CHEMISTRY LETTERS, pp. 123 - 126, 1985.

THE SYNTHESIS OF AMIDES, ESTERS, AND THIOESTERS[1)]

Muneharu MIYAKE, Makoto KIRISAWA, and Norio TOKUTAKE*
Department of Pharmacy, College of Science and Technology, Nihon University, 1-8 Kandasurugadai, Chiyoda-ku, Tokyo 101

Diethyl 2-(3-oxo-2,3-dihydro-1,2-benzisosulfonazolyl)phosphonate is a highly reactive condensing agent, which provides good yield route to amides, esters, and thioesters from a variety of amines, active hydroxylamines, and thiols and acids.

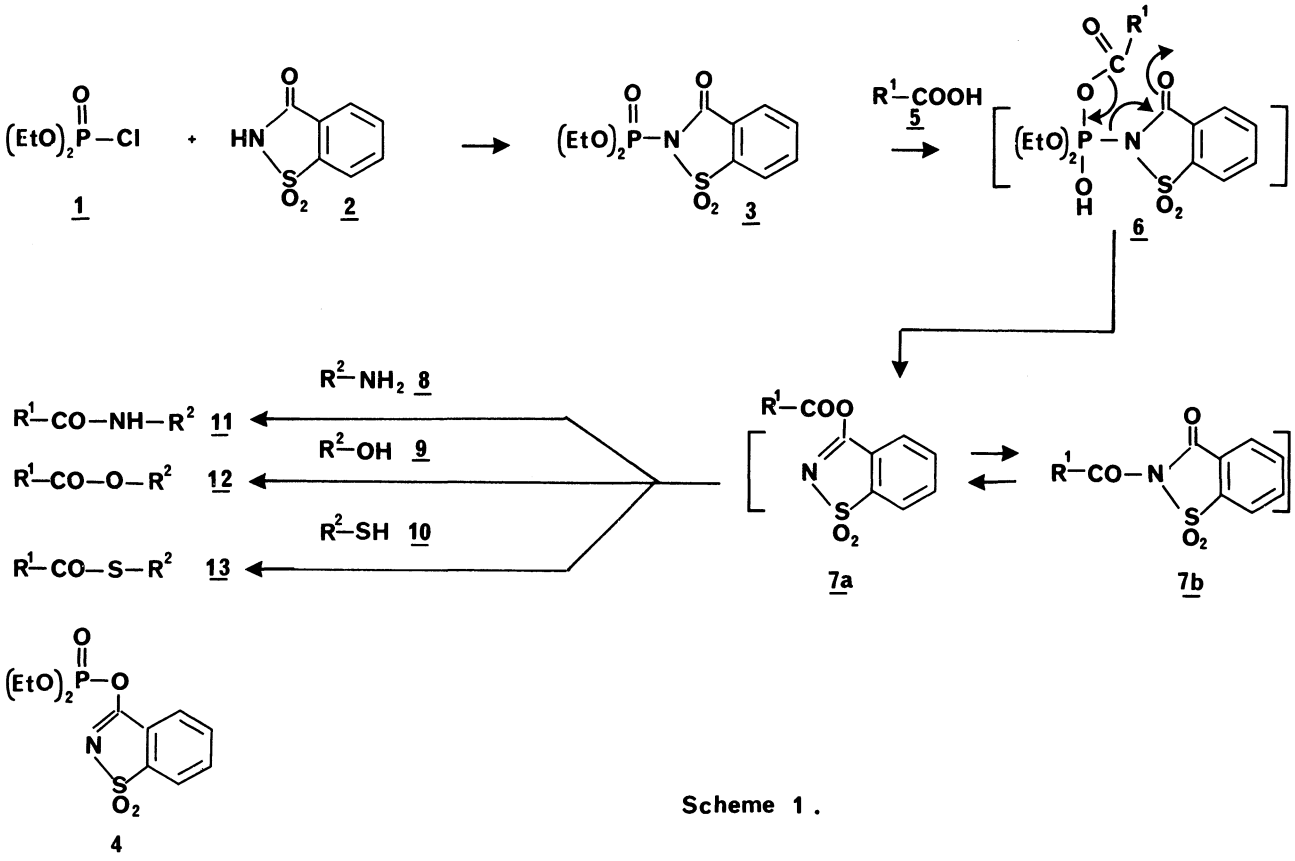
In recent years, some new syntheses of amides, esters, and thioesters, using new condensing agents have been described.[2-6)] F.Micheel et al.[7)] reported that when 3-chloro-1,2-benzisosulfonazole was allowed to react with an N-benzyloxycarbonylamino acid in dichloromethane at 0 °C, an activated ester was formed, which gave dipeptides on treatment with some α-amino acids. 3-Chloro-1,2-benzisosulfonazole, however, is not stable and difficult to handle.

