[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF STANFORD UNIVERSITY]

The Stereochemistry of Raney Nickel Action. V. Desulfurations and Dehydroxylations in the α-Substituted Phenylacetamide Series Using Deuterized Raney Nickel

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When L(+)-mandelamide was dehydroxylated with deuterized Raney in absolute deuteroethanol, the phenylacetamide obtained was optically inactive. That this inactivity was probably due to an exchange reaction at the α-position was shown by the fact that when stock phenylacetamide was subjected to the same reaction conditions, it took on three D atoms per molecule by exchange. When the latter product was oxidized, the resulting benzoic acid had 1.7 D atoms per molecule, showing that the catalytic action of Raney nickel brought about H–D exchange not only at the α-position, but also in the aromatic nucleus.

Since the desulfuration of optically active sulfones[1] and the dehydroxylation of optically active benzyl alcohols[2] occur without loss of optical activity when accomplished by the action of Raney nickel, it seemed of interest to attempt the preparation of optically active α-deuterophenylacetamide by action of deuterized Raney nickel on optically active α-benzenesulfonylphenylacetamide and/or mandelamide. α-Benzenesulfonylphenylacetamide was prepared by oxidation of the corresponding optically active sulfide, but complete racemization attended the oxidation, a result which accords with the observation[3] that optically active α-benzenesulfonylphenylacetic acid is racemized during recrystallization. Apparently the α-hydrogen on the sulfone is too acidic to permit optical stability.

Attention was next turned to the dehydroxylation of optically active mandelamides. Raney nickel in refluxing ethanol (but not methanol) smoothly converted mandelamide to phenylacetamide. When deuterized Raney nickel and L(+)-mandelamide reacted in refluxing deuteroethanol, the deuterated phenylacetamide obtained proved optically inactive.

The inactivity of the deuterated phenylacetamide was considered probably due to an exchange of the α-hydrogen in the product with deuterium, giving the optically inactive species, Ph-CD$_2$-CONH$_2$. Supporting this hypothesis was the fact that the deuterated phenylacetamide from the mandelamide dehydroxylation was found by mass spectrographic analysis to contain 2.3 D atoms per molecule.

To test this hypothesis further, stock phenylacetamide was subjected to identical reaction conditions using deuterated Raney nickel in refluxing deuteroethanol. The phenylacetamide recovered had an infrared spectrum different from that of the stock starting material, and in a later duplication of this experiment the product was found to contain 3.1 D atoms per molecule.

Since all the above samples of deuterated phenylacetamides contained *more* deuterium than accountable on the basis of exchange involving two α-hydrogens, the location of the excess deuterium in the samples was next sought. When phenylacetamide was merely recrystallized from deuteroethanol a product was obtained showing a different infrared absorption spectrum than that of phenylacetamide, and containing 1.3 D atoms per molecule. When this was recrystallized from ethanol, however, the infrared spectrum was again identical with that of the starting phenylacetamide. Since all of the above deuterated phenylacetamide samples had been recrystallized from mixtures containing ethanol, the likelihood that there was a significant amount of nitrogen bound deuterium in the samples seemed remote.

Accordingly, the above deuterated phenylacetamide sample containing 3.1 D atoms per molecule was hydrolyzed and oxidized to remove the side chain. The resulting benzoic acid showed an infrared pattern significantly different from that of stock benzoic acid, and itself proved mass spectrographically to contain 1.7 D atoms per molecule. This leaves 1.4 D atoms allocatable to the α-position of the deuterated phenylacetamide. Thus the action of deuterized Raney nickel in deuteroethanol on phenylacetamide is not only to catalyze exchange at the α-hydrogen position, but also to effect D–H exchange in the benzene ring itself. The mechanism of this latter process is currently under investigation. Hydrogen–deuterium exchange in aromatic rings under the influence of acidic or basic catalysts is a well investigated phenomenon,[4] but the present observations seem to be the first recorded examples of heterogeneous catalytic exchange processes involving nuclear hydrogen atoms.

