS JOURNAL*, **76**, 3719 (1954).

(7) H. O. House and E. J. Grubbs, *ibid.*, **81**, 4733 (1959).

multaneous<sup>8,9</sup> or subsequent<sup>10</sup> migration of one of the groups R or R' to form the ketones III. The apparent similarity of diazomethane ketone reactions and deaminations of the amino alcohols V suggested that a study of the products derived from ketones and diazomethane might provide a rapid and convenient measure of the relative migratory aptitudes of a variety of groups to an electron-deficient carbon atom. Such a measure of migratory aptitude, like the deamination of the amino alcohols V,<sup>5-7</sup> would minimize the importance of steric effects which have determined the course of molecular rearrangements in other systems.<sup>9</sup>



However, any study of the reaction of diazomethane with ketones could be expected to be complicated by the facts that the reaction proceeds very slowly except with very reactive ketones, that oxide by-products IV (or their rearrangement products, the aldehydes VI) are usually formed in addition to the desired ketones III, and that the initially formed products III are capable of further reaction with diazomethane.<sup>3,4</sup> The observation<sup>3</sup> that the reaction rates of ketones with diazomethane parallel the rates of reaction of these ketones in other carbonyl-addition reactions indicates that the rate-determining step in diazomethane-ketone reactions is the reaction of diazomethane with either the ketone VII or its conjugate acid VIII. The pronounced catalysis of the reaction by hydroxylic compounds (e.g., water or methanol)<sup>3,4</sup> suggests that diazomethane, like other nucleophilic reagents, undergoes acid-catalyzed additions to carbonyl functions, the reaction of diazomethane with the conjugate acid VIII to form the diazonium ion II being more rapid than the reaction with the ketone VII to form,

(8) A. Streitwieser, Jr., and W. D. Schaeffer, *THIS JOURNAL*, **79**, 2888 (1957); A. Streitwieser, Jr., *J. Org. Chem.*, **22**, 861 (1957).

(9) The importance of stereochemical factors in determining the products of molecular rearrangements suggests that most deaminations accompanied by rearrangement are concerted processes. For examples see (a) D. Y. Curtin, *Rec. Chem. Progress.*, **15**, 111 (1954); (b) D. J. Cram in M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, pp. 249-279; (c) R. J. W. Cremlyn, D. L. Garmaise and C. W. Shoppee, *J. Chem. Soc.*, 1847 (1953); (d) F. Ramirez and S. Stafiej, *THIS JOURNAL*, **77**, 134 (1955); **78**, 644 (1956).

(10) (a) D. J. Cram and J. E. McCarty, *ibid.*, **79**, 2866 (1957); (b) B. M. Benjamin, H. J. Schaeffer and C. J. Collins, *ibid.*, **79**, 6160 (1957); (c) D. Semenow, C. Shih and W. G. Young, *ibid.*, **80**, 5472 (1958); (d) H. Felkin, *Bull. soc. chim. France*, 20 (1959).

the zwitterion I. The formation of the oxide IV, presumably by the intramolecular nucleophilic displacement depicted by structure IX, should be favored when the displacing group is an alkoxide ion (as in intermediate I) rather than a less nucleophilic<sup>11</sup> hydroxyl group (as in intermediate II). In agreement with these considerations, the deaminations of the amino alcohols V, a process which very probably involves the diazonium ion II, produces little, if any, of the oxides IV or their by-products.<sup>5-7</sup> Thus one is led to the tentative conclusion that an increase in the concentration of the conjugate acid VIII with respect to the ketone VII should not only enhance the rate of the diazomethane-ketone reaction, but should also reduce the amount of oxide by-product formed.

In order to increase the amount of ketone VII present as its conjugate acid VIII, it was apparent that an acid stronger than methanol should be employed as a catalyst. It did not appear profitable to explore stronger protonic acids, since these materials are known to react rapidly with diazomethane to form products which would complicate the reaction mixture.<sup>3,4</sup> Several common Lewis acids have been reported to decompose diazomethane rapidly with the formation of polymethylene as well as other products.<sup>12-15</sup> For example, the reaction of diazomethane with boron trifluoride has been found to yield polymethylene and fluoromethylboron difluoride.<sup>15</sup> Although this reaction was rapid, the successful use of boron trifluoride as a catalyst for the methylation of alcohols with diazomethane<sup>16,17</sup> demonstrated that the reaction of diazomethane with organic compounds can successfully compete with the diazomethane-boron trifluoride reaction. Since boron trifluoride has been found to form relatively stable conjugate acids with ketones,<sup>18</sup> this catalyst was selected for study.

Ethereal solutions of the ketones to be studied, containing either one molar equivalent of boron trifluoride or an excess of methanol, were treated with an ethereal solution containing a known concentration of diazomethane. The methanol-catalyzed reactions were allowed to stand for one to four days; the diazomethane was consumed as rapidly as it was added in the boron trifluoride-catalyzed reactions. In order to minimize further reaction of the ketonic products III with diazomethane to form higher homologs, the reactions were not run to completion. When necessary, corrections for the consumption of the initially formed products were made. The product analyses were obtained by gas chromatography. In all cases the ketonic reaction products III were identified by comparison with au-

(11) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956, p. 140.

(12) G. Caronna and B. Sansone, *Atti. Congr. intern. chim.*, **3**, 77 (1939); *C. A.*, **34**, 980 (1940).

(13) H. Meerwein, *Angew. Chem.*, **60**, 78 (1948).

(14) G. D. Buckley and N. H. Ray, *J. Chem. Soc.*, 3701 (1952).

(15) J. Goubeau and K. H. Rohwedder, *Ann.*, **604**, 168 (1957).

(16) M. S. Newman and P. F. Beal, *THIS JOURNAL*, **72**, 5161 (1950).

(17) M. Neeman, M. C. Caserio, J. D. Roberts and W. S. Johnson, *Tetrahedron*, **6**, 36 (1959).

(18) R. Lombard and J. P. Stephan, *Bull. soc. chim. France*, 1369 (1957).

TABLE I  
 THE REACTION OF KETONES WITH DIAZOMETHANE

Reactant, RCOR', and conditions					Recovd. react. ant. %	Products, %				
R	R'	Reacn. time	Equiv. CH <sub>2</sub> N <sub>2</sub>	Catalyst (equiv.)		RR'C-CH <sub>2</sub> O	RR'CHCHO	RCOCH <sub>2</sub> R'	RCH <sub>2</sub> COR'	RCOCH <sub>2</sub> R' RCH <sub>2</sub> COR'
C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	4 days	7.1	CH <sub>3</sub> OH(xs.)	44.2	14.9 <sup>a</sup>	.. <sup>a</sup>	2.4	(11.9)38.6 <sup>b</sup>	0.062
		2 min.	2	BF <sub>3</sub> (1.0)	63.7	..	..	8.0	(21.0)28.2 <sup>b</sup>	0.28
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	CH <sub>3</sub>	3 days	3.1	CH <sub>3</sub> OH(xs.)	34.6	30.9 <sup>c</sup>	..	21.2	13.3	1.59
		2 min.	2	BF <sub>3</sub> (1.0)	63.5	..	..	28.7	7.9	3.63
		3.5 min.	2	BF <sub>3</sub> (1.0) at -45°	87.4	3.43 <sup>c</sup>	..	7.12	2.0	3.56
CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub>	CH <sub>3</sub>	3 days	1.1	CH <sub>3</sub> OH(xs.)	75.0	8.3 <sup>c</sup>	..	8.29	8.42	0.96
		4 min.	1.1	BF <sub>3</sub> (1.0)	81.0	..	..	9.61	9.38	1.02
(CH <sub>3</sub> ) <sub>2</sub> CH	CH <sub>3</sub>	1 day	1.0	CH <sub>3</sub> OH(xs.)	95.1	.. <sup>d</sup>	..	3.19	1.67	1.91
		2 min.	1.0	BF <sub>3</sub> (1.0)	93.2	..	2.12 <sup>e</sup>	3.12	1.53	2.04
(CH <sub>3</sub> ) <sub>3</sub> C <sup>f</sup>	CH <sub>3</sub>	2 min.	0.67 <sup>g</sup>	BF <sub>3</sub> (1.0)	99.2	..	0.286 <sup>e</sup>	0.312	0.109	2.86

