PYRIMIDINYLCYCLOPROPANES. SYNTHESIS AND REACTIONS

Tetsuzo Kato,* Nobuya Katagiri, Akihiro Wagai, and Yumiko Katagiri
Pharmaceutical Institute, Tohoku University, Aobayama, Sendai
980, Japan

Abstract —— Reactions of trichloromethylpyrimidines (1 - 4) with dimethyl fumarate in the presence of *t*-butyl isocyanide and copper powder in benzene gave the corresponding dimethyl 3-chloro-3-(4- or 6-pyrimidinyl)cyclopropane-1,2-*trans*-dicarboxylates (5 - 8). Similar reactions with methyl vinyl ketone afforded the corresponding 2-acetyl-1-chloro-1-(4- or 6-pyrimidinyl)cyclopropanes (9 - 12). Pyrimidinylcyclopropanes (10 and 12), on treatment with sodium ethoxide, underwent ring opening of cyclopropane to give 1-pyrimidinyl-4-oxopentanes (13 - 16).

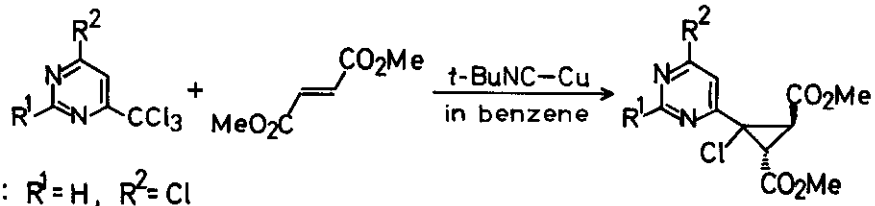
In the previous paper,[1] we have reported that 4-trichloromethylpyrimidines, obtained from the reaction of 4-methylpyrimidines with phosphorus pentachloride in phosphorus oxychloride,[2] reacted with triphenylphosphine to give chloropyrimidinylmethylenephosphoranes which were submitted to Wittig reaction with aldehydes to afford 4-alkenylpyrimidines. As a continuation and extension of our studies on *N*-heterocycles bearing trichloromethyl group,[2-5] we now report the synthesis of pyrimidinylcyclopropanes from 4-trichloromethylpyrimidines and electron-deficient olefins. Moreover, it appeared to be of interest to investigate further the scope of the reactivity of these novel products, pyrimidinylcyclopropanes, which is another subject of the present paper.

According to the procedure reported by Saegusa *et al.*,[6] 4-chloro-6-trichloromethylpyrimidine (1) was allowed to react with dimethyl fumarate (3 molar equivalents) in the presence of *t*-butyl isocyanide (2 molar equivalents) and copper powder (4 molar equivalents) in dry benzene under nitrogen atmosphere at reflux to afford dimethyl 3-chloro-3-(4-chloro-6-pyrimidinyl)cyclopropane-1,2-dicarboxylate (5) in 25% yield.[7] Since the coupling constant between two protons [3.21 ppm (d) and

3.53 ppm (d)] of cyclopropane ring was 8 Hz, we assigned the *trans* dicarboxylate structure to this compound (5).

Similar reactions of trichloromethylpyrimidines (2 - 4) with dimethyl fumarate gave the corresponding pyrimidinylcyclopropanes (6 - 8). Results are summarized in Table I.

Table I. Formation of Dimethyl 3-Chloro-3-(4 or 6-pyrimidinyl)-cyclopropane-1,2-*trans*-dicarboxylates (5 - 8).



1: R^1 = H, R^2 = Cl
2: R^1 = Me, R^2 = Cl
3: R^1 = Ph, R^2 = H
4: R^1 = Ph, R^2 = Cl

5 — 8

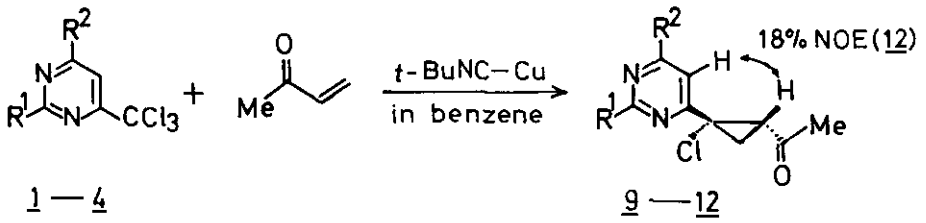
Compd.	R^1	R^2	Reaction time (hr)	Yield (%)	mp (°C)*	Formula	Analysis (%) Calcd. (Found) C	H	N
5	H	Cl	4	25	80 - 81	$C_{11}H_{10}Cl_2N_2O_4$	43.29 (43.41)	3.28 (3.24)	9.28 (9.31)
6	Me	Cl	6	18	82 - 84	$C_{12}H_{12}Cl_2N_2O_4$	45.15 (45.31)	3.76 (3.61)	8.75 (8.59)
7	Ph	H	18	18	97 - 98	$C_{17}H_{15}ClN_2O_4$	58.88 (58.89)	4.33 (4.23)	8.08 (8.07)
8	Ph	Cl	10	63	103 - 104	$C_{17}H_{14}Cl_2N_2O_4$	53.55 (53.79)	3.63 (3.67)	7.35 (7.17)

* Recrystallized from ether - hexane.