H–D exchange, either at the α-hydrogen or in the ring, failed to occur in the absence of the deuterized nickel catalyst. Thus when methyl diphenylacetate was twice refluxed with and recrystallized from deuteroethanol, the recovered product showed an infrared spectrum identical with that of the starting material.

One experiment suggests that the nickel-catalyzed exchange of deuterium for hydrogen in the present system may be subject to a considerable isotope effect. When one of the above deuterated phenylacetamide samples was treated under identical conditions with ordinary Raney nickel in refluxing ethanol, the infrared spectra of the final and starting samples were identical, and the final

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(1) W. A. Bonner, THIS JOURNAL, **74**, 1034 (1952).

(2) W. A. Bonner, J. A. Zderic and G. A. Casaletto, *ibid.*, **74**, 5086 (1952).

(3) W. Piechulek and J. Suszko, *Bull. intern. acad. polonaise, Class Sci., math. nat.*, 455 (1934A); *C. A.*, **29**, 2933 (1935).

(4) A. I. Brodskii, L. L. Chervyatsova and G. P. Miklukhin, *Zhur. Fiz. Khim.*, **24**, 968 (1950); *C. A.*, **46**, 8027 (1952); A. I. Shatenshtein, *Doklady Akad. Nauk* (S.S.S.R), **60**, 1029 (1950); *C. A.*, **44**, 5194 (1950); P. F. Tryon, W. G. Brown and M. S. Kharasch, THIS JOURNAL, **70**, 2003 (1948); W. G. Brown, M. S. Kharasch and W. R. Sprowls, *J. Org. Chem.*, **4**, 442 (1939); M. S. Kharasch, W. G. Brown and J. McNab, *ibid.*, **2**, 36 (1937); C. K. Ingold, C. G. Raisin and C. L. Wilson, *J. Chem. Soc.*, 915 (1936); A. Klit and A. Langseth, *Z. physik. Chem.*, **A176**, 65 (1936).

product proved still to contain 2.4 D atoms per molecule. Deuterium is thus apparently introduced more readily than it is removed by the action of Raney nickel on the compounds under study.

Experimental

2-Phenylmercaptophenylacetic Acid.—A mixture of thiophenol (33 g., 0.3 mole) and mandelic acid (15.2 g., 0.1 mole) was refluxed for three hours, then steam distilled to remove unreacted thiophenol. The residue was extracted with ether, and the extract was dried over anhydrous sodium sulfate, then decolorized with Norit. Solvent removal left 19.9 g. (82%) of amber sirup. This was readily crystallized from a mixture of benzene (25 ml.) and ligroin (70 ml.), giving 14.5 g. of product, m.p. 96.5–98°. Two further recrystallizations gave a sample of m.p. 98–100°. The above is essentially the procedure of Arventi and Robu-Burnuz,[5] who report an m.p. of 101–102° for 2-phenylmercaptophenylacetic acid.

2-Phenylmercaptophenylacetic Acid from D(−)-Mandelic Acid.—Thiophenol (10 ml.) and D(−)-mandelic acid (2.0 g.), $[\alpha]^{25}\mathrm{D}$ −150.0° (H_2O) were refluxed for 3.5 hours, and the resulting crude product was isolated as above, 2.45 g. of sirup (77%) having $[\alpha]^{25}\mathrm{D}$ −9.25° (*c* 2.27, 1:1 chloroform: ethanol). This was recrystallized twice from a benzene–ligroin mixture to give 0.12 g. of solid, m.p. 130°, mixed m.p. with D(−)-mandelic acid (of m.p. 132–133°) undepressed, $[\alpha]^{26}\mathrm{D}$ −138.5° (*c* 0.57, water). The mother liquors were evaporated, and the residue was recrystallized twice from a benzene–ligroin mixture and once from 50% acetic acid, giving pure 2-phenylmercaptophenylacetic acid, 0.38 g., m.p. 103.5°, optically inactive in 1:1 chloroform–ethanol solution. This experiment indicates that the reaction is not complete in a 3.5-hour period of refluxing even with a large excess of thiophenol, and that the reaction proceeds with racemization.

