Ozonolysis. XI. Kinetic Studies on the Conversion of the Molozonide into Ozonolysis Products

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Low-temperature nmr kinetic studies have shown that *trans*-3-hexene molozonide underwent decomposition to ozonolysis products in dichlorodifluoromethane and in dimethyl ether-d_6 solutions by a reaction that was first-order in molozonide concentration. In the halogenated solvent propionaldehyde, ozonide and oligomer were formed early in the reaction, the aldehyde reached a relatively stable concentration, and ozonide was the predominant reaction product. In the ether solvent much more aldehyde was formed, and, again, it reached a relatively stable concentration. Oligomer appeared early in the reaction, evidence for ozonide did not appear until near the end of the first half-life, and oligomer was the principal reaction product.

The suggestion[2] that the molozonide is an intermediate in the ozonolysis of alkenes was made in 1925. Since that time it has been established[3] with some certainty that the molozonide is indeed an intermediate in the ozonolysis of some alkenes, that it is formed by stereospecific *cis* addition of ozone to the alkene, and that the molozonide is in fact a 1,2,3-trioxolane.[3d] A plethora of speculation[4] but a dearth of facts has been published about the conversion of the molozonide to ozonolysis products.

Several kinetic studies on the ozonation reaction have been reported. The aromatic hydrocarbon–ozone and the norcaradiene derivative–ozone reactions in the liquid phase have been investigated.[5] Also, reports appear in the literature on kinetic studies of the alkene–ozone reaction both in the gas phase[6] and in the liquid phase.[7] These data, of course, give us no information about the conversion of the molozonide to ozonolysis products. The one kinetic study on the decomposition of a molozonide, that from 1-hexene, reported[8] it as a first-order reaction with $k = 0.9 \times 10^{-2}$ at $-100°$ and an energy of activation of 7 kcal/mol. Our earlier work[3e] indicated that the molozonide was the only product which resulted from the ozonation of *trans*-3-hexene in dichlorodifluoromethane solution at $-130°$, that the molozonide was stable at this temperature, and that it did not begin to convert to ozonolysis products at an appreciable rate until the solution was warmed to about $-100°$. These observations made it appear feasible to carry out kinetic studies on the conversion of the molozonide to ozonolysis products, and the results of such a study are reported herein.

The experimental procedure was to prepare dichlorodifluoromethane solutions of the molozonide at $-130°$, and to transfer the tube containing this solution to the nmr probe, which was cooled to the desired temperature. Spectra were then recorded at various intervals of time with the "gain" of the instrument being adjusted such that the methyl proton absorptions were maximized on the chart. In our first experiments we used *trans*-diisopropylethylene because its molozonide should have a less complex nmr spectrum than that from *trans*-3-hexene. However, the former molozonide proved to be too insoluble at this temperature; so all of the experiments reported herein were done with *trans*-3-hexene. The reactions could be followed for about three half-lives; by that time the area of the molozonide methine proton absorption had decreased to the point where it could not be measured on the same scale as the methyl proton absorptions with any reasonable accuracy. In obtaining the desired data from the spectra, the areas of the various proton absorptions were measured with a planimeter. The number of methyl protons in the solution should remain constant; so this area was taken as a reference and assigned an arbitrary value. A measure of the molozonide and ozonide concentrations was obtained from the areas of the appropriate[3e] methine proton absorption peaks, and the area of the two central peaks of the methylene quartet of propionaldehyde was a measure of the aldehyde formed. (The fine structure due to coupling to the aldehyde proton was not resolved under these conditions.) By means of a conversion factor, which was obtained from the methyl proton area of each spectrum, and the arbitrarily assigned methyl proton area, it was possible to convert the other areas to a common basis.

The rate constants were obtained by preparing plots of ln (molozonide methine proton area) *vs.* time; from these plots the half-life of each reaction could be determined, and the rate constant calculated from $k = \ln 2/t_{1/2}$. At -100 and $-103°$ the disappearance of molozonide was clearly first order with rate constants of 5.4×10^{-4} sec^{-1} and 3.5×10^{-4} sec^{-1}, respectively. The various rate constants are indicated in Table I, and a typical plot is shown in Figure 1.

