

TABLE II  
NUCLEAR MAGNETIC RESONANCE ASSIGNMENTS

Proton grouping	Position, $\tau$	$(\text{CH}_3\text{CH}_2)_2\text{CHCOCH}_2\text{CH}_3$	
		b' c	a' a b
a	Near 7.6	Quartet	3.0
a'	Near 7.8		
b	9.02	Triplet	9.0
b'	9.18		
c	Near 8.5	Broad multiplet	4.1

**Reduction of Sebacoïn (P).**—A 12-g. sample of crude sebacoïn<sup>24</sup> was dissolved in 100 ml. of glacial acetic acid and refluxed 2 hr. with 45 g. of 47% hydriodic acid (2.3 molar equivalents). Following the usual work-up, distillation of the crude product (10.9 g.) gave three fractions ranging in color from very light yellow to light orange. The first fraction (0.9 g.) was shown to be 50% cyclodecanone by v.p.c. analysis using a 15% phenyldiethanolamine succinate column (8 ft.  $\times$  0.25 in.) at 165°. The second fraction (6.7 g.), b.p. 103–109° (17 mm.), was 90% cyclodecanone contaminated with sebacil and two other substances present in only minor quantities. The third fraction (1.2 g.), b.p. 109–115° (17 mm.), was mainly cyclodecanone with sebacil (12%) as the main contaminant. These assignments were made by comparing v.p.c. retention times and infrared spectra with corresponding values for authentic cyclodecanone (Aldrich Chemical Co.) donated by Prof. Harold Hart.

(24) Sebacoïn was prepared by acyloin condensation of diethyl sebacate according to the directions of N. L. Allinger, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, New York, N. Y., 1963, p. 840. Analysis by v.p.c. indicated that the acyloin was contaminated with sebacil (12%). Consequently, a larger quantity of hydriodic acid should have been used in this reduction.

TABLE III  
MASS SPECTROSCOPIC ASSIGNMENTS OF ALL PEAKS HAVING AN INTENSITY GREATER THAN 10% OF THE BASE PEAK

$m/e$	abundance	Rel.	—Metastable transitions—
128	11	51.0	(99 <sup>+</sup> ) $\rightarrow$ (71 <sup>+</sup> )
100	11		
99	15	39.3	(128 <sup>+</sup> ) $\rightarrow$ (71 <sup>+</sup> )
71	90		
57	96	37.0	
55	25		
43	100	26.2	(71 <sup>+</sup> ) $\rightarrow$ (43 <sup>+</sup> )
41	29		
39	20	25.2	(128 <sup>+</sup> ) $\rightarrow$ (99 <sup>+</sup> )
29	87		
28	12		Intensity of P + 1 peak
27	58		Calcd. for C <sub>9</sub> H <sub>16</sub> O: 8.94%P
			Found: 9.3%P

**Reduction of Sebacil (R).**—A solution of crude sebacil<sup>25</sup> (3.2 g.) in glacial acetic acid (40 ml.) and 47% hydriodic acid (35 g.) was refluxed for 2.5 hr.; after the usual work-up, 2.5 g. of a yellow oil was isolated. This material proved to be 94% cyclodecanone by v.p.c. analysis.

**Acknowledgment.**—We wish to thank Mr. Robert Guynn for his help with some of these experiments, and Dr. M. Russell of this department for making the mass spectrum analysis, and to acknowledge gratefully the support of the National Institutes of Health by way of research grant AM 04936-03.

(25) Prepared by the oxidation of sebacoïn by the procedure of A. T. Blomquist and A. Goldstein, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1963, p. 838. The crude sebacil used in this experiment is greater than 92% pure.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY, NEW YORK 21, N. Y.]

## Competitive Elimination–Substitution Reactions. Some Dramatic Differences between Bromides and Tosylates

BY P. VEERAVAGU,<sup>1</sup> R. T. ARNOLD,<sup>2</sup> AND E. W. EIGENMANN<sup>3</sup>

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Typical examples of primary alkyl bromides and tosylates were treated with alkoxides under preparative conditions. Under conditions that usually lead to elimination rather than substitution, tosylates gave surprisingly good yields of substitution products while the corresponding bromides underwent predominantly the elimination reaction. This sharp difference between bromides and tosylates can be of enormous significance in the development of synthetic procedures.