<sup>a</sup> The product collected from the gas chromatogram was identified as  $\alpha$ -phenyl propionaldehyde. An authentic sample of  $\alpha$ -methylstyrene oxide was isomerized to the same aldehyde when it was passed through the same chromatographic column. <sup>b</sup> The figure in parentheses represents the actual percentage of benzyl methyl ketone present and the figure outside the parentheses represents the value after correction for further reaction of the benzyl methyl ketone with diazomethane. <sup>c</sup> These products were not characterized. In both cases peaks, believed to be either the aldehyde or oxide, were present in the gas chromatograms at retention times comparable to the retention times of the ketone peaks. <sup>d</sup> The possibility that an oxide was present, but was obscured in the gas chromatogram by the starting material peak was not excluded. <sup>e</sup> These products were only partially characterized as indicated in the Experimental section. <sup>f</sup> Attempts to achieve a measurable amount of reaction in the presence of methanol were not successful. <sup>g</sup> Because of the very low reactivity of pinacolone toward diazomethane as compared with the products IIIa, IIIb and VI, the reaction was carried to less than 1% completion in order to obtain reliable ratios of the initially formed products.

thetic samples, both the retention times and the infrared spectra of the samples being employed. The results obtained with the dialkyl ketones and alkyl aryl ketones studied are summarized in Table I. The reactions of diazomethane with acetophenone<sup>19</sup> and with 2-pentanone<sup>20</sup> have been studied previously. From acetophenone the products reported were  $\alpha$ -methylstyrene oxide (about 19% isolated as an amino alcohol derivative) and benzyl methyl ketone (about 5%); the reported products from 2-pentanone were the corresponding oxide IV (58% isolated as the diol), 2-hexanone (5%) and 3-hexanone (12%). In the present study, the methanol-catalyzed reactions of the ketones acetophenone, benzyl methyl ketone and 2-pentanone produced an additional component besides the ketones III. After separation by gas chromatography, the additional product obtained from acetophenone was identified as  $\alpha$ -phenylpropionaldehyde. Since an authentic sample of  $\alpha$ -methylstyrene oxide was also converted to the same aldehyde by gas chromatography, there is little doubt that the additional product was the expected  $\alpha$ -methylstyrene oxide. Although the corresponding products from the ketones benzyl methyl ketone and 2-pentanone were not characterized, it is probable that they were also the expected<sup>3,4,20</sup> oxides. With each of these three ketones, the boron trifluoride-catalyzed reactions produced mixtures of the ketones III but no oxide by-products IV (or aldehydes VI) were detected. Analysis of the mixture obtained from the methanol-catalyzed reaction of diazomethane with 3-methyl-2-butanone did not resolve a component corresponding to the aforementioned oxides or aldehydes. It is probable that an oxide by-product was produced in this reaction but was not resolved from the starting material by

the several chromatographic columns employed. From the boron trifluoride-catalyzed reaction of diazomethane and 3-methyl-2-butanone, a component having properties consistent with its formulation as 2,3-dimethylbutyraldehyde was isolated. Similar results were obtained in the boron trifluoride-catalyzed reaction of diazomethane with 3,3-dimethyl-2-butanone, a component believed to be 2,3,3-trimethylbutyraldehyde being separated. In the latter case, a comparison with the results of the methanol-catalyzed reaction was not obtained because the 3,3-dimethyl-2-butanone failed to react with diazomethane under the conditions employed for the previous studies.

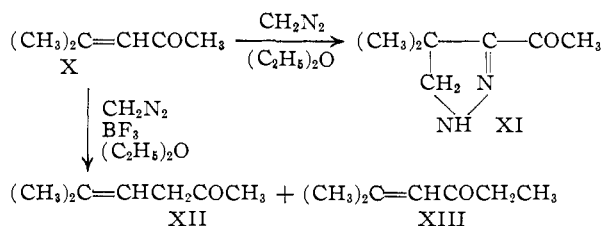
From these data it was clear that the use of boron trifluoride catalysis in the diazomethane-ketone reaction greatly accelerated the reaction and also, in the case of relatively unhindered ketones, prevented the formation of oxide IV or aldehyde VI by-products. The aldehydes obtained in the 3-methyl-2-butanone and 3,3-dimethyl-2-butanone reactions were almost certainly the rearrangement products of the initially formed oxides. Our data permit no decision as to whether or not the increased oxide formation with these hindered ketones is the result of a lower concentration of the conjugate acid VIII being present in these cases. With the relatively unreactive ketones acetophenone, 3-methyl-2-butanone and especially 3,3-dimethyl-2-butanone one of the products of the initial reaction with diazomethane was much more reactive than the starting material resulting in very appreciable formation of higher homologs of the initial products. In order to obtain reliable ratios of the products III, the reactions with 3-methyl-2-butanone and 3,3-dimethyl-2-butanone were carried to no more than a few per cent. of completion. In the case of acetophenone, a correction for this further reaction was obtained by use of the data obtained from the reaction of benzyl methyl ketone with diazomethane.

(19) E. Moseittig and L. Javanovic, *Monatsh.*, **54**, 427 (1929).

(20) P. Pöhls, Inaug. diss., University of Marburg, Marburg, 1934, as cited in ref. 3, footnote 24.

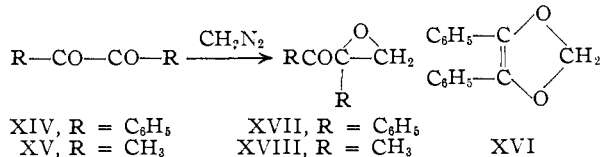
Although the ratios of ketonic products III obtained from the aliphatic ketones were similar irrespective of the nature of the catalyst, differences were observed in the ratios of ketonic products III obtained from acetophenone and from benzyl methyl ketone. In both cases when boron trifluoride was used as a catalyst, more methyl group migration was observed than when the same reactions were catalyzed by methanol. This difference can possibly be attributed to complexing of the boron trifluoride with the aromatic nucleus present in each of the two ketones.<sup>21</sup>

We next turned our attention to the reaction of  $\alpha,\beta$ -unsaturated ketones with diazomethane, this reaction has been reported<sup>3,21a</sup> previously to yield  $\Delta^1$ - or  $\Delta^2$ -pyrazolines, products of the attack of diazomethane at the carbon-carbon double bond, rather than products derived from attack of diazomethane at the carbonyl group. The reaction of 4-methyl-3-penten-2-one (X) with diazomethane in ether solution afforded the previously described<sup>22</sup> pyrazoline XI which could be assigned the  $\Delta^2$ -pyrazoline structure by virtue of its infrared and ultraviolet absorption. When the same reaction was conducted in the presence of one equivalent of boron trifluoride, none of the pyrazoline could be detected among the products. Rather, the initially formed products consisted of the unsaturated ketones XII and XIII present in a ratio of 2.40 to 1.<sup>23</sup> The ketone XII was characterized by its mass spectrum, its ultraviolet spectrum and the identity of its infrared spectrum with the spectrum of an authentic sample.<sup>24</sup> The ketone XIII was characterized by its mass spectrum, its infrared and ultraviolet spectra, and its conversion, on catalytic hydrogenation, to 5-methyl-3-hexanone which was identified by comparison with an authentic sample. The pyrazoline XI did not form either of the ketones XII or XIII when treated with a solution of boron trifluoride in ether.