2-Phenylmercaptophenylacetamide.—2-Phenylmercaptophenylacetic acid (4.0 g.) was refluxed with thionyl chloride (30 ml.) for 1.5 hours, whereupon the excess thionyl chloride was removed *in vacuo*. The residue was slowly added to chilled ammonium hydroxide, and the resulting solid was extracted into a mixture of benzene and ethyl acetate. The extract was washed, dried, and the solvent was evaporated to *ca.* 60 ml., when copious crystallization commenced in the hot. The mixture was cooled and the white solid collected, 2.5 g., m.p. 174.5–175°. The filtrate was evaporated, and the residue was crystallized from an acetone–ligroin mixture giving 0.50 g. of product, m.p. 171.5–172.5°, total yield 75%. After three recrystallizations from acetone and ligroin the pure amide had m.p. 174.5–175°.

Anal. Calcd. for $C_{14}H_{13}ONS$ (243.3): C, 69.10; H, 5.38; N, 5.76; S, 13.16. Found: C, 69.12, 69.20; H, 5.35, 5.44; N, 5.88; S, 12.97.

2-Benzenesulfonylphenylacetamide.—The above amide (1.5 g.) was dissolved in acetic acid (30 ml.). Thirty per cent. hydrogen peroxide (5 ml.) was added, and the mixture was heated at 100° for 30 minutes. Another 5 ml. of hydrogen peroxide was added, and heating continued during an additional 30 minutes. The product began to crystallize from the reaction mixture after the first 10 minutes of heating. On completion, the mixture was cooled, diluted with water, and the product was filtered and rinsed. The dried solid, fine, white needles weighed 1.70 g. (100%) and had m.p. 271–272° on a Fisher block. The material was too insoluble in the common organic solvents to permit recrystallization. It was accordingly purified by leaching with boiling acetone and filtering hot, m.p. 273° (Fisher block).

Anal. Calcd. for $C_{14}H_{13}O_3NS$ (275.3): C, 61.10; H, 4.76; N, 5.09; S, 11.64. Found: C, 61.22, 61.12; H, 4.72, 4.80; N, 5.21; S, 11.55.

2-Benzenesulfinylphenylacetamide.—2-Phenylmercaptophenylacetamide (0.5 g.) was dissolved in acetic acid (25 ml.) at 25°, and 30% hydrogen peroxide (2 ml.) was added. The mixture stood at 25° for 1.25 hours, then was thrown into water (salted and chilled to 0°). The clear solution rapidly produced white crystals, 0.3 g. These were recrystallized from a mixture of acetone and ligroin to give a product of m.p. 190°, unchanged on two further recrystallizations.

Anal. Calcd. for $C_{14}H_{13}O_2NS$ (259.3): C, 64.80; H, 5.06; S, 12.38. Found: C, 64.65, 64.76; H, 5.11, 5.16; S, 12.20.

Desulfuration of 2-Phenylmercaptophenylacetamide and 2-Benzenesulfonylphenylacetamide.—2-Phenylmercaptophenylacetamide (0.50 g.) and Raney nickel (*ca.* 8 g.) were heated in refluxing ethanol (25 ml.) for five hours. The mixture was filtered, the residue washed well with ethanol, and the filtrate was evaporated to dryness. The residue (0.19 g.; 68%) was recrystallized twice from a mixture of ethanol (0.5 ml.) and ligroin (5 ml.) to give a sample of phenylacetamide having m.p. 155–156° and showing no m.p. depression when mixed with an authentic sample.

2-Benzenesulfonylphenylacetamide (0.80 g.) was desulfurated in the above fashion, giving 0.32 g. (72%) of crude phenylacetamide. Recrystallization from an ethanol–ligroin mixture gave a sample of m.p. 155.5–156.5°, undepressed with the stock compound.

