two which always agreed within ±4%. Plots of the percentage of water collected *vs.* time gave smooth curves of the same general shape showing constantly decreasing rates. Comparison of $t_{50\%}$ values are, therefore, valid.

In both of the preceding studies[2,3] the "rate curves" showed increasing rates during the early stages of the reaction and it was suggested[3] that during this period the aldehydes required to maintain the process were being formed by dehydrogenation of the alcohol. Since in the present study carbonyl groups are already present in a reactant no such induction period was expected or found. In agreement with this U. O. P. nickel[15] did not accelerate, in fact it retarded, the reaction and no hydrogen or other gas was evolved.

Oxidation of By-products.—Infrared absorption data on the ethanol-free material from the mother liquors of the above mentioned recrystallizations from ethanol indicated, as was expected from the work of Mastagli,[9] that 1,3-diphenyl-1-propanols were the principal by-products. Each residue was dissolved in 25 ml. of glacial acetic acid and for each 0.005 mole, calculated on the assumption it was all the 1,3-diphenyl-1-propanol, 1 ml. of a solution of 10.3 g. of chromium trioxide in 30 ml. of 80% aqueous acetic acid was added dropwise with stirring while the temperature was maintained below 40°. After 24 hours at room temperature the mixture was poured into 250 ml. of ice-water and extracted with two 50-ml. portions of ether. The ether solution was washed with water, the ether boiled off and the residue recrystallized from three times its weight of ethanol. Column B of Table I gives the yield of β-phenylpropiophenones including that from the oxidation.

Effects of Changing Important Variables.—The general procedure described above was followed for comparing the effects of potassium, sodium and lithium benzylates except that the 0.002 mole of lithium was replaced by 0.005 mole of the indicated metal hydroxide and 0.130 mole of benzyl alcohol was used. The reaction of the hydroxide with the benzyl alcohol to give the metal benzylate was forced to completion by refluxing one hour in the standard apparatus before adding the acetophenone. Reaction of the acetophenone with the benzyl alcohol gave a 50% yield of water from the three experiments in 19, 35 and 455 minutes, respectively. The total yields of water were 76, 100 and 100% and the yields of pure β-phenylpropiophenone, obtained directly upon recrystallization were 26, 45 and 58%.

In a series of three experiments using the standard procedure except that the amount of lithium metal was 0.001, 0.002 and 0.005 mole and the amount of benzyl alcohol correspondingly adjusted to 0.126, 0.127 and 0.130 mole the times for a 50% yield of water were 895, 550 and 440 minutes and the yields of recrystallized β-phenylpropiophenone obtained directly were 52, 69 and 59%.

The effect of varying the temperature was studied using toluene, xylene and *p*-cymene as solvents in experiments otherwise standard. The reflux temperatures were 112, 140 and 178°. A 50% yield of water was obtained in 3450, 550 and 180 minutes and the yields of pure product were 58, 69 and 53%.

For determining the effect of varying the reactant ratio three experiments were carried out with 0.252, 0.127 and 0.127 mole of benzyl alcohol and 0.125, 0.125 and 0.250 mole of acetophenone along with 0.002 mole of lithium so that the reactant ratios were 2:1, 1:1 and 1:2. The second experiment was standard and the amount of xylene was decreased in the first and third experiments to give the same total volume. A 50% yield of water was obtained in 280, 550 and 420 minutes and the total yield of water was 97 to 102% in all three cases. The yields of pure β-phenylpropiophenone obtained directly upon recrystallization were 48, 69 and 42%.

Reactions of Phenylmethylcarbinol with Benzaldehydes.—One-eighth mole of benzaldehyde, 0.133 mole of phenylmethylcarbinol and 0.008 mole of lithium were used under conditions otherwise standard. A 50% yield of water was obtained in 180 minutes and a 95% yield in 1900 minutes. A 73% yield of β-phenylpropiophenone was obtained directly upon recrystallization and an additional 7% by oxidation of material from the mother liquors as described above. The product melted at 70° both alone and when mixed with the product prepared from benzyl alcohol and acetophenone.

When *p*-dimethylaminobenzaldehyde replaced the benzaldehyde in the procedure of the preceding paragraph a 50% yield of water was obtained in 265 minutes and a 100% yield in 900 minutes. The white crystals, obtained in 60% yield, melted at 51°.

Anal.[14] Calcd. for $C_{17}H_{19}ON$: C, 80.58; H, 7.57. Found: C, 80.72; H, 7.50.