The diketones benzil (XIV) and biacetyl (XV) were selected for study. Early studies by Biltz and Paetzold<sup>25</sup> had indicated that biacetyl does not react with diazomethane and that benzil reacts

with diazomethane to form the methylenedioxy derivative XVI. However, when the reaction with benzil was repeated in the present study the epoxy ketone XVII was formed.<sup>26</sup> This reaction was not explored further since the instability of the products at high temperatures presented their analysis by gas chromatography. A solution of biacetyl in an ether-methanol mixture reacted very rapidly with diazomethane to form the epoxy



ketone XVIII as well as smaller amounts of higher boiling materials. When the same reaction was run in ether solution catalyzed by boron trifluoride, the epoxy ketone XVIII was again the major product. None of the compounds pentane-2,3-dione, pentane-2,4-dione or the methyl enol ether of pentane-2,4-dione could be detected among the reaction products. This result is to be contrasted with the reaction of camphorquinone with diazomethane to form the isomeric enol ethers of the  $\beta$ -diketone, 1,8,8-trimethylbicyclo[3.2.1]octan-2,4-dione.<sup>27</sup> The differing behavior of the diketones XIV, XV and camphorquinone is perhaps attributable either to the relief of ring strain which will result from rearrangement of the intermediate I or II derived from camphorquinone or to steric interference with the formation of an epoxy ketone analogous to structures XVII and XVIII.

With the exception of the  $\alpha$ -diketones, the results obtained with the acyclic ketones included in this study appear to parallel previous results obtained with cyclic ketones. The reaction of diazomethane with 2-methylcyclohexanone afforded a mixture of the oxide (isolated as the diol), 3-methylcycloheptanone and 2-methylcycloheptanone, the latter ketone apparently being formed in larger amount.<sup>28</sup> 2-Phenylcyclohexanone, upon reaction with diazomethane, yielded the oxide (21%) and a mixture of 3-phenylcycloheptanone (9.4%) and 2-phenylcycloheptanone (40%).<sup>29</sup>

It was of interest to compare the ratios of products obtained from the diazomethane-ketone reactions with the corresponding values obtained by deamination of the amino alcohols V. In the present study, the cyanohydrins XIX were hydrogenated over platinum in acetic acid, the resulting reaction mixtures were diluted with water and subjected to reaction with nitrous acid. The neutral products XX and XXI were analyzed and characterized by the same methods used for the diazomethane-ketone reactions. A comparison of the ketonic product ratios for three amino alcohol deaminations and the corresponding diazomethane-ketone reactions is given in Table II. It will be

(26) The same observation has been reported recently by B. Eistert, G. Fink and R. Wollheim, *Chem. Ber.*, **91**, 2710 (1958).

(27) (a) H. Rupe and F. Hafliger, *Helv. Chim. Acta*, **23**, 139 (1940); (b) H. Rupe and C. Frey, *ibid.*, **27**, 627 (1944); (c) T. Isshiki, *J. Pharm. Soc. Japan*, **65**, No. 2A, 10 (1954); *C. A.*, **45**, 5663 (1951). (d) H. Favre, B. Marinier and J. C. Richer, *Can. J. Chem.*, **34**, 1329 (1956).

(28) D. W. Adamson and J. Kenner, *J. Chem. Soc.*, 181 (1939).

(29) C. D. Gutsche, *This Journal*, **71**, 3513 (1949).

(21) The complexes  $\text{C}_6\text{H}_6 \cdot \text{BF}_3$  and  $\text{C}_6\text{H}_5\text{CH}_3 \cdot \text{BF}_3$  have been proposed to account for charge-transfer spectra observed in boron trifluoride-benzene and boron trifluoride-toluene mixtures; see C. Reid, *This Journal*, **76**, 3264 (1954).

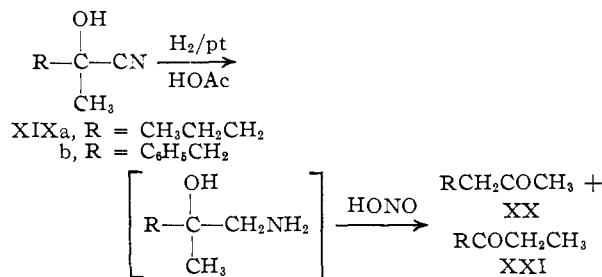
(21a) NOTE ADDED IN PROOF.—After this manuscript had been accepted for publication, preliminary experiments describing the addition of diazomethane to the carbonyl group of  $\alpha,\beta$ -unsaturated ketones were reported by W. S. Johnson, M. Neeman and S. P. Birkeland, *Tetrahedron Letters*, No. 5, 1 (1960).

(22) D. W. Adamson and J. Kenner, *J. Chem. Soc.*, 1551 (1937).

(23) This ratio of 2.40, if in error, is probably low since the unconjugated ketone XIV was slowly destroyed by the acidic reaction conditions.

(24) R. Heilmann, G. de Gaudemaris and P. Arnaud, *Compt. rend.*, **243**, 2008 (1956).

(25) H. Blitz and H. Paetzold, *Ann.*, **433**, 64 (1923).



noted that the results are similar for each of the cases compared, phenyl migration being favored over methyl migration which, in turn, was favored over the migration of a benzyl group.

TABLE II  
COMPARISON OF AMINO ALCOHOL DEAMINATIONS AND DIAZOMETHANE-KETONE REACTIONS

R	Deamination	Diazomethane-ketone rean. (CH <sub>3</sub> OH)
CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub>	0.64	0.98
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	1.71	1.59
C <sub>6</sub> H <sub>5</sub>	<0.031 <sup>a</sup>	0.062

<sup>a</sup> Data obtained from ref. 7.

