[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME]

Aromatic *N*-Oxides. III. Reaction of 2-Picoline *N*-Oxide with Phenyl Acetates[1,2]

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The reactions of 2-picoline *N*-oxide with *m*- and *p*-nitrophenyl, 2,4-dinitrophenyl, and 2,4,6-trichlorophenyl acetates produced 2-pyridylmethyl acetate in 5–43% yield and these results are interpreted in terms of the mechanism of the reaction of 2-picoline *N*-oxide with acetic anhydride. When picryl acetate and 2-picoline *N*-oxide were mixed, there formed a 1:1 complex whose structure was established as 1-acetoxy-2-methylpyridinium picrate. This adduct upon treatment with triethylamine was converted to 2-pyridylmethyl acetate and triethylamine picrate and thus provides chemical evidence in support of 1-acetoxy-2-methylpyridinium cation as the initial species in the suggested mechanisms for reaction of 2-picoline *N*-oxide with acetic anhydride or various phenyl acetates.

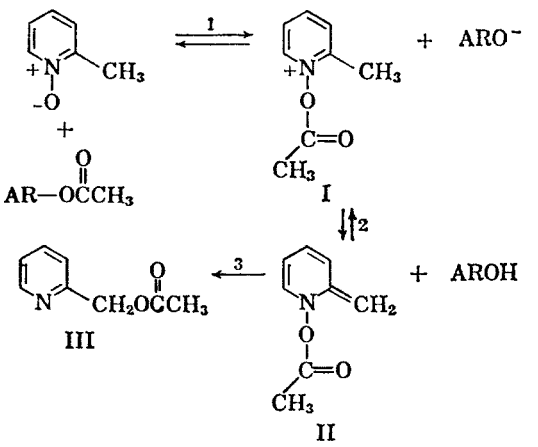
The reaction of 4-picoline *N*-oxide with 2,4,6-trichlorophenyl acetate gave 4-pyridylmethyl acetate along with some alkylpyridines.

The reaction of 2-alkylpyridine *N*-oxides and acetic anhydride to produce 2-(α-acetoxyalkyl)-pyridines has received much attention since its initial report by Boekelheide.[4,5] During the course of our study[5] of the mechanism of this reaction, we had occasion to observe the formation of 2-pyridylmethyl acetate when 2-picoline *N*-oxide was allowed to react with 2,4,6-trichlorophenyl acetate or 2,4-dinitrophenyl acetate. In this report we wish to describe our observations with these and other substituted phenyl acetates and interpret these results in terms of the mechanism for the reaction of 2-picoline *N*-oxide and acetic anhydride.

When phenyl acetate or *o*-chlorophenyl acetate and 2-picoline *N*-oxide were heated at 140–150° alone or in xylene, no observed reaction occurred and unchanged ester was recovered in 77% and 78% yield, respectively. However, *m*- and *p*-nitrophenyl acetate, 2,4-dinitrophenyl acetate, and 2,4,6-trichlorophenyl acetate did undergo reaction with 2-picoline *N*-oxide to produce 2-pyridylmethyl acetate (III) and the corresponding phenols. The yields of ester III ranged from 5–43% while the corresponding phenols were found in 12–50% yield. In addition unchanged ester was recovered from most experiments and in a few instances excellent material balance was found.

The phenols were identified by melting points and mixture melting points with authentic samples, while 2-pyridylmethyl acetate was characterized by physical constants, its picrate and comparison of the infrared spectrum with an authentic sample. In the case of the 2,4-dinitrophenyl acetate reaction, 2,4-dinitrophenol formed a 1:1 adduct with 2-picoline *N*-oxide and was isolated as such. The identity of this complex was established by: 1) analysis; 2) isolation of 2,4-dinitrophenol when the adduct was treated with hydrochloric acid; 3) formation of sodium 2,4-dinitrophenoxide by action of sodium hydroxide on the adduct; and 4) comparison with an authentic sample prepared from 2,4-dinitrophenol and 2-picoline *N*-oxide.

The mechanism of the reaction of 2-picoline *N*-oxide with acetic anhydride can easily be modified to account for the similar reaction with the phenyl acetates.