The 2,4-dinitrophenylhydrazone, prepared by standard methods, melted at 209–210°.

Anal.[14] Calcd. for $C_{23}H_{23}O_4N_5$: C, 63.71; H, 5.35. Found: C, 64.18; H, 5.36.

COLLEGE PARK, MARYLAND

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[15] (15) Universal Oil Products Co., 310 S. Michigan Ave., Chicago 4, Ill.

[CONTRIBUTION FROM THE CHEMISTRY DIVISION OF OAK RIDGE NATIONAL LABORATORY]

Molecular Rearrangements. IX. The *p*-Tolyl/Phenyl Migration Ratio in Deamination Reactions[1]

BY BEN M. BENJAMIN AND CLAIR J. COLLINS

RECEIVED APRIL 30, 1956

2-Phenyl-2-*p*-tolylethyl-1-C^{14}-amine (IV) and 2,2-diphenyl-2-*p*-tolylethyl-1-C^{14}-amine (VII) have been subjected to nitrous acid deamination. The *p*-tolyl/phenyl migration ratios have been found to be 1.18 ± 0.06.

Following the migratory aptitude work of Bachmann[2] and of Bailar,[3] and the "σ–ρ" correlation of Hammett,[4] much attention has been directed toward an understanding of the factors which determine the mobility sequence[5] of the various migrating groups which are involved in molecular rearrangements. We have obtained considerable quantitative information in this respect by the use of radioactive carbon,[6–11] with results indicating the expected preference for migration of those groups which are presumed to be better electron donors.[2–4]

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[1] (1) This paper is based upon work performed under Contract Number W-7405-eng-26 for the Atomic Energy Commission at Oak Ridge National Laboratory.

[2] (2) W. E. Bachmann and R. V. Shankland, THIS JOURNAL, **51**, 306 (1929); W. E. Bachmann and J. W. Ferguson, *ibid.*, **56**, 2081 (1934).

[3] (3) J. C. Bailar, Jr., *ibid.*, **52**, 3596 (1930).

[4] (4) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, 1940, pp. 184–206.

[5] (5) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 474–480.

[6] (6) C. J. Collins, THIS JOURNAL, **70**, 2418 (1948).

[7] (7) C. J. Collins, J. G. Burr, Jr., and D. N. Hess, *ibid.*, **73**, 5176 (1951).

[8] (8) C. J. Collins, D. N. Hess, R. H. Mayor, G. M. Toffel and A. R. Jones, *ibid.*, **75**, 397 (1953).

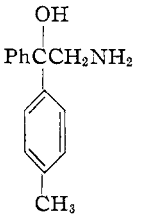
[9] (9) B. M. Benjamin and C. J. Collins, *ibid.*, **75**, 402 (1953).

[10] (10) C. J. Collins, L. S. Ciereszko and J. G. Burr, Jr., *ibid.*, **75**, 405 (1953).

[11] (11) C. J. Collins and B. M. Benjamin, *ibid.*, **75**, 1644 (1953).

Independently, Burr and his co-workers,[12–16] likewise using radioactive carbon, have obtained similar results. Among the most thoroughly studied systems have been those in which the *p*-tolyl and phenyl groups have been in migrational competition. Although the actual value of the *p*-tolyl/phenyl migration ratio may vary over a range of about 1.1 to 16[12,15,17–20] there seems little doubt that the *p*-tolyl group will always migrate in preference to phenyl, provided that the choice of the migrating group is not determined by steric requirements of the molecule,[21] for even in the apparently anomalous rearrangement of diphenyl-*p*-tolylacetaldehyde, we have been able to show[22] that the ratio of *p*-tolyl to phenyl migration is greater than one.