The general order of migratory aptitude indicated by this diazomethane-ketone study is: C<sub>6</sub>H<sub>5</sub> ~ (CH<sub>3</sub>)<sub>2</sub>C=CH- > CH<sub>3</sub> ~ CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub> > (CH<sub>3</sub>)<sub>2</sub>CH ~ C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub> ~ (CH<sub>3</sub>)<sub>3</sub>C. This order differs from that obtained from a study of the Bayer-Villiger reaction,<sup>30</sup> both in the arrangement of groups and in the order of magnitude of differences between them. The order *t*-butyl > ethyl > methyl obtained in a recent study<sup>31</sup> of the pinacol rearrangement also differs from the order observed in this study. Other studies of rearrangements involving electron-deficient carbon atoms<sup>10a,32,33</sup> suggest no obvious relationship. We therefore believe it prudent to conclude that even when the products of a molecular rearrangement are not determined by the stereochemistry of the reactant,<sup>3</sup> it is not possible to arrange groups in a unique order which will express their relative abilities to migrate to an electron-deficient carbon atom in all types of molecular rearrangements. There does, however, appear to be one general conclusion which can be drawn from these molecular rearrangement studies. Unless opposed by stereochemical factors,<sup>9</sup> groups which possess an sp<sup>2</sup> hybridized carbon atom (*e.g.*, aryl groups, vinyl groups and acyl groups<sup>34</sup>) bonded to the atom serving as the origin of the migrating groups generally migrate more readily than alkyl groups. The ability of such groups to migrate is perhaps best ascribed to the use of the *p*-orbital in these groups for overlap with the

(30) M. F. Hawthorne, W. D. Emmons and K. S. McCallum, *THIS JOURNAL*, **81**, 6393 (1959); M. F. Hawthorne and W. D. Emmons, *ibid.*, **81**, 6398 (1959).

(31) M. Stiles and R. P. Mayer, *ibid.*, **81**, 1497 (1959).

(32) D. J. Cram and J. D. Knight, *ibid.*, **74**, 5839 (1952).

(33) M. Tiffeneau, J. Levy and co-workers, *Bull. soc. chim. France*, [4] **49**, 1595 (1931).

(34) See H. O. House and D. J. Reif, *THIS JOURNAL*, **79**, 6491 (1957), and references cited therein as well as ref. 27.

developing vacant orbitals present at both the origin and the terminus of the migration.

The problem of the relative migratory aptitudes of various alkyl groups is more perplexing, especially the changes of orders observed in the various reactions studied. The differences among the alkyl groups methyl, propyl, isopropyl, *t*-butyl and benzyl included in this study, while reproducible, are so small as to make any interpretation of their meaning especially hazardous. However, it does appear pertinent to note that the product ratios are clearly not in the direction which would be predicted if the most stable ground-state conformations of the reactants determined the products of the rearrangements.<sup>7,8</sup>

### Experimental<sup>35</sup>

**Preparation of Diazomethane.**—Ethereal solutions of diazomethane were prepared by heating du Pont product EXR-101<sup>36</sup> in a mixture of 40% aqueous sodium hydroxide and reagent ether. The ethereal diazomethane which distilled from the mixture was collected in a cold (0°) receiver, dried over potassium hydroxide pellets and an aliquot titrated directly with a standard solution of benzoic acid in ether. Consistent yields of 80–90% were obtained.

**Reaction of Acetophenone with Diazomethane. A-Boron Trifluoride Catalysis.**—To a solution of 0.485 g. (0.00404 mole) of acetophenone in 30 ml. of absolute ether was added 0.568 g. (0.00400 mole) of boron trifluoride etherate.<sup>37</sup> The solution was cooled to 0° in an ice-bath and to it was added, slowly and with swirling over a 2-min. period, 30 ml. of an ether solution containing 0.0080 mole of diazomethane. The resulting colorless solution was washed with water and dried over magnesium sulfate. The ether was then removed by distillation through a Vigreux column leaving 0.570 g. of a pale-yellow liquid. The gas chromatogram<sup>38</sup> of the liquid exhibited five peaks whose retention times corresponded to acetophenone (63.7%), benzyl methyl ketone<sup>39</sup> (21%), propiophenone (8.0%), 1-phenyl-2-butanone<sup>40</sup> (5.6%) and 4-phenyl-2-butanone<sup>41</sup> (1.63%), respectively.<sup>42</sup> Samples of the products having retention times corresponding to benzyl methyl ketone and propiophenone were collected from the gas chromatogram<sup>38</sup> and further identified by comparison of their infrared spectra<sup>43</sup> with the spectra of authentic samples. The two phenyl-butanones were identified by their retention times as compared with both authentic samples and with the product mixture obtained from the subsequently described reaction of

(35) All melting points are corrected; all boiling points are uncorrected. The infrared spectra were determined with a Perkin-Elmer, Model 21, infrared recording spectrophotometer fitted with a sodium chloride prism. The ultraviolet spectra were determined with a Cary recording spectrophotometer, model 11 MS.

(36) du Pont EXR-101 contains 70% N,N'-dinitroso-N,N'-dimethyl terephthalamide and 30% mineral oil. For further information see du Pont Products Bulletin EXR-101.

(37) A commercial sample of boron trifluoride etherate was distilled under atmospheric pressure immediately prior to its use. The fraction boiling at 126–127° was used in each case.

(38) The chromatogram was obtained with a column packed with Dow Silicone Fluid No. 550 suspended on ground firebrick.

(39) An authentic sample was commercially available from the Eastman Kodak Co.

(40) An authentic sample was obtained from the reaction of propiophenone [1.70 g. (0.0127 mole)] and 1.80 g. (0.0127 mole) of boron trifluoride etherate in 107 ml. of ether with 0.025 mole of diazomethane. The crude product (1.46 g.) was composed of propiophenone (55%), 1-phenyl-2-butanone (21%), butyrophenone (15%) and higher boiling products (9%). The pure sample of 1-phenyl-2-butanone, collected from the gas chromatogram (ref. 38) of the mixture, had a strong band at 1714 cm.<sup>-1</sup> (unconj. C=O) in the infrared. This ketone had been reported [M. Montagne and M. Roch, *Compt. rend.*, **218**, 679 (1944)] to boil at 121–122° (23 mm.).

(41) Y. Chen and W. F. Barthel, *THIS JOURNAL*, **75**, 4287 (1953).

(42) In all cases the percentage compositions reported do not include small amounts of ether and the low-boiling solvents which remain in the crude reaction product.

(43) Determined in carbon tetrachloride solution.

benzyl methyl ketone with diazomethane. The similarity of the ratio of 1-phenyl-2-butanone to 4-phenyl-2-butanone obtained in this experiment (3.44 to 1) to the corresponding product ratio (3.63 to 1) in the benzyl methyl ketone-diazomethane experiment indicates that essentially all of these higher boiling products are derived from benzyl methyl ketone. Similarly, the reaction of 0.261 g. (0.00217 mole) of acetophenone and 0.299 g. (0.00210 mole) of boron trifluoride etherate in 310 ml. of absolute ether with 0.083 mole of diazomethane afforded a crude product (0.777 g.) containing acetophenone (19.5%), benzyl methyl ketone (11.7%), propiophenone (18.1%), 1-phenyl-2-butanone (30.6%) 4-phenyl-2-butanone (9.4%) and higher boiling products (10.6%).<sup>38,42</sup>

