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Studies on Ketene and Its Derivatives. CXXII.[1] Reaction of Haloketenes with 1,3-Diaza-1,3-diene Compounds

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The reaction of haloketenes with 1,3-diaza-1,3-diene compounds, prepared by condensation of 2-amino-heterocycles with aromatic aldehydes, gave the [2+4] cycloadducts, fused pyrimidinones (**6**—**17**). However, haloketenes underwent the cycloaddition with 2-(*p*-anisylideneamino)-benzimidazole (**5**) to give both pyrimido[1,2-*a*]benzimidazoles (**18** and **19**) and 2-azetidinones (**20**—**22**).

Keywords——haloketene; 1,3-diaza-1,3-diene; [2+2] cycloaddition; [2+4] cycloaddition; fused pyrimidinone; 2-azetidinone

The reaction of haloketenes with C=N double bonds such as those of imines[2-4] and carbodiimides[5-7] is reported to give the [2+2] cycloadducts, 2-azetidinone derivatives. On the other hand, the reaction of haloketenes with compounds bearing a conjugated C=N double bond gives the [2+4] cycloadducts.[2,8] For example, dichloroketene reacts with *N*-cinnamylidenearylamine to give the 3,4-dihydro-2-pyridone, from which hydrogen chloride is eliminated to yield the 2-pyridone.[2]

Previously, we have reported that haloketenes react with ethyl *N*-(2-pyridyl)formimidates and 2-arylideneaminopyridines, all of which have a C=N bond conjugated with the ring C=N bond, to give the [2+4] cycloadducts, pyrido[1,2-*a*]pyrimidin-4(4*H*)-ones, together with the [2+2] cycloadducts, 2-azetidinones.[9,10] On the other hand, Tomimatsu *et al.*[11] reported the reaction of diphenylketene with 1,3-diaza-1,3-diene compounds to give the [2+4] cycloadducts.

As a continuation and extension of our studies on the reactivities of haloketenes toward the C=N bond, we now wish to report the reaction of haloketenes with 1,3-diaza-1,3-diene compounds (**1**—**5**), which are prepared by the condensation of aromatic aldehydes with 2-amino-heterocycles such as 2-aminobenzothiazole, 2-aminothiazole, 2-amino-1,3,4-thiadiazole, 2-aminobenzoxazole, and 2-aminobenzimidazole, according to the literature.[11]

When dichloroacetyl chloride was added dropwise to a solution of 2-(*p*-anisylideneamino)benzothiazole (**1**) in 1,2-dimethoxyethane (DME) in the presence of triethylamine, 3-chloro-2-(*p*-methoxyphenyl)-4*H*-pyrimido[2,1-*b*]benzothiazol-4-one (**6**) was obtained in 44% yield. The infrared (IR) spectrum of **6** showed a carbonyl absorption band at 1680 cm^{-1}, and the proton nuclear magnetic resonance (^{1}H-NMR) spectrum showed the signal due to the ring proton at the 6-position at 9.20 ppm (1H, ddd). Similar reaction of **1** with chlorophenylketene and monochloroketene gave the corresponding pyrimido[2,1-*b*]benzothiazoles **7** and **8**.

Similarly, the azadienes **2**—**4**, prepared from the corresponding amines and aldehydes, reacted with haloketenes to give the [2+4] cycloadducts (**9**—**17**). The results are shown in Table I.

TABLE I. Reactions of Haloketenes with 2-Arylideneamino-heterocycles (**1**—**5**)