(+)-2-Phenylmercaptophenylacetic Acid.—Phenylmercaptophenylacetic acid (38.1 g.) and anhydrous brucine (61.5 g.) were dissolved in hot benzene (150 ml.). On cooling, 41.1 g. of salt was obtained. After five systematic recrystallizations from benzene 19.3 g. of brucine salt having $[\alpha]^{25}\mathrm{D}$ +55.4° (*c* 2.64, 1:1 chloroform–ethanol) resulted, and the mother liquors produced on standing an additional 3.1 g. of salt having $[\alpha]^{25}\mathrm{D}$ +54.8° (*c* 1.94). Piechulek and Suszko[3] gave 55° for the specific rotation of the brucine salt of (+)-2-phenylmercaptophenylacetic acid. The 22.4 g. of salt above was suspended in benzene (100 ml.), and the suspension was shaken with dilute (1:3) sulfuric acid (100 ml.). The aqueous layer was rewashed with benzene, and the combined benzene solutions were dried and evaporated to give 7.4 g. (87%) of clean, white product, m.p. 127.5–128.5°, $[\alpha]^{25}\mathrm{D}$ +201° (*c* 1.58, 1:1 chloroform–ethanol). The literature reports[3] m.p. 129–130° and $[\alpha]^{18}\mathrm{D}$ +216° for the optically pure product. The present sample thus appears about 97% optically pure, and was used without further resolution.

(+)-2-Phenylmercaptophenylacetamide.—The above resolved acid (5.0 g.) was converted *via* its acid chloride to the amide in the manner described above for preparation of racemic 2-phenylmercaptophenylacetamide. The crude product (4.2 g.; 84%) was recrystallized twice from acetone to give the pure product, m.p. 202–202.5°, $[\alpha]^{25}\mathrm{D}$ +193.0° (*c* 0.773, acetone). From the mother liquors an additional quantity of product was obtained, m.p. 199–200.5°, $[\alpha]^{25}\mathrm{D}$ +191.5° (*c* 0.543, acetone).

Anal. Calcd. for $C_{14}H_{13}ONS$ (243.3): C, 69.10; H, 5.38; N, 5.76. Found: C, 69.15, 69.16; H, 5.20, 5.39; N, 5.72.

Oxidation of (+)-2-Phenylmercaptophenylacetamide.—The above dextrorotatory amide (1.5 g.) was dissolved in acetic acid (25 ml.) and oxidized with a total of 12 ml. of 30% hydrogen peroxide at 100° in the manner described above for the racemic analog. The product, 1.6 g. (95%) of fine needles, had m.p. 270–271° (Fisher block) and was optically inactive in 0.1% solution in acetic acid. It gave no mixed melting point depression with racemic 2-benzenesulfonylphenylacetamide of m.p. 273°. The present oxidation thus proceeds with racemization.

Optically Active Mandelamides.—Ethyl L(+)-mandelate, $[\alpha]^{25}\mathrm{D}$ +129.5° (*c* 1.44, chloroform), and ethyl D(−)-mandelate, $[\alpha]^{25}\mathrm{D}$ −133° (*c* 1.57), were prepared in practically quantitative yield by Fischer esterification of L(+)-, $[\alpha]^{25}\mathrm{D}$ +150.0° (water), and D(−)-mandelic, $[\alpha]^{25}\mathrm{D}$ −150.5° (water), acids. These esters were ammonolyzed by dissolving in absolute ethanol, adding excess liquid ammonia, and permitting the mixture to stand over Dry Ice in a Dewar flask for several days. Solvent evaporation and recrystallization of the residues from benzene gave samples of L-(+)- and D(−)-mandelamides having m.p.'s of 122–122.5° and specific rotations (25°), respectively, of +69.0° (*c* 2.09, acetone) and −76.6° (*c* 1.29, acetone). Freudenberg and Markert[6] give $[\alpha]^{18}\mathrm{D}$ −74.0° (acetone) for the specific rotation of D(−)-mandelamide.

