

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE 39 MASS.]

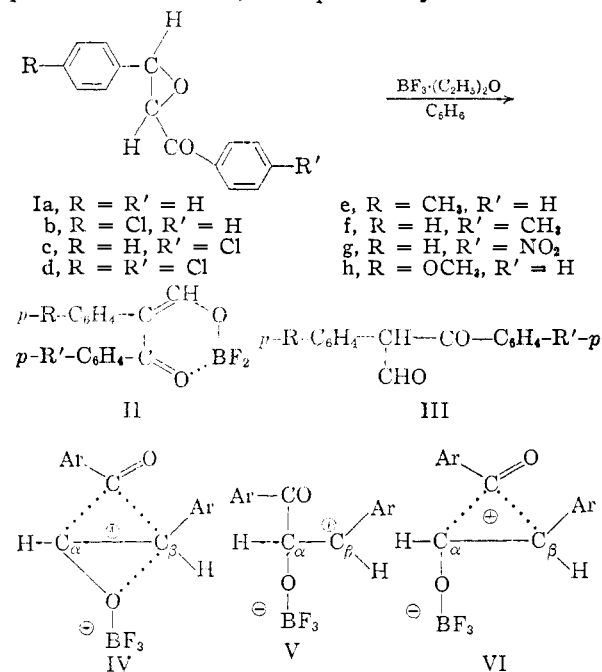
The Rearrangement of  $\alpha,\beta$ -Epoxy Ketones. VIII. Effect of Substituents on the Rate of RearrangementBY HERBERT O. HOUSE AND GEORGE D. RYERSON<sup>1</sup>

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The relative rates of rearrangement of *trans*-benzalacetophenone oxide and the 4-chloro-, 4'-chloro-, 4,4'-dichloro-, 4-methyl-, 4'-methyl-, 4-methoxy- and 4'-nitro-*trans*-benzalacetophenone oxides to the corresponding  $\alpha$ -formyldeoxybenzoin derivatives have been determined. The rate of isomerization was accelerated by electron-donating substituents on either benzene ring and retarded by electron-withdrawing substituents on either benzene ring.

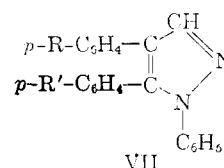
The conversion of *trans*-benzalacetophenone oxide (Ia), in the presence of boron trifluoride, to the borofluoride complex IIa of  $\alpha$ -formyldeoxybenzoin (IIIa) has been demonstrated<sup>2</sup> to involve the intramolecular migration of a benzoyl group as depicted in structure IV. Efforts to learn whether cleavage of the oxide ring and migration of the benzoyl group were concerted processes (as in structure IV) by the use of stereochemical criteria<sup>3</sup> were ambiguous since stereochemical control of the rearranged products was noted in some cases but not in others.<sup>4</sup> In order to learn whether the distribution of positive charge in the transition state for the rearrangement is better represented by structure V or by structure VI the relative rates of rearrangement of the oxides I to the borofluoride complexes II have been measured.

Each of the oxides I (Table II) was prepared by the alkaline epoxidation of the corresponding unsaturated ketone (Table I). Since two of these products, Ia and Id, have previously been shown<sup>2,5</sup>



- (1) National Science Foundation Predoctoral Fellow, 1957-1958.  
(2) H. O. House, *J. Am. Chem. Soc.*, **78**, 2298 (1956).  
(3) H. O. House and D. J. Reif, *ibid.*, **77**, 6525 (1955); **79**, 6491 (1957).  
(4) For a general discussion, see R. E. Parker and N. S. Isaacs, *Chem. Revs.* **59**, 737 (1959).  
(5) H. H. Wasserman and N. E. Aubrey, *J. Am. Chem. Soc.*, **77**, 590 (1955).

to possess the expected<sup>6,7</sup> *trans* stereochemistry, the remaining products may safely be assigned the same configuration. Isomerization of each of the oxides in the presence of a benzene solution of boron trifluoride etherate afforded the borofluoride complexes II (Table III) which were further characterized as the pyrazoles VII (Table IV). The



relative rates of rearrangement (Table V) of the oxides I were determined by reaction of dilute (approximately 10<sup>-4</sup> molar) benzene solutions of the oxides with excess (approximately 0.05 molar) boron trifluoride etherate. In every case the reaction rates exhibited a first-order dependence on the oxide concentration.

