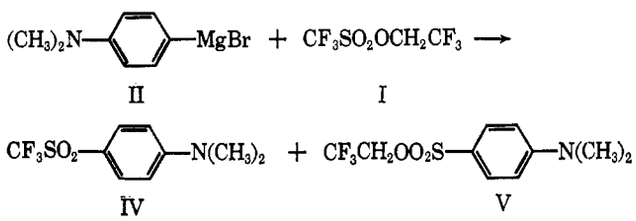
ever, in this investigation, the reaction of compound I with the Grignard reagent II afforded, instead of compound III, two acid-insoluble products, *p*-dimethylaminophenyl trifluoromethyl sulfone (IV) and 2,2,2-trifluoroethyl *p*-dimethylaminobenzenesulfonate (V). These two compounds, obtained in low yield, were characterized by elementary and spectroscopic analyses (see the Experimental Section).



Although no evidence (*via* infrared) for compound III was noted, an acid-soluble, nonfluorine-containing (*via* infrared), purple material was isolated. Attempts to purify this material by chromatography failed. It was not further characterized. Analogous reaction of *p*-dimethylaminophenyllithium with compound I afforded a large amount of acid-soluble, purple semisolid which was not characterized. An acid-insoluble product was not obtained.

Experimental Section[5]

Reaction of *p*-Dimethylaminophenylmagnesium Bromide with 2,2,2-Trifluoroethyl Trifluoromethanesulfonate.—The experiment was conducted in a purified nitrogen atmosphere. The Grignard reagent, prepared from 2.04 g (0.084 g-atom) of "activated" magnesium[2] and 16.8 g (0.084 mole) of purified *p*-bromodimethylaniline[2] in 150 ml of purified tetrahydrofuran[2] was added dropwise over 30 min at room temperature to 23.2 g (0.1 mole) of pure ester I[1] in 100 ml of anhydrous ether. Thereafter the product was heated under reflux for 1 hr and poured into water. The mixture was acidified and extracted with ether. The separated ether extract was dried (anhydrous magnesium sulfate) and filtered. Upon evaporation of the filtrate, there was obtained 4.64 g of off-white solid melting at 100–105°. Qualitative elementary analyses for nitrogen, sulfur, and fluorine were positive for this solid. Infrared analysis of this sample indicated possible *para* substitution (12.25 μ), sulfone and/or sulfonate ester (*ca.* 7.4 μ, *ca.* 8.85 μ), and carbon–fluorine bonds (*ca.* 8.5 μ). On the basis of a broad melting range and proton and fluorine magnetic resonance studies, the sample was thought to be a mixture with identification of a trifluoroethyl group (τ 5.25), a trifluoromethyl group (ϕ^* 79.6), and the methyl groups on the nitrogen atom (τ 7.14). The aromatic region was complicated owing to the nature of the solvent mixture. [Basification of the aqueous extract afforded 8.4 g of nonfluorine-containing (*via* infrared), purple solid of a dye nature, which was not further investigated.]

Isolation of *p*-Dimethylaminophenyl Trifluoromethyl Sulfone (IV).—The 4.64 g of off-white solid was dissolved in benzene and chromatographed on a column (85 × 30 mm) of 70 g of neutral alumina, activity II (Calbiochem alumina). Elution with 100-ml portions of 10% benzene–petroleum ether (fractions 1–4, see below) followed by elution with 100-ml portions of benzene (fractions 5–8, see below) comprised chromatogram I [fraction number, weight (mg), melting point where applicable, fraction description]: 1, 1637, white-yellow solid; 2, 326, 102–111°, white solid; 3, 33, 98–99°, white solid; 4, 30, 99–110°, white solid; 5, 623, 103–111°, white solid; 6, 386, 103–117°, white solid; 7, 73, 115–117°, white solid; 8, 10, yellow oil.