The initial step would involve nucleophilic attack of the ester carbonyl by the negative oxygen of 2-picoline *N*-oxide with subsequent formation of the 1-acetoxy-2-methylpyridinium (I) cation and aryloxide anion. After removal of an acidic proton from the 2-methyl group of I and the generation of a phenol and the anhydro base II, intramolecular rearrangement of II would give 2-pyridylmethyl acetate (III). In the proposed mechanism for reaction of 2-picoline *N*-oxide with acetic anhydride both cation I and the anhydro base II were suggested and evidence was offered for an intramolecular process leading to III.[5] This evidence excluded an alternate possibility for the formation of III which would involve a nucleophilic attack of

(1) For paper II in this series see V. J. Traynelis and R. F. Martello, *J. Am. Chem. Soc.*, 82, 2744 (1960).

(2) Presented in part at the 133rd Meeting of the American Chemical Society at San Francisco, Calif., in April 1958.

(3)(a) Abstracted in part from the Masters Dissertation submitted by Sr. Ann Immaculata Gallagher, I.H.M., in August 1959; (b) Peter C. Reilly Fellow 1957–58. Abstracted in part from the Ph.D. dissertation of R. F. Martello, May 1959.

(4) V. Boekelheide and W. J. Linn, *J. Am. Chem. Soc.*, 76, 1286 (1954).

(5) For leading references see V. J. Traynelis and R. F. Martello, *J. Am. Chem. Soc.*, 80, 6590 (1958).

acetate anion (generated in a manner analogous to step 1 above) upon the exocyclic methylene group of II with expulsion of the acetate function attached to nitrogen. In the ester reactions, such an attack of the aryl oxide anion on II would produce ethers; and, since such compounds were not found, especially in those cases where a good material balance was available, the results of these ester studies also reject this alternate path and add support to the evidence favoring the intramolecular conversion of II and III.

Since the displacement of the aryl oxide anion from the ester by the *N*-oxide oxygen should become more dificult as the basicity of the leaving anion increases, one attractive possibility for explaining the absence of reaction in the case of phenyl acetate and *o*-chlorophenyl acetate would be the failure of step 1 in the suggested reaction sequence. As the basicity of the phenoxide ion formed in step 1 was decreased by using acetate esters of more acidic phenols, reaction proceeded smoothly although not to the extent observed when acetic anhydride and 2-picoline *N*-oxide were allowed to react.

On the other end of the scale esters of highly acidic phenols may fail in reaction with 2-picoline *N*-oxide because the phenoxide ion may be too weak a base to promote step 2. Such an example was found in picryl acetate. When picryl acetate and 2-picoline *N*-oxide were mixed in benzene, an immediate precipitate (94%) appeared which was a 1:1 adduct of the two reactants. On evidence of elemental analysis, infrared spectrum, and chemical behavior, the structure assigned to the adduct was 1-acetoxy-2-methylpyridinium (I) picrate.

The characteristic carbonyl absorption bands of a series of phenyl acetates are listed in Table I and clearly indicate that electron-withdrawing nitro groups shift the carbonyl absorption to shorter wave lengths. Inspection of the carbonyl band in the adduct shows it is displaced to an even shorter wave length. This observation is consistent with the assigned structure since the electron withdrawing effect of a positively charged pyridinium ring should be more pronounced than a number of nitro groups.

TABLE I

CARBONYL ABSORPTION IN THE INFRARED OF SOME PHENYL ACETATES

Ester	μ
Phenyl acetate	5.70[a]
m-Nitrophenyl acetate	5.66
p-Nitrophenyl acetate	5.65
2,4-Dinitrophenyl acetate	5.60
2,4,6-Trinitrophenyl acetate	5.55
1-Acetoxy-2-methylpyridinium picrate	5.44

[a] Taken from the work of Rasmussen and Brattain.[6]

(6) R. S. Rasmussen and R. B. Brattain, *J. Am. Chem. Soc.*, **71**, 1073 (1949).