In the preceding paper[8a)] we have described the application of 2-acyl-3-oxo-2,3-dihydro-1,2-benzisosulfonazole to the preparation of β-lactams from imines. We now wish to report here that diethyl 2-(3-oxo-2,3-dihydro-1,2-benzisosulfonazolyl)phosphonate(DEBP) (3) gave amides(11), esters(12), and thioesters(13) in good yields from a variety of amines(8), active hydroxylamines(9), and thiols(10) and acids(5) under mild conditions. The reaction proceeded without any detectable racemization. Compound 3 is obtained easily by the reaction of diethyl phosphorochloridate(1) with 3-oxo-2,3-dihydro-1,2-benzisosulfonazole(Saccharin) (2) in dichloromethane in the presence of an equivalent amount of triethylamine(TEA). Of the two possible structures (3 and 4) of the phosphate obtained, 3 is more likely because the phosphate exhibits carbonyl absorption at 1740 cm^{-1} in its IR spectrum.

The acylation seems to proceed via mixed anhydride(6), which affords O-acyl-1,2-benzisosulfonazole(7a) by consecutive acyl migration. Thus, when phenoxyacetic acid was allowed to react with an equivalent amount of 3 in the presence of TEA in dichloromethane, 2-phenoxyacetyl-3-oxo-2,3-dihydro-1,2-benzisosulfonazole(7b, R^1= $C_6H_5OCH_2CO$-) (mp 175-176 °C, lit.,[7)] mp 175-176 °C) was isolated in 83% yield. The IR spectrum of the product shows carbonyl absorption at 1735 and 1750 cm^{-1}, while its ^{1}H-NMR spectrum two kinds of methylene protons of the acetyl group. The data would be interpreted by assuming tautomerism of 7 between O-acyl(7a) and N-acyl(7b) derivatives as shown in Scheme 1. However, 7's were used without isolation in the present experiments.

The experimental conditions are as follows. A solution of 1(1.72 g,10 mmol), 2(1.83 g,10 mmol), and TEA(1.4 ml,10 mmol) in dichloromethane(15 ml) was stirred

at room temperature for 2 h to afford, in 75% yield, DEBP(3), mp 108-109 °C, IR (KBr): 1160, 1350, 1740 cm^{-1}, ^{1}H-NMR(DMSO-d_6 δ): 1.23(6H,t,J=7 Hz), 3.72-4.19 (4H,m), 7.50-8.30(4H,m). A solution of 3(319 mg,1 mmol), 5(1 mmol), and TEA (0.14 ml,1 mmol) in dichloromethane(5 ml) was stirred for 30 min at room temperature followed by addition of 8(1 mmol), 9(1 mmol), or 10(1 mmol). The reaction mixture was stirred for the period shown in Table 1 and Table 2 at room temperature and worked up in the usual manner to afford amides 11, esters 12, or thioesters 13 in good yields. The results obtained are listed in Table 1 and Table 2. DEBP 3 can be stored at room temperature for several months in a desiccator without interception of light. It is crystalline compound and handled more easily than acyl chlorides. Further studies are in progress in our laboratory on the application of the method to the synthesis of other organic compounds.



Scheme 1.

Table 1. Formation of Amides 11

Product[a]		Yield/%	Mp/°C[b]	$[\alpha]_D$/° (temp/°C, c, solv.)	React.time
11a	Z-Phe-Gly-OEt	75	110-111 (110-112)[2]	-17.0 (19, 2, EtOH) -17.4 (- , 2.01, EtOH)[2]	10 min
11b	Z-Ala-Gly-OEt	64	98-99 (99-100)[2]	-22.0 (19, 2, EtOH) -22.1 (- , 3.08, EtOH)[2]	10 min
11c	Z-Val-Val-OMe	85	115-116 (116)[9]	-24.0 (18, 1, MeOH) -24.3 (25, 0.3, MeOH)[9]	10 min

