4,4′-Difluorodiphenylmethane.—A mixture of 1.22 g. (0.01 mole) of iodine, 3.5 g. (0.113 mole) of red phosphorus, and 100 ml. of glacial acetic acid was allowed to stand at room temperature for thirty minutes. Then 1.22 ml. of water and 7.0 g. (0.034 mole) of 4,4′-difluorobenzhydrol were added, and the resultant mixture was refluxed forty-four hours then filtered into 300 ml. of cold 2.5% sodium bisulfite solution to yield a tan oil which crystallized upon being seeded.[7] After one recrystallization from ethanol, the difluorodiphenylmethane occurred as 4.88 g. (75% of the theoretical) of white prisms, m. p. 27–29°. Several recrystallizations from petroleum ether (b. p. 30–60°) raised the melting point to 28.5–29.5°.

Anal. Calcd. for $C_{13}H_{10}F_2$: C, 76.46; H, 4.94; mol. wt., 204. Found: C, 76.90; H, 5.19; mol. wt. (Rast), 206.

4,4′-Difluoro-3,3′-dinitrodiphenylmethane.—One gram of the fluorophenylmethane was dissolved in 8 g. of concd. nitric acid (d. 1.50) with external cooling. This was poured into ice water and the resultant solid filtered and recrystallized; pale-yellow needles from glacial acetic acid, m. p. 177.5–178.5° (constant).

Anal. Calcd. for $C_{13}H_8N_2O_4F$: C, 53.07; H, 2.74. Found: C, 53.26; H, 2.94.

Oxidation of 4,4′-Difluorodiphenylmethane.—One gram of the above methane was mixed with 5 g. of chromic anhydride and 30 ml. of glacial acetic acid and refluxed five hours. Processing in the usual manner afforded 0.9 g. (83% of the theoretical) of colorless prisms of 4,4′-difluorobenzophenone from ligroin, m. p. 106–108°. Neither this compound nor its 2,4-dinitrophenylhydrazone, m. p. 196–198°, resulted in depression when melted with authentic samples.

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(7) Crystallizes with extreme difficulty unless seeded.

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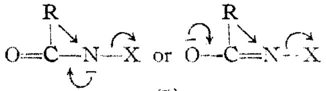
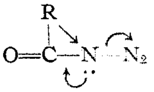
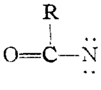
Some Observations on the Hofmann, Lossen and Curtius Rearrangements

BY CHARLES R. HAUSER AND SIMON W. KANTOR

The univalent nitrogen radical (III) has often been represented as an intermediate in the Hofmann–Lossen and Curtius types of rearrangements of (I) and (II), respectively. If (III) had an appreciable life period it might be expected to add the elements of water to form a hydroxamic acid as well as undergo rearrangement. Radicals similar to (III) from the decompositions of hydrazoic acid[1] and phenyl azide[2] and the divalent carbon radical from diazoacetic ester[3] appear to add water readily. However, N-bromobenzamide (I, R = C_6H_5, X = Br) and benzazide (II, R = C_6H_5) undergo rearrangement in the presence of water without producing a detectable amount of benzhydroxamic acid (see experimental). Therefore the elimination of X^- from (I) and of N_2 from (II) is probably accompanied by the essentially simultaneous migration of R to form directly the isocyanate.


(I)


(II)


(III)

The relative rates of elimination of the anion X^- (substituted carboxylate anion) from anion (I) in the Lossen rearrangement have previously been shown to decrease as the eliminated anion X^- is made progressively a stronger base.[4] We have found that, at least under the usual conditions, the elimination and the rearrangement fail with the anion of benzhydroxamic acid ethyl ester, $(C_6H_5CONOC_2H_5)^-$, which would have to eliminate the more strongly basic ethoxide ion. Thus, the elimination of a weaker base than the anion (I) appears to be required for the rearrangement to be realized, the main driving force apparently being the formation of the weaker base. However, the rearrangement of the ethyl ester, $C_6H_5CONHOC_2H_5$, as well as of benzhydroxamic acid may be effected thermally especially in the presence of acids[5] which facilitate the removal of X with its bonding pair of electrons.