**B. Methanol Catalysis.**—A solution of 2.018 g. (0.0168 mole) of acetophenone in 50 ml. of absolute methanol was treated with 300 ml. of an ethereal solution containing 0.060 mole of diazomethane. After a period of 40 hr. analysis<sup>38</sup> of an aliquot of the reaction mixture showed that 90% of the acetophenone remained unchanged. After the reaction mixture had been concentrated under reduced pressure to a volume of 50 ml., an additional 50 ml. of absolute methanol was added and the solution was treated with 195 ml. of an ethereal solution containing 0.060 mole of diazomethane. After the mixture had been allowed to stand for 2 days at room temperature, the resulting colorless solution was washed with water, dried over magnesium sulfate and concentrated to leave 1.90 g. of the crude product mixture. This mixture contained acetophenone (44.2%)  $\alpha$ -phenylpropionaldehyde<sup>44</sup> (14.9%), benzyl methyl ketone (11.9%), propiophenone (2.4%), an unidentified component (10.7%), 1-phenyl-2-butanone (10.8%) and 4-phenyl-2-butanone (5.2%).<sup>38,42</sup> The last three products have the same retention times and are present in approximately the same relative concentrations as the three products derived from the subsequently described reaction of benzyl methyl ketone with diazomethane. The retention time of the unidentified component suggests that it is either the oxide IV or the aldehyde VI derived from benzyl methyl ketone. The product corresponding in retention time to  $\alpha$ -phenylpropionaldehyde was collected from the gas chromatogram<sup>38</sup> and identified by comparison of its infrared spectrum<sup>43</sup> with the spectrum of an authentic sample. The gas chromatogram<sup>38</sup> of an authentic sample of  $\alpha$ -methylstyrene oxide<sup>45</sup> exhibited a single peak corresponding in retention time to  $\alpha$ -phenylpropionaldehyde. The infrared spectrum<sup>43</sup> of a sample collected from the peak confirmed the identity of the material.<sup>46</sup>

#### Reaction of Benzyl Methyl Ketone with Diazomethane.

**A. Boron Trifluoride Catalysis.**—The reaction of 0.543 g. (0.00405 mole) of benzyl methyl ketone and 0.568 g. (0.00400 mole) of boron trifluoride etherate in 60 ml. of absolute ether with 0.0080 mole of diazomethane for 2 min. at 0° afforded 0.590 g. of a crude product containing benzyl methyl ketone (63.5%), 1-phenyl-2-butanone (28.7%) and 4-phenyl-2-butanone (7.9%).<sup>38,42</sup> The two ketonic products were collected<sup>38</sup> and identified by comparison of their infrared spectra<sup>43</sup> with the spectra of authentic samples. Similarly, the reaction of 1.00 g. (0.00756 mole) of benzyl methyl ketone and 1.06 g. (0.00746 mole) of boron trifluoride etherate in 77 ml. of absolute ether, cooled to -45°, with 0.0149 mole of diazomethane afforded a crude product (1.51 g.) containing benzyl methyl ketone (87.4%), an unidentified component (3.43%), 1-phenyl-2-butanone (7.12%) and 4-phenyl-2-butanone (2.0%).<sup>38,42</sup> The unidentified component had the same retention time as the additional component present in the methanol-catalyzed reaction of benzyl methyl ketone with diazomethane.

**B. Methanol Catalysis.**—The reaction of 1.31 g. (0.00976 mole) of benzyl methyl ketone in 123 ml. of ether and 30 ml. of absolute methanol with 0.030 mole of diazomethane at room temperature for 3 days afforded 1.44 g. of a crude

product which contained benzyl methyl ketone (34.6%) an unidentified component (30.9%), 1-phenyl-2-butanone (21.2%) and 4-phenyl-2-butanone (13.3%).<sup>38,42</sup>

**Reaction of 2-Pentanone with Diazomethane. A. Boron Trifluoride Catalysis.**—The reaction of 1.09 g. (0.00127 mole) of 2-pentanone and 1.80 g. (0.0127 mole) of boron trifluoride etherate in 105 ml. of absolute ether with 0.019 mole diazomethane at 0° for 5 min. afforded a crude product (1.31 g.) containing 2-pentanone (40.8%), 3-hexanone<sup>47</sup> (23.4%) and 2-hexanone<sup>48</sup> (22.0%). In addition, three small peaks corresponding to 13.8% of higher boiling products were present.<sup>42,49</sup> The two components corresponding to 3-hexanone and 2-hexanone were collected<sup>49</sup> and identified by comparison of their infrared spectra with the spectra of authentic samples. In an additional experiment designed to minimize the production of higher boiling products the reaction of 1.00 g. (0.0116 mole) of 2-pentanone and 1.65 g. (0.0116 mole) of boron trifluoride etherate in 79 ml. of absolute ether with 0.0130 mole of diazomethane afforded a crude product (0.966 g.) containing 2-pentanone (81%) 3-hexanone (9.61%) and 2-hexanone (9.38%).<sup>42,49</sup>

**B. Methanol Catalysis.**—The reaction of 1.09 g. (0.0127 mole) of 2-pentanone in 105 ml. of absolute ether and 30 ml. of absolute methanol with 0.019 mole of diazomethane at room temperature for 2 days afforded 0.830 g. of a crude product containing 2-pentanone (41.0%), an unidentified component presumed to be either the oxide or aldehyde (11.3%), 3-hexanone (23.9%) and 2-hexanone (23.8%).<sup>42,49</sup> Similarly, 1.00 g. (0.0116 mole) of 2-pentanone in 84 ml. of absolute ether and 30 ml. of methanol reacted with 0.0130 mole of diazomethane to yield a crude product (0.911 g.) containing 2-pentanone (75.0%), an unidentified component (8.30%) 3-hexanone (8.29%) and 2-hexanone (8.42%), respectively.<sup>42,49</sup>

#### Reaction of 3-Methyl-2-butanone with Diazomethane.

**A. Boron Trifluoride Catalysis.**—The reaction of 0.950 g. (0.0110 mole) of 3-methyl-2-butanone and 1.56 g. (0.0110 mole) of boron trifluoride etherate in 66 ml. of absolute ether with 0.0100 mole of diazomethane at 0° for 2 min. afforded a crude product (1.78 g.) containing 3-methyl-2-butanone (93.2%), 2,3-dimethylbutyraldehyde (2.12%), 2-methyl-3-pentanone<sup>50</sup> (3.12%) and 4-methyl-2-pentanone<sup>51</sup> (1.53%).<sup>42,51</sup> The combined products were separated from the starting material by collection from a preparative-scale (1 cm.  $\times$  280 cm.) gas chromatographic column packed with di-2-ethylhexyl sebacate suspended on ground firebrick. The three products were then collected,<sup>51</sup> the infrared spectra<sup>43</sup> of the two ketonic products were identical with the spectra of authentic samples. The infrared spectrum<sup>43</sup> of the component believed to be 2,3-dimethylbutyraldehyde<sup>52</sup> showed a weak band at 2690  $\text{cm}^{-1}$  (aldehyde C—H) and a broad band centered at 1712  $\text{cm}^{-1}$  (C=O). The mass spectrum<sup>53</sup> exhibits a parent peak at mass 100 with additional peaks at mass 85 [(CH<sub>3</sub>)<sub>2</sub>CHCHCHO] and mass 71 [(CH<sub>3</sub>)<sub>2</sub>CHCHCH<sub>3</sub>] as

(47) A sample of 3-hexanone was obtained by the reaction of 1.09 g. (0.0127 mole) of 3-pentanone and 1.80 g. (0.0127 mole) of boron trifluoride etherate in 105 ml. of ether with 0.0190 mole of diazomethane. The crude product (1.43 g.) was composed of 61.6% starting material, 30.2% 3-hexanone and 8.3% of higher boiling products. A sample of the pure 3-hexanone, collected from this mixture, has infrared absorption at 1713  $\text{cm}^{-1}$  (unconj. C=O). This ketone has been reported [D. M. Cowan, G. H. Jeffery and A. I. Vogel, *J. Chem. Soc.*, 171 (1940)] to boil at 125°,  $n_{\text{D}}^{20}$  1.4007.