A primary alkyl halide or tosylate possessing at least one hydrogen at carbon 2 can, simultaneously, undergo bimolecular substitution and elimination on treatment with a nucleophilic reagent. The relative extents of substitution and elimination depend on the nature of the alkyl group of the substrate,<sup>4–6</sup> the leaving group,<sup>7–9</sup> the attacking nucleophilic reagent,<sup>6,10</sup> the solvent,<sup>11</sup> and temperature.<sup>12</sup> Of these various fac-

tors which influence competitive elimination–substitution reactions, the effect of the nature of the leaving group appears to have received little attention.

In the case of alkyl chlorides, bromides, and iodides, it is known<sup>7</sup> that the SN2/E2 ratio is not markedly dependent on the nature of the halide, although the ratio is reported to decrease in the order RCl > RBr > RI. Previous kinetic studies with 2-phenylethyl bromides and tosylates<sup>8,9</sup> have led to suggested differences between bromides and tosylates in their tendency to undergo substitution and elimination but no uniform pattern,<sup>13</sup> useful to the synthetic organic chemist, has evolved. Since 2-phenylethyl halides and tosylates represent special cases, elimination being promoted in each of these by the phenyl group, we report here the

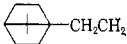
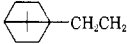
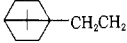
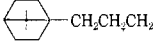
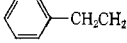
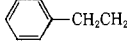
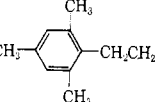
- (1) Postdoctoral Research Associate (1958–1960).
- (2) Alfred P. Sloan Research Associate. Correspondence should be addressed to Mead Johnson and Co., Evansville, Indiana.
- (3) Postdoctoral Research Associate (1956–1957).
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TABLE I  
RATE CONSTANTS AND E2 AND S<sub>N</sub>2 YIELDS FROM *n*-OCTADECYL BROMIDE AND TOSYLATE WHEN TREATED WITH 0.09 *N* POTASSIUM *t*-BUTOXIDE IN *t*-BUTYL ALCOHOL

Compound	<i>t</i> , °C.	<i>k</i> × 10 <sup>6</sup> , l./mole/sec.	Elimination, %	Substitution, %
Bromide	40	2.32	83.7	16.3
Tosylate	40	15.10	..	100.0

TABLE II  
PRODUCT ANALYSIS OF THE REACTION OF ALKOXIDES WITH BROMIDES AND TOSYLATES

	Compound RY		Alkoxide (1.0 <i>N</i> )	Elimination, Substitution, %		Total yield, %
	R =	Y =		Elimination, %	Substitution, %	
I	<i>n</i> -C <sub>18</sub> H <sub>37</sub>	Br	(a) NaOCH <sub>3</sub>	1	96	97
	<i>n</i> -C <sub>18</sub> H <sub>37</sub>	Br	(b) KO- <i>t</i> -C <sub>4</sub> H <sub>9</sub>	85	12	97
II	<i>n</i> -C <sub>18</sub> H <sub>37</sub>	OTs	(a) NaOCH <sub>3</sub>	1	95	96
	<i>n</i> -C <sub>18</sub> H <sub>37</sub>	OTs	(b) KO- <i>t</i> -C <sub>4</sub> H <sub>9</sub>	1	99	100
III		Br	KO- <i>t</i> -C <sub>4</sub> H <sub>9</sub>	1	19	92
IV		OTs	(a) NaOCH <sub>3</sub>	73	80	85
		OTs	(b) KO- <i>t</i> -C <sub>4</sub> H <sub>9</sub>	1	84	81
V		OTs	KO- <i>t</i> -C <sub>4</sub> H <sub>9</sub>	1	88	89
VI		Br	KO- <i>t</i> -C <sub>4</sub> H <sub>9</sub>	100	00	100 <sup>a</sup>
VII		OTs	KO- <i>t</i> -C <sub>4</sub> H <sub>9</sub>	100	00	100 <sup>a</sup>
						
