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Studies on Ketene and Its Derivatives. CXIII.[1] Reaction of Dichloroketene with Aromatic Amine *N*-Oxides

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Reaction of dichloroketene with pyridine 1-oxide (**1**) gave four products, namely, 2-dichloromethylpyridine (**2**), 4-dichloromethylpyridine (**3**), 3,3,7-trichloro-6-dichloroacetyl-2-oxo-2,3,3a,6,7,7a-hexahydrofuro[2,3-*c*]pyridine (**4**), and 3,3-dichloro-6-dichloroacetyl-7-hydroxy-2-oxo-2,3,3a,6,7,7a-hexahydrofuro[2,3-*c*]pyridine (**5**). Reaction of dichloroketene with **1**, followed by treatment with abs. methanol gave **3**, methyl 2,2-dichloro-2-(2-pyridyl)acetate (**6**), and methyl 2,2-dichloro-2-(4-pyridyl)acetate (**7**). Similar reaction of dichloroketene with methylpyridine 1-oxides gave the corresponding 2-dichloro and 4-dichloro methylpyridines. On the other hand, reaction of dichloroketene with 2,6-dimethylpyridine 1-oxide (**18**), followed by treatment with abs. methanol gave 4-dichloromethyl-2,6-dimethylpyridine (**19**) and bis(2,6-dimethyl-4-pyridyl)dichloromethane (**21**). Dichloroketene also reacted with quinoline 1-oxide (**24**) and isoquinoline 2-oxide (**29**) to give the corresponding dichloromethyl derivatives (**25** and **26**, and **30**, respectively).

Keywords——aromatic amine *N*-oxide; dichloroketene; dichloromethylpyridine; dichloromethylquinoline; dichloromethylisoquinoline

There is extensive literature dealing with the reaction of dichloroketene with compounds bearing a C=C double bond to give 2,2-dichlorocyclobutanones, but only a few references are available concerning such reactions with C=N double bonds.[2]

On the other hand, it has been reported that the reaction of ketene with 2-methylpyridine 1-oxide[3] and 2-methylquinoline 1-oxide[4] gives the corresponding 2-acetoxymethyl derivatives. During the course of extensive studies on the reaction of aromatic amine *N*-oxides with nucleophiles, Hamana and his co-workers reported that aromatic amine *N*-oxides reacted with active methylene compounds in the presence of acid chlorides such as benzoyl chloride or tosyl chloride to give 2-substituted heterocycles.[5] The present paper reports the reaction of dichloroketene with aromatic amine *N*-oxides to give dichloromethyl compounds.

When pyridine 1-oxide (**1**) was allowed to react with dichloroacetyl chloride (2 mol eq) in the presence of triethylamine (2.5 mol eq) in 1,2-dimethoxyethane (DME) at −10——5 °C, 2-dichloromethylpyridine (**2**), 4-dichloromethylpyridine (**3**), colorless needles (**4**) of mp 149—151 °C, and colorless prisms (**5**) of mp 186—189 °C were obtained in 11.2, 52.3, 4.7, and 2.9% yields, respectively. When this reaction was carried out using three molar equivalents of dichloroacetyl chloride at −50 °C, the yield of **5** was slightly improved but the yields of **2**—**4** decreased. The yield of **4** increased with the use of chloroform as a solvent, but a trace of **5** was obtained. The results are summarized in Table I.

Based upon the following spectral data, the structures of **4** and **5** were determined to be 3,3,7-trichloro-6-dichloroacetyl-2-oxo-2,3,3a,6,7,7a-hexahydrofuro[2,3-*c*]pyridine and 3,3-dichloro-6-dichloroacetyl-7-hydroxy-2-oxo-2,3,3a,6,7,7a-hexahydrofuro[2,3-*c*]pyridine, respectively. The empirical formula of **4**, $C_9H_6Cl_5NO_3$, was determined by mass spectrometry and elemental analyses; it was formed by the reaction of two molar equivalents of dichloroketene with the 1-oxide **1**, followed by addition of hydrogen chloride.

On the other hand, compound **5**, $C_9H_7Cl_4NO_4$, was formed by a similar reaction, followed by addition of water instead of hydrogen chloride. The infrared (IR) spectrum of **4** shows two carbonyl absorptions at 1810 and 1710 cm^{-1}. In the proton nuclear magnetic resonance (^{1}H-NMR) spectrum (Table II) of **4** a signal due to H_{3a} is observed at 3.77 ppm as a double

doublet, further split into a multiplet (ddd) by allylic coupling ($J_{3a,5}$=1.6 Hz) with H_5. H_{7a}, whose signal is observed at 5.10 ppm (ddd), is coupled with H_4 due to a planar W-path ($J_{7a,4}$= 1.6 Hz). Therefore, H_{7a} is equatorial and has α-configuration.[6] The signals due to H_4 and H_9 are observed at 5.26 (ddd) and 6.18 ppm (s), respectively. H_7 is also presumed to be equatorial because coupling ($J_{5,7}$=1.2 Hz) between H_5 and H_7 (6.54 ppm) is observed. Though the ^{1}H-NMR spectrum of **5** resembles that of **4**, as shown in Table II, the signal due to H_7 is shifted to higher field (6.26 ppm) because of the effect of a hydroxyl group. The ^{13}C-NMR spectra of **4** and **5** also support the hexahydrofuro[2,3-*c*]pyridine structures. The ^{1}H- and ^{13}C-NMR spectral data for **4** and **5** are summarized in Table II.

In order to confirm further the structure of **4**, compound **4** was allowed to react with aniline in absolute ethanol to give dichloroacetanilide.

