[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

Migration Ratios in the Rearrangement of 2-Amino-1,1-diarylethanols[1]

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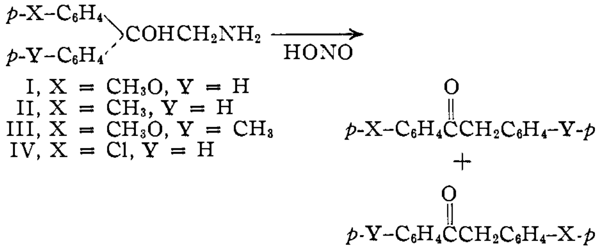
RECEIVED MARCH 15, 1954

The rearrangements of 2-amino-1-*p*-anisyl-1-phenylethanol and 2-amino-1-phenyl-1-*p*-tolylethanol, previously reported to yield only the product formed with migration of the *p*-anisyl or *p*-tolyl group, respectively, have been re-examined and the migration ratio of *p*-anisyl/phenyl has been found to be only 1.5 while that of *p*-tolyl/phenyl is 1.3 contrary to the previous reports. Rearrangement of similar amino alcohols leads to the migration ratios for *p*-chlorophenyl/phenyl of 0.9 and for *p*-anisyl/*p*-tolyl of 1.2.

The rearrangement of 2-amino-1-*p*-anisyl-1-phenylethanol (I) with nitrous acid has been reported to lead to *p*-methoxybenzyl phenyl ketone (formed by migration of the *p*-anisyl group) and none of the other isomer, *p*-anisyl benzyl ketone was isolated.[3] The corresponding *p*-ethoxyphenyl amino alcohol gave similar results although in this case a small amount of *p*-ethoxyphenyl benzyl ketone could be isolated in addition to the *p*-ethoxybenzyl phenyl ketone which was reported to be formed in much larger quantity. A different group of investigators[4] examined the rearrangement of 2-amino-1-phenyl-1-*p*-tolylethanol (II) and reported *p*-methylbenzyl phenyl ketone (formed with *p*-tolyl migration) to be the sole product isolated.

In connection with other work, it was desired to know more exactly the migration ratios in the rearrangement of amino alcohols of this type.

For this reason we have prepared the amino alcohols I and II and also 2-amino-1-*p*-anisyl-1-*p*-tolylethanol (III) and 2-amino-1-*p*-chlorophenyl-1-phenylethanol (IV) and examined the products of rearrangement with nitrous acid in 50% acetic acid at 0°.



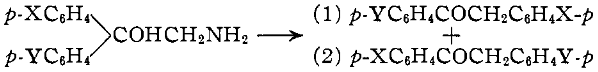
$$p\text{-X-C}_6\text{H}_4(p\text{-Y-C}_6\text{H}_4)\text{COHCH}_2\text{NH}_2 \xrightarrow{\text{HONO}} p\text{-X-C}_6\text{H}_4\overset{\text{O}}{\overset{\|}{\text{C}}}\text{CH}_2\text{C}_6\text{H}_4\text{-Y-}p + p\text{-Y-C}_6\text{H}_4\overset{\text{O}}{\overset{\|}{\text{C}}}\text{CH}_2\text{C}_6\text{H}_4\text{-X-}p$$

I, X = CH_3O, Y = H
II, X = CH_3, Y = H
III, X = CH_3O, Y = CH_3
IV, X = Cl, Y = H

The entire neutral fraction of each reaction mixture was analyzed by means of the ultraviolet spectrum together with the spectra of the two possible ketonic products. Known mixtures of the two ketonic products with the composition indicated by the ultraviolet analysis were then prepared and their infrared spectra compared with infrared spectra of the product mixtures. In each case the infrared results agree well with those obtained from the ultraviolet spectra.

Our results were in only partial agreement with those of earlier workers. Although 60% of the mixture from I was *p*-methoxybenzyl phenyl ketone formed by *p*-anisyl migration, there was 40% of the ketone formed by phenyl migration. The mixture from II consisted of only 55% of *p*-methylbenzyl phenyl ketone (*p*-tolyl migration) and there was 45% of benzyl *p*-tolyl ketone formed with phenyl migration. The *p*-chloro compound III gave 53% phenyl migration and only 47% *p*-chlorophenyl migration. These results are summarized in Table I.