Dehydroxylation of D,L-Mandelamide.—The racemic amide (0.5 g.) was treated with Raney nickel (*ca.* 4 g.) which had been rinsed several times with purified dioxane. The mixture was placed in ethanol (25 ml.) and refluxing continued for five hours. The catalyst was filtered and

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(5) B. I. Arventi and M. Robu-Burnuz, *Ann. sci. univ. Jassy, Sect. I*, **26**, 602 (1940); *C. A.*, **35**, 3239 (1941).

(6) K. Freudenberg and L. Markert, *Ber.*, **58**, 1759 (1925)

rinsed, and the filtrate evaporated to dryness, leaving 0.50 g. (89%) of crude product. This was recrystallized from a mixture of ethanol (1 ml.) and ligroin (12 ml.), giving 0.30 g. of pure phenylacetamide, m.p. 157.5–158°, undepressed when mixed with an authentic sample.

When the above reaction was repeated using methanol as solvent during a six-hour refluxing period, the recrystallized product had m.p. 132–136° (preliminary sintering). Since the starting material had m.p. 132–133°, it appeared as though little reaction occurred with methanol as solvent.

Deuterized Raney Nickel.—Ordinary Raney nickel (*ca.* 40 g.) in ethanol was filtered free of solvent on a sintered funnel, then rinsed four times with purified dioxane, stirring well and sucking approximately dry with each rinse. 99+% heavy water (25 ml.) was added to the catalyst, the mixture was stirred, the funnel was stoppered well, and equilibration was allowed to proceed for 2.5 days. The D_2O was sucked away, and the residue was suspended in an additional 25 ml. of fresh D_2O. After standing for one week the D_2O was again removed, and the catalyst was rinsed three times on the funnel with purified dioxane, then stored under purified dioxane until use (preparation **1**).

A later preparation (preparation 2) of deuterized Raney nickel was conducted in the same way, except that the D_2O from the above preparation was used for the first two equilibration rinses, and the catalyst was given a third equilibration in fresh 99+% D_2O. This sample was allowed to stand in contact with its third equilibration rinse until used, when it was sucked dry and rapidly washed once with purified dioxane. The above equilibration procedures are essentially those of Khan.[7]

Absolute Deuteroethanol.—Sodium (23 g.) was converted to "dust" by vigorous shaking in hot xylene. The xylene was decanted from the cooled product, and the sodium was washed with 400 ml. of dry ether in six or seven portions. The sodium was transferred, using 250 ml. of dry ether, to a three-necked flask equipped with stirrer, dropping funnel and calcium chloride protected reflux condenser, and containing glass beads. Ethanol (46 g., 1 mole) mixed with dry ether (60 ml.) was added dropwise with vigorous stirring to the sodium suspension at such a rate that gentle refluxing was maintained. After the addition, the mixture was stirred under reflux for an hour, after which 99+% heavy water (20 g., 1 mole) was added dropwise with vigorous stirring. The mixture was allowed to stir overnight, when the ether was distilled from the mixture with vigorous stirring. The ether-free residue was heated at 1 mm. pressure with a free flame, condensing all of the liquid so distilled in a liquid nitrogen cooled trap. Fifty ml. of liquid was so obtained. The above reaction was duplicated exactly on a twofold scale, when the combined quantity of crude deuteroethanol was 125.2 g. The ether distillates from the above were combined, filtered and distilled through an 18-inch glass spiral column. The residue (3.0 g.) was combined with the above crude deuteroethanol, giving a total yield of 128.2 g. (91%). The crude product was distilled again through the 18-inch spiral column. After a 12-ml. forerun (b.p. 34–77.5°), the remainder of the sample had b.p. 77.5–78°. A portion of the 77.5° distillate was found to have $d^{20}{}_{4}$ 0.820; a portion of the 78° distillate had $d^{20}{}_{4}$ 0.822. The combined product weighed 119.0 g. (85%) and had $n^{26}\mathrm{D}$ 1.3670. Mass spectrographic analysis of the water obtained by combustion of this deuteroethanol, conducted as described below, indicated it to contain 18.8% by weight of D_2O. This corresponds to 1.02 D atoms per molecule; theoretical, 1.00. For deuteroethanol $d^{25}{}_{4}$ has previously been reported as 0.801[8] and 0.8033.[9]