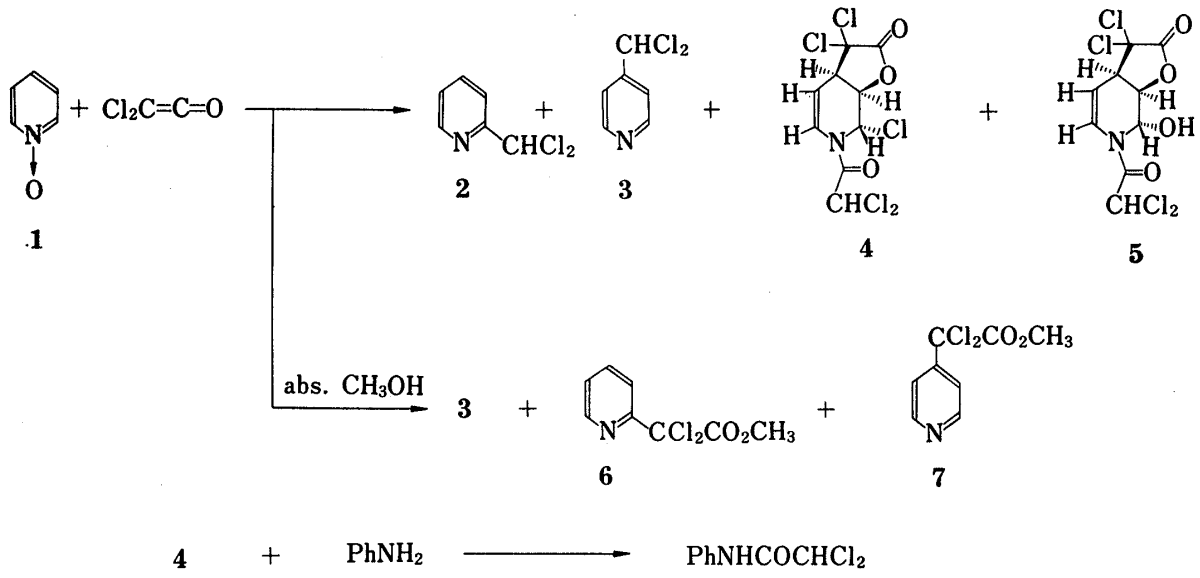


Chart 1

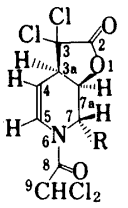
TABLE I. Reaction of Dichloroketene with Pyridine 1-Oxide (**1**)

Molar ratio		Solvent	Reaction temp. (°C)	Yield (%)			
Cl_2C=C=O	**1**			**2**	**3**	**4**	**5**
2	1	DME	−10—−5	11.2	52.3	4.7	2.9
3	1	DME	−50	8.3	27.8	3.4	4.1
2	1	$CHCl_3$	−10—−5	9.9	22.9	5.5	Trace
3	1	$CHCl_3$	−50	22.8	36.4	7.9	Trace

The mechanisms of the formation of **2**—**5** can be rationalized as follows; 1,3-cycloaddition and 1,5-cycloaddition of dichloroketene (or two molecules of dichloroketene) to the *N*-oxide **1** give intermediates A (or A′) and B (or B′), respectively, then decarboxylation (or decarboxylation with elimination of dichloroketene) gives **2** and **3**, respectively. On the other hand, the intermediate B can undergo allylic shift[7] to give an intermediate C, to which the C=O double bond of another molecule of dichloroketene adds from the α-site to give an intermediate D. Addition of hydrogen chloride or water to D gives **4** or **5**, respectively.

To trap intermediates A and B (A′ and B′), the reaction mixture was treated with abs. methanol, and methyl 2,2-dichloro-2-(2-pyridyl)acetate (**6**) and a mixture of **3** and methyl 2,2-dichloro-2-(4-pyridyl)acetate (**7**) were obtained.

TABLE II. ^{1}H- and ^{13}C-NMR Spectral Data for Compounds **4** and **5**[a]



4 : R=Cl
5 : R=OH

Position	Chemical shift (δ, ppm)			
	4		**5**	
	Proton (J=Hz)[b]	Carbon[d]	Proton (J=Hz)[c]	Carbon[d]
2		166.10 (s)		166.44 (s)
3		80.32 (s)		80.79 (s)
3a	3.77 (1H, ddd, $J_{3a,4}$=3.2, $J_{3a,5}$=1.6, $J_{3a,7a}$=4.8)	45.09 (d)	3.81 (1H, ddd, $J_{3a,4}$=3.5, $J_{3a,5}$=1.7, $J_{3a,7a}$=4.8)	45.38 (d)
4	5.26 (1H, ddd, $J_{4,3a}$=3.2, $J_{4,5}$=8.8, $J_{4,7a}$=1.6)	103.27 (d)	5.30 (1H, ddd, $J_{4,3a}$=3.5, $J_{4,5}$=8.5, $J_{4,7a}$=1.8)	102.51 (d)
5	6.96 (1H, ddd, $J_{5,3a}$=1.6, $J_{5,4}$=8.8, $J_{5,7}$= 1.2)	124.52 (d)	7.02 (1H, ddd, $J_{5,3a}$=1.7, $J_{5,4}$=8.5, $J_{5,7}$=1.2)	125.34 (d)
7	6.54 (1H, dd, $J_{7,5}$=1.2, $J_{7,7a}$=3.2)	61.65 (d)	6.26 (1H, dd, $J_{7,5}$=1.2, $J_{7,7a}$=3.0)	70.63 (d)
7a	5.10 (1H, ddd, $J_{7a,3a}$=4.8, $J_{7a,4}$= 1.6, $J_{7a,7}$=3.2)	74.97 (d)	5.15 (1H, ddd, $J_{7a,3a}$=4.8, $J_{7a,4}$=1.8, $J_{7a,7}$=3.0)	75.15 (d)
8		162.57 (s)		162.28 (s)
9	6.18 (1H, s)	65.05 (d)	6.42 (1H, s) 3.82 (1H, s, 7-OH)	65.29 (d)

a) The spectra were recorded on a JEOL JNM FX-100 spectrometer with tetramethylsilane as an internal standard.
b) In $CDCl_3$ (100 MHz).
c) In CD_3OD-$CDCl_3$ (100 MHz).
d) In DMSO-d_6 (25 MHz).