Experimental

Rearrangement of N-Bromobenzamide.—N-Bromobenzamide (1.0 g., 0.005 mole), m. p. 128–129°,[6] was dissolved in 110 ml. of approximately 1.0 *N* sodium hydroxide and the solution allowed to stand at room temperature for two hours. The reaction mixture, a drop of which gave a negative test for active bromine with a solution of potassium iodide, acetic acid and starch, was acidified with iced hydrochloric acid. To one ml. of this solution was added several drops of 2% ferric chloride solution, failing to produce the red-violet color characteristic of hydroxamic acids.[7] The remainder of the acidified solution was heated on a water-bath for one hour, made basic and aniline isolated; m. p. of the benzenesulfonamide, 111–112°.[8]

In a blank experiment, benzhydroxamic acid (0.001 g.), m. p. 129–131°,[9] was treated with alkali as described above. One ml. of the acidified solution gave a positive ferric chloride test for the hydroxamic acid, as did a ml. of the solution after it had been diluted with 3 ml. of water, showing that as little as 0.025% of benzhydroxamic acid is detectable.

Rearrangement of Benzazide.—Benzazide (1.0 g., 0.007 mole), m. p. 29–30°,[10] was heated with 110 ml. of water on a steam-bath for one-half hour. Decomposition accompanied by the evolution of nitrogen started at 40° and was very rapid at 70°. The evolution of nitrogen was over after fifteen minutes. The mixture was cooled and filtered. The filtrate after acidification gave a negative test for hydroxamic acid with ferric chloride. Diphenylurea, m. p. 237–239° after one recrystallization from alco-

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(1) Schmidt, *Ber.*, **57**, 704 (1924).

(2) Bamberger, *Ann.*, **443**, 192 (1925); see also Sidgwick, "The Organic Chemistry of Nitrogen," Oxford University Press, London, England, 1942, p. 369.

(3) Bredig and Fränkel, *Z. Elektrochem.*, **11**, 525 (1905).

(4) Bright and Hauser, THIS JOURNAL, **61**, 618 (1939).

(5) Waldstein, *Ann.*, **181**, 384 (1876).

(6) Hauser and Renfrow, THIS JOURNAL, **59**, 121 (1937).

(7) Feigl, "Spot Tests," Elsevier Publishing Co., Inc., New York, N. Y., 1946, p. 355.

(8) Shriner and Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1940, p. 193.

(9) Hauser and Renfrow, "Organic Syntheses," John Wiley and Sons, New York, N. Y., 1943, Coll. Vol. II, p. 67.

(10) Barrett and Porter, THIS JOURNAL, **63**, 3434 (1941).

hol (reported m. p. 238–239°),[11] was obtained as the sole product.

The hydroxamic acid is stable under the conditions of the experiment since a positive test with ferric chloride was obtained with a solution of benzhydroxamic acid (0.001 g.) in 50 ml. of water which had previously been heated on the steam-bath for one half hour.

Failure of the Ethyl Ester Derivative to Rearrange.—Benzhydroxamic acid ethyl ester, m. p. 62–63°,[6] was recovered unchanged when dissolved in sodium hydroxide as described above for bromobenzamide. No trace of aniline could be detected even with such a sensitive test for aniline as calcium hypochlorite.[12]

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[11] Young and Clark, *J. Chem. Soc.*, **73**, 367 (1898).

[12] Elvove, *Chem. Zentr.*, **89**, I, 1074 (1918).

CONTRIBUTION FROM THE
DEPARTMENT OF CHEMISTRY
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A Synthesis of β-(3,4,5-Trimethoxyphenyl)-propionic Acid[1]

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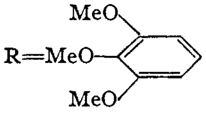
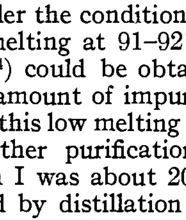
β-(3,4,5-Trimethoxyphenyl)-propionic acid, IV, a compound with possible synthetic applications in the colchicine series, has been previously synthesized in a variety of ways.[2,3,4] The best of these[4] involves the reduction of II to 3,4,5-trimethoxybenzaldehyde, condensation of the aldehyde with diethyl malonate, and catalytic hydrogenation to yield IV. The present communication describes a three-step sequence from I to IV involving conversion of II to 3,4,5-trimethoxypropiophenone, III, followed by a Willgerodt–Kindler reaction to yield IV. Although the overall yield is lower (24–28%) than is obtained by the previously published method[4] (about 40%), the steps are simple and require neither the purification of intermediates nor the preparation of catalysts.