Fraction 1 of chromatogram I was dissolved in benzene and rechromatographed on a column (111 × 20 mm) of 40 g of neutral alumina, activity I (Calbiochem alumina). Elution with 50-ml portions of benzene (fractions 1–5, see below) followed by elution with 50-ml portions of anhydrous ether (fractions 6–8, see below) embraced chromatogram II [fraction number, weight (mg), melting point where applicable, fraction description]: 1, 420, semisolid; 2, 696, 144.5–146°, white solid; 3, 84, 138–142°, white solid; 4, 43, 97–103°, white solid; 5, 29, 110–112°, white solid; 6, 75, 115–117°, white solid; 7, 34, 117–118°, white solid; 8, 10, 115–116°, white solid.

Fraction 1 of chromatogram II was washed with acetone and filtered. Evaporation of the acetone filtrate left 181 mg of white solid, mp 140–144°, which was combined with fractions 2 and 3 of chromatogram II. Recrystallization (cyclohexane–Darco) of these combined fractions afforded 800 mg of compound IV, as white platelets, mp 144–145°.

Anal. Calcd for $C_9H_{10}F_3NO_2S$: C, 42.7; H, 4.0; F, 22.5; N, 5.5. Found: C, 42.5; H, 4.1; F, 22.2; N, 5.4.

Pmr studies of compound IV indicate a single peak at τ 7.14 which is consistent for the methyl groups on the nitrogen atom. F^{19} nmr studies show a single peak at ϕ^* 79.6 which is in agreement for a trifluoromethylsulfonyl group. Both spectra were taken on a 25-mg sample of compound IV dissolved in a mixture of 0.125 ml of $CFCl_3$ qnd 0.08 ml of pyridine.

Isolation of 2,2,2-Trifluoroethyl *p*-Dimethylaminobenzenesulfonate (V).—The following chromatographic fractions were combined (fractions 2–7, inclusive, of chromatogram I and fractions 4–8, inclusive, of chromatogram II) and recrystallized from cyclohexane (Darco) to yield 1.6 g of compound V as long, white needles, mp 117–118°.

Anal. Calcd for $C_{10}H_{12}F_3NO_3S$: C, 42.4; F, 20.1; N, 5.0; mol wt, 283. Found: C, 42.3; F, 19.6; N, 4.8; mol wt, 281.

Pmr studies of compound V show a single peak at τ 7.13 for the methyl groups on the nitrogen atom and a quadruplet centered at 5.25 (with a J value of 8.5 cps) which is in agreement for the trifluoroethoxy group.

F^{19} nmr studies of compound V show a triplet centered at ϕ^* 73.4 (with a J value of 8.5 cps) which is consistent for the trifluoroethoxy group. Both spectra were taken on a 60-mg sample of compound V dissolved in 500 mg of a 75% pyridine–25% $CFCl_3$ solvent mixture.

Acknowledgment.—The author thanks Dr. Robert L. Hansen for a sample of 2,2,2-trifluoroethyl trifluoromethanesulfonate and Dr. Charles E. Ring of the molecular spectroscopy group of the Minnesota Mining and Manufacturing Company for the spectral data.

(5) Melting points are corrected. They were taken with a Thomas–Hoover capillary melting point apparatus. Infrared spectra were taken with a Perkin-Elmer Model 21 spectrophotometer. Proton magnetic resonance spectra were taken with a Varian Model A-60 instrument. Values are reported in τ units using tetramethylsilane as internal reference. Fluorine magnetic resonance spectra were taken with a Varian Model V-43002 40-Mcps spectrophotometer. Values are reported in ϕ^* ($CFCl_3$ reference). Chromatographic alumina was purchased from California Corporation for Biochemical Research. Petroleum ether (bp 30–60°) was used. Analyses were performed by the microanalytical section of these laboratories. Molecular weights were determined by the thermistor method; see J. J. Neumayer, *Anal. Chim. Acta*, **20**, 519 (1959).