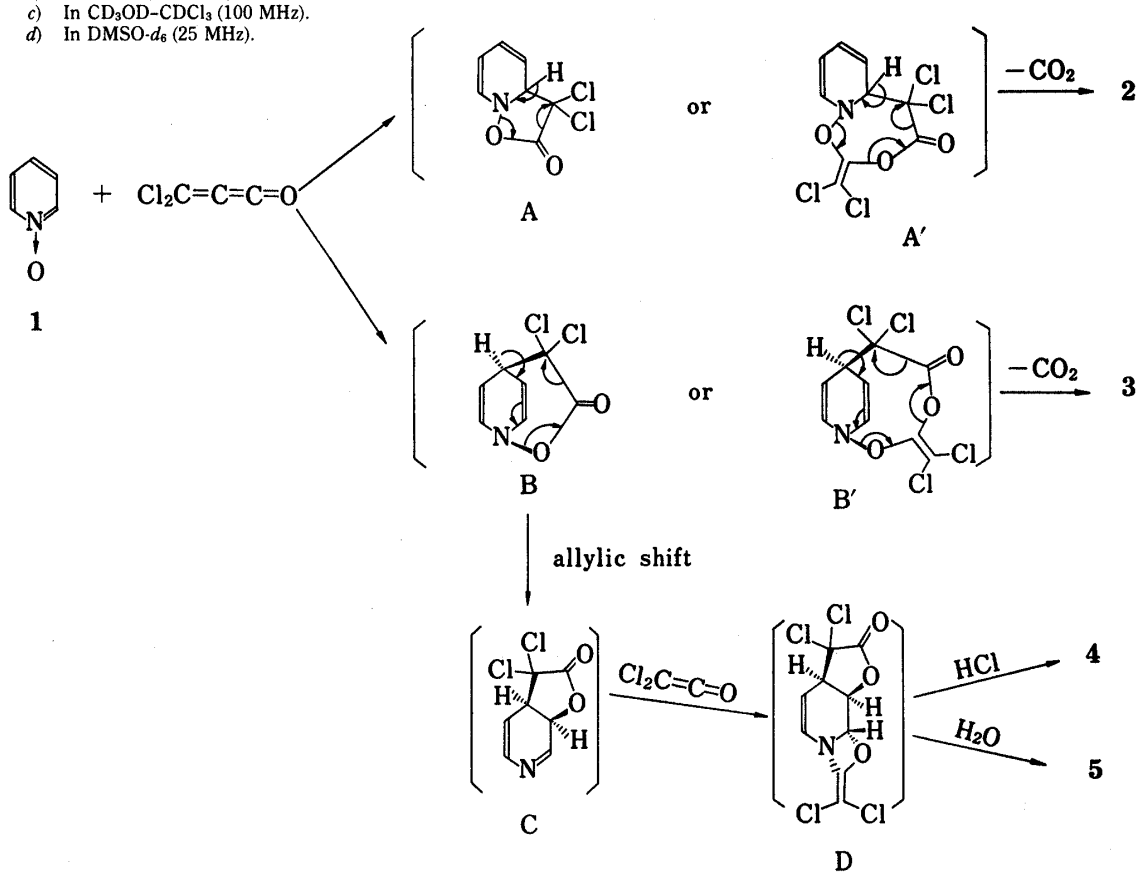


Chart 2

Next, the reaction of dichloroketene with methylpyridines was investigated. 2-Methylpyridine 1-oxide (**8**) reacted with dichloroketene in DME to give 2-dichloromethyl-6-methylpyridine (**9**) and 4-dichloromethyl-2-methylpyridine (**10**) in 28.6 and 44.5% yields, respectively. Similar reaction of 3-methylpyridine 1-oxide (**11**) with dichloroketene gave 4-dichloromethyl-3-methylpyridine (**14**) and a mixture (*ca.* **12**: **13**=4: 3) of 2-dichloromethyl-3-methylpyridine (**12**) and 2-dichloromethyl-5-methylpyridine (**13**) in 31.8 and 52.2% yields, respectively.

On the other hand, reaction of 4-methylpyridine 1-oxide (**15**) with dichloroketene produced 2-dichloromethyl-4-methylpyridine (**16**) in 22.2% yield. In this case, when the reaction mixture was treated with abs. methanol, a mixture of **16** and methyl 2,2-dichloro-2-(4-methyl-2-pyridyl)acetate (**17**), which were inseparable by column chromatography, was obtained.