VIII		OTs	(a) NaOCH <sub>3</sub>	5	79	84
		OTs	(b) KO- <i>t</i> -C <sub>4</sub> H <sub>9</sub>	71	..	71

reactions of a number of typical primary alkyl bromides and tosylates with alkoxides under preparative conditions. The results obtained indicate that the differences between primary alkyl bromides and tosylates become magnified in an environment which strongly favors the elimination reaction. The alkyl bromides, when treated with potassium *t*-butoxide (in *t*-butyl alcohol) largely undergo elimination as expected, but even under these conditions the corresponding tosylates give predominantly substitution products.

As a preliminary step in this investigation, the kinetics of the reaction of *n*-octadecyl bromide (I) and *n*-octadecyl tosylate (II) with 0.09 *N* potassium *t*-butoxide in *t*-butyl alcohol was studied at 40°. The bromide and tosylate followed bimolecular kinetics; the former gave 83.7% elimination, while the latter gave 100% substitution (Table I). Such a dramatic difference between a bromide and its corresponding tosylate has, to our knowledge, never before been reported. A similar difference was also observed under preparative conditions, when I and II were refluxed with 1 *N* solution of potassium *t*-butoxide in anhydrous *t*-butyl alcohol (80°) for 20 hr. The ratio of bimolecular substitution and elimination was determined by product analysis.

Another primary alkyl bromide, 2'-5,5-dimethylbicyclo[2.2.1]heptan-1-ylethyl bromide (III), and two other primary alkyl tosylates, 2'-5,5-dimethylbicyclo[2.2.1]heptan-1-ylethyl tosylate (IV) and 3',5,5-dimethylbicyclo[2.2.1]heptan-1-ylpropyl tosylate (V) were allowed to react with potassium *t*-butoxide under the preparative conditions already described. The

bromide III gave largely elimination while the tosylates gave predominantly substitution products (Table II), thereby confirming the observation made with I and II. The somewhat higher substitution-elimination ratio (*ca.* 1:4) obtained with the bromide III as compared with the ratio (*ca.* 1:7) obtained with the bromide I is probably due to the presence of the bulky 5,5-dimethylbicyclo[2.2.1]heptan-1-yl group in III which sterically

interferes with the abstraction of an adjacent proton by *t*-butoxide ion.<sup>14</sup>

In a comparative study under experimental conditions employing a weaker base, the bromide I and the tosylates II and IV were refluxed for 12 hr. with 1 *N* sodium methoxide in anhydrous methanol (65°). Under these conditions, the bromide and tosylates gave almost identical results, the reaction in all these cases being predominantly substitution (Table II). It is known that with a given substrate the more nucleophilic *t*-butoxide leads to a lower substitution-elimination ratio than the less nucleophilic methoxide. However, a comparison of the results obtained when *t*-butoxide and methoxide, respectively, were the attacking nucleophiles brings out the significant fact that the greater reactivity of tosylates in bimolecular substitution, as compared with that of bromides, becomes most pronounced under reaction conditions that favor elimination rather than substitution. Herein lies the importance of tosylates in organic syntheses. In those cases in which bromides or iodides yield olefins, we believe that the corresponding tosylates can be used to advantage in the preparation of ethers, amines,<sup>15</sup> and alkyl derivatives of compounds containing active methylene groups.<sup>16,17</sup>

The characteristic of tosylates to undergo substitution rather than elimination is masked when there is a 2-phenyl substituent. 2-Phenylethyl bromide (VI)

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TABLE III  
 COMPOUNDS, THEIR PHYSICAL CONSTANTS AND ELEMENTAL ANALYSIS

