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Preparation of Carboxamide using Halosulfonium Salt[1]

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The equimolar reaction of carboxylic acids and amines with halosulfonium chloride afforded the corresponding carboxamides. Mechanism is discussed on the basis of sulfoxide formation.

Keywords——oxidation of sulfide; halosulfonium complex; carboxamide; sulfoxide; dehydration;

Recently, Corey and Kim[3] reported a new oxidation method of alcohols to carbonyl compounds with the halosulfonium salt or the azasulfonium salt without the formation of sulfoxide. On the other hand, Oae *et al.*[4] reported that halosulfonium salts were successfully oxidized to corresponding sulfoxides with water or acetic acid.

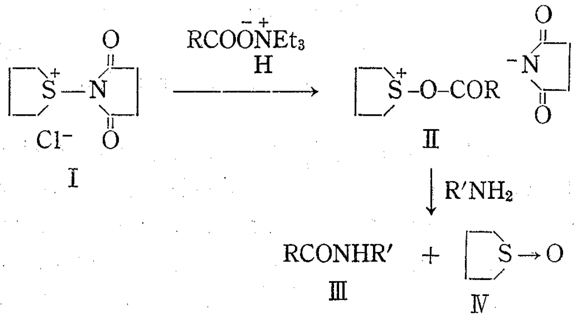

Fig. 1

We explored the applicabitity of the reagents for carboxyl activation. The halo-

TABLE I

RCOOH	R′	RCONHR′ (III) mp (°)	Reported	Yield (%)	IR cm^{-1}: $\nu_{C=O}$ (KBr)
CH_3	$PhCH_2$	59— 62 White needles	61[a]	50 (15[i])	1630
C_2H_5	$PhCH_2$	42— 43 White needles	42[b]	5	1630
	Ph	104—106 White needles	105[c]	6	1665
t-C_4H_9	Ph	Oil	Oil[d]	9	1640 (film)
Ph	$PhCH_2$	105—106 White needles	105[e]	6	1635
	n-C_4H_9	40— 42 White needles	41— 42[f]	6	1630
	t-C_4H_9	134—136 White needles	134[g]	11	1630
$PhCH_2$	$PhCH_2$	121—122 White needles	121—122[d]	60	1640
	n-C_4H_9	54— 56 White needles	55—56[h]	40	1650
	t-C_4H_9	112—114 White needles	115—116[g]	78	1635

a) H.O. Nicholas and J.L. Erickson, *J. Am. Chem. Soc.*, **48**, 2174 (1926).
b) C.A. Buehler and C.A. Mckenzie, *J. Am. Chem. Soc.*, **59**, 421 (1937).
c) E.C. Gilbert and L. Clarke, *J. Am. Chem. Soc.*, **49**, 2296 (1927).
d) O.C. Dermer and J. King, *J. Org. Chem.*, **8**, 168 (1943).
e) A.E. Martell and M. Herbst, *J. Org. Chem.*, **6**, 878 (1941).
f) H.W. Grimmel and A. Guenther, Brit. Patent 610952 (1948) [*C.A.*, 43, 4686 (1949)].
g) J.J. Ritter and P.P. Minieri, *J. Am. Chem. Soc.*, **70**, 4045 (1948).
h) O.M. Behr, G. Eglinton, I.A. Lardy, and R.A. Ruphael, *J. Chem. Soc.*, **1964**, 1147.
i) Sodium acetate was used instead of NEt_3.

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1) This constitutes part XXIV of a series entitled Studies on Heterocyclic Compounds.
2) Location: *Shirokane, Minato-ku, Tokyo 108, Japan.*
3) E.J. Corey and C.U. Kim, *J. Am. Chem. Soc.*, **94**, 7586 (1972).
4) W. Tagaki, K. Kikukawa, K. Ando, and S. Oae, *Chem. Ind.* (London), **1964**, 1924; S. Oae, Y. Ohnishi, S. Kozuka, and W. Tagaki, *Bull. Chem. Soc. Jpn*, **39**, 364 (1966).

sulfonium salt or the azasulfonium salt might be expected to react with carboxylic acids under the presence of tertiary amines, and further reaction with primary amines to form carboxamide and sulfoxide. In this report, we show a carboxamide formation using the azasulfonium salt.

The reaction of azasulfonium salt(I) and phenylacetic acid afforded N-benzylphenylacetamide(III) and tetrahydrothiophen-1-oxide(IV) both in 60% yields. The sulfoxide was identified by comparisons of infrared (IR) ($\nu_{S\rightarrow O}$ 1030 cm^{-1}), thin-layer Chromatography (TLC) and mass spectrum (MS) (M^+: *m/e* 104) with those of an authentic sample.

The reaction mechanism of the formation of carboxamides suggests that an intermediate salt (II) formation may play an important role. Nucleophilic attack with amines to the intermediate (II) yields carboxamide (III) and sulfoxide (IV). The oxygen of the sulfoxide is originated from the starting acid through the intermediate(II) (Fig. 1 and Table I).

Experimental

N-Benzylphenylacetamide(General Procedure: Table I)——Tetrahydrothiophen (0.53 g; 0.006 mol) was added to a stirred solution of N-chlorosuccinimide (0.8 g; 0.006 mol) in toluene (20 ml) at 0° under argon. A white precipitate appeared immediately after addition of the tetrahydrothiophene. To the cooled (−45°) mixture, a solution of phenylacetic acid (0.68 g; 0.005 mol) and NEt_3 (0.5 g; 0.005 mol) in toluene was added dropwise under stirring. After the mixture had been stirred for 1 hr at −45°, a solution of benzylamine (0.54 g; 0.005 mol) in toluene was added dropwise. After the reaction mixture was refluxed for 6 hr, the cooled reaction mixture was quenched with H_2O and the product was extracted with EtOAc. The organic layer was washed with aqueous $NaHCO_3$, 1 N HCl, and H_2O, successively, and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was separated by TLC (silica gel) to afford 0.69 g (60%) of N-benzylphenylacetamide, as white needles, mp 121—122°. IR cm^{-1}: ν_{CO} 1640 (KBr).

From the reaction mixture above obtained, separation of the TLC afforded 0.37 g (60%) of tetrahydrothiophen-1-oxide, identifide to an authentic sample with IR ($\nu_{S\rightarrow O}$ 1030 cm^{-1}) TLC and MS (M^+ *m/e* 104).