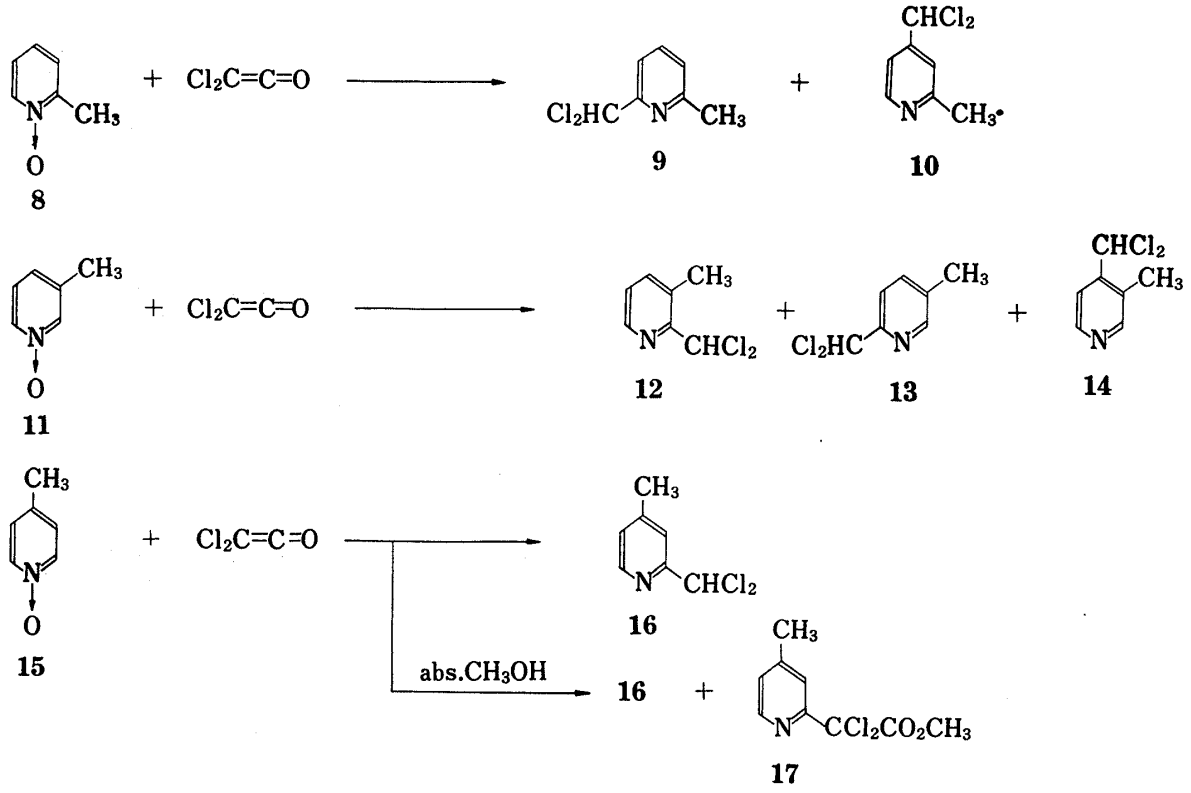


Chart 3

Similarly, 2,6-dimethylpyridine 1-oxide (**18**) reacted with two molar equivalents of dichloroketene in DME to give 4-dichloromethyl-2,6-dimethylpyridine (**19**) in 8.9% yield. On the other hand, treatment of the reaction mixture with abs. methanol did not give methyl 2,2-dichloro-2-(2,6-dimethyl-4-pyridyl)acetate (**20**) but gave **19** and bis (2,6-dimethyl-4-pyridyl)dichloromethane (**21**) in 21.6 and 29.2% yields, respectively. In a similar manner, the reaction of 3,5-dimethylpyridine 1-oxide (**22**) with dichloroketene gave 2-dichloromethyl-3,5-dimethylpyridine (**23**) in 42.0% yield.

A plausible mechanism for the formation of **21** is shown in Chart 5; namely, addition of dichloroketene to **18** gives a bicyclic intermediate E and a betain intermediate F. Addition between these two, followed by decarboxylation gives rise to the intermediate G, from which dichloroacetic acid is eliminated to give the product **21**. However, it is not clear why only **21** was obtained when the reaction mixture was treated with abs. methanol.

When quinoline 1-oxide (**24**) was allowed to react with dichloroketene in DME, 2-dichloromethylquinoline (**25**) and 4-dichloromethylquinoline (**26**) were obtained in 11.2 and 6.6%

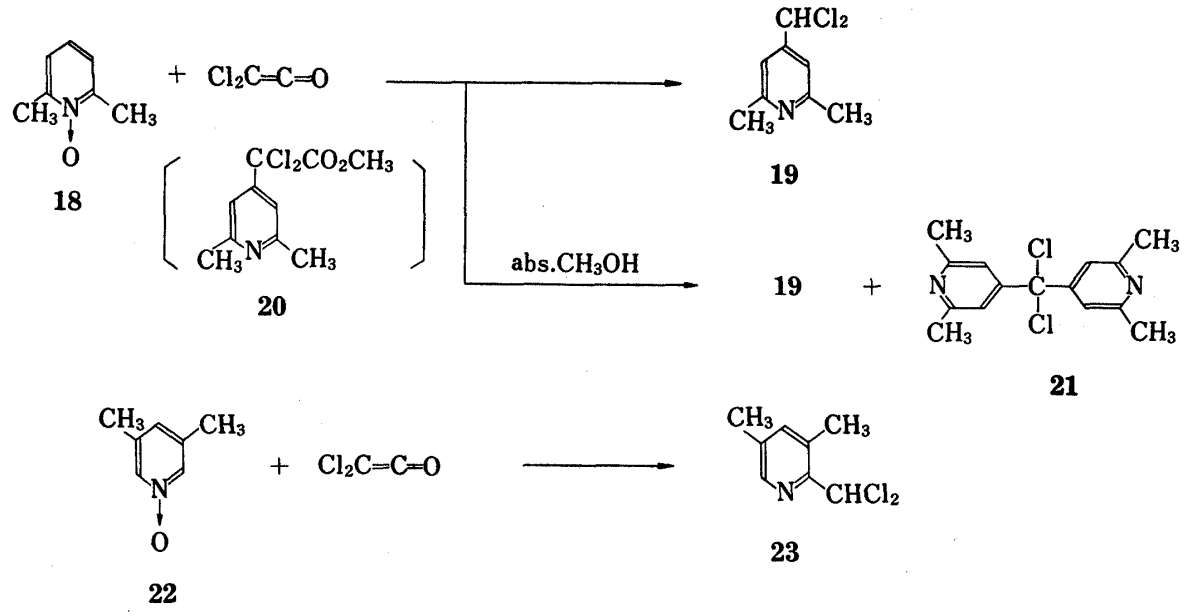


Chart 4

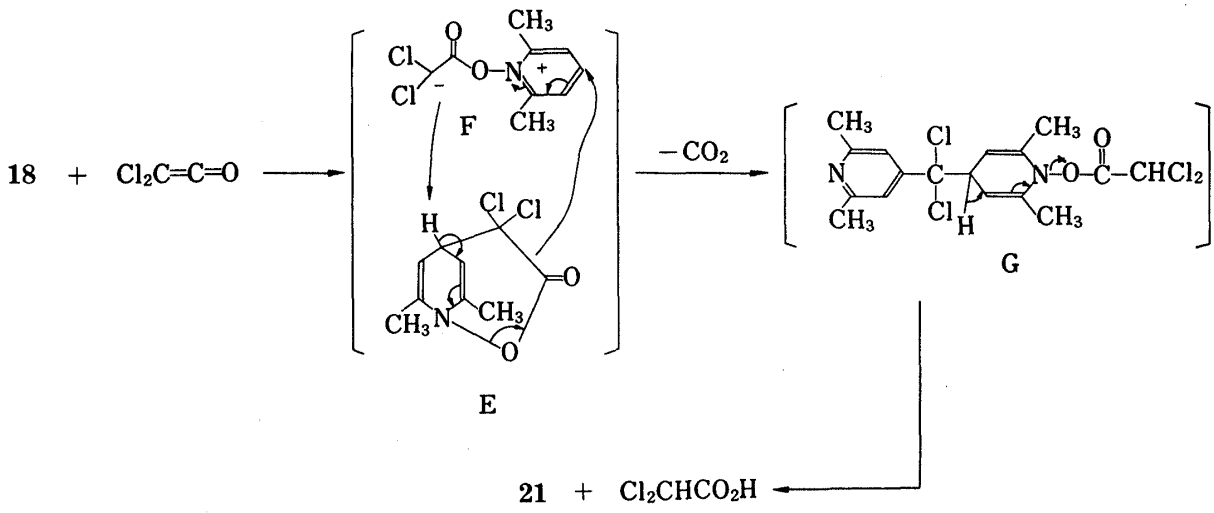


Chart 5

yields, respectively. However, the reaction in chloroform gave **25**, 4-quinolinol (**27**), and bis(2-quinolyl)dichloromethane (**28**) in 12.4, 4.6, and 5.4% yields, respectively. The mechanism of the formation of **28** seems to be similar to that of **21**.