TABLE I  
PROPERTIES OF THE *trans*-BENZALACETOPHENONES  
 $p\text{-R-C}_6\text{H}_4\text{-CH=CHCO-C}_6\text{H}_4\text{-R}'\text{-}p$

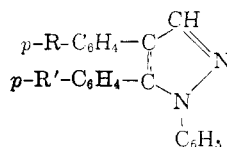
R	R'	M.p., °C.	Lit. m.p., °C.	$\lambda_{\text{max}}$ , m $\mu$ ( $\epsilon$ ) in EtOH	$\nu_{\text{C=O}}$ , cm. <sup>-1</sup> (medium)
H	H			227 (10,200) 311 (24,000)	1687 (CCl <sub>4</sub> )
Cl	H	112.6-113.4	114 <sup>a</sup>	230 (11,600) 314 (25,500)	1670 (CCl <sub>4</sub> )
H	Cl	96.2-97.6	96 <sup>b</sup>	225 (11,600) 315 (25,800)	1665 (CCl <sub>4</sub> )
Cl	Cl	155-157 <sup>c</sup>		228 (13,200) 318 (29,000)	1660 (CHCl <sub>3</sub> )
CH <sub>3</sub>	H	95.8-96.4	96.5 <sup>d</sup>	233 (11,400) 322 (25,200)	1665 (CCl <sub>4</sub> )
H	CH <sub>3</sub>	74.3-75.1	77 <sup>e</sup>	226 (12,100) 312 (27,300)	1665 (CCl <sub>4</sub> )
H	NO <sub>2</sub>	146.1-148.3	149-150 <sup>f</sup>	269 (17,900) 321 (18,300)	1660 (KBr)
OCH <sub>3</sub>	H	73.8-74.9	76-78 <sup>g</sup>	244 (12,700) 343 (22,200)	1655 (KBr)

- <sup>a</sup> W. Davey and J. R. Gwilt, *J. Chem. Soc.*, 1008 (1957).  
<sup>b</sup> C. F. H. Allen and G. F. Frame, *Can. J. Chem.*, **6**, 605 (1932).  
<sup>c</sup> Data from ref. 2. <sup>d</sup> V. Hanzlik and A. Bianchi, *Ber.*, **32**, 2282 (1899). <sup>e</sup> S. V. Kostanecki and G. Rossbach, *ibid.*, **29**, 2245 (1896). <sup>f</sup> W. Dilthey, L. Neuhaus and W. Schommer, *J. prakt. Chem.*, [2] **123**, 235 (1929). <sup>g</sup> W. B. Black and R. E. Lutz, *J. Am. Chem. Soc.*, **77**, 5134 (1955).

It is clear from these data that electron-donating substituents R or R' enhance the rate of isomerization while electron-withdrawing substituents R or R' have the reverse effect. Furthermore, the

- (6) H. O. House and R. S. Ro, *ibid.*, **80**, 2428 (1958).  
(7) H. E. Zimmerman, L. Singer and B. S. Thyagarajan, *ibid.*, **81**, 108 (1959).