In chemical behavior the adduct contains a labile acetyl group which is readily removed by water or ethanol with the formation of the picrate of 2-picoline *N*-oxide. The action of sodium acetate in acetic acid on the adduct gave a quantitative recovery of picric acid and 55% 2-picoline *N*-oxide isolated as its picrate with no evidence for the presence of 2-pyridylmethyl acetate. Failure to observe rearrangement here may be attributed to attack of acetate anion at the 1-acetoxy carbonyl group to produce sodium picrate, 2-picoline *N*-oxide, and acetic anhydride, and these reactants were present in such low concentration that normal reaction either failed or occurred to a very small extent. However, when the adduct was heated with triethylamine in anhydrous dioxane followed by chromatography, equal amounts of triethylamine picrate (20%) and 2-pyridylmethyl acetate (20%), isolated and characterized as its picrate, were found. This last reaction can be rationalized according to the mechanism described previously with the triethylamine serving as the base to convert I to II.

These results now provide evidence that cation I can be formed in the first step of the reaction of 2-picoline *N*-oxide with phenyl acetates or acetic anhydride, and that I by action of base and subsequent rearrangement leads to III by an intramolecular process.

Reaction of 2,4,6-trichlorophenyl acetate with 4-picoline *N*-oxide in xylene gave 4-pyridylmethyl acetate (10%) and a mixture of pyridine bases: 4-picoline (13%), 2,4-dimethylpyridine (2.5%), and 4-ethylpyridine (2.7%). The bases were separated by vapor phase chromatography and identified by comparison of the infrared spectra with those of authentic samples. 2,4,6-Trichlorophenol was isolated in 34% yield and identified by melting point and mixture melting point. These results can be rationalized according to the scheme described previously[1] with the modifications introduced for the 2-picoline *N*-oxide-phenyl acetates reaction.

EXPERIMENTAL[7]

Starting esters. Phenyl acetate, b.p. 90° (20 mm.), n_D^{20} 1.5030, was prepared by the procedure of Vogel,[8] while the method of Wohlleben[9] was used to make *o-chlorophenyl acetate*, b.p. 108° (16 mm.), n_D^{25} 1.5145 [lit.[9] b.p. 108° (15 mm.)]. *m-Nitrophenyl acetate*, (97%), m.p. 54–56° (lit.[10] m.p. 55–56°); *p-nitrophenyl* acetate (83%), m.p. 76.5–78° (lit.[11] m.p. 82°); *2,4-dinitrophenyl acetate* (79%), m.p. 70–72° (lit.[12] m.p.

(7) All melting points and boiling points are uncorrected. The microanalyses were carried out by Midwest Microlab Inc., Indianapolis, Ind.

(8) A. I. Vogel, *Textbook of Practical Organic Chemistry*, 3rd Edition, Longmans, Green and Co., N. Y., 1956, p. 66.

(9) W. J. Wohlleben, *Ber.*, **42**, 4370 (1909).

(10) F. Arnall, *J. Chem. Soc.*, **125**, 816 (1924).

(11) P. Grammaticakis, *Bull. soc. chim. France*, 544 (1951).

(12) J. J. Blanksma, *Chem. Weekblad*, **6**, 717–27 (1909); *Chem. Abstr.*, **4**, 752 (1910).

72°); and *2,4,6-trichlorophenyl acetate* (94%), m.p. 49° (lit.[13] m.p. 49–51°) were prepared from the corresponding phenol, acetic anhydride, and 1–3 ml. of concd. sulfuric acid as described by Blanksma.[12]

2,4,6-Trinitrophenyl acetate. Following the procedure of Tommasi and David,[14] picric acid (10 g., 0.044 mole) and acetic anhydride (21.6 g., 0.21 mole) gave after several crystallizations from anhydrous ether 6 g. (51%) of colorless 2,4,6-trinitrophenyl acetate, m.p. 86–87° (lit. m.p.[14,15] 75–76°, m.p. [16] 96.5–97.5).

Reaction of 2-picoline N-oxide with the phenyl esters. General procedure. A mixture of equal molar amounts of 2-picoline *N*-oxide and a phenyl ester was heated alone or in xylene at 140–150°, or in other refluxing solvents for a period of 2.5 to 9 hr. When no solvent was used, benzene or ether was added after the heating period. In some cases the unchanged 2-picoline *N*-oxide was removed by extraction with water. An acid wash (10% hydrochloric acid) removed the basic component which was liberated when the solution was made alkaline, extracted into ether, dried, and isolated by distillation. On some occassions a direct distillation of the reaction mixture was used to obtain the 2-pyridylmethyl acetate. The phenol was removed by extraction with 5% sodium hydroxide and was liberated upon acidification, while unchanged phenyl ester in the remaining reaction residue was isolated by distillation or evaporation followed by crystallization.