Lastly, isoquinoline 2-oxide (**29**) reacted with dichloroketene in DME and chloroform to give 1-dichloromethylisoquinoline (**30**) in 42.4 and 24.0% yields, respectively.

Experimental

Melting and boiling points are uncorrected. IR spectra were taken with a JASCO A-102 spectrophotometer. ^{1}H-NMR spectra were recorded by using tetramethylsilane as an internal standard on JEOL JNM-PMX 60 and JEOL JNM FX-100 spectrometers at 60 and 100 MHz, respectively. ^{13}C-NMR spectra were recorded with a JEOL JNM FX-100 spectrometer with tetramethylsilane as an internal standard.

Dichloroketene was generated by the reaction of dichloroacetyl chloride with triethylamine.

Reaction of Dichloroketene with Pyridine 1-Oxide (1)——1) A solution of dichloroacetyl chloride (14.75 g, 0.1 mol) in DME (50 ml) was added dropwise to a solution of **1** (4.76 g, 0.05 mol) and triethylamine (12.63 g, 0.125 mol) under a nitrogen atmosphere with stirring and ice-salt cooling (−10——5°C).

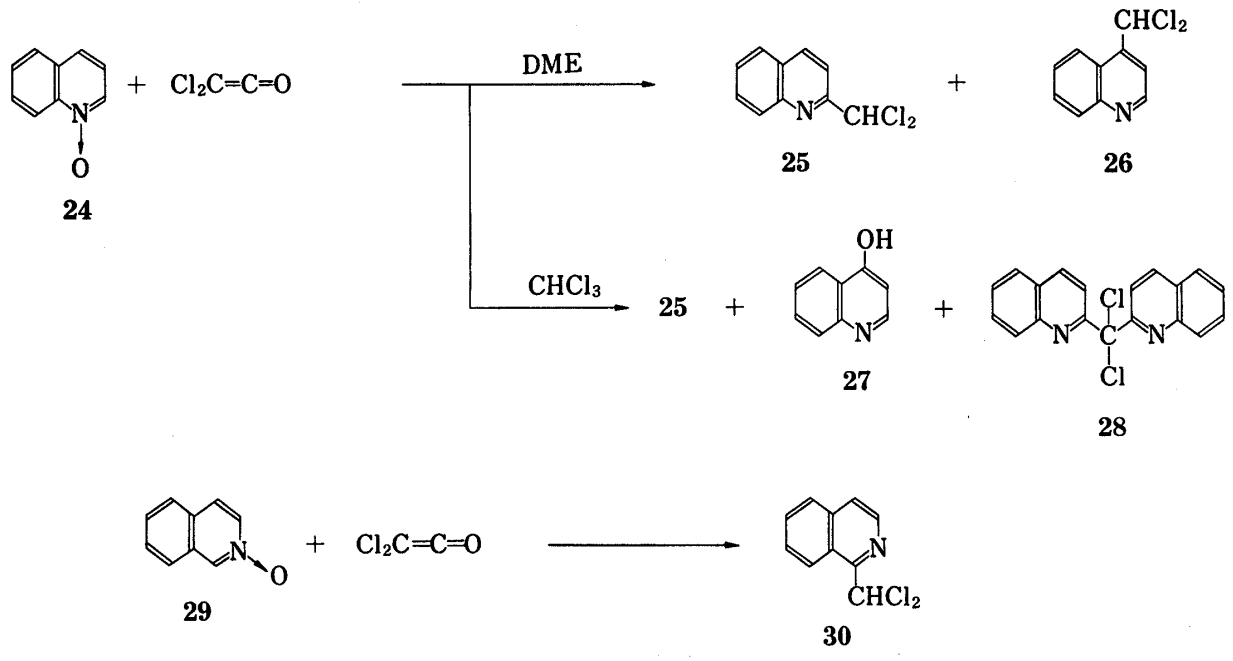


Chart 6

The mixture was stirred for 1 h at room temperature. The precipitated triethylamine hydrochloride was filtered off, and the filtrate was concentrated under reduced pressure to give an oily residue (15.1 g), which was subjected to silica gel (300 g) column chromatography. Elution with hexane–ethyl acetate (20: 1) gave an oily substance which was distilled under reduced pressure to give 2-dichloromethylpyridine (**2**), bp 66—69°C (17 mmHg) [lit.[8] bp 90—92°C (18 mmHg)], 0.91 g (11.2%). Subsequent elution with hexane–ethyl acetate (10: 1) gave a crystalline substance, which was recrystallized from hexane–chloroform (2: 1) to give the product **4**, colorless needles, mp 149—151°C, 0.83 g (4.7%). Elution was continued with hexane–ethyl acetate (5: 1) to give 4-dichloromethylpyridine (**3**), bp 90—92°C (20 mmHg) [lit.[8] 78—80°C (15 mmHg)], colorless oil, 4.24 g (52.3%). Further elution with the same solvent gave a crystalline substance, which was recrystallized from chloroform to give the product **5**, mp 186—189°C, colorless prisms, 0.48 g (2.9%).

4: IR (KBr): 1810, 1710 cm^{-1}. mass spectra (MS) *m/e*: 351 (M^+). *Anal.* Calcd for $C_9H_6Cl_5NO_3$ (**4**): C, 30.58; H, 1.71; Cl, 50.16; N, 3.96. Found: C, 30.94; H, 1.84; Cl, 50.62; N, 4.07.

5: IR (KBr): 3400, 1805, 1685 cm^{-1}. MS *m/e*: 333 (M^+). *Anal.* Calcd for $C_9H_7Cl_4NO_4$ (**5**): C, 32.27; H, 2.11; N, 4.18. Found: C, 32.19; H, 2.12; N, 4.25.