Experiments carried out at $-108°$ were very erratic. Data which were obtained from most of these experiments gave so much scatter of points that no correlation could be made when plots of ln (molozonide methine proton area) *vs.* time were prepared. However, three experiments (two with 25 μl and one with 15 μl of alkene) did give good first-order plots. These had half-lives of 56, 55, and 52 min with $k = 2.1 \times 10^{-4}$. From the rate constants which were obtained at -100

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(1) (a) Tufts University; (b) Stanford University.

(2) H. Staudinger, *Ber.*, **58**, 1088 (1925).

(3) (a) R. Criegee and G. Schröder, *Chem. Ber.*, **93**, 689 (1960); (b) F. L. Greenwood, *J. Org. Chem.*, **29**, 1321 (1964); (c) F. L. Greenwood, *ibid.*, **30**, 3108 (1965); (d) P. S. Bailey, J. A. Thompson, and B. A. Shoulders, *J. Amer. Chem. Soc.*, **88**, 4098 (1966); (e) L. J. Durham and F. L. Greenwood, *J. Org. Chem.*, **33**, 1629 (1968).

(4) *Cf.* references cited in R. W. Murray, *Accounts Chem. Res.*, **1**, 313 (1968).

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(6) T. Vrbaski and R. J. Cvetanović, *Can. J. Chem.*, **38**, 1053 (1960); Y. K. Wei and R. J. Cvetanović, *ibid.*, **41**, 913 (1963); J. Heicklen, *J. Phys. Chem.*, **70**, 477 (1966).

(7) (a) T. W. Nakagawa, L. J. Andrews, and R. M. Keefer, *J. Amer. Chem. Soc.*, **82**, 269 (1960); D. G. Williamson and R. J. Cvetanović, *ibid.*, **90**, 3668, 4248 (1968); (b) G. Wagner and A. Greiner, *Z. Phys. Chem.*, **215**, 92 (1960).

(8) S. D. Razumovskiy and L. V. Berezova, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **1**, 207 (1968).

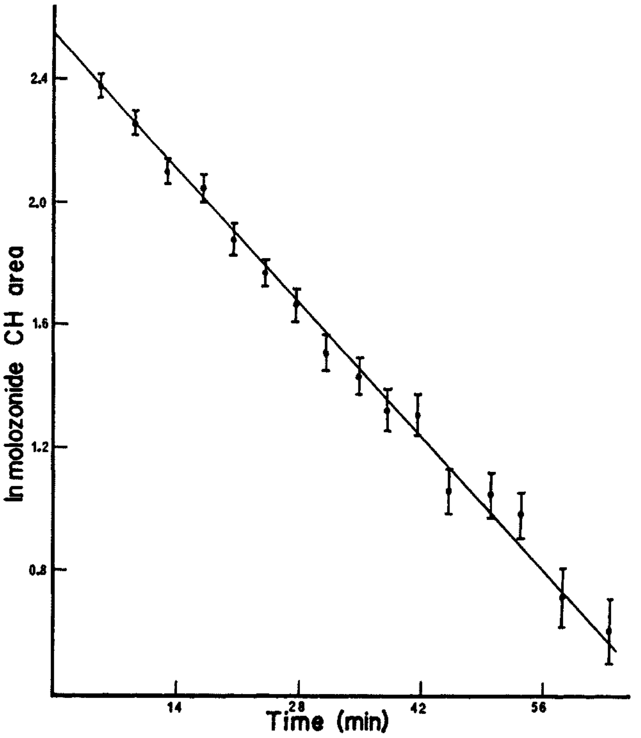

Figure 1.—Plot of ln (molozonide methine proton area) *vs.* time: 25 μl of alkene, temp −100°, solvent CCl_2F_2.

