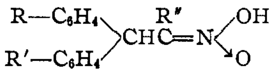
[CONTRIBUTION FROM THE PHARMACEUTICAL RESEARCH DIVISION OF COMMERCIAL SOLVENTS CORPORATION]

Some New *aci*-Nitro Compounds

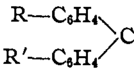
BY E. B. HODGE

The preparation and properties of a series of compounds believed to have the formula  $(R{-}C_6H_4)(R'{-}C_6H_4){>}CHC(R'')=N(OH)\rightarrow O$ where R and R′ = H, Me, or halogen and R″ = Me or Et are described. These compounds do not revert to the original nitro compound, but decompose at various rates. Boiling them with methanol produces the corresponding oximes.

The number of *aci*-nitro compounds reported in the literature is small. Most of these interesting compounds revert in a few hours or less to the original nitro compound. Kohler and Stone,[1] however, prepared several *aci*-nitro compounds which were derivatives of nitrostilbene and which were, in general, considerably more stable than previously described *aci*-nitro compounds. The nitrostilbene derivatives also differed from previously described *aci*-nitro compounds by undergoing complex decompositions and not reverting to the original nitro compound.

We were studying reactions of some diarylalkyl nitro compounds whose structures are shown in Table I. These nitro compounds were prepared by the method of Müller[2] as modified by the writer and others.[3,4] As part of this study we wished to prepare the ketones in which the positions of the carbonyl group corresponded to that of the nitro group. For this conversion a reaction described by Nef[5] was tried. This reaction consists in acidifying a salt of an *aci*-nitro compound with a strong mineral acid.

TABLE I

SOME NITRO COMPOUNDS OF THE FORMULA  $(R{-}C_6H_4)(R'{-}C_6H_4){>}CHCHNO_2R''$ AND THE CORRESPONDING *aci*-NITRO COMPOUNDS AND OXIMES

R	R′	R″	Yield[a] of nitro compound, %	Analyses of nitro compound, % Chlorine Calcd.	Chlorine Found	Nitrogen Calcd.	Nitrogen Found	M.p. of nitro compound °C. cor.	M.p. range of *aci*-nitro compound °C.	Time for *aci*-nitro compound to liquefy	M.p. of oxime °C. cor.	Analyses of oxime, % Chlorine Calcd.	Chlorine Found	Nitrogen Calcd.	Nitrogen Found
H	H	CH_3	30			5.81	5.59	88–90[b]	70–77	4–20 hours	164–165[d]			6.22	5.99
4-Cl	4-Cl	CH_3	71	22.86	22.74	4.52	4.38	84–85[c]	42–55	4–20 hours	170.4–171.4[e]	24.11	24.12	4.76	4.54
4-Cl	4-Br	CH_3	36	10.00	10.03	3.95	3.85	82.5–83.5	48–65	4–20 hours	172–173	10.47	10.47	4.14	3.99
4-Cl	2,4-Di-CH_3	C_2H_5	52	11.16	11.17	4.41	4.50	124–125.9	47–70	4–20 hours	177.5–179	11.79	12.07	4.66	4.57
2-Cl	4-CH_3	CH_3	12	12.23	11.92	4.84	4.90	98–99	89–94	8 days	172.5–174	12.95	12.76	5.12	5.24
2-Cl	4-Cl	CH_3	68	22.86	22.90	4.52	4.51	117–118	75–80	6 weeks	170–171.5	24.11	24.20	4.76	4.63
2-Cl	4-Br	CH_3	82	10.00	10.08	3.95	4.13	125.5–127.2	101–118	> 6 months	186–188	10.47	10.45	4.14	4.15
2-Cl	4-I	CH_3	38	8.83	9.04	3.49	3.60	138–138.5	116–130	> 6 months	196–197.5	9.20	9.01	3.63	3.31

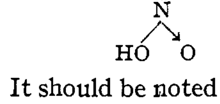
[a] Yield of crude crystalline product based on nitro alcohol. [b] Neher[3] gives 89–90°. [c] Blickenstaff[4] gives 80.5–81.5°. [d] R. Stoermer, *Ber.*, **39**, 2303 (1906), gives 164.5°. [e] H. Erlenmeyer, P. Bitterli and E. Sorkin, *Helv. Chim. Acta*, **31**, 469 (1948), give 170–171°.