TABLE IV  
 PROPERTIES OF THE PYRAZOLES VII


R	R'	M.p., °C.	Yield, %	Molecular formula	C	Calcd., %		Cl	C	Found, %		Cl	$\lambda_{\max}$ , $m\mu$ ( $\epsilon$ in EtOH)
						H	N			H	N		
H	H	207.8-208.7 <sup>a</sup>	78										233 (21,300) 266 (15,900)
Cl	H	194.9-195.3	56	C <sub>21</sub> H <sub>15</sub> ClN <sub>2</sub>	76.24	4.57	8.47	10.72	75.96	4.79	8.28	10.64	241 (21,500) 268 (19,100)
H	Cl	201.2-201.8	91	C <sub>21</sub> H <sub>15</sub> ClN <sub>2</sub>	76.24	4.57	8.47	10.72	76.16	4.56	8.45	10.53	233 (26,000) 265 (16,000)
Cl	Cl	181.5-183 <sup>b</sup>											243 (23,900) 268 (18,700)
CH <sub>3</sub>	H	162.2-169.9	91	C <sub>22</sub> H <sub>15</sub> N <sub>2</sub>	85.13	5.85	9.03	...	84.92	5.78	9.02	...	237 (23,100) 269 (16,100)
H	CH <sub>3</sub>	217.6-218.3	92	C <sub>22</sub> H <sub>15</sub> N <sub>2</sub>	85.13	5.85	9.03	...	85.11	5.74	9.00	...	235 (22,600) 266 (17,300)
H	NO <sub>2</sub>	221.6-222.4	50	C <sub>21</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub>	73.89	4.43	12.31	...	73.92	4.32	12.42	...	229 (22,600) 246 (23,000)
OCH <sub>3</sub>	H	148.5-149.4 <sup>c</sup>	62										239 (23,200) 274 (14,800)

<sup>a</sup> Lit. m.p. 210-211°; W. Wislicenus and A. Ruthing, *Ann.*, **379**, 299 (1911). <sup>b</sup> Data from ref. 2. <sup>c</sup> Lit. m.p. 150-151°; J. Algar and J. McKenna, *Proc Royal Irish Acad.*, **49**, 225 (1944); *C. A.*, **38**, 5502 (1944).

 TABLE V  
 RELATIVE RATES OF REARRANGEMENT OF THE BENZAL-  
 ACETOPHENONE OXIDES

Oxide I	Relative rate (no. of measurements)
Ia, R = R' = H	1.00
Ib, R = Cl, R' = H	0.72 ± 0.02 (3)
Ie, R = CH <sub>3</sub> , R' = H	1.63 ± .29 (6)
Ih, R = OCH <sub>3</sub> , R' = H	1.88 ± .14 (5)
Ig, R = H, R' = NO <sub>2</sub>	0.71 ± .05 (4)
Ic, R = H, R' = Cl	0.76 ± .08 (4)
If, R = H, R' = CH <sub>3</sub>	1.94 ± .23 (7)
Id, R = R' = Cl	0.55 ± .02 (3)

tion at the carbon atom where displacement occurs. However, the observation<sup>10</sup> that the fluorohydrin IXa has the same configuration as its precursor, the oxide Ia, removes this objection. The opening of the oxide ring with retention of configuration could be explained by the scheme represented in structure X.

The pseudo-first-order rate of rearrangement of the fluorohydrin IXa to the borofluoride complex IIa (see Table VI) was found to increase steadily during the reaction. In the final portion of the reaction the rate became approximately equal to that observed with the oxide Ia. These results would be compatible with either the conversion of fluorohydrin IXa to the oxide Ia or the conversion of the fluorohydrin IXa to the ester IXb at a rate slightly less than the rate of rearrangement of Ia of IXb to IIa. Consequently, there is no evidence at hand which will distinguish between rearrangement of the fluorohydrin ester IXb *via* transition state VIIIa and rearrangement of the oxide Ia *via* transition state IV or VIIIb. In the absence of evidence to the contrary, a transition

(10) H. O. House, *J. Org. Chem.*, **21**, 1306 (1956).

state of the type VIII seems more probable than IV.