Deuterium Assays.—Deuterium contents of the products from reactions involving deuterized Raney nickel were determined as follows. Approximately 20 mg. of the compound to be assayed was placed in a combustion boat and burned to CO_2 and water in the customary semi-micro combustion line.[10] The combustion gases were lead directly from the combustion tube into a small U-tube equipped with two stopcocks, and the combustion water was condensed by surrounding this U-tube with ice. When combustion was complete the stopcocks were closed and the U-tube was disconnected and attached directly to a Model 21-401 Mass Spectrometer (Consolidated Engineering Corporation, Pasadena, California). The U-tube was evacuated into the spectrometer several times, then permitted to stand about 30 minutes when the 20- and 18-peak heights were measured. This process was repeated several times, until the 20/18 ratio was constant, when the weight % D_2O in the combustion water was calculated. To test the accuracy of the method, a carefully weighed "synthetic" mixture containing 25.80% D_2O and 74.20% H_2O was furnished, composition unknown, to the analyst. Found composition: D_2O, 25.74; H_2O, 74.26. The mass spectrographic data were furnished by Dr. H. Eding of Standard Research Institute.

Dehydroxylation of L(+)-Mandelamide with Deuterized Raney Nickel.—The above (+)-amide (0.75 g.) was placed in a flask with *ca.* 6 g. of deuterized Raney nickel (preparation 1) which had been filtered free of dioxane and rinsed once with deuteroethanol. The mixture was covered with deuteroethanol (35 ml.), protected with a calcium chloride tube, and refluxed during five hours. The catalyst was filtered and rinsed twice with hot deuteroethanol. The solvent was recovered from the filtrate by distillation, and the residue was vacuum-dried, 0.57 g. The product was recrystallized from a mixture of 2.5 ml. of ethanol and 14 ml. of ligroin, giving 0.48 g. of product having m.p. 159.5–160.5° and showing no detectable optical activity in a 4-dcm. tube (*c* 2.60, acetone). Combustion of the product gave water containing 27.6% D_2O, indicating that the substance possessed 2.3 D atoms per molecule.

When the above reaction was repeated with preparation 2 deuterized nickel and D(−)-mandelamide during a 25-minute refluxing period, it was found that dehydroxylation was incomplete. The specific rotation of the crude product corresponded to that expected for approximately 30% unreacted D(−)-mandelamide.

Deuterized Raney Nickel on Phenylacetamide. Run 1.—Phenylacetamide (1.00 g.), deuterized Raney nickel (*ca.* 6 g., preparation 1) and deuteroethanol (35 ml.) were refluxed under $CaCl_2$ protection for five hours, when the product (0.92 g.) was isolated as described above. A portion (0.45 g.) of this was recrystallized from an ethanol–ligroin mixture giving 0.25 g. of pure material, m.p. 157.5–158.5°, which showed an infrared spectrum identical with that of the deuterated phenylacetamide obtained above, and slightly different than that of stock phenylacetamide. The purified product was dissolved in a little ethanol, and the solution was diluted with water and strongly acidified (H_2SO_4), then refluxed overnight to effect hydrolysis of the amide. The product, recovered by continuous ether extraction, was then oxidized with alkaline potassium permanganate solution, giving 0.25 g. of benzoic acid, m.p. 122–122.5°. The infrared spectrum of this product showed marked dissimilarities with that of stock benzoic acid, suggesting the presence of ring-bound deuterium.