TABLE I

RATE CONSTANTS FOR THE DECOMPOSITION OF MOLOZONIDE

Temp, °C	*trans*-3-Hexene, μl[a]	$t_{1/2}$, min	10^4k, sec^{-1}
−100	15	18	6.4
	15	23	5.0
	20	24	4.8
	20	22	5.3
	25	20	5.8
	25	22	5.3
−103	15	36	3.2
	15	35	3.3
	20	32	3.6
	20	32	3.6
	20	30	3.8
	25	33	3.5
	25	32	3.6

[a] Amount of alkene added to reaction vessel. For preparation of reaction solutions, *cf.* Experimental Section.

and −103°, the energy of activation for this reaction can be estimated from the equation

$$\ln \frac{k_2}{k_1} = \frac{E_a}{R}\left(\frac{T_2 - T_1}{T_2T_1}\right)$$

as 8 kcal/mol. With this value and the rate constant for −103° one obtained a calculated $k = 1.7 \times 10^{-4}$ at −108°. This value is in reasonable agreement with the experimentally obtained value of 2.1×10^{-4}.

The temperature range over which the rate decomposition of an explosive species in reasonable concentration can be studied will be rather narrow. There should be some rather well-defined temperature at which the rate of decomposition will occur at a reasonable rate. The molozonide is certainly an explosive species,[3c] and the only explanation that we can offer for the erratic results which were obtained at −108° is that the molozonide has the characteristics outlined above, and that a temperature of −108° is near that well-defined temperature. We have found[3e] that this *trans*-molozonide showed no evidence of decomposition when kept at −130° for 7 hr. Because of the time required to record the nmr spectrum, a temperature of −100° is about as high as one can study this particular system in this manner. It would be our guess from observing this system and other experiences with molozonides that any attempt to study this system at a temperature much above −100° would result in an explosion.

Murray, *et al.*,[9] have proposed a mechanism for ozonolysis which envisages an initial decomposition of the molozonide to give rise to some aldehyde, and after this the dominant pathway becomes the reaction of aldehyde with molozonide. In their latest publication[10] it was stated that it is reasonable to postulate that this dominant pathway is bimolecular in nature, and that possible pathways include the reaction of two alkene–ozone adducts or that of one such adduct with an aldehyde molecule. In the case of the system being presently reported, the disappearance of molozonide is clearly a first-order reaction, and this is not consistent with the collision of two molecules of molozonide or the reaction of the molozonide with aldehyde as rate-controlling processes. The known facts about the ozonolysis of alkenes indicate that the molozonide does not go directly to the ozonide, and this is substantiated by the presently reported studies. Plots of ln (ozonide methine proton areas) *vs.* time were prepared and these showed that the reaction was not first order in ozonide. The data are best explained by the fragmentation of the molozonide as the rate-controlling process.

In this fragmentation, propionaldehyde was clearly a product. In the first spectra, which were obtained *ca.* 4 min after insertion of the nmr tube into the probe which was cooled to −100°, the areas of the methylene protons of the aldehyde were measurable. The amount of aldehyde had doubled by the end of the first half-life (*ca.* 24 min), and then remained relatively constant for the remainder of the run. The same pattern was followed in the experiments at −103° except that the aldehyde methylene proton areas were not measurable until after *ca.* 20 min. These data, studies on the alkene ozonation oligomer,[11] ozonolysis in the presence of aldehyde, and ozonolysis of unsymmetrical alkenes[4] support the formation of aldehyde and its subsequent reaction with other species to form the observed ozonolysis products. Whatever other molozonide fragmentation species were formed, they did not accumulate in sufficient concentration to be observable in the nmr spectra.

Ozonide and oligomer were formed in the very early stages of the reaction, as evidenced by methine proton absoroption[3e] for these two products in the first spectra. From the area of the first molozonide methine proton area and the last ozonide methine proton area, it was possible to estimate that some 60–75% of the molozonide was converted to ozonide. This percentage conversion is quite approximate for various reasons: some molozonide had disappeared by the time the first spectra were obtained, there was some overlap of the

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[9] R. W. Murray, R. D. Youssefyeh, and P. R. Story, *J. Amer. Chem. Soc.*, **89**, 2429 (1967).

[10] R. W. Murray, R. D. Youssefyeh, G. J. Williams, and P. R. Story, *Tetrahedron*, **24**, 4347 (1968).