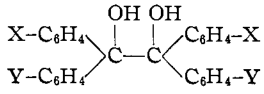
TABLE I



$$p\text{-XC}_6\text{H}_4(p\text{-YC}_6\text{H}_4)\text{COHCH}_2\text{NH}_2 \longrightarrow (1)\ p\text{-YC}_6\text{H}_4\text{COCH}_2\text{C}_6\text{H}_4\text{X-}p + (2)\ p\text{-XC}_6\text{H}_4\text{COCH}_2\text{C}_6\text{H}_4\text{Y-}p$$

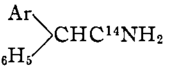
X	Y	Run	Yield (1), %	Av. (1) %	Av. (2), %
CH_3O	H	1	60.1 ± 0.4	61	39
		2	61.8 ± 0.4		
CH_3	H	1	55.4 ± 1.8	56	44
		2	57.0 ± 1.9		
CH_3O	CH_3	1	54.3 ± 0.9	55	45
		2	55.7 ± 0.5		
H	Cl	1	52.9 ± 0.4	53	47
		2	53.5 ± 0.1		

It is of interest to compare our results with those obtained in a study by Bachmann, Ferguson and Moser[5] of the rearrangement of symmetrical pinacols of the general structure V and also with the results of the recent study[6] of the rearrangement



V

with nitrous acid of amines of the type VI



$$\text{Ar}(\text{C}_6\text{H}_5)\text{CHC}^{14}\text{NH}_2$$

VI

which differ from our compounds only in the absence of the hydroxyl group. This comparison is made in Table II.

TABLE II

	Migration ratios (Ar/C_6H_5)		
Ar	Bachmann pinacols V	Amino alcohols (present work)	Amines VI (Ciereszko and Burr)
p-$CH_3OC_6H_4$	500	1.56 ± 0.05	1.5
p-$CH_3C_6H_4$	16	1.28 ± .09	0.9
p-ClC_6H_4	0.66	0.88 ± .01	..

The value of *p*-anisyl/*p*-tolyl, 1.22 ± 0.03, is in what is perhaps partially fortuitously good agree-

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[1] From the Ph.D. Dissertation submitted to Columbia University by Malcolm C. Crew. Presented in part at the Thirteenth National Organic Chemistry Symposium of the American Chemical Society, Ann Arbor, Mich., June, 1935.

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[3] M. Tiffeneau, A. P. Orekhoff and M. Roger, *Bull. soc. chim.*, **49**, 1757 (1931).

[4] A. McKenzie, A. K. Mills and J. R. Myles, *Ber.*, **63**, 904 (1930).

[5] W. E. Bachmann and J. W. Ferguson, THIS JOURNAL, **56**, 2081 (1934); W. E. Bachmann and F. H. Moser, *ibid.*, **54**, 1124 (1932).

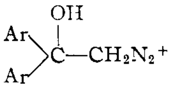
[6] L. S. Ciereszko and J. G. Burr, *ibid.*, **74**, 5431 (1952).

ment with the value of 1.22 calculated by taking the quotient of the *p*-anisyl/phenyl and *p*-tolyl/phenyl migration ratios using the relationship between migration ratios which was observed by Bachmann.[5]

It is seen that the effect of substituents in the present work is qualitatively the same as in the pinacol rearrangements studied by Bachmann but the amino alcohol rearrangement is very much less sensitive to the effects of substituents. Similar differences were noted by Ciereszko and Burr[6] who compared the results obtained with the amines of type VI with those obtained in the rearrangement of the corresponding alcohols with phosphorus pentoxide.[7] It is of interest that the *p*-anisyl/phenyl ratio found in the rearrangement of the amino alcohol I is unchanged when the β-hydroxyl group is replaced by hydrogen. We do not understand the difference between the *p*-tolyl/phenyl ratio in the amine of Ciereszko and Burr as compared with the amino alcohol II; their value of less than 1 is particularly puzzling in view of the work of Bachmann and the qualitative similarity between *p*-methyl and *p*-methoxyl generally observed.[8]

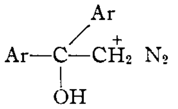
The insensitivity to substituents of the amino alcohol rearrangement could be explained by postulating an intermediate diazo oxide as was suggested by McKenzie and Richardson[9] and which could rearrange with simultaneous ring opening and aryl migration by a molecular mechanism in which no large amount of positive charge is developed in the transition state.