Next, trichloromethylpyrimidines (1 - 4) were allowed to react with methyl vinyl ketone under the similar conditions to give the corresponding pyrimidinylcyclopropanes (9 - 12). Results are summarized in Table II. In the NMR spectrum of compound (12), an 18% nuclear Overhauser effect (NOE) was observed between the

pyrimidine ring proton (7.81 ppm, s) and methine proton (3.29 ppm, dd) of cyclopropane ring. Therefore, the configuration of compound (12) was characterized as the *cis*.

Table II. Formation of 2-Acetyl-1-chloro-1-(4 or 6-pyrimidinyl)-cyclopropanes (9 - 12).



1 — 4 9 — 12

Compd.	R^1	R^2	Reaction time (hr)	Yield (%)	mp (°C)**	Formula	Analysis (%) Calcd. (Found) C	H	N
9	H	Cl	5	20	99 - 100	$C_9H_8Cl_2N_2O$	46.77 (47.16	3.46 3.51	12.12 11.96)
10	Me	Cl	2	25	92 - 93	$C_{10}H_{10}Cl_2N_2O$	49.00 (49.15	4.11 4.08	11.43 11.41)
11	Ph	H	4	34 (17*)	120 - 121	$C_{15}H_{13}ClN_2O$	66.06 (65.63	4.77 4.74	10.20 10.23)
12	Ph	Cl	2.5	22	170 - 171	$C_{15}H_{12}Cl_2N_2O$	58.65 (58.54	3.91 3.84	9.12 8.88)

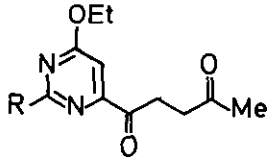
* Cyclohexyl isocyanide was used instead of *t*-butyl isocyanide.

** Recrystallized from hexane.

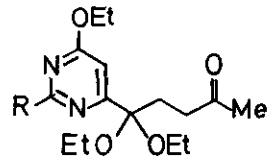
Compound (10), on treatment with excess sodium ethoxide (10 molar equivalents) in ethanol at room temperature for 20 hr, underwent ring opening of cyclopropane to give 1-(4-ethoxy-2-methyl-6-pyrimidinyl)-1,4-dioxopentane [13, bp 75° (0.007 mmHg), *Anal.* Calcd. for $C_{12}H_{16}N_2O_3$: C, 61.00; H, 6.83; N, 11.86. Found: C, 60.69; H, 6.84; N, 11.63.] and 1,1-diethoxy-1-(4-ethoxy-2-methyl-6-pyrimidinyl)-4-oxopentane [14, mp 51 - 53° (hexane). *Anal.* Calcd. for $C_{16}H_{26}N_2O_4$: C, 61.91; H, 8.44; N, 9.03. Found: C, 61.71; H, 8.57; N, 9.06.] in 8% and 52% yield, respectively.

Similar treatment of compound (12) gave 1-(4-ethoxy-2-phenyl-6-pyrimidinyl)-1,4-dioxopentane [15, mp 52 - 54° (hexane), *Anal.* Calcd. for $C_{17}H_{18}N_2O_3$: C, 68.44; H, 6.08; N, 9.39. Found: C, 68.51; H, 6.12; N, 9.29.] and 1,1-diethoxy-1-(4-ethoxy-2-phenyl-6-pyrimidinyl)-4-oxopentane [16, mp 59 - 60° (hexane), *Anal.* Calcd. for $C_{21}H_{28}N_2O_4$: C, 67.72; H, 7.58; N, 7.52. Found: C, 67.45; H, 7.77; N, 7.62.] in 30% and 32% yield, respectively.

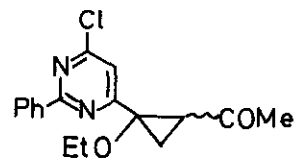
When this reaction was carried out for shorter time (1 hr), 2-acetyl-1-(4-chloro-2-phenyl-6-pyrimidinyl)-1-ethoxycyclopropane (17) was obtained in 32% yield, together with 15 (13%) and 16 (5%). [compound (17), mp 130° (hexane), *Anal.* Calcd. for $C_{17}H_{17}ClN_2O_2$: C, 64.46; H, 5.41; Cl, 11.19; N, 8.84. Found: C, 64.35; H, 5.54; Cl, 11.12; N, 8.79.].



13 : R = Me
15 : R = Ph



14 : R = Me
16 : R = Ph



17

Scheme I

REFERENCES AND NOTES

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7. Satisfactory spectral data were obtained for all new compounds herein reported.

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