11d	Z-Val-Gly-OEt	73	169-170 (170-171)[10]	-32.5 (18, 2, dioxan) -32.4 (20, 1.85, dioxan)[10]	10 min
11e	Z-Gly-Gly-OEt	75	78-79 (79-80)[2]	- -	10 min
11f	Boc-Phe-Ala-OMe	75	96-97 (98-99)[11]	-18.0 (19, 1, MeOH) -18.0 (25, 1, MeOH)[11]	10 min
11g	Boc-Leu-Leu-OMe	64	135-136 (132-133)[11]	-50.0 (19, 1, MeOH) -50.4 (25, 1, MeOH)[11]	10 min
11h	Boc-Phe-Val-OMe	75	116-117 (117-118)[3]	-10.0 (20, 2, DMF) -11.0 (- , 1.89, DMF)[3]	10 min
11i	Pht-$CH_2CONH-C_6H_5$	72	233-234 (231-232)[12]	- -	30 min
11j	$C_6H_5OCH_2CONH-C_{10}H_7$	69	131-132 (129-131)[13]	- -	2.5 h
11k	$C_6H_5OCH_2CONH-C_6H_4-OMe$	78	132-133 (135-136)[14]	- -	5 min

a) These compounds 11 were characterized by spectra(IR and ^{1}H-NMR) and elemental analyses. Optically active amino acids were of the L-form. 11a-11h were purified by a short column chromatography on silica gel with ethyl acetate and benzene (1:1). 11i-11k were recrystallized from acetone-hexane. Two equivalent amounts of TEA were used in the cases of preparing 11a-11h because α-amino acid ester hydrochlorides were used as amine component. Z:benzyloxycarbonyl group; Boc:t-butoxycarbonyl group; Pht:phthalimido group.
b) Not corrected.

Table 2. Formation of Esters 12 and Thioesters 13

Product[a]		Yield/%	Mp/°C[b]	$[\alpha]_D$/° (temp/°C, c, solv.)	React.time
12a	Z-Phe-OSu	71	139-140 (140-140.5)[15]	-17.0 (20, 1, dioxan) -17.3 (25, 1, dioxan)[15]	15 min
12b	Z-Ala-OSu	73	121-122 (123-123.5)[15]	-37.0 (20, 2, dioxan) -37.2 (25, 2, dioxan)[15]	15 min
13a	Boc-Phe-SPy	71	123-125 (123-125)[16]	-86.0 (20, 1, EtOAc) -86.0 (20, 1, EtOAc)[16]	1 h
13b	Boc-Leu-SPy	68	91-92 (93-95)[16]	-90.0 (20, 1, DMF) -90.0 (20, 1, DMF)[16]	1 h
13c	Pht-$CH_2COS-C_6H_5$	67	99-100 (100-101)[17]	- -	3 h

a) These compounds 12 and 13 were characterized by spectra(IR and ^{1}H-NMR) and elemental analyses. Optically active amino acids were of the L-form. All products were purified by a short column chromatography on silica gel with ethyl acetate and benzene(1:1). Su:succinimido group; Py:2-pyridyl group.
b) Not corrected.

References

1) Diethyl 2-(3-oxo-2,3-dihydro-1,2-benzisosulfonazolyl)phosphonate as a New Condensing Agent. Part 1.
2) M.Furukawa, N.Hokama, and T.Okawara, Synthesis, 1983, 42.
3) H.Kinoshita, K.Inomata, O.Miyano, and H.Kotake, Bull. Chem. Soc. Jpn., 52, 2619 (1979).
4) M.Ueda, H.Oikawa, N.Kawaharasaki, and Y.Imai, Bull. Chem. Soc. Jpn., 56, 2485 (1983).
5) T.Kunieda, Y.Abe, T.Higuchi, and M.Hirobe, Tetrahedron Lett., 22, 1257 (1981).
6) T.Kunieda, Y.Abe, and M.Hirobe, Chem. Lett., 1981, 1427.
7) F.Michhel and M.Lorenz, Tetrahedron Lett., 1963, 2119.
8) a) M.Miyake, N.Tokutake, and M.Kirisawa, Synth. Commun., 14, 353 (1984); b) E.Stephen and H.Stephen, J. Chem. Soc., 1957, 492.
9) J.E.Shields, S.T.McDowell, J.Pavols, and G.R.Gray, J. Am. Chem. Soc., 90, 3549 (1968).
10) M.Ueda, N.Kawaharasaki, and Y.Imai, Synthesis, 1982, 933.
11) D.E.Nitecki, B.Halpern, and J.W.Westley, J. Org. Chem., 33, 864 (1968).
12) J.Scheiber, Chem. Ber., 46, 1103 (1913).
13) L.G.S.Brooker and F.L.White, U.S.Patent 2494031 (1950).[Chem. Abstr., 44,7687 (1950)].
14) Lederer, D.R.P. 82105; Friedländers Fortschritte der Teerfarbenfabrikation (Berlin, Julius Springer) 4, 1161.
15) G.W.Anderson, J.E.Zimmerman, and F.M.Callahan, J. Am. Chem. Soc., 86, 1839 (1964).
16) K.Lloyd and G.T.Young, J. Chem. Soc., C, 1971, 2890.
17) A.Arrieta, T.Garcia, and J.M.Palomo, Synth. Commun., 13, 471 (1983).

(Received October 17, 1984)