It seems more probable, however, that the species which undergoes rearrangement is the hydroxydiazonium ion (VIII). The small substituent effects suggest that when N≡N (rather than $-OH_2$, OTs^-, etc.) is the leaving group, relatively little driving force by aryl migration is required for reaction and thus resonance structures of the type IX rather than X make a relatively large contribution to the transition state. Brown and Nelson[10] have offered a similar explanation for the relation between reactivity and isomer distribution in aromatic substitution (of which rearrangements of the pinacol type may be regarded as internal examples). A similar explanation stated somewhat differently was one of the two originally offered by Ciereszko and Burr[6] for the very much smaller effect of the *p*-methoxyl group on the rearrangement of the amine VI as compared with the corresponding alcohol. Bailey and Burr,[11] however, prefer an explanation in terms of a cyclic molecular rearrangement of the diazo-hydroxide.



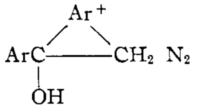
$Ar_2C(OH)-CH_2N_2^+$

VIII



$Ar-C(OH)(Ar)-\overset{+}{C}H_2\ N_2$

IX



$ArC(OH)(Ar^+)-CH_2\ N_2$

X

Experimental[12]

***p*-Methoxyphenacyl bromide**, m.p. 65–68°, was prepared by the method of Lutz,[13] in 20% yield by the bromination of *p*-methoxyacetophenone in the presence of aluminum chloride. The literature m.p. is 71–72°.[14]

Phenacylamine and *p*-methoxyphenacylamine were prepared by the method of Mannich and Hahn[15] and used as the mixed hydrobromide and hydrochloride salts after recrystallization from absolute ethanol.

2-Amino-1-*p*-anisyl-1-phenylethanol (I) was prepared from the mixed phenacylammonium salts above and *p*-anisylmagnesium bromide. After purification by recrystallization from benzene-hexane the yield was 24% of amino alcohol, m.p. 136–136.5° (lit.[3] 134–135°).

2-Amino-1-phenyl-1-*p*-tolylethanol (II), m.p. 107–107.5°, was prepared from the phenacylammonium halides above and *p*-tolylmagnesium bromide. Recrystallization from benzene–hexane gave a 47% yield of II, m.p. 107–107.5° (lit.[4] 106°).[16]

2-Amino-1-*p*-anisyl-1-*p*-tolylethanol (III).—To a solution of *p*-tolylmagnesium bromide prepared from 12.2 g. (0.50 mole) of magnesium turnings and 85.5 g. (0.50 mole) of *p*-bromotoluene in 600 ml. of ether was added in small portions 22.5 g. (0.091 mole) of *p*-methoxyphenacylammonium halides prepared above. The mixture was refluxed for 2 hours, decomposed with ammonium chloride solution, made alkaline, extracted with ether and the dried ether solution treated with hydrogen chloride to precipitate the crude hydrochloride of III. Decomposition of the hydrochloride with 10% sodium hydroxide, extraction with ether and evaporation of the ether gave 10.9 g. (47% yield) of an oil which slowly crystallized on standing. Eight recrystallizations from benzene–hexane yielded 2.2 g. (9%) of III, m.p. 102.5–104°.

Anal. Calcd. for $C_{16}H_{19}NO_2$: C, 74.7; H, 7.4; N, 5.4. Found: C, 74.9; H, 7.3; N, 5.4.

2-Amino-1-*p*-chlorophenyl-1-phenylethanol (IV) was prepared from *p*-chlorophenylmagnesium bromide and the phenacylammonium halide mixture above. After recrystallization from benzene–hexane a 40% yield of IV, m.p. 119.5–120°, was obtained.

Anal. Calcd. for $C_{14}H_{14}ClNO$: C, 67.9; H, 5.7; N, 5.7. Found: C, 68.4, 68.1, 67.9; H, 5.8, 5.5, 5.6; N, 5.7, 5.4, 5.6.

***p*-Anisyl benzyl ketone**, m.p. 75–76°, was prepared from phenylacetyl chloride and anisole with aluminum chloride in carbon disulfide. The reported m.p. is 77°.[17]

***p*-Methoxybenzyl phenyl ketone** was prepared from 4-methoxybenzoin[17] by reduction with thioglycolic acid followed by sodium carbonate.[18] The yield was 37% of product, m.p. 94.5–95° (reported[17] 96.5°).

***p*-Tolyl benzyl ketone**, prepared in 93% yield from phenylacetyl chloride and toluene, melted at 109–110° (reported[19] 110°).

***p*-Methylbenzyl phenyl ketone**, prepared from *p*-tolylacetyl chloride and benzene in 60% yield, melted at 95.5–96.5° (reported[20] 94–95°).