[11] F. L. Greenwood and H. Rubenstein, *J. Org. Chem.*, **32**, 3369 (1967).

ozonide methine proton and unreacted alkene methine proton absorptions, part of the oligomer methine proton absorption lies in the same region as that of the ozonide methine proton, and the reactions were not carried beyond three half-lives. In dichlorodifluoromethane solution the chemical shifts of the methine protons of the stereoisomeric ozonides were sufficiently different that these absorptions appeared as overlapping triplets.[3e] From the relative heights of the two central peaks of each triplet, it was possible to observe that the *cis* and *trans* ozonides were formed in approximately equal amounts throughout the decomposition of the molozonide.

To explain some earlier results,[3c] it was postulated that an ether solvent facilitated the conversion of molozonide to ozonolysis products. The higher yield of ozonide[10,11] from *trans* alkenes in ether solution may also be explained in this fashion. To test this hypothesis, *trans*-3-hexene was ozonized in dimethyl ether-d_6 solution at −130°. To our chagrin, the −130° nmr spectrum of this solution had no absorption whatsoever in the ozonide methine proton region. A kinetic run was carried out with this solution at −103°, and the results were strikingly different from those obtained in dichlorodifluoromethane solution. In the latter solvent, the aldehyde methylene proton area was not measurable until *ca.* 25 min after the start of the run. In the ether solvent, the first spectrum (7 min) indicated that now there was about twice as much aldehyde present as there was after 25 min in the halogenated solvent. Again, the aldehyde concentration increased quite rapidly to a relatively stable concentration which was about twice that in the halogenated solvent. The formation of the other ozonolysis products was even more remarkable. Broad, structureless methine proton absorption between the molozonide methine proton and alkene methine proton absorptions was the first evidence of other ozonolysis products. This absorption was attributed to oligomer, since authentic oligomer has methine proton absorption[11] in this region. This broad absorption increased with time, and it wasn't until the 44-min spectrum that the first suggestion of the two central methine proton peaks of the *cis* and *trans* ozonides was observable above the oligomer methine proton absorption. The quadruplet of the ozonide stereoisomers was not observable until the 63-min spectrum. In the ether solvent, the difference in chemical shifts of the *cis* and *trans* ozonide methine protons was such that they appeared as a quartet instead of the overlapping triplets which were observed in the halogenated solvent. In the ether solvent, the two central ozonide methine proton peaks indicated that the *cis* and *trans* ozonides were being formed in about equal amounts throughout that portion of the reaction during which ozonide was observable. A plot of ln (molozonide methine proton area) *vs.* time showed that in dimethyl ether the reaction was clearly first-order with a half-life of 52 min and $k = 2.2 \times 10^{-4}\ \text{sec}^{-1}$.

The differences in the relative amounts of products which result from the decomposition of the molozonide in the two solvents were very marked. In dichlorodifluoromethane, not much aldehyde was formed, ozonide and oligomer were formed at the very beginning of the reaction, and, finally, the ozonide was the predominant product. In the dimethyl ether, much more aldehyde was formed, in the early stages of the reaction, oligomer was formed to the virtual exclusion of ozonide, ozonide was not observable until nearly half of the molozonide had disappeared, and the oligomer was the principal product of the reaction. In some fashion, the ether would appear to be preventing the formation of ozonide from molozonide. This is the opposite of our hoped-for result, but perhaps it should not be so dismaying. In these experiments we were observing the decomposition of molozonide in a solvent, and in the earlier work the ozonation of an alkene in ether solution was carried out. These are two different reactions.

The influence of the ether solvent on the reaction outlined above emphasizes again the remarkable effect such a solvent exerts on the ozonolysis of alkenes. In a conventional ozonolysis[12] of the stereoisomers of 2-butene and of 3-hexene, an ether solvent effected a marked enhancement of the yield of *trans* ozonide over that obtained in a hydrocarbon solvent. Similarly, with the 2-pentene stereoisomers, there was an enhancement of the *trans* isomers of each of the ozonides and, also, a marked increase in the amounts of "crossed ozonides" in an ether solvent compared with a hydrocarbon solvent.

Despite the beautiful resolution which was achieved in many of the spectra, it was impossible to reach any conclusion about the conformation of the molozonide.