When this reaction was applied to the compounds studied, white solids were formed. Most of these solids decomposed at various rates to yellow or green oils, but two of them stayed solid for at least six months. The less stable of these solids had an odor of nitrogen oxides as soon as formed and it was impossible to get significant analyses on most of them. Nitrogen and halogen analyses corresponding to those of the original nitro compound were obtained on one of the more stable of the compounds, however.

These solids were formed in amounts equal to those of the nitro compounds from which they were prepared. They were insoluble in water and not more than slightly soluble in the common organic solvents. When ferric chloride solution was added to methanol which had been in contact with one of them a deep red color developed. The solids did not have definite melting points, but decomposed over a range of temperature.

When these solids were boiled with methanol they gradually dissolved, and on cooling and concentrating the solution, the corresponding oximes separated.

From the above discussion it appears that the solids prepared were the *aci*-nitro compounds corresponding to the nitro compounds used. The general formula for the compounds would thus be



R, R′ = H, Me, or halogen
R″ = Me or Et

It should be noted that the low solubility of these products in organic solvents seems unexpected on the basis of the proposed structure.

However, in absence of other evidence to the contrary, they are considered to be *aci*-nitro compounds.

Some of the properties of the nitro compounds used, of the *aci*-nitro compounds formed, and of the corresponding oximes, are given in Table I. All compounds in this table are new except those for which previously determined melting points are given.

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[1] E. P. Kohler and J. F. Stone, THIS JOURNAL, **52**, 761 (1930).

[2] P. Müller, U. S. Patent 2,397,802, Apr. 2, 1946.

[3] M. B. Neher, Ph.D. Dissertation, Purdue University, 1947.

[4] R. T. Blickenstaff, Ph.D. Dissertation, Purdue University, 1948.

[5] J. U. Nef, *Ann.*, **280**, 263 (1894).

As can be seen from this table the stability of this type of *aci*-nitro compound is dependent to a considerable extent on the position and nature of the substituents on the benzene rings.

Since the preparation of the diarylalkyl nitro compounds of the type used is rather simple, the *aci*-nitro compounds described and other similar ones are probably more readily available than any previously described compounds of this class.

The formation of the oxime by the action of methanol is believed to take place through the intermediate formation of the ester of the *aci*-nitro compound. Such esters are known to decompose to oximes.[6] The other product from this decomposition would be formaldehyde. This would be expected to react to some extent at least with methanol to form methylal. The presence of methylal in one of the reaction mixtures was demonstrated by the formation of formaldehyde 2,4-dinitrophenylhydrazone after hydrolysis of a distillate from the reaction mixture.

Experimental

Preparation of Nitro Compounds.—The nitro compounds were all prepared in about the same manner. The preparation of 1-*o*-chlorophenyl-1-*p*-chlorophenyl-2-nitropropane will be given as an example.

To a stirred mixture of 125 g. (1.11 moles) of chlorobenzene and 200 g. of 96% sulfuric acid held at about 25° by water cooling was added dropwise 100 g. (0.465 mole) of 1-*o*-chlorophenyl-2-nitro-1-propanol. The addition took 33 minutes and stirring was continued for another 27 minutes. Then 50 ml. of chlorobenzene was added (to prevent crystallization) and the organic layer was separated and washed with 200 g. of 5% sodium carbonate solution. It was then distilled in the presence of water to a vapor temperature of 99° and the organic residue was cooled and stirred for one-half hour with 300 ml. of petroleum ether. Filtration gave 99.1 g. (68%) of white solid; m.p. 101–110°. Recrystallization from a methanol–benzene mixture gave 68.1 g. (47%); m.p. 115–116°. One further crystallization from benzene raised the m.p. to 117–118°.

In condensations in which xylene and toluene took part, 85% and 90% sulfuric acids were used, respectively.

Preparation of *aci*-Nitro Compounds.—The preparation of the *aci*-nitro compounds will be illustrated by a description of the preparation of the *aci*-form of 1-*p*-bromophenyl-1-*o*-chlorophenyl-2-nitropropane.

To a solution of 4.4 g. (0.012 mole) of 1-*p*-bromophenyl-1-*o*-chlorophenyl-2-nitropropane and 0.75 g. (0.013 mole) of potassium hydroxide in 10 ml. of methanol was added 20 ml. of water. This solution was then added dropwise with stirring to a solution of 5 ml. of concentrated hydrochloric acid in 40 ml. of water which was held at 20°. The white precipitate was filtered and washed with 10 ml. of water. After two hours in a vacuum desiccator and further drying in the air overnight, there were 4.5 g. of white solid.