When phenyl acetate (0.093 mole) and 2-picoline *N*-oxide (0.093 mole) were heated at 140–150° for 2 hr. or refluxed in xylene for 8 hr., only the starting ester (77% and 35%, respectively) was isolated; *o*-chlorophenyl acetate (0.058 mole) and 2-picoline *N*-oxide (0.058 mole) in xylene refluxed for 8 hr. gave only the starting ester (78%). In these two experiments, the basic extract of the reaction mixture gave negative ferric chloride and bromine tests for phenols.

m-Nitrophenyl acetate (0.059 mole) and 2-picoline *N*-oxide (0.059 mole) in xylene were refluxed for 4 hr. and produced 5% 2-pyridylmethyl acetate, isolated as the picrate, 12% *m*-nitrophenyl, m.p. 95–97°, and 80% unchanged ester, m.p. 54–56°; while *p*-nitrophenyl acetate (0.095 mole) under similar conditions gave 37% 2-pyridymethyl acetate, b.p. 112–116° (12 mm.), n_D^{25} 1.5062, and 52% *p*-nitrophenol, m.p. 110–114°. When 2,4,6-trichlorophenyl acetate (0.067 mole) and 2-picoline *N*-oxide (0.15 mole) in tetrachloroethane were refluxed for 4 hr., 22% 2-pyridylmethyl acetate, 24% 2,4,6-trichlorophenol, and 65% unchanged ester were found, while 9 hr. of reflux in xylene produced 43% 2-pyridylmethyl acetate and 50% 2,4,6-trichlorophenol.

The reaction of 2-picoline *N*-oxide (0.10 mole) and 2,4-dinitrophenyl acetate (0.11 mole) in refluxing toluene for 2.5 hr. formed 28% 2-pyridylmethyl acetate, 26% starting ester, m.p. 68–70° and 34% of a yellow 1:1 molecular complex of 2-picoline *N*-oxide and 2,4-dinitrophenol, m.p. 137–141°.

Anal. Calcd. for $C_{12}H_{11}N_3O_6$: C, 49.15; H, 3.78. Found: C, 49.39; H, 3.84.

Treatment of the yellow complex with dilute sodium bicarbonate produced a bright yellow solid which did not melt and upon acidification with hydrochloric acid gave 2,4-dinitrophenol, m.p. 112–114°. A mixture melting point with an authentic sample was not depressed. The molecular complex upon treatment with dilute hydrochloric acid also liberated 2,4-dinitrophenol, m.p. 112–114°.

The reaction of 2,4-dinitrophenol with 2-picoline N-oxide. A solution of 2-picoline *N*-oxide (1.0 g., 0.009 mole), 2,4-dinitrophenol (1.7 g., 0.009 mole) in ethanol (20 ml.) was refluxed for 25 min., filtered, and after cooling gave 2.1 g. (77%) of the 1:1 molecular complex, m.p. 137–141°. A mixture melting point with the material in the above experiment showed no depression.

Reaction of 2-picoline N-oxide and 2,4,6-trinitrophenyl acetate (picryl acetate). Equimolar solutions of picryl acetate (9.3 g., 0.034 mole) in 50 ml. of dry benzene and 2-picoline *N*-oxide (3.7 g., 0.034 mole) in 50 ml. of dry benzene were added with vigorous stirring at the same rate to 15 ml. of anhydrous benzene. A bright yellow solid appeared immediately upon mixing and filtration gave 12.2 g. (95%) of 1-acetoxy-2-methylpyridinium picrate (the adduct), m.p. 105–109° dec. (sealed tube).

Anal. Calcd. for $C_{14}H_{12}N_4O_9$: C, 44.22; H, 3.18. Found: C, 43.82, 43.73; H, 3.31, 3.32.

This yellow solid was very hygroscopic and upon standing exposed to air liberated acetic acid and gave 2-piccline *N*-oxide picrate. Also upon crystallization from ethanol 2-picoline *N*-oxide picrate, m.p. 123.5–125° (mixture melting point with authentic sample, 123.5–125°) was isolated. When the adduct was heated under nitrogen, decomposition occurred at 106° and gave a black residue.