2) A solution of dichloroacetyl chloride (8.85 g, 0.06 mol) in DME (10 ml) was added dropwise to a solution of **1** (1.90 g, 0.02 mol) and triethylamine (6.06 g, 0.06 mol) in DME (50 ml) under a nitrogen atmosphere with stirring at −50°C. The mixture was stirred at room temperature for 2 h, then concentrated under reduced pressure to give an oily residue, which was dissolved in chloroform (150 ml). The solution was washed with water (100 ml × 5), and dried over anhydrous sodium sulfate. Evaporation of the solvent gave an oily substance (8.0 g), which was subjected to silica gel (200 g) column chromatography. Elution with hexane–ethyl acetate (15: 1) gave the product **2**, 0.27 g (8.3%). Subsequent elution with hexane–ethyl acetate (10: 1) gave the product **4**, 0.24 g (3.4%). Elution was continued with hexane–ethyl acetate (5: 1) to give 0.90 g (27.8%) of **3** and 0.27 g (4.1%) of **5**.

3) A solution of dichloroacetyl chloride (14.75 g, 0.1 mol) in chloroform (50 ml) was added dropwise to a solution of **1** (4.76 g, 0.05 mol) and triethylamine (12.63 g, 0.125 mol) in chloroform (50 ml) with stirring and ice-salt cooling (−10——5 °C). The mixture was stirred at room temperature for 1 h. The reaction mixture was washed with water (100 ml × 4), and the chloroform layer was dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure gave an oily residue (19.1 g), which was subjected to silica gel (300 g) column chromatography. Elution with hexane–ethyl acetate (20: 1) gave the product **2**, 0.80 g (9.9%). Subsequent elution with hexane–ethyl acetate (10: 1) gave the product **4**, 0.98 g (5.5%). Elution was continued with hexane–ethyl acetate (5: 1) to give the product **3**, 1.85 g (22.9%).

4) A solution of dichloroacetyl chloride (8.85 g, 0.06 mol) in chloroform (10 ml) was added dropwise to a solution of **1** (1.90 g, 0.02 mol) and triethylamine (6.06 g, 0.06 mol) in chloroform (50 ml) with stirring at −50°C. The reaction temperature was raised to room temperature when the starting material **1** was no longer detectable on the thin-layer chromatography (TLC) plate. The reaction mixture was washed with water (100 ml × 5), and the chloroform layer was dried over anhydrous sodium sulfate. Removal of the solvent *in vacuo* gave an oily residue (9.0 g), which was subjected to silica gel (200 g) column chromatography.

Elution with benzene gave the product **4**, 0.56 g (7.9%). Further elution with the same solvent gave the product **2**, 0.74 g, (22.8%). Subsequent elution with chloroform gave the product **3**, 1.18 g (36.4%).

5) A solution of dichloroacetyl chloride (2.95 g, 0.02 mol) in DME (10 ml) was added dropwise to a solution of **1** (0.95 g, 0.01 mol) and triethylamine (2.53 g, 0.025 mol) in DME (10 ml) under a nitrogen atmosphere with stirring and ice-salt cooling (−10——5°C). Abs. methanol (*ca.* 20 ml) was added to the mixture, and the whole was kept at room temperature for 15 h. The reaction mixture was concentrated *in vacuo* to give an oily residue, which was dissolved in chloroform (150 ml). The chloroform solution was washed with water (100 ml × 5), and dried over anhydrous sodium sulfate. Removal of the solvent *in vacuo* gave a residue (3.1 g), which was subjected to silica gel (80 g) column chromatography. Elution with hexane–ethyl acetate (15: 1) gave an oily substance, which was distilled under reduced pressure to give methyl 2,2-dichloro-2-(2-pyridyl)acetate (**6**), bp 93—95°C (4 mmHg), colorless oil, 0.56 g (25.5%). Further elution with the same solvent gave a mixture of **3** and methyl 2,2-dichloro-2-(4-pyridyl)acetate (**7**).

6: IR ($CHCl_3$): 1765 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.87 (3H, s), 7.29 (1H, m), 7.82 (2H, m), 8.56 (1H, m). MS *m/e*: 219 (M^+). *Anal.* Calcd for $C_8H_7Cl_2NO_2 \cdot 1/4H_2O$ (**6**): C, 42.79; H, 3.37; Cl, 31.58; N, 6.24. Found: C, 43.07; H, 3.18; Cl, 31.82; N, 6.15.

7: ^{1}H-NMR ($CDCl_3$) δ: 3.87 (3H, s, OCH_3), 7.45 (2H, d, J=4.8 Hz, 3,5-H), 8.68 (2H, d, J=4.8 Hz, 2,6-H).

The signals of compound **3** were also observed in the ^{1}H-NMR spectrum. **3**: ^{1}H-NMR ($CDCl_3$) δ: 6.63 (s, C<u>H</u>Cl_2).

Reaction of Compound 4 with Aniline——A solution of **4** (0.1 g) and aniline (0.08 g) in abs. ethanol (10 ml) was refluxed for 5 h. After removal of the solvent, the residue was extracted with chloroform (30 ml). The chloroform extract was washed with water, and dried over anhydrous sodium sulfate. After removal of the solvent, the resulting residue was subjected to silica gel column chromatography. Elution with benzene gave dichloroacetanilide, mp 119—120°C (lit.[9] mp 117—118°C).

General Procedure for the Reaction of Dichloroketene with Methylpyridine 1-Oxides 8, 11, and 15——1) A solution of dichloroacetyl chloride (2.95 g, 0.02 mol) in DME (10 ml) was added dropwise to a solution of methylpyridine 1-oxide (0.01 mol) and triethylamine (2.53 g, 0.025 mol) in DME (10 ml) under a nitrogen atmosphere with stirring and ice-salt cooling (−10——5°C). The mixture was stirred for 1 h at room tem-