Run 2.—Deuterized Raney nickel of preparation 2 (*ca.* 7 g.) was rinsed with purified dioxane on a sintered funnel, then placed in deuteroethanol (25 ml.) with phenylacetamide (1.00 g.). After a reflux period of five hours the 0.90 g. of crude product was isolated as before. Recrystallization from the usual ethanol–ligroin mixture gave a product whose infrared spectrum was identical with that of the above deuterated phenylacetamide samples, and which was found mass spectrographically to contain 3.1 D atoms per molecule (weight per cent. D_2O in combustion water, 36.9). The product was next hydrolyzed and oxidized to benzoic acid in the manner described under run 1 above. The acid obtained showed an infrared spectrum identical with that of the deuterated benzoic acid above, and was found to contain 1.7 D atoms per molecule (combustion water, 30.6% D_2O).

Ordinary Raney Nickel on Deuterophenylacetamide.—A portion (0.45 g.) of the product from run 1 above was heated for five hours with ordinary Raney nickel (*ca.* 6 g.) in refluxing ethanol (40 ml.). The crude product (0.38 g.) was isolated as usual, when recrystallized to give a pure product of m.p. 158–158.5°. This material showed an infrared spectrum identical with that of the starting product and was found to contain 2.4 D atoms per molecule (combustion water, 28.8% D_2O). This ordinary Raney nickel was incapable, under identical conditions, of catalyzing the removal of deuterium from deuterated phenylacetamide.

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(7) N. A Khan, THIS JOURNAL, **74**, 3021 (1952).

(8) T. L. Chang and Y. C. Wei, *Science Repts. Ntl. Tsing Hua Univ., Ser. A*, **4**, 451 (1947); *C. A.*. **42**, 7236 (1948).

(9) E. de Salas and C. L. Wilson, *J. Chem. Soc.*, 319 (1938).

(10) L. F. Fieser. "Experiments in Organic Chemistry," D. C. Heath and Co., New York, N. Y., 1941, p. 465 ff.

Deuteroethanol and Phenylacetamide.—One-half gram of phenylacetamide was dissolved in deuteroethanol (4 ml.) and the mixture was refluxed for two hours, then diluted with ligroin. The crystalline product was filtered, rinsed with ligroin and dried *in vacuo* over phosphoric anhydride. It was found to contain 1.3 D atoms per molecule (combustion water, 16.1% D$_2$O). This product was next recrystallized from ordinary ethanol, heating for 15 minutes prior to crystallization. The infrared spectrum of the product was now identical with that of stock phenylacetamide, indicating the removal of N-bound deuterium.

Deuterized Raney Nickel on Methyl Benzyl Ketone.—Deuterized nickel (preparation 2, *ca.* 7 g.), methyl benzyl ketone (2.5 ml.) and deuteroethanol (25 ml.) were mixed and the mixture was refluxed for 13 hours. The crude product was isolated as usual, then purified by distillation. The purified product was found to contain 2.35 D atoms per molecule (combustion water, 21.2% D$_2$O). Its infrared spectrum contained no carbonyl band, and showed only minor differences from the spectrum of methylbenzylcarbinol. A portion of the product was oxidized as usual with alkaline permanganate. The benzoic acid obtained had an infrared spectrum identical with that of stock benzoic acid, suggesting no significant amount of ring-bound deuterium.

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Electrophilic Substitution by Hydrogen in the Xylenes. The Kinetics of Acid Cleavage of the Trimethylsilylxylenes

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Pseudo first-order rate constants for the cleavage of the six isomeric trimethylsilylxylenes by *p*-toluenesulfonic acid in acetic acid have been determined at 25°. The reactions were followed by a dilatometric method. Although the cleavage reactions parallel usual electrophilic substitutions, they are considerably influenced by buttressing and steric strain effects. The order of increase in the rate of acid cleavage for the trimethylsilylxylenes is (R = trimethylsilyl): 5-R-*m*-xylene < 4-R-*o*-xylene < 2-R-*p*-xylene < 3-R-*o*-xylene < 4-R-*m*-xylene < 2-R-*m*-xylene. A plot of the logarithms of the rate constants for each of the cleavage reactions *vs.* the logarithms of the partial relative rate factors for the corresponding positions in the xylenes derived from halogenation and nitration data yields a good linear relationship. This general cleavage technique is thus indicated to be a reliable method for determining the relative rates of electrophilic substitution by hydrogen at a particular position in an aromatic ring.