No.	R	Yield (%)	Appearance (Recryst. solvent)	mp (°C)	Formula	Analysis (%) Calcd (Found)			ν_{max} (KBr) cm^{-1}	^{1}H-NMR δ (CF_3CO_2H–$CDCl_3$)
						C	H	N		
6	Cl	44	Prisms (Acetone)	194—195	$C_{17}H_{11}ClN_2O_2S$	59.56 (59.29	3.23 3.02	8.17 8.09)	1680 1600	3.98 (3H, s), 7.07—8.07 (7H, m), 9.20 (1H, ddd)
7	Ph	69	Needles (Acetone)	233—234	$C_{23}H_{16}N_2O_2S$	71.85 (71.80	4.20 4.29	7.29 7.10)	1665 1600	3.90 (3H, s), 6.82—8.03 (12H, m), 9.10 (1H, ddd)
8	H	49	Needles (Acetone)	225—226	$C_{17}H_{12}N_2O_2S \cdot 1/6H_2O$	65.58 (65.77	3.99 3.81	9.00 9.08)	1675 1600	3.92 (3H, s), 7.00—8.03 (8H, m), 9.08 (1H, ddd)
9	Cl	75	Needles (Acetone)	285—286	$C_{12}H_6ClN_3O_3S$	46.84 (46.78	1.97 1.88	13.66 13.57)	1690 1600	7.52—8.55 (6H, m)
10	Ph	66	Needles (Acetone)	266—268	$C_{18}H_{11}N_3O_3S \cdot 1/4H_2O$	61.09 (61.34	3.28 3.25	11.88 11.70)	1650 1590	7.00—8.47 (11H, m)
11	H	73	Needles (Acetone)	244—245	$C_{12}H_7N_3O_3S$	52.74 (52.59	2.58 2.53	15.38 15.46)	1685 1600	7.00 (1H, s), 7.47—8.50 (6H, m)
12	Cl	40	Needles (Acetone)	200—201	$C_{13}H_{10}ClN_3O_2S$	50.73 (50.97	3.28 3.32	13.66 13.55)	1695 1605	2.77 (3H, s), 3.87 (3H, s), 6.93 (d), 7.78 (d)[a]
13	Ph	50	Needles (Acetone)	242—243	$C_{19}H_{15}N_3O_2S$	65.31 (65.30	4.33 4.37	12.03 11.83)	1665 1600	2.80 (3H, s), 3.77 (3H, s), 6.67 (d), 7.23 (d)[b]

14	H	32	Prisms (Ethyl acetate)	233—234	$C_{13}H_{11}N_3O_2S \cdot 1/6H_2O$	56.51 (56.39	4.13 4.05	15.41 15.66)	1695 1600	2.80 (3H, s), 3.87 (3H, s), 7.00 (d), 7.85 (d)
15	Cl	34	Leaves (Ethanol)	231—232	$C_{17}H_{10}Cl_2N_2O_3$	56.53 (56.29	2.79 2.78	7.76 7.78)	1690 1630 1600	3.93 (3H, s), 7.58 (2H, s), 8.43 (1H, s)
16	Ph	58	Needles (Ethanol)	214	$C_{23}H_{15}ClN_2O_3$ $1/6C_2H_5OH$	68.27 (68.46	3.93 4.11	6.82 6.51)	1675 1635 1600	3.83 (3H, s), 7.67 (2H, s), 8.46 (1H, s)
17	H	22	Needles (Ethanol)	248—249	$C_{17}H_{11}ClN_2O_3$	62.49 (62.48	3.39 3.27	8.57 8.28)	1710 1625 1600	3.93 (3H, s), 7.55 (2H, s), 8.37 (1H, s)
18	Ph	21	Needles (Ethanol)	310<	$C_{23}H_{17}N_3O_2 \cdot 1/2H_2O$	73.39 (73.59	4.82 4.85	11.16 10.94)	1650 1605	3.80 (3H, s), 6.67—7.83 (12H, m), 8.58 (1H, ddd)
19	H	17	Needles (Acetone)	299—301	$C_{17}H_{13}N_3O_2$	70.09 (70.32	4.50 4.47	14.43 14.48)	1685 1605	3.97 (3H, s), 7.00—7.93 (8H, m), 8.58 (1H, ddd)
20	Cl	47	Needles (Ethyl acetate)	310<	$C_{17}H_{13}Cl_2N_3O_2$	56.37 (56.68	3.62 3.71	11.60 11.69)	1750 1655	5.40 (1H, s, 4-H)
21	Ph	25	Needles (Ethyl acetate–benzene)	218—219	$C_{23}H_{18}ClN_3O_2$ $1/6C_6H_6$	69.14 (69.29	4.59 4.39	10.08 10.07)	1745 1645	5.37 (1H, s, 4-H)
22	H	36	Needles (Ethanol)	290—292	$C_{17}H_{14}ClN_3O_2$	62.29 (62.32	4.31 4.35	12.82 13.01)	1740 1640	4.85 (1H, d, J=4 Hz, 3-H), 5.37 (1H, d, J=4 Hz, 4-H)

a) In $CDCl_3$. *b*) In $CDCl_3$–CD_3OD.