Compound	M.p., °C. <sup>a</sup>	B.p.			Yield, %	—Calculated, %—		—Found, %—	
		°C.	mm.	<i>n</i> <sup>25D</sup>		Carbon	Hydro- gen	Carbon	Hydro- gen
1. 3'-5,5-Dimethylbicyclo[2.2.1]heptan-1-ylpropionitrile	33	82-85	0.3	.....	94	81.31	10.79	81.53	10.78
2. 3'-5,5-Dimethylbicyclo[2.2.1]heptan-1-ylpropionic acid	121-122 P	.....	..	.....	91	73.44	10.26	73.29	10.04
3. Ethyl 3'-5,5-dimethylbicyclo[2.2.1]heptan-1-ylpropionate	.....	100	0.7	1.4750	90	74.95	10.78	75.05	10.91
4. 3'-5,5-Dimethylbicyclo[2.2.1]heptan-1-ylpropanol	.....	99-101	0.1	1.4850	78	79.06	12.16	78.98	12.09
5. 2-Mesitylethanol	83.5 N	.....	..	.....	76	80.45	9.83	80.49	9.66
6. <i>n</i> -Octadecyl bromide <sup>18</sup>	28 M	.....	..	.....	..	..	..	..	..
7. 2'-5,5-Dimethylbicyclo[2.2.1]heptan-1-ylethyl bromide	68 MW	.....	..	.....	80	57.20	8.29	57.21	8.24
8. Octadecyl tosylate <sup>17</sup>	56 P	.....	..	.....	..	..	..	..	..
9. 2'-5,5-Dimethylbicyclo[2.2.1]heptan-1-ylethyl tosylate	77-78 P	.....	..	.....	94	67.04	8.13	67.17	8.19
10. 3'-5,5-Dimethylbicyclo[2.2.1]heptan-1-ylpropyl tosylate	67 H	.....	..	.....	76	67.83	8.39	67.95	8.37
11. 2-Mesitylethyl tosylate	70-71 H	.....	..	.....	68	67.89	6.97	67.98	7.02
12. <i>n</i> -Octadecyl methyl ether <sup>19,c</sup>	30.5 EM	.....	..	.....	<sup>b</sup>	..	..	..	..
13. 2'-5,5-Dimethylbicyclo[2.2.1]heptan-1-ylethyl methyl ether <sup>c</sup>	.....	99-100	15.0	1.4675	<sup>b</sup>	79.06	12.16	79.30	12.15
14. 2-Mesitylethyl methyl ether <sup>c</sup>	.....	117-118	15.0	1.5080	<sup>b</sup>	80.85	10.18	80.97	10.06
15. <i>n</i> -Octadecyl <i>t</i> -butyl ether <sup>c</sup>	52-53 P	.....	..	.....	<sup>b</sup>	81.10	14.16	80.90	14.20
16. 2'-5,5-Dimethylbicyclo[2.2.1]heptan-1-ylethyl <i>t</i> -butyl ether <sup>c</sup>	.....	106	3.0	1.4606	<sup>b</sup>	80.29	12.58	80.45	12.31
17. 3'-5,5-Dimethylbicyclo[2.2.1]heptan-1-ylpropyl <i>t</i> -butyl ether <sup>c</sup>	.....	137-138	15.0	1.4640	<sup>b</sup>	80.60	12.68	80.70	12.75
18. Octadecene <sup>20,d</sup>	.....	144-146	3.0	1.4430	<sup>b</sup>	..	..	..	..
19. 5,5-Dimethylbicyclo[2.2.1]heptan-1-ylethylene <sup>d</sup>	.....	48	15.0	1.4750	<sup>b</sup>	87.92	12.08	87.73	12.13
20. 2,4,6-Trimethylstyrene <sup>21,d,e</sup>	.....	88.5	15.0	1.5310	<sup>b</sup>	..	..	..	..

<sup>a</sup> Solvents for recrystallization: H, *n*-hexane; M, methanol; N, nitromethane; P, *n*-pentane; W, water. <sup>b</sup> See Table II. <sup>c</sup> Infrared absorption 1120-1070 cm.<sup>-1</sup> region (C-O-C). <sup>d</sup> Infrared absorption: 915-905 cm.<sup>-1</sup> region (>C=CH<sub>2</sub>). <sup>e</sup> Ultraviolet absorption: λ<sub>max</sub> 242 mμ, log ε 3.9.<sup>22</sup>

and tosylate (VII) yielded 100% elimination with *t*-butoxide.<sup>9</sup> We treated 2-mesitylethyl tosylate (VIII) with sodium methoxide and potassium *t*-butoxide. With methoxide, VIII gave 79% substitution and 5% elimination (Table II), but complete elimination was obtained with *t*-butoxide. This demonstrates that the bulky *t*-butoxide group is able to abstract a proton situated adjacent to the mesityl group, and that, in spite of the two *o*-methyl groups, the mesityl ring (like the phenyl ring) promotes E2 elimination through conjugation with the incipient double bond of the E2 transition state.