TABLE III. Dichloromethyl-methylpyridines **9**, **10**, **12—14**, and **16**

Compd. No.	Yield (%)	bp °C (mmHg)	Solvent for column chromatography hexane-ethyl acetate	Formula	Analysis (%) Calcd (Found) C	H	N
9	28.6	75—78 (3)	20 : 1	$C_7H_7Cl_2N \cdot 1/6AcOEt$	48.28 (48.29	4.40 4.16	7.34 7.24)
10	44.5	75—78 (4)	10 : 1	$C_7H_7Cl_2N$	47.76 (47.89	4.01 4.04	7.96 7.81)
12 and **13** (4:3)	52.2	75—78 (4)	20 : 1	$C_7H_7Cl_2N$	47.76 (47.77	4.01 3.93	7.96 7.85)
14	31.8	77—79 (4)	5 : 1	$C_7H_7Cl_2N \cdot 1/4H_2O$	46.56 (46.60	4.19 3.99	7.76 7.58)
16	22.2	75—76 (4) (mp 34—35°C)	20 : 1	$C_7H_7Cl_2N \cdot 1/3H_2O$	46.18 (46.01	4.25 3.90	7.69 7.60)

Compd. No.	^{1}H-NMR ($CDCl_3$) δ ppm
9	2.55 (3H, s, CH_3), 6.70 (1H, s, C<u>H</u>Cl_2)
	7.12 (1H, dd, $J_{3,4}$=6 Hz, $J_{3,5}$=2 Hz, 5-H), 7.47 (2H, m, 3, 4-H)
10	2.58 (3H, s, CH_3), 6.65 (1H, s, C<u>H</u>Cl_2)
	7.23 (1H, d, J=5 Hz, 5-H), 7.30 (1H, s, 3-H), 8.50 (1H, d, J=5 Hz, 6-H)
12	2.37 (3H, s, CH_3), 6.73 (1H, s, C<u>H</u>Cl_2)
13	2.57 (3H, s, CH_3), 6.97 (1H, s, C<u>H</u>Cl_2)
14	2.42 (3H, s, CH_3), 6.85 (1H, s, C<u>H</u>Cl_2)
	7.63 (1H, d, J=5 Hz, 5-H), 8.45 (1H, s, 2-H), 8.53 (1H, d, J=5 Hz, 6-H)
16	2.39 (3H, s, CH_3), 6.68 (1H, s, C<u>H</u>Cl_2)
	7.10 (1H, d, J= 5.4Hz, 5-H), 7.55 (1H, s, 3-H), 8.37 (1H, d, J=5.4Hz, 6-H)

perature. After removal of the solvent, the residue was dissolved in chloroform (150 ml). The chloroform solution was washed with water (100 ml×3), and dried over anhydrous sodium sulfate. After removal of the solvent, the residue was subjected to silica gel (100 g) column chromatography. Elution with hexane–ethyl acetate gave dichloromethylpyridines **9**, **10**, **12**—**14**, and **16**. The results are summarized in Table III.

2) A solution of dichloroacetyl chloride (2.95 g, 0.02 mol) in $CHCl_3$ (10 ml) was added dropwise to a solution of 4-methylpyridine 1-oxide (1.09 g, 0.01 mol) and triethylamine (2.53 g, 0.025 mol) in chloroform (10 ml) with stirring and ice-salt cooling (−10——5°C). After stirring for 1 h at room temperature, abs. methanol (*ca.* 20 ml) was added to the mixture. The whole was kept for 48 h at room temperature. The reaction mixture was concentrated *in vacuo* to give an oily residue, which was dissolved in chloroform (150 ml). The chloroform solution was washed with water (100 ml×3), and dried over anhydrous sodium sulfate. After removal of the solvent, the residue (2.6 g) was subjected to silica gel (60 g) column chromatography. Elution with hexane-ethyl acetate (20: 1) gave a mixture of **16** and methyl 2,2-dichloro-2-(4-methyl-2-pyridyl)acetate (**17**), 0.49 g (16: 17=1: 3).

17: IR ($CHCl_3$): 1765 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.42 (3H, s), 3.88 (3H, s), 7.10 (1H, d, J=5.4 Hz), 7.76 (1H, s), 8.37 (1H, d, J=5.4 Hz). MS *m/e*: 233 (M^+).

Reaction of Dichloroketene with 2,6-Dimethylpyridine 1-Oxide (18)——1) A solution of dichloroacetyl chloride (2.95 g, 0.02 mol) in DME (10 ml) was added dropwise to a solution of **18** (1.23 g, 0.01 mol) and triethylamine (2.53 g, 0.025 mol) in DME (10 ml) under a nitrogen atmosphere with stirring and ice-salt cooling (−10——5°C). The mixture was stirred for 1 h at room temperature. After removal of the solvent, the residue was dissolved in chloroform (150 ml). The chloroform solution was washed with water (100 ml×3), and dried over anhydrous sodium sulfate. After removal of the solvent, the residue (3.0 g) was subjected to silica gel (80 g) column chromatography. Elution with hexane-ethyl acetate (18: 1) gave an oily residue, which was distilled under reduced pressure to give 4-dichloromethyl-2,6-dimethylpyridine (**19**), bp 90—92°C (5 mmHg), colorless oil, 0.17 g (8.9%). ^{1}H-NMR ($CDCl_3$) δ: 2.54 (6H, s), 6.55 (1H, s), 7.10 (2H, s). MS *m/e*: 189 (M^+). *Anal.* Calcd for $C_8H_9Cl_2N$ (**19**): C, 50.55; H, 4.77; Cl, 37.31; N, 7.37. Found: C, 50.37; H, 4.85; Cl, 36.84; N, 7.61.

2) A solution of dichloroacetyl chloride (2.95 g, 0.02 mol) in DME (10 ml) was added dropwise to a solution of **18** (1.23 g, 0.01 mol) and triethylamine (2.53 g, 0.025 mol) in DME (10 ml) under a nitrogen atmosphere with stirring and ice-salt cooling (−10——5°C). Stirring was continued for 1 h at room temperature, then abs. methanol (*ca.* 20 ml) was added to the mixture. The whole was kept for 72 h at room temperature. The reaction mixture was concentrated *in vacuo* to give a residue, which was dissolved in chloroform (150 ml). The chloroform solution was washed with water (100 ml×3), and dried over sodium sulfate. After removal of the solvent, the residue (4.0 g) was subjected to silica gel (100 g) column chromatography. Elution with hexane–ethyl acetate (18: 1) gave the product **19**, 0.41 g (21.6%). Subsequent elution with hexane–ethyl acetate (10: 1) gave an oily residue, which was distilled under reduced pressure to give bis(2,6-dimethyl-4-pyridyl)dichloromethane (**21**), bp 110—112°C (1.5 mmHg), mp 77—80°C, 0.43 g (29.2%). ^{1}H-NMR ($CDCl_3$) δ: 2.55 (12H, s), 7.13 (4H, s). MS *m/e*: 294 (M^+). *Anal.* Calcd for $C_{15}H_{16}Cl_2N_2$ (**21**): C, 61.03; H, 5.46; N, 9.49. Found: C, 60.89; H, 5.17; N, 9.42.