On the other hand, the reaction of 2-(*p*-anisylideneamino)benzimidazole (**5**) with monochloroketene in a mixture of DME and *N*, *N*-dimethylformamide (DMF) gave two products, 2-(*p*-methoxyphenyl)-4*H*-pyrimido[1,2-*a*]benzimidazol-4-one (**19**), mp 299—301 °C, and 1-(2-benzimidazolyl)-3-chloro-4-(*p*-methoxyphenyl)-2-azetidinone (**22**), mp 290—292 °C, in 17 and 36% yields, respectively.

The IR spectrum of **22** showed a carbonyl absorption band due to 2-azetidinone at 1740 cm^{-1} whereas the ^{1}H-NMR spectrum revealed two ring protons of 2-azetidinone at 4.85 and 5.37 ppm. Since the coupling constant between these protons is $J=4$ Hz, the configuration with respect to the 3- and 4-positions is *trans*.

Similar reaction of **5** with chlorophenylketene gave the pyrimido[1,2-*a*]benzimidazole **18** and 2-azetidinone **21** in 21 and 25% yields, respectively. However, reaction of **5** with dichloroketene did not give the [2+4] cycloadduct, but gave a 47% yield of a [2+2] cycloadduct, the 2-azetidinone **20**, as the sole product. Although the reaction of haloketenes with **4** in the presence of DMF was carried out, the [2+2] cycloadducts were not detected. Instead, the [2+4] cycloadducts were obtained exclusively. It is not clear why only the reaction of haloketenes with **5** gives 2-azetidinones.