The oxime, after repeated recrystallization from benzene-hexane and hexane melted at 102–103° (reported[21] 109°).

The 2,4-dinitrophenylhydrazone melted at 194–195°.

Anal. Calcd. for $C_{21}H_{18}N_4O_4$: C, 64.6; H, 4.7; N, 14.4. Found: C, 64.8, 65.0; H, 4.1, 4.8; N, 14.1, 14.3.

***p*-Anisyl *p*-Methylbenzyl Ketone**.—Anhydrous aluminum chloride (16 g., 0.12 mole) was added in small portions to a chilled solution of 16.7 g. (0.100 mole) of *p*-tolylacetyl chloride and 13.0 g. (0.12 mole) of anisole in 65 ml. of carbon

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(7) J. G. Burr, Jr., and L. S. Ciereszko, This Journal, **74**, 5426 (1952).

(8) H. H. Jaffe, *Chem. Revs.*, **53**, 191 (1953).

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(11) P. S. Bailey and J. G. Burr, *ibid.*, **75**, 2951 (1953).

(12) All melting points are corrected unless indicated otherwise. All analyses were carried out by the Schwarzkopf Microanalytical Laboratory, Middle Village, N. Y.

(13) R. E. Lutz and co-workers, *J. Org. Chem.*, **12**, 617 (1947).

(14) A. Horeau and J. Jacques, *Bull. soc. chim. France*, 382 (1946).

(15) C. Mannich and F. L. Hahn, *Ber.*, **44**, 1452 (1911); see also K. H. Slotta and H. Heller, *ibid.*, **63**, 1024 (1930).

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(17) S. S. Jenkins, This Journal, **54**, 1159 (1932).

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(20) M. Tiffeneau, *Ann. chim.*, [8] **10**, 360 (1907).

(21) H. Strassman, *Ber.*, **22**, 1230 (1889).