$$\underset{\mathrm{I}}{\mathrm{RCOOH}} \longrightarrow \underset{\mathrm{II}}{\mathrm{RCOCl}} \longrightarrow \underset{\mathrm{III}}{\mathrm{RCOCH_2CH_3}} \longrightarrow \underset{\mathrm{IV}}{\mathrm{RCH_2CH_2COOH}}$$



The over-all yield of this synthesis fell short of anticipations mainly because of an unexpected complication in the reaction of II with diethylcadmium. Numerous examples of this general reaction have been reported,[5] and in most cases the yields of ketone are excellent, further reaction of the ketone with the organocadmium reagent being almost negligible. In the present instance, however, appreciable amounts of 3-(3′,4′,5′-trimethoxyphenyl)-pentene-2, V, were formed by addition of diethylcadmium to III followed by loss of water.[6] A fairly accurate estimate of the amount of V contaminating the ketone was obtained by catalytic hydrogenation of a molecular distillate of the crude product. The much greater rate of hydrogen absorption of V as compared with III permitted a quantitative measure of the former. In one case, also, a fractional distillation gave results which correlated satisfactorily with the hydrogenation value. The amount of V contaminating III rose when the ratio of diethylcadmium to acid chloride or the reaction time was increased. Attempts to reduce the formation of V by using only a slight excess of diethylcadmium or a shortened reflux time, however, were unavailing because of the failure then of III to react completely. The conditions finally chosen as optimum resulted in almost complete consumption of II to yield 90–98% of a product containing from 15–27% of V and from which the ketone could be obtained in 43–49% yield by fractional distillation.



$$\mathrm{R{-}\overset{\overset{\displaystyle CHCH_3}{\|}}{C}{-}CH_2CH_3}$$

V

The conversion of III to IV by the Kindler modification of the Willgerodt reaction was studied in some detail in an effort to improve the yields. Under the conditions chosen as optimum, material melting at 91–92° (reported 98°,[2] 100–102°,[3] 104°[4]) could be obtained in 35–45% yield. A small amount of impurity (probably I) may account for this low melting point and for the difficulty of further purification. The over-all yield of IV from I was about 20% when II and III were purified by distillation and about 28% when the crude intermediates were employed.

Experimental[7,8]

3,4,5-Trimethoxypropiophenone (III): (a) Optimum Reaction Conditions.—A solution of diethylcadmium was prepared according to standard procedures[5] from 47.2 g. (0.433 mole) of ethyl bromide in 470 cc. of dry, thiophene-free benzene. To this was added a solution of 50.0 g. (0.217 mole) of 3,4,5-trimethoxybenzoyl chloride (prepared in 91% yield from I and thionyl chloride; b. p. 174–176° at 15 mm.) in 120 cc. of dry, thiophene-free benzene. The mixture was stirred at room temperature for twenty minutes, refluxed for two and one-half hours, and then chilled and treated with water and dilute sulfuric acid. The organic material was extracted into benzene, the benzene washed several times with sodium bicarbonate solution (which removed 0.61 g. of I) and water, and the benzene then evaporated to leave 47.9 g. (98.5%) of an oil which slowly changed to a semi-crystalline mass. Fractional distillation through a thirty-four inch glass-

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[1] This investigation was supported in part by a research grant from the National Cancer Institute, U. S. Public Health Service.

[2] Slotta and Heller, *Ber.*, **63**, 3029 (1930).

[3] Cook, Graham, Cohen, Lapsley and Lawrence, *J. Chem. Soc.*, 322 (1944).

[4] Frank, Fanta and Tarbell, THIS JOURNAL, **70**, 2314 (1948).

[5] Cason, *Chem. Rev.*, **40**, 15 (1947).

[6] The addition of a dialkylcadmium to carbonyl groups has been reported in several instances [Gilman and Nelson, *Rec. trav. chim.*, **55**, 518 (1936); Christensen, *et al.*, THIS JOURNAL, **69**, 1909 (1947); Baker and Squire, *ibid.*, **70**, 1487 (1948)] and has been thought to be due to the activating influence of an electron withdrawing group adjacent to the carbonyl group.

[7] All melting points are corrected.

[8] We are indebted to Dorothy Kuenne for performing the microanalyses.