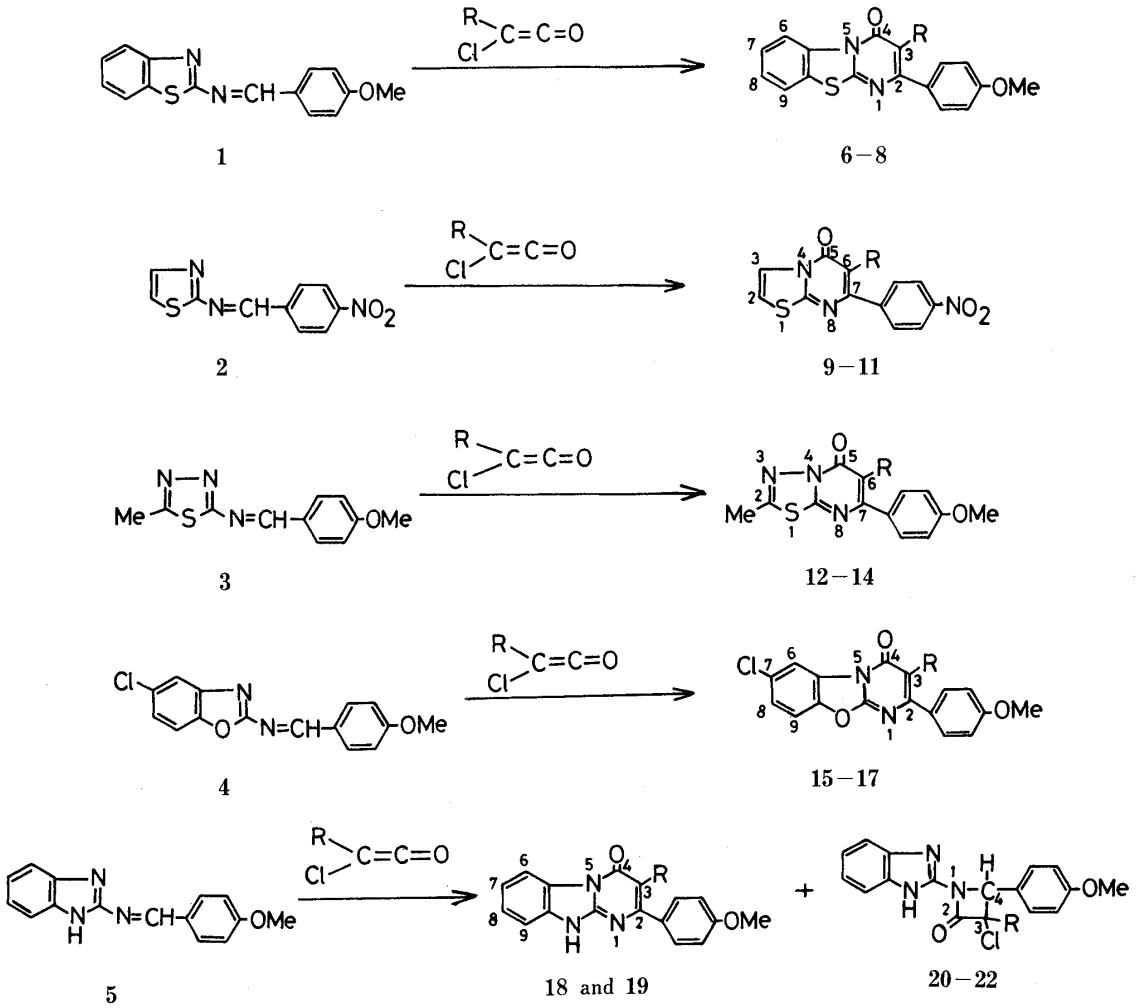

Chart 1

Experimental

Melting points were determined on a Yanaco model MP, and are uncorrected. IR spectra were taken with a JASCO A-102 spectrophotometer. ^{1}H-NMR spectra were recorded on a JEOL JNM-PMX-60 spectrometer using

tetramethylsilane as an internal standard.

General Procedure for the Synthesis of Compounds 6—17——A solution of dichloroacetyl chloride, α-chlorophenylacetyl chloride, or monochloroacetyl chloride (0.012 mol) in anhydrous DME was added dropwise to a solution of **1—4** (0.01 mol) and triethylamine (1.52 g, 0.015 mol) in anhydrous DME (120—140 ml) with stirring at −15——10 °C. The mixture was stirred for 2—3 h at room temperature. The solvent was evaporated off under reduced pressure and the residue was dissolved in chloroform (100 ml). The chloroform solution was washed with water (100 ml × 3), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. Crystals thus obtained were recrystallized from the appropriate solvent to give products **6—12** and **15—17**. Compounds **13** and **14** were purified by silica gel (100 g) column chromatography with ethyl acetate as the eluent.

1-(2-Benzimidazolyl)-3,3-dichloro-4-(*p*-methoxyphenyl)-2-azetidinone (20)——A solution of dichloroacetyl chloride (1.77 g, 0.012 mol) in DME (10 ml) was added dropwise to a solution of **5** (2.51 g, 0.01 mol) and triethylamine (1.52 g, 0.015 mol) in a mixture of DME (160 ml) and DMF (10 ml) with stirring at −15——10 °C. The mixture was stirred for 16 h at room temperature. The solvent was evaporated off under reduced pressure and the residue was dissolved in chloroform (300 ml). The chloroform solution was washed with water (100 ml × 3), dried over anhydrous sodium sulfate, and evaporated under reduced pressure to give a crystalline substance, which was recrystallized from ethyl acetate to give 1.70 g (47%) of the product **20**.

Reaction of Chlorophenylketene with 2-(*p*-Anisylideneamino)benzimidazole (5)——A solution of chlorophenylacetyl chloride (2.27 g, 0.012 mol) in anhydrous DME (10 ml) was added dropwise to a solution of **5** (2.51 g, 0.01 mol) and triethylamine (1.52 g, 0.015 mol) in anhydrous DME (180 ml) and DMF (10 ml) with stirring at −15——10 °C. The mixture was stirred for 16 h at room temperature. The solvent was evaporated off under reduced pressure, and the residue was dissolved in chloroform (300 ml). The chloroform solution was washed with water (100 ml × 3), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The crystalline residue was washed with acetone (50 ml), and recrystallized to give 0.78 g (21%) of the product **18**. The washing and mother liquor were combined and concentrated under reduced pressure. The residue was subjected to silica gel (50 g) column chromatography. Elution with hexane–ethyl acetate (1 : 1) gave a crystalline product, which was recrystallized to give 1.0 g (25%) of **21**.

Reaction of Monochloroketene with 2-(*p*-Anisylideneamino)benzimidazole (5)——A solution of monochloroacetyl chloride (1.36 g, 0.012 mol) in anhydrous DME (10 ml) was added dropwise to a solution of **5** (2.51 g, 0.01 mol) and triethylamine (1.52 g, 0.015 mol) in DME (160 ml) and DMF (10 ml) with stirring at −15——10 °C. The mixture was stirred for 3 h at room temperature. The solvent was evaporated off under reduced pressure and the residue was dissolved in chloroform (300 ml). The chloroform solution was washed with water (100 ml × 3), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. Crystals thus obtained were washed with acetone (50 ml), and recrystallized to give 1.18 g (36%) of **22**. The washing and mother liquor were combined, and concentrated to give a crystalline residue, which was washed with ether (200 ml), and recrystallized to give 0.50 g (17%) of **19**.

References and Notes

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