### Experimental

The physical constants and elemental analysis of compounds not included in this section are given in Table III.

**2'-5,5-Dimethylbicyclo[2.2.1]heptan-1-ylethanol.**—The procedure outlined below was found to be a distinct improvement over that reported earlier.<sup>23</sup>

A solution of 2'-2-chloro-5,5-dimethylbicyclo[2.2.1]heptan-1-ylethyl acetate (100 g.) in ether (500 ml.) was added slowly to a solution of sodium (60 g.) in liquid ammonia (2500 ml.). When all the chloroacetate had been added, the blue sodium color was discharged by adding ethanol (95%), and the ammonia was allowed to evaporate.

Water and dilute hydrochloric acid (4 N) were added to acidify and dissolve the residue; the product was extracted with ether. The ether solution yielded upon distillation 65 g. of crude product (b.p. 80-100° (0.5 mm.)).

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This material was heated under reflux for 5 hr. with potassium hydroxide (10 g.) in ethanol (100 ml.) to saponify any unchanged ester. The organic material was extracted with ether and was fractionally distilled to give 62 g. (90%) of colorless oil, b.p. 78-80° (0.2 mm.), *n*<sup>25D</sup> 1.4844. This oil crystallized at room temperature to form long needles, m.p. 33°. The acid phthalate of this alcohol melted at 147-148°.<sup>23</sup>

**2'-5,5-Dimethylbicyclo[2.2.1]heptan-1-ylethyl Tosylate.**—Finely powdered *p*-toluenesulfonyl chloride (342 g., 6% excess) was added in small portions over a period of 1 hr. to a well-stirred solution of 2'-5,5-dimethylbicyclo[2.2.1]heptan-1-ylethanol (285 g., 1.7 moles) in pyridine (550 ml.). The temperature was maintained below 5° during this addition by external cooling with an ice-salt bath. The mixture was stirred and maintained at 5-10° for an additional 5 hr. during which time ether (600 ml.) was added in small portions to keep the mixture fluid enough to be stirred. The slurry so formed was poured into cold dilute hydrochloric acid and the crystalline tosylate was extracted with ether. The ether was evaporated and the solid residue was washed thoroughly with cold *n*-pentane to obtain a tosylate of satisfactory purity (m.p. 76-78°) for further syntheses.

Other tosylates used in this study were prepared from the corresponding alcohols by a similar procedure (see Table III).

**3'-5,5-Dimethylbicyclo[2.2.1]heptan-1-ylpropionitrile.**—A mixture of 2'-5,5-dimethylbicyclo[2.2.1]heptan-1-ylethyl tosylate (100 g., 0.31 mole), sodium cyanide (31 g., 0.62 mole), and dimethyl sulfoxide (225 ml.) was heated with stirring at 125° for 60 hr. in an atmosphere of nitrogen. This mixture was poured into a large volume of water and the nitrile was extracted with ether. The ether solution was evaporated and the residue was distilled under reduced pressure to give the expected nitrile.

**3'-5,5-Dimethylbicyclo[2.2.1]heptan-1-ylpropionic Acid.**—3'-5,5-Dimethylbicyclo[2.2.1]heptan-1-ylpropionitrile (51.4 g.) was added slowly to a stirred mixture of sulfuric acid (250 ml. of 75 vol. %) and sodium chloride (2 g.). The temperature was maintained at 100° during this addition and at 185-190° for 2 hr. thereafter.