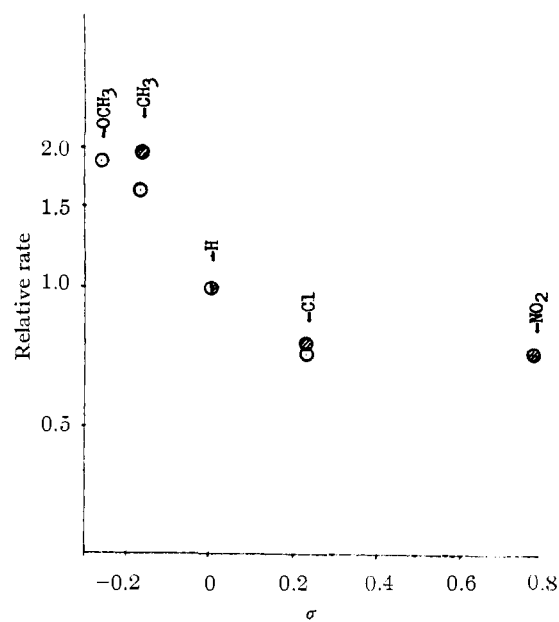
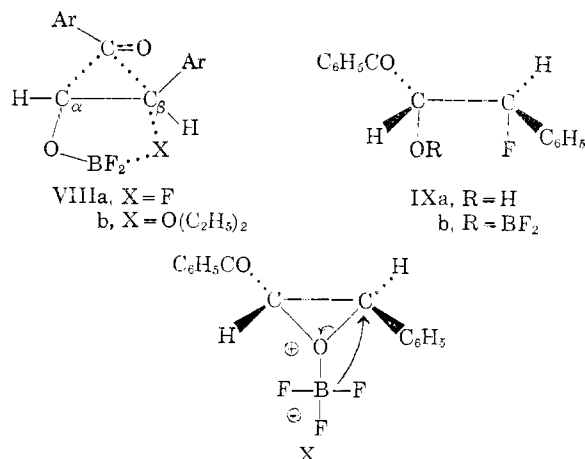


Fig. 1.—Substituent effects on the rate of rearrangement of *trans*-benzalacetophenone oxides: O substituents R (structure I); ● substituents R' (structure I).

In an effort to determine the dependence of the reaction on the boron trifluoride etherate concentration, kinetic runs at several boron trifluoride concentrations were made (Table VII). The approximately first-order dependence of the calculated pseudo-first-order rate constant on the stoichiometric boron trifluoride etherate concentration observed with the lower concentrations increased with increasing concentration of the Lewis acid.



These observations may well be the result of an increased association of the polar, boron trifluoride-containing species (particularly boron trifluoride etherate) at higher concentrations in the non-polar solvent, benzene. In any event, the data suggest that no more than one molecule of boron trifluoride

TABLE VI  
COMPARISON OF THE RATE OF REARRANGEMENT OF  $8.06 \times 10^{-5} M$  *trans*-BENZALACETOPHENONE OXIDE (Ia) WITH THAT OF  $9.42 \times 10^{-5} M$  1,3-DIPHENYL-3-FLUORO-2-HYDROXY-PROPANONE (IXa) IN THE PRESENCE OF 0.0548 *M* BORON TRIFLUORIDE ETHERATE

Reacn., %	$k \times 10^4$ , sec. <sup>-1</sup>	
	Ia	IXa
10	2.12	1.74
20	2.12	1.88
30	2.14	1.93
40	2.15	1.96
50	2.16	2.03
60	2.17	2.06
70	2.19	2.11
80	2.20	2.14
90	2.18	2.22

(or its etherate) need be involved in the transition state leading to rearrangement and are in agreement with the rapid prior equilibrium illustrated in the accompanying equation. The relatively low basicity of ethylene oxide compared with other ethers<sup>11</sup> is consistent with the reversible formation of the complex XI prior to rearrangement.

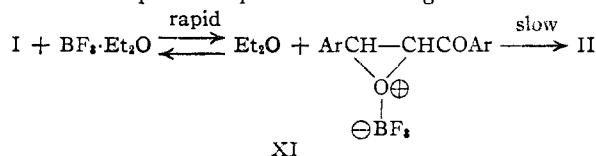


TABLE VII  
DEPENDENCE OF THE RATE OF ISOMERIZATION OF  $8.06 \times 10^{-5} M$  *trans*-BENZALACETOPHENONE OXIDE ON BORON TRIFLUORIDE ETHERATE CONCENTRATION

Stoichiometric BF <sub>3</sub> ·(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> O concn., <i>M</i>	Pseudo-first order rate constant, sec. <sup>-1</sup>
0.0216	$8.55 \times 10^{-4}$
.0432	$2.50 \times 10^{-3}$
.0864	$3.28 \times 10^{-3}$
.1728	$5.05 \times 10^{-3}$

(11) S. Searles, M. Tamres and E. R. Lippincott, *J. Am. Chem. Soc.*, **75**, 2775 (1953).

