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Reaction of Acyl Oxime with Mercaptan

Rokuro SUDO, Akira KANEDA and Nobuo FURUOYA

Laboratory of Organic Chemistry, Tokyo Institute of Technology, Meguro-ku, Tokyo

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The acyl derivative of oxime, derived from a strong acid, is generally unstable. However, acyl oximes of the ethyl α-oximinoacetate derivative were prepared and were found to be more stable than ordinary acyl oxime. Acetyl, carbethoxy, benzoyl, and even tosyl ester were prepared, and their reactions with the mercaptide anion were investigated.

In general, acyl derivatives of oxime can be readily isolated as long as the acyl group is not derived from a very strong acid.[1] Recently, however, tosyl ester of α-oximinobenzylcyanide[2] and ethyl α-oximinophenylacetate[3] were found to be more stable than ordinary oxime tosylate. In our study[3] of the nucleophilic attack of the mercaptide anion on the carbon of the C=N function, some acyl esters of ethyl α-oximininopropionate (**1**) and ethyl α-oximinophenylacetate (**2**) were prepared, and their reactions with the mercaptide anion were investigated. The characteristics of these acyl oximes, prepared from the corresponding ethyl α-oximinoacetate derivative and acyl chloride, are summarized in Table 1.

TABLE 1. ACYL OXIMES $R-\underset{\underset{N-OR_1}{\|}}{C}-COOC_2H_5$

R_1	Mp (bp) °C	Yield %	Recryst. solvent	Compound number
R=CH₃				
CH_3CO	113/8 mmHg	47		**3**
C_6H_5CO	55	81	ligroin	**4**
C_2H_5-OCO	136/7 mmHg	86	isopropyl alcohol	**5**
p-$CH_3C_6H_4SO_2$	39	80		**6**
R=C₆H₅				
CH_3CO	145/1 mmHg	75		**7**
p-$CH_3C_6H_4SO_2$	96	35	ethanol	**8**

When acetyl ester (**3**) of ethyl α-oximinopropionate was treated with benzyl mercaptan in benzene, no reaction occurred, but in benzene containing an equivalent amount of triethylamine, it afforded four products: ethyl α-oximinopropionate (**1**), benzyl thioacetate (**9**), ethyl α-benzylsulfeniminopropionate (**11**), and triethylammonium acetate (**12**) (Fig. 1). **11** was characterized by elementary analysis and by a study of its IR and NMR spectra. The IR spectrum had absorptions at 1712 cm^{-1} (C=O of the ester) and at 1586 cm^{-1} (C=N), and the NMR spectrum had a CH_3-singlet at τ 7.88, indicating that the methyl group is attached to carbon, while that of the C=N-CH_3 singlet in the 2-methyliminodithiolane[4] (**13**) is at τ 6.9.

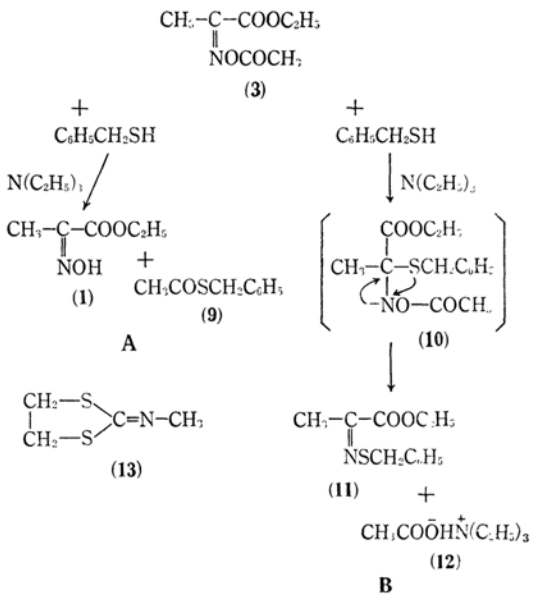

Fig. 1.