Anal. Calcd. for $C_{15}H_{13}BrClNO_2$: Br, 22.54; Cl, 10.00; N, 3.95. Found: Br, 22.85; Cl, 10.14; N, 3.73.

Preparation of Oximes.—These were also all prepared in the same manner. Their preparation will be illustrated by a description of the conversion of 1-*p*-bromophenyl-1-*o*-chlorophenyl-2-nitropropane to 1-*p*-bromophenyl-1-*o*-chlorophenyl-2-propanone oxime.

The *aci*-nitro compound was prepared as described in the preceding example, but was dried only the two hours in a vacuum desiccator. Then it was added to 25 ml. of methanol and the mixture was heated on a steam-bath for one-half hour. It was then left standing in an open erlenmeyer flask. After three weeks the residue in the flask was crystallized three times from methanol to give 1.3 g. (16%) of the oxime.

The yield given is about typical for the series. All of the oximes were impure as first recovered and some required as many as five crystallizations to give pure compounds.

Identification of Formaldehyde.—Thirty-seven grams (0.12 mole) of the *aci*-form of 1-*o*-chlorophenyl-1-*p*-chlorophenyl-2-nitropropane was mixed with 80 ml. of methanol and refluxed for 5 hours under a 14 × 2 cm. packed column. The temperature at the top of the column dropped from 64 to 50° during this time. Then 15 ml. was slowly distilled and this distillate was heated to boiling with a solution of 1.5 g. of 2,4-dinitrophenylhydrazine in 100 ml. of ethanol and 2 ml. of concentrated hydrochloric acid. On cooling, 0.7 g. (0.003 mole) of formaldehyde 2,4-dinitrophenylhydrazone crystallized. After recrystallization from ethanol this had a m.p. of 162–164°; a mixed melting point with an authentic sample was also 162–164°.

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[6] See J. T. Thurston and R. L. Shriner, *J. Org. Chem.*, **2**, 183 (1937).

[CONTRIBUTION FROM THE UNIVERSITY OF COLORADO]

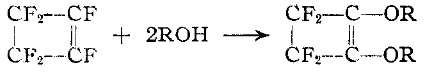
Action of Alcohols on 3,3,4,4-Tetrafluoro-1,2-dichlorocyclobutene-1[1,2]

BY J. D. PARK, C. M. SNOW[3] AND J. R. LACHER

The reaction of alkanols with 3,3,4,4-tetrafluoro-1,2-dichlorocyclobutene-1 in the presence of a base under control conditions results in the formation of 1-alkoxy-2-chloro-3,3,4,4-tetrafluorocyclobutene-1, as contrasted to the production of 1,2-dialkoxy-3,3,4,4-tetrafluorocyclobutene-1 from the analogous hexafluorocyclobutene reported previously. When an excess of alcoholic alkali solution was used with 3,3,4,4-tetrafluoro-1,2-dichlorocyclobutene-1, a cyclic triether having the empirical formula $C_4F_2Cl(OR)_3$ was formed. Various mechanisms are discussed. Some of the physical properties of the ethers including magnetic susceptibilities, along with their ultraviolet and infrared absorption spectra, are presented.

A review of the art on the preparation of fluorinated ethers has been previously covered.[4,5]

It has been shown[5] that the reaction of alcohols with hexafluorocyclobutene in the presence of a base resulted in the unexpected production of a diether as shown by the equation



Substitution of the vinylic fluorine atoms by the –OR groups was postulated, with a mechanism similar to the formation of a substituted anisole from a substituted phenyl halide. The addition

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[1] Presented before the Fluorine Section of the Division of Industrial and Engineering Chemistry, 118th Meeting of the American Chemical Society, Chicago, Illinois, September 3–8, 1950.

[2] This paper represents part of a thesis submitted by C. M. Snow to the Graduate School, University of Colorado, in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1950. This work was supported in part by Contract N6-onr-231, Task Order 6, with the Office of Naval Research, United States Navy.

[3] Agricultural Processing Industries, Inc., Denver, Colorado.

[4] J. D. Park, J. R. Lacher, *et al.*, THIS JOURNAL, **70**, 1550 (1948).

[5] J. D. Park, M. L. Sharrah and J. R. Lacher, *ibid.*, **71**, 2337 (1949).