## Experimental<sup>12</sup>

The *trans*-Benzalacetophenone Oxides (I).—Each of the oxides (Table II) was prepared by the alkaline epoxidation<sup>13</sup> of the corresponding unsaturated ketone (Table I), the reaction solvent being either aqueous methanol or aqueous acetone. The infrared spectra of all the oxides which were measured in carbon tetrachloride solution exhibited a double carbonyl band, the two peaks being at approximately 1695 and 1677 cm.<sup>-1</sup>. In each case the absorption band found at the higher frequency was the more intense, as would be expected<sup>14</sup> for derivatives of *trans*-benzalacetophenone oxide.

The Borofluoride Complexes (II).—Solutions of the oxides I in reagent benzene (20–100 ml./g. of oxide) were treated with three molar equivalents of redistilled boron trifluoride etherate. After the solutions had been allowed to stand for from 2 to 30 min., they were washed with water, dried over magnesium sulfate, and concentrated under reduced pressure. The residual crude complexes were purified by repeated crystallization from hexane or mixtures of benzene with either hexane or cyclohexane. The yields reported (Table III) represent the quantities of pure borofluoride complexes isolated in the preparative experiments and not the maximum yields obtainable. The ultraviolet spectra were measured in benzene solutions containing concentrations of boron trifluoride etherate ranging from 0.02 to 0.09 *M*. Neither the position nor the intensity of the ultraviolet absorption was found to vary with the boron trifluoride concentration in the range studied. In all cases the molecular extinction coefficients reported are the average values obtained from several measurements at different boron trifluoride etherate concentrations. It was necessary to measure these spectra in the presence of excess boron trifluoride to avoid extensive hydrolysis of the borofluoride complexes. Thus, the spectrum of a solution of the borofluoride complex IIa in reagent diethyl ether exhibited maxima at 222 mμ ( $\epsilon$  10,570) and 329 mμ ( $\epsilon$  7,740) and resembled closely the spectrum of an ether solution of  $\alpha$ -formyldeoxybenzoin (IIIa),  $\lambda_{\text{max}}$  231 mμ ( $\epsilon$  13,800) and 323 mμ ( $\epsilon$  8,740).

The Pyrazoles (VII).—The pyrazoles were obtained by the reaction of the corresponding borofluoride complexes II with two molar equivalents of phenylhydrazine in boiling ethanol for 10 to 15 min. The cold, ethanolic solutions deposited the crude pyrazoles which were collected on a filter and recrystallized from either ethanol or aqueous ethanol. The properties of the pyrazoles are summarized on Table IV.

Purification of Materials for Kinetic Measurements.—Commercial boron trifluoride etherate was distilled twice and stored under nitrogen. Samples to be used for kinetic runs were distilled just prior to their use. Reagent grade benzene was distilled from freshly cut sodium just prior to its use. Each oxide was recrystallized to a constant melting point and then dried under reduced pressure and stored in a desiccator.

Procedure for Kinetic Measurements.—All apparatus employed was dried overnight at >110° and then stored in a desiccator. Weighed quantities (approximately 0.02 g. or 10<sup>-4</sup> mole) of the oxides were dissolved in benzene and the solutions were diluted to 100 ml. and brought to 30.20 ± 0.02° in a constant temperature bath. A weighed sample (approximately 1 g. or 10<sup>-2</sup> mole) of boron trifluoride etherate was diluted to 100 ml. with benzene. To a 50-ml. volumetric flask were added a 20-ml. aliquot of the boron trifluoride solution and approximately 23 ml. of benzene. When the flask and its contents had reached thermal equilibrium in the constant temperature bath, a 5-ml. aliquot of the oxide solution was added and the resulting solution was diluted to 50 ml. and mixed. A portion of the solution was transferred to a glass-stoppered silica cell which was thermostated to 30.20 ± 0.02° in a Beckman spectrometer,