Cleavage of Oximes with Bisulfite. A General Procedure

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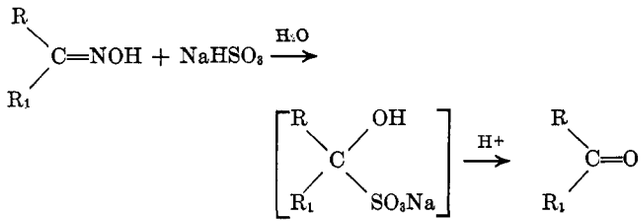
Received April 28, 1966

Of the methods available for the cleavage of oximes to the parent oxo compounds, either direct acid hydrolysis or acid-catalyzed exchange with formaldehyde, pyruvic, or levulinic acids is commonly used.[1]

In connection with other synthetic work, we have found a simple, inexpensive, mild procedure for accomplishing this task. Moreover, the reaction is car-

(1) For example, see C. H. DePuy and B. W. Ponder, *J. Am. Chem. Soc.*, **81**, 4629 (1959); E. B. Hershberg, *J. Org. Chem.*, **13**, 542 (1948); M. P. Cava, R. L. Little, and D. R. Napier, *J. Am. Chem. Soc.*, **80**, 2260 (1958).

ried out under neutral, nonreversible conditions; brief exposure to acid (in the cold) is required only for the isolation of the product.



The reaction was first described by von Pechmann[2] in 1887 at which time he characterized a crystalline intermediate in the case of benzaldoxime.[3,4] The failure to find references to this excellent procedure in the modern literature, coupled with our finding of its general utility prompt us to report the results of the hydrolysis of several representative oximes.

Our results are tabulated in Table I. Reaction times are not necessarily optimized; thin layer chromatography was used extensively to assess the progress of the hydrolysis.

TABLE I

BISULFITE CLEAVAGE OF OXIMES

Oxo compd[a,b]	Reaction time, hr	Yield, %[c]
3,4-Diphenyl-2-butanone (1)	2	84
Acetophenone (2)	6	83
Benzophenone (3)	24	98
2′,3′-α-Tetrahydrofuran-2′-spiro-17-(4-androsten-3-one)[d] (4)	16	86
Heptaldehyde (5)	2	87
5-Chlorosalicylaldehyde (6)	6	77

[a] Oximes corresponding to **2**, **3**, **5**, and **6** were purchased from Eastman Chemicals. [b] Thin layer chromatography was run on silica gel G plates (Analtech, Inc.). Benzene was used as solvent in all cases; with the oxime of **4**, 5% ether was added to enhance mobility. Approximate R_f values (oximes): **1**, 0.2; **2**, 0.3; **3**, 0.2; **4**, 0.15; **5**, 0.15; **6**, 0.25. The corresponding oxo compounds showed greater mobility. The developed spots were visualized by exposure to iodine vapor. [c] Yields are of purified products: liquids by distillation and solids by crystallization from appropriate solvents. [d] G. E. Arth, H. Schwam, L. H. Sarett, and M. Glitzer, *J. Med. Chem.*, 6, 617 (1963). The oxime was made in the usual fashion.

Experimental Section

The oxime, dissolved in 10 to 12 vol. of 50% aqueous ethanol, was refluxed with 3.5 molar equiv of sodium bisulfite until thin layer chromatography indicated complete reaction. After removal of the ethanol by distillation, the residue was admixed with chloroform and an excess of dilute hydrochloric acid, and the ketone or aldehyde was extracted into the organic layer. In the case of the aldehydes, hydrolysis of the bisulfite adduct required stirring with acid for up to 30 min to obtain two clear layers.

The extracts gave near-quantitative yields of "crude" product, usually single spot by tlc.

(2) H. von Pechmann, *Ber.*, **20**, 2539 (1887).

(3) In the equation shown, we have chosen to depict the bisulfite adduct of the oxo compound as an intermediate for the sake of simplicity. We have proven its intermediacy in the case of heptaldehyde, and would expect it in all cases where it would not be excluded on steric grounds (*e.g.*, aldehydes and cyclic and methyl ketones). Von Pechmann[2] isolated a product which he characterized as $C_6H_5CH(SO_3Na)NH(SO_3Na)\cdot 3H_2O$ by elemental analysis.