Furthermore, the fact that the reaction of this compound with hydrochloric acid in ethanol yielded dibenzyl disulfide (**14**) and ammonium chloride supported the sulfenimino structure of **11**. The presence of **14** and ammonium chloride in the

1) P. A. S. Smith, "The Chemistry of Open-Chain Organic Nitrogen Compounds," Vol. II, W. A. Benjamin, Inc., New York, (1966), p. 46.

2) T. E. Stevens, *J. Org. Chem.*, **28**, 2436 (1963).

3) A. Kaneda, M. Nagatsuka and R. Sudo, This Bulletin, **40**, 2705 (1967).

4) T. Nakai and S. Ohkawara, presented at the 21st Annual Meeting of The Chemical Society of Japan, Okaka, April 1968.

products indicates that the intermediates of the reaction are ethyl α-iminopropionate (**15**) and benzylsulfenchloride (**16**) (Fig. 2).

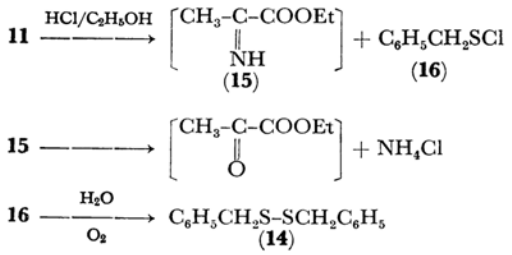

Fig. 2

Thus, acetyl ester of ethyl α-oximinopropionate can be expected to manifest its nucleophilic activity at two sites: at the carbon of the carbonyl in the acyl group, yielding **1** (A route), and at the carbon of the C=N function (B route) yielding ethyl α-benzylmercapto-α-acetoxyaminopropionate (**10**) (B route). **10** seems to have been converted to **11** through a migration of the benzylmercapto group from carbon to nitrogen, accompanied by the elimination of the acetoxy group, instead of through the Beckmann rearrangement, which usually occurs with acyl oxime. Another mechanism is possible, that in which the mercaptide anion attacks nitrogen directly, leading to a nucleophilic substitution. In a similar method, other acyl esters of the ethyl α-oximinoacetate derivative were treated with benzyl mercaptan; these results are summarized in Table 2. In the case of tosyl ester, only the

Table 2. Reaction products of acyl oximes with benzyl mercaptan

R_1 in $R\text{-}C(=N\text{-}OR_1)\text{-}COOC_2H_5$	Products: $R\text{-}C(=N\text{-}SCH_2C_6H_5)\text{-}COOC_2H_5$ %	Products: $R\text{-}C(=NOH)\text{-}COOC_2H_5$ %
R=CH$_3$		
H	0	no reaction
CH_3CO	8	69
C_6H_5CO	38	36
C_2H_5OCO	52	23
p-$CH_3C_6H_4SO_2$	quantitative	0
R_1=C$_6$H$_5$		
H	0	no reaction
CH_3CO	2	60
p-$CH_3C_6H_4SO_2$	quantitative	0

product from the **B** route was obtained; thus, the reaction with benzyl mercaptan gave the benzylsulfenimino compound, and also ethyl α-ethylsulfeniminopropionate (**17**) with ethyl mercaptan. On the other hand, the ethyl trichloroacetylpropionate **18** and diethyl phosphate **19** of ethyl α-oximinopropionate, which were prepared from **1** and the corresponding acid chloride, were carefully treated with benzyl mercaptan to give the original oxime **1** quantitatively (A route). Because, they appeared to undergo hydrolysis very easily and to give **1**.

It has been reported[3] that the tosyl ester of α-oximinobenzylcyanide (**20**) afforded α-benzylmercapto-α-phenylimino acetonitrile (**21**) through the Beckmann rearrangement in a similar reaction. This is erroneous, for the product was α-benzylsulfeniminobenzyl cyanide (**22**). This compound was very stable even when it was refluxed in an aqueous hydrochloric acid or sodium hydroxide solution, but it was converted to ethyl benzoate, dibenzyl disulfide(**14**), and anmmonium chloride when it was treated with hydrochloric acid in ethanol under cooling. Similarly, the tosyl ester **20′** of ethyl α-oximinophenylacetate afforded ethyl α-benzylsulfeniminophenylacetate (**22′**), which was then converted to ethyl benzoyl formate, dibenzyl disulfide, and ammonium chloride (Fig. 3).