(12) All melting points are corrected and all boiling points are uncorrected. The infrared spectra were determined with either a Baird, model B, or a Perkin-Elmer, model 21, infrared recording spectrophotometer fitted with a sodium chloride prism. The ultraviolet spectra were determined with either a Cary recording spectrophotometer, model 11MS or a Beckman, model DU, spectrometer. The microanalyses were performed by Dr. S. M. Nagy and his associates and by the Scandinavian Microanalytical Laboratory.

(13) R. L. Wasson and H. O. House, *Org. Syntheses*, **37**, 58 (1957).

(14) H. O. House and J. W. Blaker, *J. Am. Chem. Soc.*, **80**, 6389 (1958).

model DU. Reagent benzene was used as a reference for the spectroscopic measurements. Before each set of kinetic runs the optical density of a standard solution of formaldehyde 2,4-dinitrophenylhydrazone [ $\lambda_{\max}$  345 m $\mu$  ( $\epsilon$  18,500)] in benzene was measured in order to check the reproducibility of the spectrometer. The maximum variation of these optical density measurements from their mean was less than 1%. The reactions were followed by measuring the optical densities of the reaction mixtures at the wave length of maximum absorption of the borofluoride complexes (approximately 360 m $\mu$ ; see Table III). For the 4-methoxy-*trans*-benzalacetophenone oxide runs, the maximum at 383 m $\mu$  was employed. The oxides, benzene and boron trifluoride etherate all have negligible absorption in this region. For the purpose of calculation the first optical density reading taken was considered to be 0% reaction and the final, maximum optical density reading was taken as 100% reaction. In several of the cases the final optical density reading was demonstrated to remain constant for at least an hour. In all cases the pseudo-first order rate constants were determined graphically from plots of time vs. log [(final - init. optical density)/(final - obsd. optical density)]. For the rearrangement of *trans*-benzalacetophenone oxide, Table VII summarizes the effect of change in boron trifluoride etherate concentration at a constant oxide concentration and Table VIII demonstrates that changes in the oxide concentration at constant boron trifluoride etherate concentration do not alter the rate constant. The deliberate addition of a small amount of water (to make the solution 0.0037 *M* in water) prior to a kinetic run had a small effect on the rate ( $k = 1.77 \times 10^{-3}$  with added water,  $k = 1.27 \times 10^{-3}$  without added water). Addition of greater amounts of water caused the reaction mixture to become turbid precluding optical measurements. For each set of kinetic runs a sample of *trans*-benzalacetophenone oxide was run as a standard in an effort to minimize possible errors in the relative rates which would result from differing concentrations of boron trifluoride etherate and differing amounts of water which might be present. Table V lists the average relative rates obtained with the average deviation from the mean. Each of the entries in the table represents the average of at least three kinetic runs.<sup>15</sup>

In two cases (I<sub>g</sub> and I<sub>h</sub>) the rearrangements were run under the conditions of the kinetic measurements but on a

(15) The kinetic data may be found in the Ph.D. dissertation of George D. Ryerson, Massachusetts Institute of Technology, September, 1960.

sufficient scale to permit the isolation of the products. A solution of 25.3 mg. ( $9.40 \times 10^{-5}$  mole) of the oxide I<sub>g</sub> and 6 ml. (0.048 mole) of boron trifluoride etherate in 1000 ml. of benzene was allowed to stand at 30° for 2.5 hr., after which period the optical density indicated 70% reaction. The solution was washed with aqueous sodium acetate and then with water and concentrated under reduced pressure to

TABLE VIII

EFFECT OF VARIOUS CONCENTRATIONS OF *trans*-BENZALACETOPHENONE OXIDE ON THE RATE OF REARRANGEMENT IN THE PRESENCE OF A 0.0424 *M* SOLUTION OF BORON TRIFLUORIDE ETHERATE