Reaction of 1-acetoxy-2-methylpyridinium picrate and sodium acetate. A mixture of the adduct (2.5 g., 0.006 mole) and sodium acetate (1 g., 0.012 mole) in 15 ml. of glacial acetic acid was refluxed for 2 hr., cooled, and acidified with 10% hydrochloric acid. The picric acid, m.p. 120–122° (0.9 g., 60%) was filtered and the remainder (0.6 g., 40%) was isolated by extraction with benzene followed by removal of the solvent. The remaining acid solution was made strongly alkaline and extracted with chloroform. After removal of the chloroform, the residue was converted to a picrate and gave 1.1 g. (55%) of picrate of 2-picoline *N*-oxide, m.p. 123–125°. A mixture melting point with an authentic sample was not depressed.

Reaction of 1-acetoxy-2-methylpyridinium picrate and triethylamine. Triethylamine (0.8 g., 0.079 mole) was added to a solution of the adduct (2.5 g., 0.006 mole) in 20 ml. of dry dioxane. The solution immediately changed to a red color. After 1 hr. of reflux, the reaction mixture was cooled, placed on 60 g. of Merck acid-washed alumina packed in a 2 × 2.5-cm. column and eluted with anhydrous ether. The fifth 50-ml. fraction contained 2-pyridylmethyl acetate which was isolated as the picrate (0.5 g., 20%), m.p. 163–165° (lit.[4] m.p. 168–168.5°). A mixture melting point with an authentic sample was not depressed. Fractions 6–9 upon recrystallization from ethanol after a charcoal treatment gave 0.4 g. (20%) of the picrate of triethylamine, m.p. 173–174° (lit. m.p.[17] 175°). A mixture melting point with an authentic sample was the same.

Reaction of 4-picoline N-oxide and 2,4,6-trichlorophenyl acetate. A solution of 4-picoline *N*-oxide (22.0 g., 0.20 mole), 2,4,6-trichlorophenyl acetate (23.7 g., 0.0099 mole) and xylene (60 ml.) was refluxed for 10 hr. and after cooling was washed with 10% hydrochloric acid. The aqueous solution was made alkaline with potassium carbonate and extracted with ether. After the ether was removed, distillation gave fraction I, 1.8 g. of a colorless liquid, b.p. 70–75° (50 mm.) and fraction II, 1.5 g. (10%) of 4-pyridylmethyl acetate, b.p. 118–120° (14 mm.), $n_D^{18.5}$ (1.5045). Fraction I was analyzed by vapor phase chromatography under conditions described previously[1] and contained 4-picoline (13.3%), 2,4-dimethylpyridine (2.5%) and 4-ethylpyridine (2.7%).[18]

The reaction mixture was extracted with sodium bicarbonate solution, which upon acidification gave 6.2 g. (34%) of 2,4,6-trichlorophenol, m.p. 65–67°.

(13) K. V. Auwers and W. Mauss, *Ann.*, **464**, 310 (1928).
(14) D. Tommasi and H. David, *Compt. rend.*, **77**, 207 (1873).
(15) A. Hantzsch, *Ber.*, **39**, 1097 (1906).
(16) S. C. J. Olivier and G. Berger, *Rec. trav. chim.*, **46**, 610 (1927).
(17) C. K. Ingold and J. A. Jessop, *J. Chem. Soc.*, 2361 (1929).
(18) Identification of these was as described previously.[1]

Infrared spectra. The infrared spectra of the compounds listed in Table I were recorded from a potassium bromide disk on a Perkin-Elmer, Model 21, recording spectrophotometer with sodium chloride optics. Other spectra were taken on the above instrument or a Baird Associates infrared spectrophotometer.

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NOTRE DAME, IND.

[CONTRIBUTION FROM THE CHEMICAL DIVISION, AEROJET-GENERAL CORP.]

The Preparation and Reactions of 1,1,3,3-Tetranitropropane[1]

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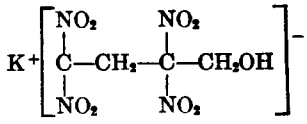
1,1,3,3-Tetranitropropane has been prepared by deformylation of aqueous potassium *aci*-2,2,4,4-tetranito-1-butanol (I). The alcohol I was prepared by partial acidification of potassium *aci*-2,2-dinitroethanol. 1,1,3,3-Tetranitropropane is a low-melting unstable solid which in the form of its dipotassium salt was found to undergo reactions typical of terminal *gem*-dinitro groups. It reacted as a bifunctional compound upon condensation with formaldehyde, yielding 2,2,4,4-tetranitro-1,5-pentanediol; with methyl acrylate, however, it reacted as a monofunctional compound, yielding only methyl potassium *aci*-4,4,6,6-tetranitrohexanoate.