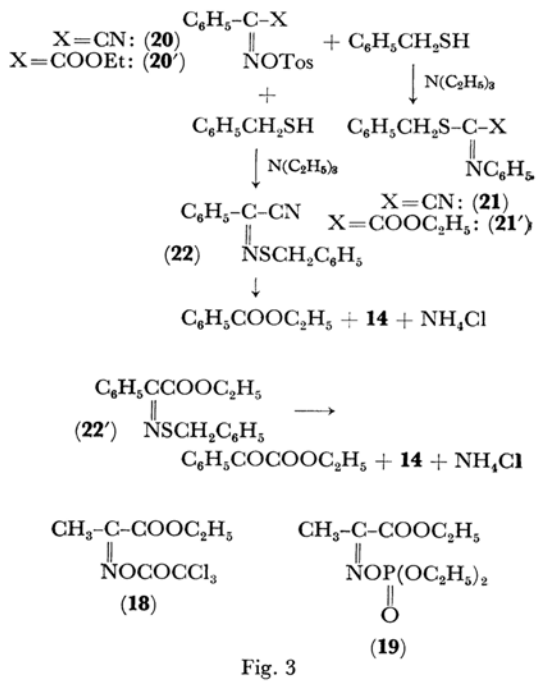

Fig. 3

Experimental

Ethyl α-oximinopropionate (**1**)[5] and ethyl α-oximinophenylacetate (**2**)[6] were prepared by the nitrosation of ethyl α-methylacetoacetate and ethyl phenylacetate; they melted at 96°C and 95—96°C respectively.

Acetylation of the Ethyl α-Oximinopropionate

5) W. Wislicenus, *Ber.*, **42**, 1934 (1909).
6) K. E. Hamlin and W. H. Hartung, *J. Biol. Chem.*, **145**, 355 (1942).

Derivatives (3, 4, 5 and 6). To a solution of 0.1 mol of **1** and 0.1 mol of triethylamine in 50 m*l* of ether there was added 0.1 mol of the corresponding acetyl chloride derivative. The mixture was then refluxed for 2 hr and, after cooling, washed with 50 m*l* of water. The ether solution was concentrated to give a crude product, which was purified by distillation or by recrystallization. The physical constants are summarized in Table 1 and Table 3.

Ethyl α-Acetoximinophenylacetate (7). Sodium salt[3] of **2** (21.5 g, 0.1 mol) was suspended in 50 m*l* of benzene. To this solution, which was stirred vigorously, there was then added, drop by drop, 8 g (0.1 mol) of acetyl chloride under cooling. After the addition had been completed, the mixture was warmed at 40°C for 30 min. After cooling, it was poured into water. The benzene layer was separated and dried over anhydrous sodium sulfate. It was concentrated to give an oil, which was distilled at 145°C/1 mmHg, giving **7**. Yield, 17.7 g (75%).

Tosyl Ester of α-Oximinophenylacetate (8). Sodium salt[3] of **2** (21.5 g, 0.1 mol) was suspended in 50 m*l* of benzene. To this solution, which was stirred vigorously, there were then added, drop by drop, 19 g of *p*-toluenesulfonyl chloride dissolved in 30 m*l* of benzene. After the addition was completed, the mixture was refluxed for 1 hr. After cooling, the mixture was washed with water and was dried over anhydrous sodium sulfate. The mixture was concentrated to give crystals which were recrystallized from ethanol. Mp 95—96°C Yield, 12.1 g (35%). The physical constants of **7** and **8** are listed in Table 1 and Table 3.