Initial oxide concn., <i>M</i>	Pseudo-first order rate constant, sec. <sup>-1</sup> × 10 <sup>3</sup>
$8.74 \times 10^{-5}$	1.33
$4.37 \times 10^{-5}$	1.27
$2.62 \times 10^{-5}$	1.35

approximately 30 ml. The resulting solution was diluted with ether, washed with water, and then concentrated to dryness under reduced pressure. A solution of the residue in 5 ml. of ethanol was treated with 18.3 mg. ( $1.69 \times 10^{-4}$  mole) of phenylhydrazine and one drop of acetic acid. The resulting solution was refluxed for 30 min., diluted with water and cooled. The crude pyrazole VII<sub>g</sub> which separated (16.8 mg. or 53%, m.p. 220.6–223.8°) was chromatographed on 2 g. of Merck acid washed alumina and then recrystallized from aqueous ethanol. The pure pyrazole VII<sub>g</sub>, m.p. 222.5–224.2°, yield 12.0 mg. (38%), was identified by a mixed melting point determination and by comparison of the infrared spectrum with the spectrum of an authentic sample.

In a similar experiment in which a solution of 32.8 mg. ( $1.29 \times 10^{-4}$  mole) of the oxide I<sub>h</sub> and 6 ml. (0.048 mole) of boron trifluoride etherate in 1000 ml. of benzene was allowed to react for 3 hr., the optical density of the solution indicated 69% reaction. Use of the previously described isolation procedure, employing 19.7 mg. ( $1.82 \times 10^{-4}$  mole) of phenylhydrazine, afforded 12.6 mg. (30%) of the crude pyrazole VII<sub>h</sub>, m.p. 139.4–143.5°, which was identified by comparison of its infrared spectrum with the spectrum of an authentic sample.

[CONTRIBUTION FROM THE IPATIEFF HIGH PRESSURE AND CATALYTIC LABORATORY, DEPARTMENT OF CHEMISTRY, NORTHWESTERN UNIVERSITY, EVANSTON, ILL.]

## High Pressure Thermal Alkylation of Xylenes and Related Compounds by Propylene<sup>1, 2</sup>

BY C. N. PILLAI AND HERMAN PINES

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The high pressure thermal alkylation reactions of toluene, the three xylenes and *p*-methylanisole by propylene were studied in a flow system at 430° and 410 atmospheres pressure. The alkylation products were *n*-butyl- and isobutylbenzene derivatives. Comparison of the selectivity of these reactions with the previously reported results with other alkylbenzenes lead to the conclusion that steric factors are of greater importance than resonance factors in determining the selectivity of addition. Ring methylation and formation of phenolic materials were also observed during the reaction of *p*-methylanisole.

In the earlier papers of this series, the high pressure thermal alkylation of monoalkylbenzenes by simple olefins has been reported.<sup>3, 4</sup> It was found that the addition of a benzyl-type radical to an unsymmetrical olefin at high pressure and temperature had a certain amount of selectivity. The mode of addition resulting in the more stable

intermediate free radical (I < II < III) predominated. It was also found that the magnitude of this selectivity was dependent on the structure of the benzyl-type radical as well as on the structure of the olefin.

Benzyl radicals derived from toluene, ethylbenzene and cumene showed progressively increasing selectivity in their addition to unsymmetrical olefins like propylene<sup>3</sup> and 1-butene.<sup>4</sup> This progressive change in selectivity was considered to be due to one or both of two factors, namely the progressive increase in steric hindrance around the benzylic carbon atom in the series toluene, ethyl-

(1) Part IV of the series, "Thermal Alkylation Reactions." For Part III, see H. Pines and C. N. Pillai, *J. Am. Chem. Soc.*, **82**, 2921 (1960).

(2) This research was supported in part by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is hereby made to the donors of this fund.

(3) H. Pines and J. T. Arrigo, *J. Am. Chem. Soc.*, **79**, 4958 (1957).

(4) H. Pines and C. N. Pillai, *ibid.*, **81**, 3629 (1959).