Several energy values for the alkene–ozone reaction have appeared in the literature. Wagner and Greiner[7b] reported that ozone reacts with an alkene with an activation energy of virtually zero. The present work indicated that the decomposition of the molozonide of *trans*-3-hexene requires an activation energy of 8 kcal/mol, and a value of 7 kcal/mole has been reported[8] for the molozonide of 1-hexene. This may be compared with an activation energy of 31 kcal/mol which has been reported for ascaridole.[13] Criegee and Schröder[3a] found an enthalpy of 39 kcal/mol for the decomposition of the molozonide of *trans*-di-*t*-butylethylene. For the reaction of stilbene and ozone, Briner and Dallwigk[14] reported an enthalpy of 103 kcal/mol.

Experimental Section

The *trans*-3-hexene was an API standard sample. The fluorocarbons were purchased from Matheson Scientific Company and the dimethyl ether-d_6 from Merck Sharpe and Dohme of Canada.

Dichlorodifluoromethane (0.32 ml of liquid) was condensed in an nmr tube which was cooled to −130°. Dichlorofluoromethane (16 ml of gas) was condensed in the tube as an internal standard, and then 15 μl (0.12 mmol), 20 μl (0.15 mmol), or 25 μl (0.20 mmol) of alkene was added. In the reaction carried out in dimethyl ether-d_6, 0.32 ml of the liquid ether (−130°), 16 ml of gaseous internal standard, and 20 μl of alkene were used. To these solutions was added 92% of the theoretical amount of ozone which was generated by an ozonizer of the type described by Bonner,[15] which, at an oxygen flow rate of 1.35 l./hr, produced 2–3 vol. % ozone. Addition of more than 92% of the theoretical amount of ozone gave erratic results, apparently due to the formation of oxidation products which catalyzed the decomposition of the molozonide. After the ozonation, helium was bubbled through the reaction mixture for 10 min to remove dissolved oxygen, and the nmr tube was then transferred to the probe, which was cooled to the desired temperature.

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(12) F. L. Greenwood, *J. Amer. Chem. Soc.*, **88**, 3146 (1966).

(13) J. Boche and O. Runquist, *J. Org. Chem.*, **33**, 4285 (1968).

(14) E. Briner and E. Dallwigk, *Helv. Chim. Acta*, **40**, 1978 (1957).

(15) W. A. Bonner, *J. Chem. Educ.*, **30**, 452 (1953).

Spectra were recorded with a Varian HR-60, Model 4300-B, using a V-4331 nmr probe which was equipped with a V6040 temperature controller. To determine the temperature in the reaction mixture, an nmr tube, containing some liquid into which a thermocouple was inserted, was placed in the probe. In this way it was determined at what temperature the thermocouple in the probe had to be maintained in order to get a certain temperature in the reaction mixture. By constant monitoring of the temperature controlling device it was possible to maintain the temperature to within ±0.5° of the desired temperature. The various peak areas were measured with a Keuffel and Esser planimeter which measured areas to 0.1 cm^2. The times mentioned throughout the text are the times after insertion of the reaction mixture into the probe that the spectrum was scanned through the molozonide methine proton absorption.

There is a question of the solubility of the ozonolysis products, particularly the oligomer, in the reaction mixture. The total methine proton areas of the first and last spectra were about the same. The dimethyl ether solution was finally warmed to $-50°$, and the total methine proton areas of the spectrum which was obtained at this temperature agreed well with that from the first spectrum which was recorded at $-103°$. This was some indication that the oligomer was in solution.

The molozonide had nmr (CCl$_2$F$_2$) δ 4.07 (t, CH), 1.60 (m, CH$_2$), 0.90 (t, CH$_3$); nmr (CD$_3$OCD$_3$) δ 4.28 (t, CH), 1.67 (m, CH$_2$), 0.95 (t, CH$_3$). Authentic ozonide had nmr (CCl$_4$) δ 4.94 (t, J = 5 Hz, CH), 4.89 (*t*, J = 5 Hz, CH), 1.55 (m, CH$_2$), 0.82 (t, J = 8 Hz, CH$_3$), 0.84 (t, J = 8 Hz, CH$_3$); nmr (CD$_3$OCD$_3$) δ 5.15 (t, J = 5 Hz, CH), 5.07 (t, J = 5 Hz, CH), 1.65 (m, CH$_2$), 0.97 (t, J = 8 Hz, CH$_3$), 0.93 (t, J = 8 Hz, CH$_3$).