Recently Curtin and Crew[23] studied the deamination of 2-amino-1-phenyl-1-*p*-tolylethanol (I) and found the products II/III, representing the *p*-tolyl/phenyl migration, to be formed in the ratio 1.28 ± 0.09. This rather small value for the deamination reaction, as contrasted with the much higher values for the *p*-tolyl/phenyl migratory abilities in other reactions,[12,15–20] had already been observed by Burr and his co-workers,[13,14] who deaminated 2-phenyl-2-*p*-tolylethyl-1-C^{14} amine (IV) to the carbinols V and VI. The ratio of *p*-tolyl/phenyl migration actually reported by Burr[13,14] was slightly less than one (see also ref. 23). These results were apparently not considered to indicate an actual preference for phenyl over *p*-tolyl migration, since they were employed by Burr[13,14] merely to illustrate the decrease in selectivity between the migratory abilities of these two groups in the deamination reaction.[24]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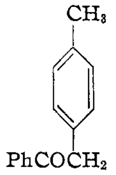
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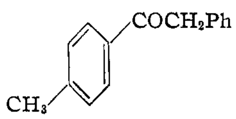
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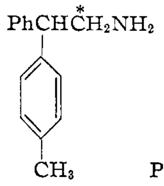
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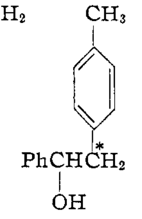
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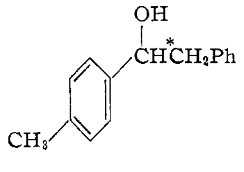
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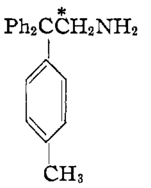
In order to establish whether the different ratios reported by Curtin and Crew[23] and by Burr and his co-workers[13,14] are a reflection of the structural differences of compounds I and IV, we have repeated the nitrous acid deamination of IV, and have determined the ratio of the products V and VI by the carbon-14 dilution method.[25] For comparison, the closely related amine VII has been subjected to the same deamination conditions, and the ratio of the products VIII/IX has been established. The results are summarized in Table I. It can be seen from Table I that the combined yields of carbinols V and VI, from deamination of IV, represent 80–84% of the reaction product. We were unable to identify the remaining 16–20% of material. That this product did not contain a significant amount of 4-methylstilbene was demonstrated, however, by the addition to it of non-radioactive 4-methylstilbene, reisolation of this material, and subsequent radioactivity assay. Similarly, we were unable to obtain the carbinols VIII and IX in quantitative yields. In the deamination product of VII, however, the presence of the olefins X and XI was demonstrated, and in one experiment (no. 5, Table I) the combined yield of VIII and X (corresponding to *p*-tolyl migration) was determined by the dilution technique[25] upon conversion of both the carbinol VIII and the olefin X to 1,1-diphenyl-2-*p*-tolyl-2-bromoethylene (XII). From this experiment the yields of IX plus XI were calculated by difference. The ratio of *p*-tolyl/phenyl migration obtained in this way was 1.24. The combined yields of IX and XI could not be obtained directly because of the complication arising from the existence of *cis* and *trans* isomers of the bromo derivative of olefin XI. In the deamination of compound IV, our inability to account for 16–20% of the reaction product requires some caution in transposing the ratio of the carbinols V/VI into the ratio of the migratory abilities of the *p*-tolyl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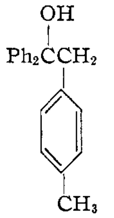
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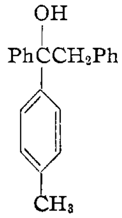
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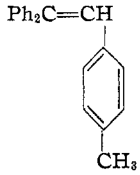
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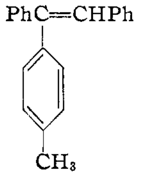
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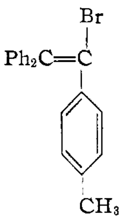
XII

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[12] J. G. Burr, Jr., and L. S. Ciereszko, THIS JOURNAL, **74**, 5426 (1952).

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

[14] P. S. Bailey and J. G. Burr, Jr., *ibid.*, **75**, 2951 (1953).

[15] J. G. Burr, Jr., *ibid.*, **75**, 5008 (1953); **77**, 6721 (1955).

[16] J. G. Burr, Jr., *Chemistry & Industry*, 850 (1954).

[17] R. F. Tietz and W. E. McEwen, THIS JOURNAL, **77**, 4011 (1955).

[18] W. E. McEwen, M. Gilliland and B. I. Sparr, *ibid.*, **72**, 3212 (1950).

[19] S. N. Ege and K. W. Sherk, *ibid.*, **75**, 354 (1953).

[20] Bachmann (ref. 2) reports a *p*-tolyl/phenyl "migratory aptitude" of 16/1 in the rearrangement of symmetrical diphenyl-di-*p*-tolylethylene glycol. This appears to be the largest *p*-tolyl/phenyl migration ratio yet reported, all others (refs. 12–19) lying between 1.1 and 5.0.

[21] See, for example, D. Y. Curtin and co-workers, THIS JOURNAL, **72**, 961 (1950); **73**, 992 (1951); **73**, 3453 (1951); **74**, 5905 (1952); **75**, 6011 (1953).

[22] B. M. Benjamin and C. J. Collins, *ibid.*, **78**, 4329 (1956).