Reaction of Dichloroketene with 3,5-Dimethylpyridine 1-Oxide (22)——A solution of dichloroacetyl chloride (2.95 g, 0.02 mol) in DME (10 ml) was added dropwise to a solution of **22** (1.23 g, 0.01 mol) and triethylamine (2.53 g, 0.025 mol) in DME (10 ml) under a nitrogen atmosphere with stirring and ice-salt cooling (−10——5°C). The mixture was stirred for 1 h at room temperature. After removal of the solvent, the residue was dissolved in chloroform (150 ml). The chloroform solution was washed with water (100 ml×3), and dried over sodium sulfate. After removal of the chloroform *in vacuo*, the residue (2.5 g) was subjected to silica gel (100 g) column chromatography. Elution with hexane–ethyl acetate (20: 1) gave an oily residue, which was distilled under reduced pressure to yield 2-dichloromethyl-3,5-dimethylpyridine (**23**), bp 79—82°C (3 mmHg), 0.80 g (42.0%). ^{1}H-NMR ($CDCl_3$) δ: 2.30 (3H, s), 2.48 (3H, s), 6.90 (1H, s), 7.32 (1H, s), 8.25 (1H, s). MS *m/e*: 189 (M^+). *Anal.* Calcd for $C_8H_9Cl_2N$ (**23**): C, 50.55; H, 4.77; Cl, 37.31; N, 7.37. Found: C, 50.61; H, 4.74; Cl, 37.55; N, 7.35.

Reaction of Dichloroketene with Quinoline 1-Oxide (24)——1) A solution of dichloroacetyl chloride (2.95g, 0.02 mol) in DME (10 ml) was added dropwise to a solution of **24** (1.45 g, 0.01 mol) and triethylamine (2.53 g, 0.025 mol) in DME (10 ml) under a nitrogen atmosphere with stirring and ice-salt cooling (−10——5°C). The mixture was stirred for 0.5 h at room temperature. Triethylamine hydrochloride precipitated was filtered off, and the filtrate was concentrated *in vacuo* to give a residue, which was extracted with ether. The ether fraction was concentrated to give an oily residue (1.98 g), which was subjected to silica gel (60 g) column chromatography. Elution with hexane–benzene (4: 1) gave a crystalline substance, which was recrystallized from petroleum ether to give 2-dichloromethylquinoline (**25**), mp 82—84°C (lit.[10] mp 82°C), 0.24 g (11.2%). Subsequent elution with hexane–benzene (1: 3) gave an oily substance, which was distilled under reduced pressure to give 4-dichloromethylquinoline (**26**), bp 118—120°C (4 mmHg) [lit.[11] bp 109—110°C (3 mmHg)], 0.14 g (6.6%).

2) A solution of dichloroacetyl chloride (2.95 g, 0.02 mol) in chloroform (10 ml) was added dropwise to a solution of **24** (1.45 g, 0.01 mol) and triethylamine (2.53 g, 0.025 mol) in chloroform (10 ml) with stirring and ice-salt cooling (−10——5°C). The mixture was stirred for 2 h at room temperature, and allowed to

stand for 9 h. The reaction mixture was washed with water (15 ml × 4), and the organic layer was dried over anhydrous sodium sulfate. After removal of the solvent, the residue (4.0 g) was subjected to silica gel (80 g) column chromatography. Elution with hexane–benzene (4: 1) gave **25**, 0.26 g (12.4%). Subsequent elution with hexane–benzene (1: 1) gave a crystalline substance, which was recrystallized from hexane to give bis(2-quinolyl)dichloromethane (**28**), mp 99—101°C, colorless needles, 0.09 g (5.4%). ^{1}H-NMR ($CDCl_3$) δ: 7.8 (12H, m). MS *m/e*: 338 (M^+). *Anal.* Calcd for $C_{19}H_{12}Cl_2N_2$ (**28**): C, 67.27; H, 3.57; Cl, 20.90; N, 8.26. Found: C, 67.67; H, 3.37; Cl, 21.13; N, 8.27

Elution was continued with benzene–ethyl acetate (3: 1) to give 4-quinolinol (**27**), mp 205—206°C (ethyl acetate) (lit.[12] mp 201°C), 0.07 g (4.6%). *Anal.* Calcd for C_9H_7NO (**27**): C, 74.48; H, 4.83; N, 9.66. Found: C, 74.57; H, 4.66; N, 9.69.

Reaction of Dichloroketene with Isoquinoline 2-Oxide (29)——1) Employing the procedure given for compound **23**, **29** (1.45 g, 0.01 mol) was allowed to react with dichloroacetyl chloride (2.95 g, 0.02 mol) in the presence of triethylamine 2.53 g, 0.025 mol) in DME (60 ml). After removal of the solvent, the residue was dissolved in chloroform (150 ml). The chloroform solution was washed with water (100 ml × 3), and dried over anhydrous sodium sulfate. After removal of the solvent, the residue (5.3 g) was subjected to silica gel (100 g) column chromatography. Elution with hexane–chloroform (1: 1) gave 1-dichloromethylisoquinoline (**30**), mp 57—59°C (petroleum ether), 0.90 g (42.4%). ^{1}H-NMR ($CDCl_3$) δ: 7.23 (1H, s), 7.73 (4H, m), 8.52 (2H, m). MS *m/e*: 211 (M^+). *Anal.* Calcd for $C_{10}H_7Cl_2N$ (**30**): C, 56.63; H, 3.33; Cl, 33.44; N, 6.61. Found: C, 56.75; H, 3.28; Cl, 33.67; N, 6.68.

2) According to the procedure described above, **29** was allowed to react with dichloroacetyl chloride (2.95 g, 0.02 mol) in the presence of triethylamine (2.53 g, 0.025 mol) in chloroform (30 ml). Work-up as above gave **30**, 0.51 g (24.0%).

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