(48) 2-Hexanone was prepared by the oxidation of 2-hexanol with chromium trioxide in aqueous acetic acid. The pure ketone (42% yield) was collected at 125–126°,  $n_{\text{D}}^{20}$  1.3984. A. L. Henne and P. Hill [THIS JOURNAL, 65, 752 (1943)] reported b.p. 124–124.5°,  $n_{\text{D}}^{20}$  1.4002.

(49) The chromatogram was obtained with a column packed with di-2-ethylhexyl sebacate suspended on ground firebrick.

(50) An authentic sample of 2-methyl-3-pentanone was obtained by the reaction of an ethereal solution of ethylmagnesium bromide with isobutyramide. The pure ketone, b.p. 112–115°,  $n_{\text{D}}^{20}$  1.3938, was obtained in 62% yield; C. G. Overberger, W. F. Hale, M. B. Berenbaum and A. B. Finestone [THIS JOURNAL, 76, 6185 (1954)], report b.p. 113.7–111.5°,  $n_{\text{D}}^{20}$  1.3951.

(51) The chromatogram was obtained with a column packed with 1-methyl-4-nitrophenol-nitrile suspended on ground firebrick.

(52) This aldehyde has been described by R. A. Barnes and W. M. Budde, THIS JOURNAL, 63, 2339 (1945).

(53) The mass spectra were determined with a CEI 21-103C mass spectrometer equipped with a heated inlet system.

(44) Authentic samples were obtained by the subsequently described pyrolysis of  $\alpha$ -methylstyrene oxide and as previously described [H. O. House and J. W. Blaker, THIS JOURNAL, 80, 6398 (1958)].

(45) Prepared by the reaction of  $\alpha$ -methylstyrene bromohydrin [see C. O. Cuss and R. Rosenthal, *ibid.*, 77, 2549 (1955)] with aqueous ammonia. The product, obtained in 41% yield, was collected at 30–36° (0.25–0.35 mm.),  $n_{\text{D}}^{20}$  1.5108; J. Hoffman [*ibid.*, 79, 503 (1957)] reported the compound to boil at 84.5–85.5° (17 mm.),  $n_{\text{D}}^{20}$  1.5208.

(46) See A. Klages, *Ber.*, 38, 1971 (1905), for the same transformation under similar conditions.

well as an additional peak at mass 101 attributable either to the fragment  $(\text{CH}_3)_2\text{CCHCO}_2\text{H}$  derived from 2,3-dimethylbutyric acid, the expected oxidation product of the aldehyde, or to the protonated parent aldehyde.

**B. Methanol Catalysis.**—The reaction of 0.500 g. (0.00581 mole) of 2-methyl-2-butanone in 29 ml. of absolute ether and 10 ml. of absolute methanol with 0.0058 mole of diazomethane for 1 day at room temperature afforded 0.210 g. of crude product containing 3-methyl-2-butanone (95.1%), 2-methyl-3-pentanone (3.19%) and 4-methyl-2-pentanone (1.67%).<sup>42,51</sup> The gas chromatogram exhibited no peak corresponding to the previously described component believed to be 2,3-dimethylbutyraldehyde. It is probable that any oxide produced in this reaction was not resolved from the starting ketone in the gas chromatographic analysis.

**Reaction of 3,3-Dimethyl-2-butanone with Diazomethane in the Presence of Boron Trifluoride.**—The reaction of 0.900 g. (0.00900 mole) of 3,3-dimethyl-2-butanone and 1.28 g. (0.00901 mole) of boron trifluoride etherate in 35 ml. of absolute ether with 0.0060 mole of diazomethane at 0° for 2 min. afforded a crude product (1.02 g.) containing 3,3-dimethyl-2-butanone (99.2%), 4,4-dimethyl-2-pentanone<sup>54</sup> (0.109%), 2,2-dimethyl-3-pentanone<sup>55</sup> (0.312%) and a component believed to be 2,3,3-trimethylbutyraldehyde (0.286%).<sup>38,42</sup> Similarly, the reaction of 1.50 g. (0.0150 mole) of 3,3-dimethyl-2-butanone and 1.42 g. (0.0100 mole) of boron trifluoride etherate in 90 ml. of ether with 0.0150 mole of diazomethane afforded a crude product (1.54 g.) containing 3,3-dimethyl-2-butanone (86.0%), 4,4-dimethyl-2-pentanone (2.82%), 2,2-dimethyl-3-pentanone (7.25%), a component believed to be 2,3,3-trimethylbutyraldehyde (2.56%) and two peaks corresponding to higher boiling products (1.46%).<sup>38,42</sup> The infrared spectra<sup>43</sup> of the two ketonic products collected from the reaction mixture were identical with those of authentic samples. The infrared spectrum<sup>43</sup> of the component believed to be 2,3,3-trimethylbutyraldehyde showed a weak band at 2717  $\text{cm}^{-1}$  (aldehyde C—H) and a broad band in the carbonyl region with two peaks of nearly equal intensity at 1723 and 1705  $\text{cm}^{-1}$  (C=O). It is possible that the aldehyde sample is contaminated with its oxidation product, the corresponding acid. The mass spectrum<sup>53</sup> of the material exhibits peaks attributable to the aldehyde at mass 114 (parent peak), 99  $[(\text{CH}_3)_3\text{CCHCHO}]$  and 85  $[(\text{CH}_3)_3\text{CCHCH}_3]$  as well as a peak at mass 115 which is attributable either to the fragment  $(\text{CH}_3)_3\text{CCHCO}_2\text{H}$  derived from 2,3,3-trimethylbutyric acid or to the protonated parent aldehyde.

**Reaction of Benzil with Diazomethane.**—To 2.61 g. (0.0124 mole) of benzil in 40 ml. of absolute ether was added 0.10 mole of diazomethane in 100 ml. of anhydrous ether. After the solution had been allowed to stand for 7 days at room temperature, it was concentrated to a volume of 50 ml. and treated with an additional 0.028 mole of diazomethane in 100 ml. of absolute ether. The resulting solution was allowed to stand for 5 days and then concentrated to leave 3.12 g. of an orange oil. A 1.97-g. portion of the crude product was chromatographed on 100 g. of Merck acid-washed alumina.  $\alpha$ -Phenyl- $\alpha,\beta$ -epoxy-propionophenone [0.634 g. (36%)] eluted as an oil with a 50–50 petroleum ether–benzene mixture, was identified by comparison of its infrared spectrum<sup>48</sup> with the spectrum of an authentic sample.<sup>56</sup> A 244-mg. (0.00109 mole) sample of the oxide was converted by previously described procedures<sup>56</sup> to 1,4,5-triphenylpyrazole, m.p. 210.5–211.5°, yield 149 mg. (46%), which was identified by a mixed melting-point determination with an authentic sample.