TABLE 3. ELEMENTARY ANALYSIS OF ACYL OXIMES

Compound number	Anal. % Calcd C	H	N	Found C	H	N
R=CH_3						
3	48.55	6.40	8.09	48.46	6.12	8.32
4	61.27	5.57	5.96	61.44	5.68	6.17
5	47.29	6.45	6.89	47.88	6.59	6.47
6	50.52	5.30	4.91	50.63	5.29	5.01
R=C_6H_5						
7	61.27	5.57	5.96	61.45	5.43	6.09
8	58.79	4.93	4.03	58.73	4.89	3.80

Reaction of Ethyl α-Acetoximinopropionate (3) with Benzyl Mercaptan. To a solution of 17.3 g (0.1 mol) of **3** in 50 m*l* of dry benzene containing 10.1 g (0.1 mol) of triethylamine, 12.4 g (0.1 mol) of benzyl mercaptan were added. The mixture was then refluxed for 6 hr. After cooling, water was added to the mixture. The benzene layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure; 50 m*l* of ligroin were then added. The precipitated crystals were collected by filtration and were found to be the original oxime (**1**) by a mixed-melting-point procedure. The ligroin filtrate was concentrated to give an oil, which was then purified by distillation and which was identified as ethyl α-benzylmercaptiminopropionate (**11**), bp 135°C/1 mmHg, mp 36—37°C. The yields of **1** and **11** are listed in Table 2. IR bands (KBr): 1712 cm^{-1} (C=O), 1586 cm^{-1} (C=N). NMR spectrum, $CDCl_3$ (TMS as internal reference): τ 8.69 (3H, triplet) for $-CH_2-C\underline{H}_3$, τ 7.88 (3H, singlet) for $-CH_3$, τ 5.74 (2H, quartet) for $-C\underline{H}_2-CH_3$, and τ 5.57 (2H singlet) for $-C\underline{H}_2-C_6H_5$. In a similar procedure, other acyl oximes, (**4**, **5** and **6**), were treated with benzyl mercaptan; the results are summarized in Table 2.

Ethyl α-Ethylsulfeniminopropionate (17). In a procedure similar to **11**, **6** was treated with ethyl mercaptan and was converted to **17**. **17** was distilled at 103°C/8 mmHg. Yield, 96%. IR bands (NaCl): 1712 cm^{-1} (C=O), 1586 cm^{-1} (C=N); NMR ($CDCl_3$, TMS as the internal reference): τ 8.67 (3H, triplet) for $-COOCH_2C\underline{H}_3$, τ 8.59 (3H, triplet) for $-S-CH_2-C\underline{H}_3$, τ 7.81 (3H, singlet) for $-CH_3$, τ 6.83 (2H, quartet) for $-S-C\underline{H}_2-CH_3$, and τ 5.72 (2H, quartet) for $-COOC\underline{H}_2-CH_3$.

Reaction of Ethyl α-Benzylsulfeniminopropionate (11) with Hydrochloric Acid in Ethanol. The propionate, **11** (11.6 g, 0.05 mol), was added under cooling to 30 m*l* of ethanol containing hydrochloric acid. The solution was then kept at room temperature overnight. The precipitated crystals were collected by filtration and found to be ammonium chloride. Yield, 1.8 g. The filtrate was concentrated to one third of the original volume and kept at room temperature. The precipitated crystals were collected by filtration and found to be dibenzyl disulfide (yield, 7 g) by a mixed-melting-point procedure. The filtrate was concentrated to an oil. The isolation of the product from this oil, by either distillation or recrystallization, was not successful.

Reaction of α-Benzylsulfeniminobenzyl Cyanide (22) with Hydrochloric Acid in Ethanol. In a procedure similar to that described above, **22**[3] was treated with hydrochloric acid. Dibenzyl disulfide and ammonium chloride were obtained, and the final oily residue was distilled to give an oil which was identified as ethyl benzoate by a study of its IR spectrum.

Reaction of Ethyl α-Benzylsulfeniminophenylacetate (22′) with Hydrochloric Acid in Ethanol. In a procedure similar to that used in the reaction of **22**, **22′** [3] was treated with hydrochloric acid to give dibenzyl disulfide, ammonium chloride, and ethyl benzoylformate, which was identified by means of the IR spectrum.