The mixture was cooled and poured into cold water. The precipitated acid was extracted with ether and from the ether solution into dilute potassium hydroxide solution. This alkaline solution was acidified to precipitate the acid uncontaminated by amide. The acid was taken up in ether and the solution was dried and evaporated. Washing the residue with *n*-pentane (to remove a yellow coloration) gave white platelets.

**Ethyl 3'-5,5-Dimethylbicyclo[2.2.1]heptan-1-ylpropionate.**—A solution of 3'-5,5-dimethylbicyclo[2.2.1]heptan-1-ylpropionitrile (33 g.) in absolute ethanol (30 ml.) and dry ether (150 ml.) was saturated with hydrogen chloride, while being kept cooled in a freezing mixture. After storage overnight at  $-10^{\circ}$ , the reaction mixture was concentrated by evaporation under reduced pressure. The solid imino-ester that separated was removed by filtration and then shaken up with water (750 ml.). The liberated ester was extracted with ether and purified by distillation.

**3'-5,5-Dimethylbicyclo[2.2.1]heptan-1-ylpropanol.**—Lithium aluminum hydride (2 g., 50% excess) was added to tetrahydrofuran (100 ml.) and refluxed with stirring for 30 min. After cooling the reaction vessel to room temperature, ethyl 3'-5,5-dimethylbicyclo[2.2.1]heptan-1-ylpropionate (31.4 g., 1.4 moles) was added dropwise with stirring. At the end of 12 hr., the excess of lithium aluminum hydride was decomposed by slow addition of water; sulfuric acid (4 *N*) was added to dissolve the aluminum hydroxide. Extraction with ether, followed by distillation, gave the desired alcohol.

**2-Mesitylethanol.**—In this preparation, the procedure described for the synthesis of mesitoic acid<sup>24</sup> from mesityl bromide was followed with the necessary modifications.

Into a 3-l. three-necked round-bottomed flask fitted with a condenser, stirrer, and dropping funnel was placed 16.8 g. (0.7 g.-atom) of magnesium turnings and 500 ml. of dry ether. A solution of ethyl bromide (38.5 g., 0.35 mole) and mesityl bromide (69.7 g., 0.35 mole) in ether (100 ml.) was added gradually over a period of 30 min. The reaction started as soon as the first portion of the bromide mixture was added. The reaction was completed by refluxing for another 30 min.

The reaction vessel was cooled in a bath of freezing mixture, and a solution of ethylene oxide (61.6 g., 70 ml., 1.4 moles) in ice-cold ether (100 ml.) was run in over 20 min. Within an hour, the reaction mixture turned into a gel. It was kept stirred overnight at room temperature. The Grignard complex was decomposed with 4 *N* sulfuric acid (500 ml.), the ether layer was removed, and the aqueous portion was extracted with ether. The combined ether extracts were dried and evaporated. The white solid residue was dried under vacuum and sublimed; white shiny crystalline scales were obtained.

**2'-5,5-Dimethylbicyclo[2.2.1]heptan-1-ylethyl Bromide.**—A solution of 2'-5,5-dimethylbicyclo[2.2.1]heptan-1-ylethyl tosylate (22.4 g., 0.07 mole) and lithium bromide (12 g., 100% ex-

(24) D. M. Bowen in "Organic Syntheses," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1953, p. 553.

cess) in dry acetone<sup>9</sup> (100 ml.) was refluxed with stirring for 24 hr. Most of the solvent was evaporated off and the residue was poured into water and extracted with ether.

**Reaction of 2'-5,5-Dimethylbicyclo[2.2.1]heptan-1-ylethyl Tosylate with Potassium *t*-Butoxide.**—The above tosylate (50 g.) was refluxed with 1 *N* solution (250 ml.) of potassium *t*-butoxide in anhydrous *t*-butyl alcohol for 20 hr. with stirring under anhydrous conditions. Potassium *p*-toluenesulfonate separated as a white precipitate during the reaction. The heterogeneous reaction mixture was poured into cold water (4000 ml.) and extracted with pentane. The dried pentane extract was evaporated and the residual liquid product was dried under vacuum. Small aliquots of the undistilled material were taken to determine the fraction of the olefin product present; the olefin present was estimated using Wij reagent.<sup>25</sup> Fractionation gave 2'-5,5-dimethylbicyclo[2.2.1]heptan-1-ylethyl *t*-butyl ether.