Registry No.—Molozonide (*trans*-3-hexene), 2028-40-2; *trans*-3-hexene, 13269-52-8.

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Reaction of Hypochlorous Acid with Ketones. A Novel Baeyer–Villiger Oxidation of Cyclobutanone with Hypochlorous Acid

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Cyclobutanone was converted into γ-butyrolactone by aqueous hypochlorous acid, apparently the first case of a Baeyer–Villiger reaction by a nonperoxidic oxidant. This reaction is accelerated by acid, unaffected by light, and does not involve the intermediacy of 4-chlorobutyric acid. Neither cyclopentanone nor cyclohexanone are oxidized to lactones by HOCl. Cyclohexanone gives 2- and 4-chlorocyclohexanone, 2,2-dichlorocyclohexanone, and 2-cyclohexenone, but no 3-chlorocyclohexanone.

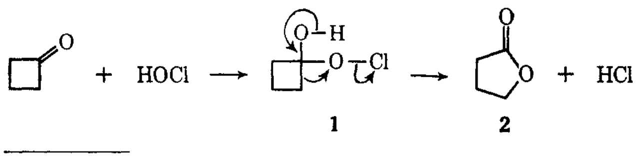
The Baeyer–Villiger oxidation of ketones to esters has been observed with various peroxy acids, including hydrogen peroxide,[2] and apparently with alkyl hydroperoxides,[3] but has been strictly limited to oxidants containing the -OOH group.

Little is known about reactions of hypochlorous acid with ketones, and it appeared possible that this acid, which resembles peroxy acids in being both a weak acid and an oxidizing agent, might also convert ketones into esters.

We have treated a few simple ketones with aqueous hypochlorous acid at various pH's and examined the products. With cyclohexanone and cyclopentanone no trace of the appropriate lactones could be detected by glpc, the major result being chlorination. However, cyclobutanone was rapidly oxidized to γ-butyrolactone in 83% yield at pH 4.

Although this oxidation of cyclobutanone appears to be a rather special case, it was of interest to subject it to some mechanistic tests. The main alternative to a Baeyer–Villiger type (ionic) mechanism (Scheme I) is a radical ring opening to give 4-chlorobutyric acid (**5**) followed by a cyclization of the chloro acid **5** to the lactone (Scheme II). A third highly unlikely possibility is an unprecedented free-radical analog of the Baeyer–Villiger reaction (Scheme III). In all these mechanisms we assume as the first step an addition of hypochlorous acid to the keto group to give **1** which is analogous to that accepted for peroxy acids in the Baeyer–Villiger reaction. Scheme II involves a radical ring opening similar to one which is well established for alkyl hypochlorites;[4,5] *e.g.*, cyclobutyl hypochlorite decomposes thermally to 4-chlorobutyraldehyde.[5] This mechanism was excluded by subjecting the proposed intermediate 4-chlorobutyric acid to the conditions of the

SCHEME I



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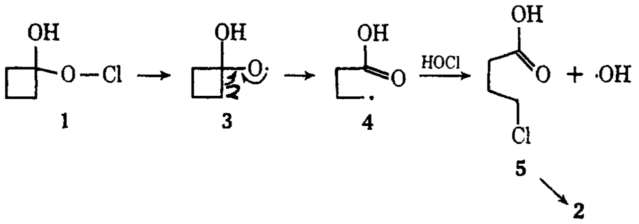

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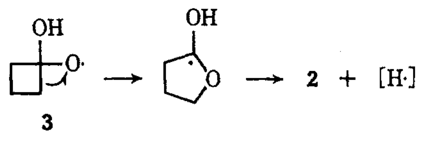

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(4) See, for example, F. D. Greene, M. L. Savitz, F. D. Osterholtz, H. H. Lau, W. N. Smith, and P. M. Zanet, *J. Org. Chem.*, **28**, 55 (1963).

(5) D. B. Denney and J. W. Hanifin, Jr., *ibid.*, **29**, 732 (1964).