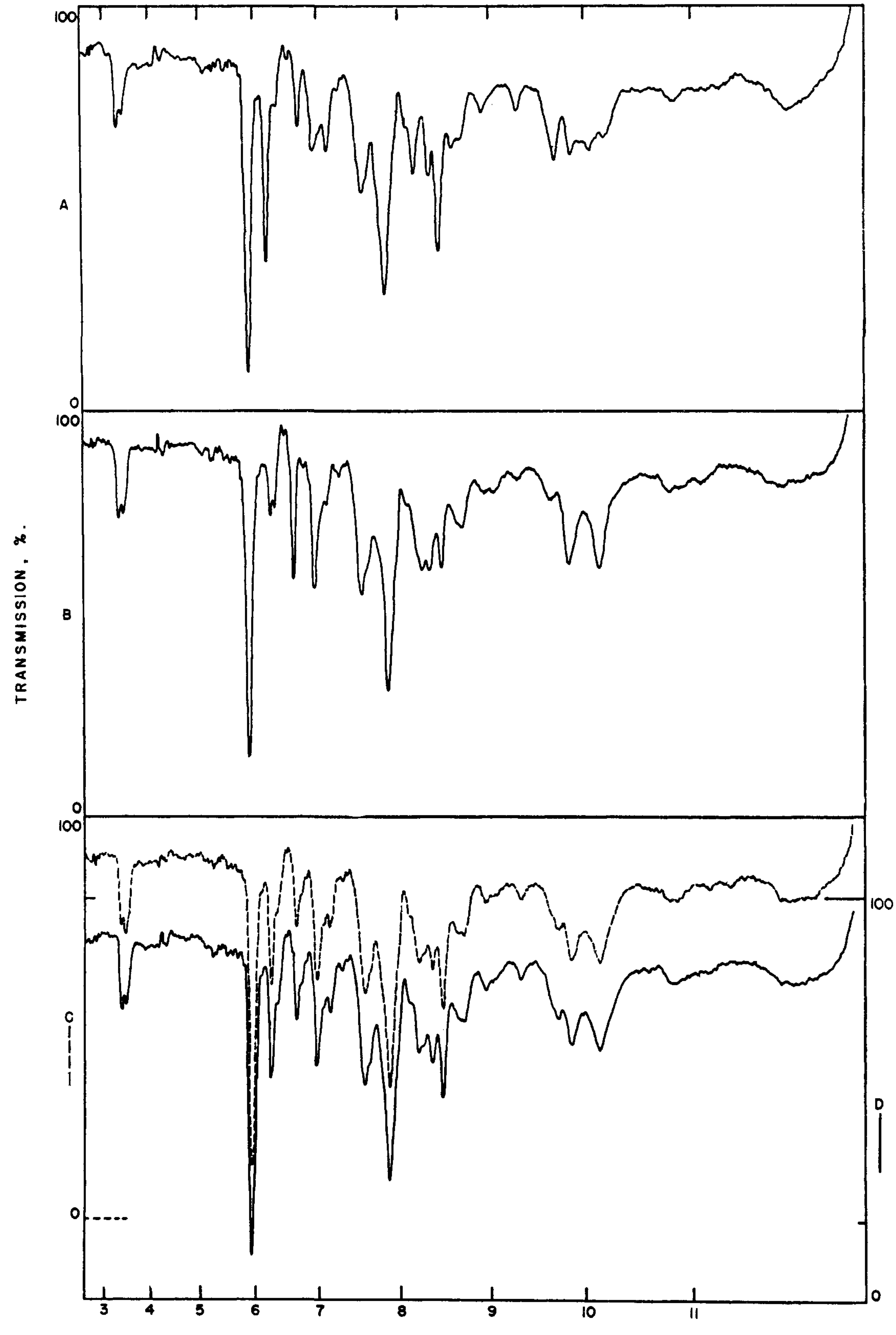

Fig. 1.—Infrared spectra of 5% solutions in carbon tetrachloride: curve A, benzyl *p*-tolyl ketone; curve B, *p*-methylbenzyl phenyl ketone; curve C, mixture, 44% benzyl *p*-tolyl ketone, 56% *p*-methylbenzyl phenyl ketone; curve D, rearrangement product.

disulfide. The mixture was heated under reflux for 15 minutes and poured onto a mixture of ice and hydrochloric acid. Extraction with benzene and removal of the benzene gave the crude ketone which after recrystallization from 95% ethanol amounted to 16 g. (67%), m.p. 90–90.5°.

Anal. Calcd. for $C_{16}H_{16}O_2$: C, 80.0; H, 6.7. Found: C, 80.1; H, 7.0.

The 2,4-dinitrophenylhydrazone melted at 197–198° (a mixture with 2,4-dinitrophenylhydrazine showed a depression).

Anal. Calcd. for $C_{22}H_{20}N_4O_5$: C, 62.9; H, 4.8; N, 13.3. Found: C, 63.6, 63.2, 63.0; H, 4.7, 5.0, 5.3; N, 11.8, 13.2, 13.0.

***p*-Methoxybenzyl *p*-Tolyl Ketone.**—To a Grignard solution prepared from 3.0 g. (0.12 mole) of *p*-bromotoluene in 200 ml. of dry ether was added 11.0 g. (0.060 mole) of anhydrous cadmium chloride in small portions. After 1 hour of stirring at room temperature a part of the ether was distilled and replaced by benzene after which 15.4 g. (0.084 mole) of *p*-methoxyphenylacetyl chloride was added at a rate just fast enough to maintain gentle reflux. The solution was heated for 15 minutes after the addition was complete, then poured onto ice and hydrochloric acid. Removal of the solvent from the organic layer gave 12.3 g. (62%) of crude ketone which after three recrystallizations from methanol and one from hexane–benzene melted at 99.5–100°.

Anal. Calcd. for $C_{16}H_{16}O_2$: C, 80.0; H, 6.7. Found: C, 80.8, 80.1, 79.9; H, 7.0, 7.6, 6.5.

The 2,4-dinitrophenylhydrazone melted at 224.5–225°.

Anal. Calcd. for $C_{22}H_{20}O_5N_4$: C, 62.9; H, 4.8; N, 13.3. Found: C, 63.2; H, 4.9; N, 13.3.

Benzyl *p*-chlorophenyl ketone was prepared in 78% yield from phenylacetyl chloride and chlorobenzene and, after recrystallization from 95% ethanol and benzene–hexane, melted at 104.5–105°. Additional recrystallizations did not raise the m.p. (reported[22] 107.5°).

***p*-Chlorobenzyl phenyl ketone** was prepared in 89% yield from *p*-chlorophenylacetyl chloride and benzene. The m.p. was 136.5–137.5° (reported[22] 138°).