The procedure described here was used without any major modification to study the reaction of alkoxides with other tosylates and bromides used in this investigation. When methoxide in methanol was used, the reaction mixture was refluxed for only 12 hr.

The relative amounts of olefin and ether formed in this and other related reactions are given in Table II.

**Kinetic Study of the Reaction of *n*-Octadecyl Bromide and Tosylate with Potassium *t*-Butoxide.**—The reaction was carried out in a 100-ml. volumetric flask. About 0.06 mole of the bromide (or tosylate) was placed in the volumetric flask and weighed. Then 0.9 *N* potassium *t*-butoxide in anhydrous *t*-butyl alcohol, already equilibrated thermally in a thermostat at 40°, was added to the calibration mark. The dissolution of the bromide was facilitated by shaking. The flask was kept in the thermostat and at suitable intervals 5.0-ml. aliquots of the contents were pipetted out into a titration flask containing 50 ml. of water. The amount of unneutralized base, and thereby the amount of bromide reacted, was determined by titrating with 0.06 *N* hydrochloric acid, using phenolphthalein as indicator.

The amount of olefin formed was determined in the following manner: the titrant from above was extracted with *n*-pentane, the extract dried ( $\text{Na}_2\text{SO}_4$ ), and pentane evaporated.<sup>26</sup> The residue was dissolved in carbon tetrachloride (50 ml.) and the amount of olefin present was determined using Wij reagent.

A plot of  $t(\text{sec.})/\log(a-x)(b-x)$  was a straight line;  $a$  and  $b$  were initial concentrations of the bromide (or tosylate) and *t*-butoxide, respectively, and  $x$  was the amount of the substrate that had reacted. The reaction constant was obtained from the slope of the linear plot. The results of this kinetic study are given in Table I.

(25) A. Polgar and J. L. Jungnickel in "Organic Analysis," Vol. 3, Interscience Publishers, Inc., New York, N. Y., 1956, p. 222.

(26) When carbon tetrachloride was used for this extraction, it was found that some *t*-butyl alcohol was also extracted, which led to anomalous values in the subsequent titration of olefin.

[CONTRIBUTION FROM THE DEFENSIVE RESEARCH DIVISION, DIRECTORATE OF DEFENSIVE SYSTEMS, U. S. ARMY CHEMICAL RESEARCH AND DEVELOPMENT LABORATORIES, EDGEWOOD ARSENAL, MD.]

## Reactions of Isopropyl Methylphosphonofluoridate with Substituted Phenols. I

BY JOSEPH EPSTEIN, ROBERT E. PLAPINGER, HARRY O. MICHEL, JAMES R. CABLE, RALPH A. STEPHANI, RALPH J. HESTER, CLYDE BILLINGTON, JR., AND GARY R. LIST

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A study has been made of the reactivity of isopropyl methylphosphonofluoridate with various substituted phenols. The data indicate that: (a) The nucleophilic displacement capability of a phenolate increases with the basicity of the anion ( $\log k_2 = 0.589pK_a - 4.172$ ). (b) Cationic sites in the phenol increase the reactivity of the phenolate and the increase is inversely related to the distance between cationic and anionic sites. (c) There are marked steric (bulk) effects due to *ortho* substituents which lower the reactivity of the phenol. (d) Substances in the *ortho* position which are capable of hydrogen bonding can markedly increase the rate constant. (e) The reactivity of phenols in which the *ortho* substituent contains a cationic site can be adequately explained on the basis that two effects, opposite in their manifestations on the reactivity, are operative, *viz.*, b and c. A mathematical relationship to predict the reactivity of phenols containing cation sites is offered, and an explanation for "abnormal" reactivities shown by cationic phenols and others is advanced.

Investigations into the reactions of the nerve gas, isopropyl methylphosphonofluoridate (GB), in dilute

aqueous solution have led to the discovery of classes of compounds which have high reactivity in displace-