A direct determination of the rate of electrophilic substitution in benzene at positions *meta* to powerful electron-releasing groups is difficult because of the preponderance of *ortho-* and *para*-substitution. The usual approach in such cases involves either a laborious separation of isomers to determine the *o–m–p* ratios, or the useful procedures of Ingold, *et al.*,[1a,b,c] in which the rate of substitution for each position in a monosubstituted[1] or polymethylsubstituted[2] benzene relative to that for any position in benzene can be calculated.

Another approach to this problem of determining relative rates of substitution at different positions in substituted benzenes has been utilized by Corwin and Naylor[3] who studied the kinetics of the acid cleavage of diphenylmercury. These authors reversed the usual electrophilic process and essentially carried out an *electrophilic substitution by hydrogen.* They pointed out that it was thus possible to isolate a particular position in a substituted benzene nucleus for the determination of its susceptibility toward electrophilic attack by "tagging" that position with the mercury moiety.[3a] Since electrophilic substitution in the xylenes was of considerable interest in the present study, an approach analogous to that employed by Corwin and Naylor was sought. It was hoped thereby to obtain useful quantitative data which might possibly be correlated with the presently accepted concepts of aromatic electrophilic substitution, and with existing data on the xylenes and their derivatives.

In the present study, the cleavage of mercury–carbon bonds was not considered suitable because of the probability of too rapid rates of cleavage, limited choice of cleaving acid[3] and the possibility of complications due to unusually large steric effects. Instead, the cleavage of the silicon–carbon bond appeared to be the reaction of choice. The silicon atom has smaller steric requirements than mercury, and steric effects should therefore be lessened. The silicon atom, having the characteristics of a metalloid, is cleaved by acids from aromatic nuclei with varying ease, depending upon the electron-releasing ability of the substituent present on the ring.[4a,b] For example, *p*-methoxyphenyltrimethylsilane is cleaved by hydrogen chloride in refluxing acetic acid much more readily than *p*-chlorophenyltrimethylsilane. Anisole and chlorobenzene, respectively, are the products of such cleavages, the silicon fragment being released as trimethylchlorosilane.[4a,b]

Experimental

Trimethylsilylxylenes.—All the trimethylsilylxylenes were prepared by the reaction of the appropriate xylyllithium compound and trimethylchlorosilane in the usual manner.[5] Color Test I[6] was used to indicate completion of reaction. In most cases, the xylyllithium intermediates were quite insoluble, and it was necessary to add a fairly large volume of ether in order to obtain efficient stirring.

Upon completion of the coupling, the reaction mixture was filtered through a glass wool plug. The filtrate was

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[1] (a) M. L. Bird and C. K. Ingold, *J. Chem. Soc.*, 918 (1938); (b) C. K. Ingold and M. S. Smith, *ibid.*, 905 (1938); (c) C. K. Ingold, A. Lapworth, E. Rothstein and D. Ward, *ibid.*, 1959 (1931).

[2] F. E. Condon, THIS JOURNAL, **70**, 1963 (1948).

[3] A. H. Corwin and M. A. Naylor, *ibid.*, **69**, 1004 (1947).

[3a] ADDED IN PROOF.—W. M. Schubert and co-workers also have measured the rate of electrophilic substitution by hydrogen in some highly hindered aldehydes, ketones, and acids; see THIS JOURNAL, **76**, 9 (1954), for pertinent references.

[4] (a) R. A. Benkeser and H. R. Krysiak, *ibid.*, **75**, 4528 (1953); (b) H. Gilman and F. J. Marshall, *ibid.*, **71**, 2066 (1949).

[5] For the preparation of organolithium compounds, see R. G. Jones and H. Gilman, "Organic Reactions," Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951, p. 352.

[6] H. Gilman and F. Shultz, THIS JOURNAL, **47**, 2002 (1925).