(4) We did not study the fate of the nitrogenous portion of the molecule. Little, if any, ammonia could be detected by warming a basified portion of the reaction. The work of H. H. Sisler and L. F. Andrieth [*J. Am. Chem. Soc.*, **61**, 3389 (1939)] suggests that it is converted to sulfamic acid.

The Reaction of α-Pyridone with Diazoalkanes[1]

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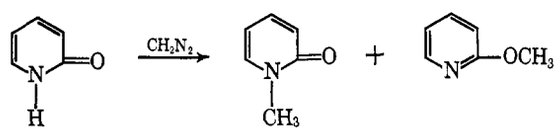
Received June 6, 1966

In 1895 it was reported that treatment of α-pyridone with diazomethane gives exclusively oxygen alkylation,[2] a view which has become widely accepted.[3-6] As part of a study of the alkylation of salts of α-pyridone, we have reexamined the reaction of α-pyridone with diazomethane. It transpires, contrary to the earlier report, that the reaction not only gives both nitrogen and oxygen methylation but actually gives more of the former, *i.e.*, about 55% N-methyl-α-pyridone and about 35% 2-methoxypyridine.



That this is a kinetically controlled result is shown by the following. (1) Both 2-methoxypyridine and N-methyl-α-pyridone are completely stable to diazomethane under the reaction conditions. (2) The product distribution does not change as a function of time. (3) The product distribution is the same whether 1 equiv of α-pyridone is treated with 2 of diazomethane or whether 2 equiv of α-pyridone are treated with 1 of diazomethane (Table I).

TABLE I

REACTIONS OF α-PYRIDONE WITH DIAZOMETHANE[a]

Solvent[b]	Reacn time	Yield of products, %[c] N-Methyl-α-pyridone	Yield of products, %[c] 2-Methoxypyridine
$(C_2H_5)_2O$ + CH_3OH (52:48)	45 min	53	39
$(C_2H_5)_2O$ + CH_3OH (52:48)	45 min	51	37
$(C_2H_5)_2O$ + CH_3OH (48:52)	24 hr	56	31
$(C_2H_5)_2O$ + CH_3OH (48:52)	48 hr	55	33
$(C_2H_5)_2O$ + CH_3OH (77:23)	24 hr	54	37
$(C_2H_5)_2O$ + CH_3OH (65:35)	24 hr	59[d]	38[d]
$(C_2H_5)_2O$ + CH_3OH (48:52)	24 hr	46[e]	30[e]
$(C_2H_5)_2O$ + CH_2Cl_2 (50:50)	96 hr	45	36

[a] At 0°. [b] Numbers in parentheses refer to mole % of solvent. [c] Material balances range from 90 to 95% (*cf.* the Experimental Section). [d] Two moles of diazomethane for each mole of α-pyridone was used. [e] One mole of diazomethane for 2 moles of α-pyridone was used.

The original methylation study[2] had been conducted in a methanol–ethyl ether solvent system and, hence, this was also employed in most of our experiments. On the chance that in an aprotic medium the reaction

(1) Paper VIII in the series "The Chemistry of Ambident Anions." Preceding paper: R. C. Kerber, G. W. Urry, and N. Kornblum, *J. Am. Chem. Soc.*, **87**, 4520 (1965).

(2) H. von Pechmann, *Ber.*, **28**, 1624 (1895).

(3) H. Meyer, *Monatsh.*, **26**, 1311 (1905).

(4) H. S. Mosher, in "Heterocyclic Compounds," Vol. I, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1950, pp 435, 534.

(5) R. Gompper, *Advan. Heterocyclic Chem.*, **2**, 252, 254 (1963).

(6) H. Meislich, in "Pyridine and Its Derivatives," Part 3, E. Klingsberg, Ed., Interscience Publishers, Inc., New York, N. Y., 1962, p 641.