**Reaction of 2,3-Butanedione with Diazomethane. A. Methanol Catalysis.**—To 2.58 g. (0.0300 mole) of 2,3-butanedione in 40 ml. of absolute methanol was added 0.060 mole of diazomethane in 275 ml. of reagent ether. After 20 min. the reaction mixture was worked up in the usual way to separate 0.816 g. of crude product which contained 1,2-epoxy-2-methyl-3-butanone (54%), 2,3-butanedione (10%)

and several higher boiling components (36%).<sup>38,42</sup> The gas chromatogram of the crude product exhibited no peak corresponding to 2,3-pentanedione,<sup>39</sup> 2,4-pentanedione<sup>39</sup> or the enol ether, 4-methoxy-3-pentene-2-one.<sup>57</sup> An appropriate control experiment demonstrated that neither of the two pentanediones would have been lost during the work-up procedure although appreciable quantities of the starting material, 2,3-butanedione, were lost during the aqueous extractions. A sample of the epoxy ketone collected from the gas chromatogram was shown to be identical with an authentic sample of 1,2-epoxy-2-methyl-3-butanone<sup>58</sup> by comparison of the infrared spectra<sup>43</sup> of the two samples.

**B. Boron Trifluoride Etherate Catalysis.**—The reaction of 1.00 g. (0.0116 mole) of 2,3-butanedione and 1.42 g. (0.0100 mole) of boron trifluoride etherate in 199 ml. of absolute ether with 0.0464 mole of diazomethane at 0° for 7 min. afforded a crude product (1.40 g.) containing 1,2-epoxy-2-methyl-3-butanone (54%), 2,3-butanedione (25%) and several higher boiling components (21%).<sup>38,42</sup> The epoxy ketone collected from the gas chromatogram, was identified as previously described. As in the previous case, no 2,3-pentanedione, 2,4-pentanedione or 4-methoxy-3-pentene-2-one was detected in the crude product.

**Reaction of 4-Methyl-3-pentene-2-one with Diazomethane. A. Uncatalyzed.**—A solution of 8.7 g. (0.085 mole) of 4-methyl-3-pentene-2-one in 335 ml. of absolute ether containing 0.085 mole of diazomethane was allowed to stand at room temperature and under an atmosphere of nitrogen for 3.5 days at which time the color of diazomethane was no longer apparent in the reaction mixture. The ether was then removed by distillation through a Vigreux column and the residue was fractionally distilled under reduced pressure. The pyrazoline, collected at 107–117° (21 mm.), amounted to 3.29 g. (41%). At all times a nitrogen atmosphere was maintained over the reaction product. A cold solution of a portion of the crude product in petroleum ether deposited the crystalline 3-acetyl-4,4-dimethyl- $\Delta^2$ -pyrazoline (XI), m.p. 43–50° [lit.<sup>22</sup> 51.5–52.5°], which exhibits infrared absorption<sup>43</sup> at 3380  $\text{cm}^{-1}$  (N—H) and 1655  $\text{cm}^{-1}$  (conj. C=O) with an ultraviolet maximum<sup>59</sup> at 309  $\text{m}\mu$  ( $\epsilon$  10,300). The gas chromatogram<sup>38</sup> of the pyrazoline exhibited a single peak. When a sample of the crystalline pyrazoline was exposed to air, the material partially liquefied. The infrared spectrum<sup>43</sup> of the partially oxidized product exhibited a peak of diminished intensity at 3380  $\text{cm}^{-1}$  attributable to N—H stretching and the gas chromatogram<sup>38</sup> of the material exhibited an additional peak. These observations suggest that the  $\Delta^2$ -pyrazoline is rapidly oxidized by air to the corresponding pyrazole.

As a control experiment, a solution of 0.70 g. (0.0072 mole) of the pyrazoline in ether was treated with 1.0 g. (0.0072 mole) of boron trifluoride etherate. The resulting red solution was washed at one with water, dried over magnesium sulfate and examined by gas chromatography.<sup>38</sup> The chromatogram indicated the presence of ether and the starting pyrazoline but not the ketonic products obtained from the subsequently described boron trifluoride-catalyzed reaction of 4-methyl-3-pentene-2-one with diazomethane.

**B. Boron Trifluoride Catalysis.**—To a solution of 4.9 g. (0.042 mole) of 4-methyl-3-pentene-2-one and 5.9 g. (0.042 mole) of boron trifluoride etherate in 10 ml. of ether was added, over a 4-min. period at 0°, an ethereal solution containing 0.094 mole of diazomethane. The resulting solution was washed with 25 ml. of water and divided into several portions. One portion of the solution was washed with aqueous sodium bicarbonate, dried over magnesium sulfate and concentrated under a Vigreux column. The residual crude product contained 4-methyl-3-pentene-2-one (83.9%), component A (4.7%) and component B (11.4%), the ratio of

(57) The enol ether was obtained as a mixture with starting diketone (20% enol ether and 80% 2,4-pentanedione) by treating 1.00 g. (0.0100 mole) of 2,4-pentanedione in 10 ml. of ether and 15 ml. of methanol with 40 ml. of an ethereal solution containing 0.010 mole of diazomethane. The solution decolorized after 1 hr. and was worked up in the usual manner. The enol-ether has been reported [B. Eistert and W. Reiss, *Ber.*, **87**, 108 (1954)] in its two forms, the *cis* isomer boiling at 65–68° (16 mm.) and the *trans* isomer at 93–95° (16 mm.).

(58) An authentic sample of 1,2-epoxy-2-methyl-3-butanone, b.p. 131–134°,  $n_D^{20}$  1.4126–1.4136, was obtained by the procedure of R. S. Wilder and A. A. Dolnick [U. S. Patent 2,431,718, Dec. 2, 1947, C. A., **42**, 3431 (1948)] who reported b.p. 130–138°,  $n_D^{20}$  1.4192.

(59) Determined in 95% ethanol solution.

(54) An authentic sample of 4,4-dimethyl-2-pentanone, b.p. 125–126.5°,  $n_D^{20}$  1.3989, was prepared by the procedure of W. A. Mosher and J. C. Cox, Jr. [THIS JOURNAL, **72**, 3701 (1950)] who reported b.p. 124–125°,  $n_D^{20}$  1.4018.

(55) An authentic sample of 2,2-dimethyl-3-pentanone, b.p. 124.5–125.8°,  $n_D^{20}$  1.4000, was prepared by the procedure of F. C. Whitmore, C. I. Noll and V. C. Meunier, *ibid.*, **61**, 683 (1939)] who reported b.p. 124.5° (729 mm.),  $n_D^{20}$  1.4044–1.4052.