[23] D. Y. Curtin and M. C. Crew, *ibid.*, **76**, 3719 (1954).

[24] In discussions with Dr. Burr, he suggested that an isotope effect in his degradative procedures might account for the apparent *p*-tolyl/phenyl ratio of less than one.

[25] R. H. Mayor and C. J. Collins, THIS JOURNAL, **73**, 471 (1951).

and phenyl groups. This is not true in interpreting the data for the deamination of VII, however, since (a) the ratio of carbinols VIII/IX is invariant, within experimental error, in three different experiments even though the combined yields of VIII and IX vary from 42–74%, and (b) in run 5 (Table I) there is close agreement between the migration ratio calculated from the observed yield of carbinol VIII plus olefin XII. The general accord in the *p*-tolyl/phenyl migratory abilities observed for compounds I,[23] IV and VII, therefore, gives us confidence in the values observed for the deamination of compound IV.

TABLE I

MIGRATION RATIOS OBSERVED IN THE DEAMINATION OF IV AND VII AS DETERMINED BY THE ISOTOPE DILUTION METHOD

Expt.	Amine	Yields, % V	VI	VIII	IX	Total yield of carbinols	Total/phenyl migration ratio
1	IV	45.4	38.8			84.2	1.17[a]
2	IV	43.8	36.6			80.4	1.20[a]
3	VII			26.6	47.2	73.8	1.13[b]
4	VII			15.2	26.6	41.8	1.14[b]
5	VII			15.4[c]	27.4	42.8	1.12[b]
6							1.24[d]

[a] This value was obtained by dividing the yield of V (column 3) by the yield of VI (column 4). [b] This value was obtained by dividing the yield of VIII (column 5) by half the yield of IX (column 6). This is necessary because amine VII contains two phenyls but only one *p*-tolyl group. [c] In this experiment a separate aliquot of the reaction mixture was diluted with non-radioactive carbinol V, and converted to the bromoölefin XII. From the molar radioactivity of XII the combined yields of VIII and X were calculated to be 38.3%. By difference, IX and XI are, therefore, 61.7%. [d] This value was obtained by dividing 38.3 (footnote *c*) by 61.7/2 (footnote *c*).

In order to have an additional check on these data, the deamination product of the amine IV was degraded by the two methods of Ciereszko and Burr.[13] In method A, the mixed carbinols V and VI were oxidized with permanganate to benzoic and terephthalic acids, whereas in method B the mixed carbinols were dehydrated to 4-methylstilbene, which was purified, and then oxidized to benzoic and terephthalic acids; the only difference in our procedure was that: (a) the benzoic acid fractions were isolated and assayed for radioactivity content, and (b) the terephthalic acid fractions were sometimes purified as the methyl ester. The results of these experiments are given in Table II. By inspection of Table II we see that the migration ratios calculated from these data vary over a considerably greater range (1.04–1.29) than do the migration ratios calculated from Table I. This is hardly surprising, however, when we consider: (1) that compounds V and VI are probably not oxidized to benzoic and terephthalic acids in exactly the same yields, (2) that carbinols V and VI do not dehydrate to 4-methylstilbene in identical yields, and (3) that the isotope effect during permanganate oxidation of carbinols V and VI or of 4-methylstilbene may cause a significant lowering in the carbon-14 content of the acids produced.[26]

It is clear, therefore, that the *p*-tolyl/phenyl migration ratio in the deamination of IV and VII is 1.18 ± 0.06.[27] These values are in agreement, within experimental error, with the value of 1.28 ± 0.09 reported by Curtin and Crew[23] in the deamination of 2-amino-1-phenyl-1-*p*-tolylethanol (I). It is interesting that these three different amines should undergo deamination with experimentally indistinguishable *p*-tolyl/phenyl migration ratios, and that this ratio should be considerably smaller than those reported for other reactions.[12,15,17–19] In view of the complicated nature[28] of the amine nitrous acid reaction, the reasons for these results are obscure. Possible explanations have been discussed by Burr,[13,14] by McEwen[17] and by Curtin.[23]

Experimental

2-Phenyl-2-*p*-tolylethylamine-1-C^{14} Hydrochloride (IV).—This compound was prepared by the method of Ciereszko and Burr[13] and was crystallized from acetone–ether mixture; m.p. 236°. The radioactivity assay was 6.569 ± 0.014 mc./mole.