Rearrangement of the Amino Alcohols I, II, III and IV with Nitrous Acid.—The rearrangements were carried out by treating 500 mg. of the amino alcohol in 35 ml. of 50% acetic at 0–2° with a threefold excess of aqueous sodium nitrite (0.4 g. in 5 cc. of water). After the addition of sodium nitrite was completed, stirring was continued at 1–2° for 24 hours. Excess nitrous acid was then destroyed by addition of 10% sulfamic acid until the mixture did not darken starch–iodide paper. The solution was then diluted with 75 ml. of water and the neutral fraction extracted with pentane. The pentane layer was dried over anhydrous sodium carbonate and evaporated to dryness. In each case a white solid was obtained which amounted to 97–100% of the theoretical weight of ketones. This solid was accurately weighed, dissolved in ethanol and the solution diluted to 100.0 ml. A 5.00-ml. portion of the solution was further diluted until the final concentration (accurately known) was about 20 mg./l. This solution was used for the ultraviolet spectra as described below.

The ethanol was removed from the remaining ethanol solution and the infrared spectrum of the mixture was determined in carbon tetrachloride as described below. Duplicate runs of each rearrangement were carried out.

Ultraviolet Spectral Analyses of the Ketone Mixtures.—The data were obtained using a Beckman DU spectrophotometer. The spectra of the eight *p*-substituted benzyl phenyl ketones described above were determined in 95% ethanol at concentrations of 30 and 15 mg./ml. and Beer's law appears to hold at the concentrations used.

The method of analysis is illustrated by a description of its application to a mixture of *p*-methoxybenzyl phenyl ketone and *p*-anisyl benzyl ketone obtained in the rearrangement of the amino ketone I. Extinction coefficients of the two pure ketones and of the unknown mixture were obtained at each of four wave lengths (229, 237, 243 and 278 mμ). Five of the six possible pairs of simultaneous equations expressing the extinction coefficients of the mixtures of products as functions of the concentrations and independently determined extinction coefficients of the product ketones were solved for the ketone concentrations, and the percentage composition of the ketone mixture calculated. The maximum error was determined and used to weight the values of the percentage composition in computing the average value.[23] These weighted averages together with their probable errors are reported in Table I.

The infrared spectra were obtained with a model 21 Perkin–Elmer double beam recording spectrophotometer. In general, 5% solutions in carbon tetrachloride were employed. However, because of the low solubilities, the *p*-chlorobenzyl phenyl ketone and benzyl 4-chlorophenyl ketone solutions were 2.5% in carbon tetrachloride.

The curves used to check the analysis of the mixture obtained by the rearrangement of the *p*-methyl amino alcohol II, the ketone mixture of which showed the largest probable errors on ultraviolet analysis, are recorded in Fig. 1.

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(22) S. S. Jenkins and E. M. Richardson, This Journal, **55**, 1618 (1933).

(23) N. Margenau and G. M. Murphy, "The Mathematics of Physics and Chemistry," D. Van Nostrand Co., Inc., New York, N. Y., 1943, p. 487 ff.

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[Contribution from the Department of Chemistry, Purdue University]

The Ionization Constants of Some New Fluorine-containing Acids[1a]

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Received January 18, 1954

The acids $CF_3CH{=}CHCO_2H$ and $C_3F_7CH{=}CHCO_2H$ are stronger than $CF_3CH_2CH_2CO_2H$ and $C_3F_7CH_2CH_2CO_2H$; and considerably stronger than their non-fluorinated analogs, but they are much weaker acids than CF_3CO_2H or $C_3F_7CO_2H$. Thus it is shown that the inductive effect of fluorine in the CF_3– and C_3F_7– groups is transmitted only partially through a vinyl group.

Compounds having the general formula $CF_3(CH_2)_nCO_2H$ show a marked decrease in acid strength as "*n*" increases from zero to two,[2] but the effect of a vinyl group or C_3F_7– group (except for $C_3F_7CO_2H$[2]) had not been studied prior to the start of this work. Therefore it was of interest to synthesize acids of this type and compare their acidity with that of their saturated analogs as well as their non-fluorine-containing analogs.

The acids selected for study were $C_3F_7CH_2CH_2CO_2H$, $C_3F_7CH{=}CHCO_2H$, $CF_3CH{=}CHCO_2H$ and, as a check on the method, $CF_3CH_2CH_2CO_2H$ inasmuch as its strength was already known.[2] The ethyl esters of these acids were synthesized starting with trifluoroacetic or heptafluorobutyric acids, reducing them to the perfluorinated aldehydes,[3] subjecting these aldehydes to the Reformatsky

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(1) (a) Part of a paper presented before the Division of Organic Chemistry, 124th National Meeting of the American Chemical Society, Chicago, Ill., September, 1953. (b) Abstracted from the doctoral dissertation of D. D. Smith, Purdue University.

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