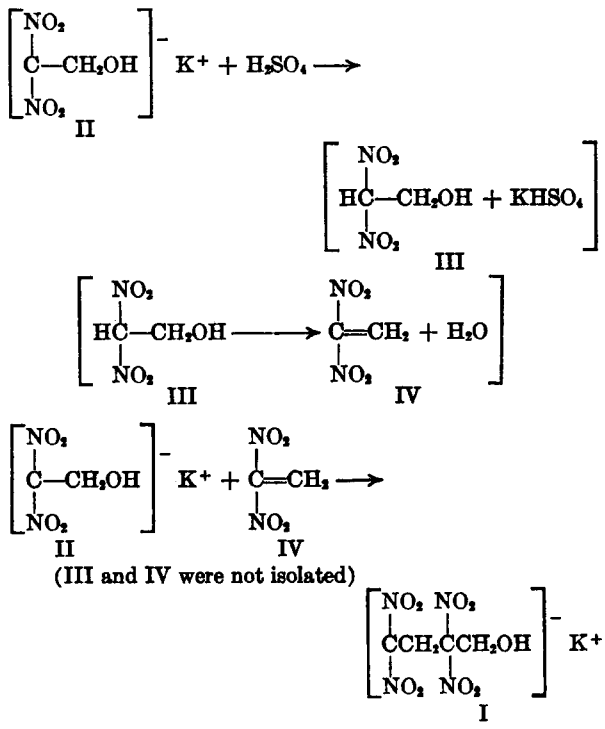
Herzog, Gold, and Geckler[2] described a new method for the preparation of potassium *aci*-2,2-dinitroethanol and a subsequent paper dealt with the reactions of this compound with α,β-unsaturated carbonyl compounds and formaldehyde.[3] Duden and Pondorf[4] had previously reported that the acidification of potassium dinitroethanol with excess mineral acid, in addition to the gases nitrogen, nitric oxide, nitrogen dioxide, carbon monoxide and carbon dioxide, gave a poor yield of a crystalline compound of unknown structure having the empirical formula $C_5H_2N_4O_7$. We have found that upon partial acidification, potassium *aci*-2,2-dinitroethanol is converted into potassium *aci*-2,2,4,4-tetranitro-1-butanol (I). The



I

facile formation of the 1,1,3,3-tetranitropropane structure stimulated a study of the influence of *p*H upon the yield of I from aqueous potassium *aci*-2,2-dinitroethanol solutions. From this study it was concluded that the optimum conditions were a *p*H of 4, 20°, and two and one-half hours' reaction time. Under these conditions, potassium *aci*-2,2-dinitroethanol was converted into I in 70% yield. The crystalline compound reported by Duden and Pondorf[4] was not isolated under these conditions.

The formation of I can be explained by the following reaction scheme:



II III IV

(III and IV were not isolated)

The potassium salt (II) was partially converted, at a *p*H of 4, into 2,2-dinitroethanol (III). Elimination of water from III would give 1,1-dinitroethylene (IV), which as an α,β-unsaturated nitro compound would react with II in a Michael addition-type reaction forming potassium tetranitro-1-butanol (I). The formation of 1,1-dinitroethylene as a reactive intermediate has been postulated in similar reactions.[5,6]

(1) This work was performed under a contract with the Office of Naval Research.

(2) L. Herzog, M. H. Gold, and R. D. Geckler, *J. Am. Chem. Soc.*, 73, 749 (1951).

(3) K. Klager, *J. Org. Chem.*, 16, 161 (1951).

(4) P. Duden and G. Pondorf, *Ber.*, 38, 2031 (1905).

(5) M. B. Frankel, *J. Org. Chem.*, 23, 813 (1958).

(6) L. Zeldin and H. Shechter, *J. Am. Chem. Soc.*, 79, 4708 (1957).