2-Phenyl-1-*p*-tolylethanol (VI).—Benzyl *p*-tolyl ketone,[29] 35 g., was reduced with 3.9 g. of lithium aluminum hydride, to produce 34 g. of a carbinol, m.p. 67–69°. The carbinol was crystallized from hexane; m.p. 68–69°,[30] phenylurethan derivative, m.p. 113–114°.

TABLE II

MIGRATION RATIOS IN THE DEAMINATION OF IV AS DETERMINED BY THE METHOD OF CIERESZKO AND BURR[13]

Expt.	Radioactivity of IV, mc./mole	Compds. oxidized	Radioactivity, mc./mole of Benzoic acid	Terephthalic acid	Total	Migration ratio, *p*-tolyl/phenyl
6	1.862 ± 0.003	Mixture V + VI	0.801 ± 0.002	1.036 ± 0.006	1.837	1.29[a] 1.25[b]
7	1.549 ± .006	Mixture V + VI	.651 ± .002	0.804 ± .006	1.455	1.24[a] 1.08[b]
8	1.549 ± .006	XVab[c]	.732	0.795 ± .005	1.468	1.09[a] 1.05[b]

[a] Ratio calculated by dividing terephthalic acid assay (column 5) by benzoic acid assay (column 4). [b] Ratio calculated by dividing terephthalic acid assay (column 5) by assay of IV (column 1) minus assay of terephthalic acid (column 5). [c] Radioactivity assay, single determination, 1.537 mc./mole.

1-Phenyl-2-*p*-tolylethanol (V).—Phenyl *p*-methylbenzyl ketone,[31] 25 g., was reduced with 3 g. of lithium aluminum hydride in ether. The carbinol was crystallized from ligroin; m.p. 46–48°.

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(26) W. A. Bonner and C. J. Collins, THIS JOURNAL, **75**, 2308 (1953), have discussed the analytical difficulties which result from an isotope effect in the oxidation of a secondary carbinol.

(27) We estimate the experimental error in the determination of the yields reported in Table I to be approximately ±1%. Thus the uncertainty in the yield of V (column 1, Table I) would be expressed as 45.4 ± 0.5%.

(28) A. T. Austin, E. D. Hughes, C. K. Ingold and J. H. Ridd, THIS JOURNAL, **74**, 555 (1952); J. H. Dusenbury and R. E. Powell, *ibid.*, **73**, 3266, 3269 (1951); H. W. T. Taylor, *J. Chem. Soc.*, 1099, 1897 (1928).

(29) H. Strassmann, *Ber.*, **22**, 1229 (1889).

(30) P. Weill and F. Kayser, *Bull. soc. chim.*, [5] **3**, 841 (1936), give m.p. 67–68°; phenylurethan, m.p. 114°.

(31) M. Tiffeneau and J. Levy, *ibid.*, [4] **49**, 1742 (1931).

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.86; H, 7.60. Found: C, 84.92; H, 7.49.

The phenylurethan derivative of the carbinol had a m.p. of 97–98° after four crystallizations from ligroin.

Anal. Calcd. for $C_{22}H_{21}NO$: C, 79.73; H, 6.39. Found: C, 79.71; H, 6.57.

4-Methylstilbene (XV).[32]—This olefin, m.p. 120°, was prepared by dehydrating samples of the carbinols V and VI in boiling, 6 *N* hydrochloric acid.

2,2-Diphenyl-2-*p*-tolylethyl-1-C^{14}-amine Hydrochloride (VII).—Diphenyl-*p*-tolylchloromethane,[33] 30 g., was mixed thoroughly with 9 g. of carbon-14 labeled copper cyanide. The mixture was slowly heated to 200° and was maintained at that temperature for two hours. The reaction mixture was then extracted with acetone to remove organic material. After removing the acetone by evaporation, the thick oily mass was dissolved in hot ethanol. Upon cooling, crystals of diphenyl-*p*-tolylacetonitrile separated. The nitrile was recrystallized from ligroin, m.p. 111°.[34] The nitrile, 15 g., was mixed with 3 g. of lithium aluminum hydride in ether. The reduction was allowed to proceed for two hours while the reaction mixture was boiled. Water was then carefully added to the mixture, the ether layer was separated, and clarified by filtration. After evaporation of the ether, there remained an oil which did not crystallize. The oil was taken up in dry ether and dry hydrogen chloride was passed through it. At first a precipitate formed but this later dissolved when an excess of hydrogen chloride was present. After about 18 hours crystals of the amine hydrochloride separated; these were purified by several crystallizations from tetrahydrofuran–ether mixture to yield a product of m.p. 200° dec. The radioactivity assay was 5.725 ± 0.029 mc./mole.