(56) H. O. House, D. J. Reif and R. L. Wasson, *ibid.*, **79**, 2490 (1957).

component B to component A being 2.40 to 1.<sup>45,52</sup> When another portion of the ether solution was dried and concentrated without having been washed with aqueous sodium bicarbonate, the ratio of component B to component A was 0.75 to 1.<sup>52</sup> Both components A and B were isolated by collection from the gas chromatogram<sup>52</sup> of the reaction mixture. Component A, subsequently identified as previously described 2-methyl-2-hexen-4-one (XIII),<sup>60</sup> exhibits infrared absorption<sup>43</sup> at 1695 (conj. C=O) and 1630 cm.<sup>-1</sup> (conj. C=C) as well as an ultraviolet maximum<sup>59</sup> at 235 m $\mu$  ( $\epsilon$  10,400). The mass spectrum<sup>53</sup> exhibits a parent peak at mass 112 with additional peaks at mass 83 [(CH<sub>3</sub>)<sub>2</sub>C=CHCO] and mass 55 [(CH<sub>3</sub>)<sub>2</sub>C=CH]. A 35-mg. (0.31 millimole) sample of component A in 5 ml. of ethanol was hydrogenated over 15 mg. of a 10% palladium-on-carbon catalyst at room temperature and atmospheric pressure, 9.8 ml. (1.2 equivalents) of hydrogen being absorbed. The hydrogenation product, collected from the gas chromatogram<sup>38</sup> of the reaction mixture, was identified as 2-methyl-4-hexanone both by its retention time and by comparison of the infrared spectrum<sup>43</sup> of the product with the spectrum of an authentic sample.<sup>61</sup> Component B, subsequently identified as the known 2-methyl-2-hexene-5-one (XII),<sup>24</sup> exhibits infrared absorption at 1720 cm.<sup>-1</sup> (unconj. C=O) with only end absorption in the ultraviolet<sup>59</sup> ( $\epsilon$  2200 at 210 m $\mu$ ). The mass spectrum<sup>53</sup> exhibits a parent peak at mass 112 with additional peaks at mass 97 [(CH<sub>3</sub>)<sub>2</sub>CH=CHCH<sub>2</sub>CO] and mass 69 [(CH<sub>3</sub>)<sub>2</sub>=CHCH<sub>2</sub>]. The infrared spectrum of the material is identical with the published<sup>24</sup> infrared spectrum of 2-methyl-2-hexen-5-one.

**2-Cyano-1-phenyl-2-propanol (XIX b).**—To a cold solution of 50.0 g. (0.481 mole) of sodium bisulfite in 125 ml. of a water-ethanol mixture was added slowly with vigorous shaking, 37.7 g. (0.281 mole) of benzyl methyl ketone. To the resultant slurry at 0° was added, dropwise and with stirring over a period of 30 min., 25.0 g. (0.384 mole) of potassium cyanide in 80 ml. of cold water. The mixture was stirred for an additional 1 hr., during which time it warmed to room temperature. The oily layer which had formed was separated and the aqueous phase extracted with three 50-ml. portions of ether. The combined organic layers were dried and concentrated. The crude product was then distilled through a modified Claisen still affording 16.4 g. (27%) of the pure cyanohydrin as a pale yellow oil, b.p. 111–112° (0.50 mm.),  $n_D^{20}$  1.5186, as well as a forerun which amounted to 8.68 g., b.p. 105.5–111° (0.45 mm.),  $n_D^{20}$  1.5184. A small sample of the cyanohydrin with boiling point 111–112° (0.50 mm.) was distilled through a short-path still (bath temperature 150°) at 0.5 mm. No change was observed in the refractive index. The infrared spectrum<sup>43</sup> of the cyanohydrin shows a strong band at 3475 cm.<sup>-1</sup> (—OH) and a very weak band at 2236 cm.<sup>-1</sup> (—C=N); the ultraviolet spectrum<sup>59</sup> shows the pattern of an alkyl-substituted benzene ring with a maximum at 258 m $\mu$  ( $\epsilon$  236).

*Anal.* Calcd. for C<sub>10</sub>H<sub>11</sub>ON: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.46; H, 6.99; N, 8.44.

(60) J. Cologne and M. Reymernier, *Bull. soc. chim. France*, 188 (1956).

(61) An authentic sample of 2-methyl-4-hexanone was commercially available from K and K Laboratories.

**Reduction and Nitrous-Acid Deamination of 2-Cyano-1-phenyl-2-propanol (XIX b).**—The cyanohydrin (8.00 g., 0.0497 mole) in 120 ml. of glacial acetic acid was hydrogenated over 0.400 g. of platinum oxide at room temperature and approximately 20 p.s.i. of hydrogen pressure. The required hydrogen uptake was complete (0.0994 mole) after 3 hr. The solution was separated from the catalyst, diluted with 100 ml. of water and then cooled to 0° and treated with a solution of 16.0 (0.232 mole) of sodium nitrite in 50 ml. of cold water. The resulting solution was stirred for 3 hr. at 0° and then allowed to stand at 0° for an additional 24 hr. The reaction mixture was treated with saturated, aqueous solution of sulfamic acid to destroy any excess nitrous acid and then diluted with 400 ml. of water and extracted with four 100-ml. portions of pentane. The combined pentane extracts were washed with 100-ml. portions of water and dried over anhydrous sodium carbonate and magnesium sulfate. The dried pentane solution was concentrated under reduced pressure to leave a yellow liquid which was distilled through a short-path still (bath temperature 150°) at 20 mm. affording 1.34 g. of a light-yellow liquid. The yield of the two phenylbutanones based upon the cyanohydrin was 15.5%. The gas chromatogram<sup>38</sup> of the liquid showed four peaks whose retention times corresponded to benzyl methyl ketone (9.60%), an unidentified component (5.50%), 1-phenyl-2-butanone (53.5%) and 4-phenyl-2-butanone (31.5%). The infrared spectra<sup>43</sup> of the two phenylbutanones collected<sup>38</sup> from the products were identical with the spectra of authentic samples. In a duplicate experiment, employing 7.22 g. (0.0448 mole) of the cyanohydrin, the crude product (1.29 g. or 17.4%) contained benzyl methyl ketone (5.33%), an unidentified component (5.33%), 1-phenyl-2-butanone (56.5%) and 4-phenyl-2-butanone (32.8%).<sup>38</sup>

**Reduction and Nitrous Acid Deamination of 2-Cyano-2-pentanol (XIX a).**—The cyanohydrin<sup>62</sup> (8.00 g., 0.0708 mole) in 120 ml. of glacial acetic acid was hydrogenated over 0.400 g. of platinum oxide as previously described. The required hydrogen uptake (0.142 mole) was complete after 1.5 hr. The solution was separated from the catalyst, diluted with 120 ml. of water, cooled to 0° and treated with a solution of 19.7 g. (0.286 mole) of sodium nitrite in 50 ml. of water. The solution was stirred at 0° for 24 hr. and then worked up as previously described. The resulting ketonic product mixture (1.49 g. or 20.4% based on the cyanohydrin) contained 2-pentanone (3.38%), 3-hexanone (38.2%) and 2-hexanone (58.5%).<sup>49</sup> The infrared spectra<sup>43</sup> of the two hexanones collected<sup>49</sup> from the ketonic product mixture were identical with the spectra of authentic samples of 3- and 2-hexanone. In a duplicate set of experiments, employing 6.20 g. (0.0548 mole) samples of the cyanohydrin, the crude products amounted to 0.768 g. (12.8%) and 1.02 g. (16.5%). The gas chromatogram<sup>49</sup> of the first product mixture indicated the presence of 2-pentanone (8.86%), 3-hexanone (35.2%) and 2-hexanone (56.0%). The gas chromatogram<sup>49</sup> of the second product mixture indicated the presence of 2-pentanone (11.2%), 3-hexanone (34.7%), and 2-hexanone (54.1%).

#### CAMBRIDGE 39, MASS.

(62) This cyanohydrin, b.p. 91–92° (9 mm.),  $n_D^{20}$  1.4170, was prepared as previously described. The compound is reported [M. A. J. Ultee, *Rec. trav. chim.*, **28**, 7 (1909)] to boil at 100° (21 mm.),  $n_D^{20}$  1.4285.