Anal. Calcd. for $C_{21}H_{22}NCl$: C, 77.88; H, 6.85. Found: C, 77.55; H, 6.91.

2,2-Diphenyl-2-*p*-tolylethylamine Nitrate.—When dilute nitric acid was added to an aqueous solution of the amine hydrochloride, the very slightly soluble amine nitrate separated. The compound was crystallized from acetone–ether mixture, m.p. 233° dec.

Anal. Calcd. for $C_{21}H_{22}N_2O_3$: C, 71.98; H, 6.27. Found: C, 72.33; H, 6.42.

2,2-Diphenyl-2-*p*-tolylethylamine Nitrite.—The amine nitrite salt was prepared by adding a solution of sodium nitrite to a solution of the amine hydrochloride in water at room temperature. The crystalline solid which separated was removed by filtration, washed with water, then with acetone, and finally with ether. The compound melted over a wide temperature range beginning at about 60° and the melt did not solidify again upon cooling.

Anal. Calcd. for $C_{21}H_{22}N_2O_2$: C, 75.42; H, 6.63. Found: C, 75.57; H, 6.63.

1,1-Diphenyl-2-*p*-tolylethanol (VIII).—Ethyl *p*-tolylacetate, 52 g., was added to the Grignard reagent from 100 g. of bromobenzene and 16 g. of magnesium. The reaction complex was hydrolyzed with water and the ether layer was decanted from the granular magnesium hydroxide. The ether was evaporated and the material remaining spontaneously crystallized. This was recrystallized twice (Norite) from ligroin. A 50% yield of the pure carbinol was obtained; m.p. 111°.

1,2-Diphenyl-1-*p*-tolylethanol (IX).—This carbinol was prepared from desoxybenzoin and *p*-tolylmagnesium bromide by the method of Roger and McGregor.[35] It was easily purified by one crystallization from ligroin, m.p. 90°.

Anal. Calcd. for $C_{21}H_{20}O$: C, 87.46; H, 6.99. Found: C, 87.61; H, 6.97.

2,2-Diphenyl-1-*p*-tolyl-1-bromoethylene (XII).—The carbinol VIII, 2.5 g., was dissolved in 60 ml. of glacial acetic acid and the mixture was boiled for a half-hour. To the cooled solution was added 1.5 g. of bromine in 10 ml. of acetic acid. The mixture was heated on the steam-bath for 20 minutes and then boiled until no more hydrogen bromide was evolved. Upon evaporation of the acetic acid, a quantitative yield of the bromide, 3.1 g., melting at 117–119° was obtained. One crystallization from ethanol gave the pure compound, m.p. 120°.

Anal. Calcd. for $C_{21}H_{18}Br$: C, 72.00; H, 5.19. Found: C, 71.59; H, 4.90.

An attempt to prepare 1,2-diphenyl-1-*p*-tolyl-2-bromoethylene[36] in a manner similar to that for XII gave, after ten crystallizations from alcohol, a small quantity of material melting at 125–130°. The residue melted at 105–110°. Upon heating the high melting material with ethanol for five minutes or more the melting point was lowered. It was possible, after continued crystallization of the low-melting material, to obtain more of the high melting material. A separation of the isomers to give a compound for reliable radioactivity assay was not possible.

Rearrangement of the Amines IV and VII.—The following is a description of the techniques used in the rearrangement reactions and yield determinations of the products. The conditions and data for the individual experiment are recorded in Tables III and IV. A solution of 1.504 g. of the hydrochloride of 2-phenyl-2-*p*-tolylethyl-1-C^{14}-amine (IV) was heated to 80° (oil-bath) and a solution of 1.5 g. of sodium nitrite in 60 ml. of water was added. The temperature was maintained at 80° for two hours after which evolution of nitrogen had stopped and the reaction was complete. The oily material was extracted with five 50-ml. portions of ether. The ether was removed by evaporation in a current of air. The residue was dissolved in alcohol and the solution was diluted to the mark in a 250-ml. volumetric flask. After complete homogeneity of the solution was ensured, 100 ml. was removed with a pipet and added to 1.5425 g. of pure 1-phenyl-2-*p*-tolylethanol (V). Another 100 ml. was added to 1.5210 g. of 2-phenyl-1-*p*-tolylethanol (VI). The remaining 50 ml. of solution was quantitatively added to 1.0039 g. of 4-methylstilbene (XV). The three separate solutions just prepared were made homogeneous and the solvent was evaporated from each one. Phenylurethan derivatives were prepared from the two carbinol portions and the phenylurethans were purified by five crystallizations from ligroin. They were then dried *in vacuo* (over Drierite for 18 hours) and assayed for radioactivity. The 4-methylstilbene was crystallized five times from ethanol and assayed for radioactivity. The results are recorded in Table III.

TABLE III

YIELDS OF PRODUCTS FROM THE DEAMINATION OF IV AS DETERMINED BY THE ISOTOPIC DILUTION METHOD

Experiment	1	2
Weight of hydrochloride of IV (grams)	1.5419	1.5040
Radioactivity of IV (mc./mole)	6.569 ± 0.014	5.463 ± 0.013
Experimental conditions	1.75 g. $NaNO_2$ 100 ml. H_2O 1.5 hr. at 80–85°	1.5 g. $NaNO_2$ 160 ml. H_2O 2 hr. at 80°
Aliquot used to determine yields		
V	45/100	2/5
VI	45/100	2/5
Weight of dead carbinol added to aliquot (grams)		
V	1.5768	1.5425
VI	1.4370	1.5210
Radioactivity of diluted carbinol (mc./mole)		
V	0.961 ± 0.001	0.6978 ± 0.0053
VI	.907 ± .002	.6026 ± .0062
Aliquot used to determine yield of XV	1/10	1/5
Weight of dead XV added to aliquot (grams)	0.3870	1.0039
Radioactivity of diluted XV (mc./mole)	.0300 ± 0.0007	0.0156 ± 0.0003

Similarly the hydrochloride of VII was mixed with sodium nitrite and the yields of the product of rearrangement were obtained by radioactivity dilution technique, the data for which are recorded in Table IV. The carbinols VIII and IX were reisolated by crystallization three times from ligroin. No derivatives were made. The aliquot used to determine the combined yield of carbinol VIII and the corresponding olefin X was added to a weighed portion of non-radioactive

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(32) R. Anschütz, *Ber.*, **18**, 1946 (1885).

(33) J. W. Copenhaver, M. F. Ray and C. S. Marvel, THIS JOURNAL, **57**, 1311 (1935).

(34) J. Hoch, *Compt. rend.*, **197**, 770 (1933).

(35) R. Roger and A. McGregor, *J. Chem. Soc.*, 1850 (1934).

(36) C. F. Koelsch, THIS JOURNAL, **54**, 2487 (1932), obtained an isomer melting at 114–116°.

Table IV

Yields of Products from the Deamination of VII as Determined by the Isotopic Dilution Method

Experiment		3	4	5
Weight of hydrochloride of VII (grams)		1.5196	1.5061	1.4379
Radioactivity of VII (mc./mole)		5.725 ± 0.029	5.725 ± 0.029	5.725 ± 0.029
Experimental conditions		0.36 g. $NaNO_2$ 115 ml. H_2O 3 hr. at 83–85°	0.37 g. $NaNO_2$ 130 ml. H_2O 1 hr. at 99°	0.36 g. $NaNO_2$ 130 ml. H_2O 6.5 hr. at 58°
Aliquot used to determine yields	IX	2/5	2/5	2/5
	VIII	2/5	2/5	2/5
Weight of dead carbinol added to aliquot (grams)	IX	2.2281	2.2136	1.6350
	VIII	1.7108	2.0514	1.6012
Radioactivity of diluted carbinol (mc./mole)	IX	0.5902	0.3585 ± 0.0014	0.4539 ± 0.0029
	VIII	.4450	.2269 ± .0012	.2682 ± .0004
Aliquot used to determine yield of VIII + X				1/5
Wt. of dead VIII added to aliquot (grams)				1.0020
Radioactivity of bromide: Derivative of VIII and X (mc./mole)				0.5104 ± 0.0048

VIII. The entire mixture was then treated in exactly the same way as described for the preparation of 1,1-diphenyl-2-*p*-tolyl-2-bromoethylene (XII), above. The bromoölefin was then purified by four crystallizations from ethanol and assayed for radioactivity. It was then calculated from the data of Table IV, experiment 5, that the combined yield of VIII and 1,1-diphenyl-2-*p*-tolyl ethylene (X) is 38.3%. The combined yield of IX and XI, obtained by difference, is 61.7%. This gives a *p*-tolyl/phenyl migration ratio of 1.24 for the rearrangement of VII to produce *both* carbinols (VIII and IX) and olefins (X and XI).

Oxidations.—The residue of mixed carbinols V and VI from the rearrangement of a sample of IV was divided into two portions. One portion was oxidized with potassium permanganate as described by Ciereszko and Burr.[13] The second portion was dehydrated with phosphorus pentoxide and the 4-methylstilbene was also oxidized as described. The benzoic and terephthalic acid fractions from the oxidations were isolated. Benzoic acid was purified by sublimation, m.p. 121.2°. Terephthalic acid was taken up in sodium carbonate solution. The solution was decolorized with Norite while hot and then acidified. The precipitated terephthalic acid was removed from the still hot solution by filtration. It was washed with hot water followed by alcohol and dried. The acid was treated with diazomethane, and the dimethyl ester was purified by crystallization from methanol, m.p. 141°, and assayed for radioactivity. The data are recorded in Table II.

Radiochemical Structure Determination of Compounds V, VII, VIII and IX.—The purified phenylurethan of carbinol V, 1.5 g., which was recovered from the carbon-14 dilution experiment 2, was treated with 5 g. of chromic oxide in acetic acid containing a small quantity of sulfuric acid. After heating the mixture on the steam-bath for 15 minutes, oxidation was complete. The oxidation mixture yielded 116 mg. of terephthalic acid and a small quantity of dark material. The terephthalic acid, after precipitation from sodium carbonate solution, had a radioactivity assay of 0.678 mc./mole. The phenylurethan of carbinol VI from experiment 2 was treated similarly and a very small quantity of terephthalic acid was obtained. This had a radioactivity assay of 0.0095 mc./mole. Carbinol VIII from experiment 3 was oxidized with chromic acid in acetic acid. Benzophenone was recovered and converted to the 2,4-dinitrophenylhydrazone derivative for purification and radioactivity assay. The derivative was non-radioactive. Likewise the 2,4-dinitrophenylhydrazone of 4-methylbenzophenone, obtained by chromic acid oxidation of carbinol IX in experiment 2, was non-radioactive. The rearrangements of compounds IV and VII, therefore, take place essentially without scrambling of the chain carbon atoms.

Analytical Determinations.—Carbon and hydrogen analyses were performed by the Huffman Microanalytical Laboratories, Wheatridge, Colorado. Carbon-14 determinations were carried out as described previously.[6-11]

Oak Ridge, Tennessee

[Contribution from the Merck Sharp & Dohme Research Laboratories, Merck & Co., Inc.]

The Reaction of Epoxides with Anhydrous Hydrogen Fluoride in the Presence of Organic Bases. The Preparation of 9α-Fluoro-4-pregnene-11β,17α,21-Triol 3,20-Dione 21-Acetate and Its 1-Dehydro Analog

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It has been possible to effect the conversion of 9β,11β-epoxy-4-pregnene-17α,21-diol-3,20-dione 21-acetate (I) to 9α-fluoro-4-pregnene-11β,17α,21-triol 21-acetate (II) in 75% yield through the use of anhydrous hydrogen fluoride in organic bases. In this manner the formation of the by-product described by Fried and Sabo is minimized. The analogous 1-dehydro-compound IV was likewise prepared in 75% yield from the corresponding epoxide III. The use of solutions of anhydrous hydrogen fluoride in organic bases, such as tetrahydrofuran, is suggested whenever a source of fluoride ions, soluble in organic media, is required.

In a recent communication[1] Fried and Sabo announced the conversion of 9β,11β-epoxy-4-pregnene-17α,21-diol-3,20-dione 21-acetate (I) to 9α-fluoro-4-pregnene-11β,17α,21-triol-3,20-dione 21-acetate (II) with anhydrous hydrogen fluoride in ethanol-free chloroform solution in about 50% yield. The product was found to be of great pharmacological importance since it possesses about ten times the glucocorticoid activity of hydrocortisone acetate.[1] In addition to II, Fried and Sabo isolated an unsaturated alcohol,[2] isomeric with I, from the hydrofluorination reaction.

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(1) J. Fried and E. F. Sabo, This Journal, **76**, 1455 (1954).

(2) R. P. Graber, C. S. Snoddy, Jr., and N. L. Wendler [*Chemistry and Industry*, 57 (1956)] have recently described the preparation of 17α-hydroxy-8(14)-dehydrocorticosterone acetate or its C_9-epimer by the reaction of I with 60% perchloric acid in chloroform solution at 0°. The characteristics of this unsaturated alcohol were found to be essentially the same as those of the by-product of Fried and Sabo.