Photo-induced Carbon-Carbon Bond Formation: Reactions of 2-Thiopyridones and 2-Quinolinethiones with Alkenes

Takehiko NISHIO*, Yoshimori OMOTE

Department of Chemistry, University of Tsukuba, Sakura-mura, Niihari-gun, Ibaraki 305, Japan

A synthetically useful method for the formation of C—C bonds involving photochemically induced addition of 2-thioxo-1,2-dihydropyridines or -quinolines to alkenes is described. The products are 2-(2-mercaptoalkyl)-pyridines and -quinolines.

It has been shown that thiones undergo photo-induced addition to alkenes to give thietanes as primary products, which are often unstable and are transformed into fragmentation products[1,2]. This ready mode of C—C bond formation suggested that 2-substituted pyridines and 2-substituted quinolines could be readily prepared by similar photochemical reactions of 2-thiopyridones and 2-quinolinethiones with alkenes. This paper describes a synthetically useful method of C—C bond formation with 2-thiopyridones (**1**) and 2-quinolinethiones (**3**) through a photo-induced addition reaction[3].

Irradiation of a solution of 2-thiopyridones (**1**) in 1,2-dimethoxyethane in the presence of an alkene (**2**) in excess in a Pyrex vessel with a high-pressure mercury lamp under an argon atmosphere at room temperature gave the 2-substituted pyridines (**3**) in good yields.

Table. 2-(2-Mercaptoalkyl)-pyridines (**3**) and 2-(2-Mercaptoalkyl)-quinolines (**5**) prepared

Product	Irradiation Time [h]	Yield	m.p. [°C] or b.p./torr[a] [°C]	Molecular Formula[b]	I.R.[c] ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3/TMS_{int}$) δ [ppm]	^{13}C-N.M.R. ($CDCl_3/TMS_{int}$) δ [ppm]
3aa	8	86	b.p. 120°/2	$C_{10}H_{13}NO_2S$ (211.2)	2575, 1725, 1585, 1570, 1465, 1430, 1275, 1230, 1150, 1105, 1085, 985, 745	1.36 (t, 1H, J = 9.3 Hz); 1.71 (s, 3H); 3.23 (d, 2H, J = 9.3 Hz); 3.70 (s, 3H); 7.09–7.33 (m, 2H); 7.57–7.76 (m, 1H); 8.50–8.59 (m, 1H)	21.5 (q); 33.0 (t); 52.3 (q); 55.0 (s); 120.9 (d); 122.0 (d); 136.4 (d); 148.9 (d); 161.0 (s); 174.5 (s)
3ab	8	92	b.p. 125°/2	$C_9H_{10}N_2S$ (178.2)	2560, 2240, 1590, 1575, 1435, 990, 785, 745	1.61 (t, 1H, J = 8.8 Hz); 1.80 (s, 3H); 3.18 (AB or ABX, 2H, J = 8.8, 9.8 Hz); 7.20–7.34 (m, 1H); 7.59–7.87 (m, 2H); 8.56–8.65 (m, 1H)	25.6 (q); 34.2 (t); 47.6 (s); 121.4 (d); 121.8 (s); 123.0 (d); 137.1 (d); 149.6 (d); 156.9 (s)
3ac	8	68	b.p. 135°/2 (dec.)	$C_8H_8N_2S$[d] (164.2)	2555, 2240, 1585, 1570, 1470, 1435, 755	1.78 (t, 1H, J = 8.8 Hz); 3.18 (dd, 2H, J = 6.4, 8.8 Hz); 4.29 (t, 1H, J = 6.4 Hz); 7.09–7.58 (m, 2H); 7.68–7.86 (m, 1H); 8.56–8.63 (m, 1H)	27.7 (t); 43.5 (d); 118.7 (s); 122.5 (d); 123.3 (d); 137.3 (d); 149.9 (d); 152.9 (s)
3ad	8	33	b.p. 145°/2	$C_{13}H_{13}NS$ (215.25)	2560, 1590, 1570, 1495, 1470, 1455, 1435, 745, 700	1.41 (t, 3H, J = 8.3 Hz); 2.95–3.66 (m, 2H); 4.23 (t, 1H, J = 7.8 Hz); 6.97–7.58 (m, 8H); 8.53–8.60 (m, 1H)	29.2 (t); 57.1 (d); 121.6 (d); 123.6 (d); 126.9 (d); 128.0 (d); 128.6 (d); 136.3 (d); 142.2 (s); 149.3 (d); 161.4 (s)
3ba	12	67	m.p. 124.5–125.5°	$C_{10}H_{13}NO_3S$ (227.2)	2590, 1738, 1595, 1580, 1450, 1285, 1235, 1200, 1100, 810	(in D_3C—OD): 1.76 (s, 3H); 3.35 (dd, 2H, J = 13.7, 31.3 Hz); 3.74 (s, 3H); 7.22 (d, 2H, J = 2.4 Hz); 8.04–8.11 (m, 1H)	(in D_3C—OD): 21.4 (q); 32.1 (t); 52.8 (q); 53.6 (s); 123.8 (d); 124.8 (d); 140.3 (d); 150.6 (s); 152.8 (s); 177.6 (s)
5aa	6	91	b.p. 150°/2	$C_{14}H_{15}NO_2S$ (261.3)	2575, 1730, 1620, 1600, 1562, 1502, 1455, 1430, 1285, 1230, 1200, 1150, 1100, 835, 760	1.54 (t, 1H, J = 8.8 Hz); 1.78 (s, 3H); 3.37 (dd, 2H, J = 2.0, 8.8 Hz); 3.70 (s, 3H); 7.31–7.78 (m, 4H); 8.06 (br. d, 2H)	22.0 (q); 32.8 (t); 52.3 (q); 55.7 (s); 119.0 (d); 126.4 (d); 126.8 (s); 127.3 (d); 129.4 (2 x d); 136.4 (d); 147.2 (s); 160.9 (s); 174.4 (s)
5ab	6	86	b.p. 145°/2	$C_{13}H_{12}N_2S$ (228.3)	2560, 2240, 1618, 1597, 1560, 1502, 1450, 1430, 815, 755	1.71 (X of ABX, 1H, J = 8.8, 9.8 Hz); 1.87 (s, 3H); 3.29 (AB of ABX, 2H, J = 8.8, 9.8 Hz); 7.32–7.85 (m, 4H); 8.01–8.22 (m, 2H)	25.9 (q); 34.1 (t); 48.1 (s); 118.8 (d); 122.1 (s); 126.9 (d); 127.0 (s); 127.5 (d); 129.2 (d); 129.9 (d); 137.3 (d); 147.4 (s); 156.9 (s)
5ba	2	89	b.p. 150°/2 m.p. 106–107°	$C_{15}H_{17}NO_2S$ (275.3)	2560, 1735, 1615, 1595, 1555, 1510, 1450, 1435, 1277, 1235, 1160, 1130, 1095, 905, 760	1.52 (t, 1H, J = 9.3 Hz); 1.78 (s, 3H); 2.68 (d, 3H, J = 1.0 Hz); 3.37 (dd, 2H, J = 1.5, 9.3 Hz); 3.72 (s, 3H); 7.20 (d, 1H, J = 1.0 Hz); 7.42–7.75 (m, 2H); 7.89–8.09 (m, 2H)	18.9 (q); 22.0 (q); 32.7 (t); 52.3 (q); 55.6 (s); 119.6 (d); 123.5 (d); 126.2 (d); 127.0 (s); 129.1 (d); 130.1 (d); 144.6 (s); 147.1 (s); 160.5 (s); 174.7 (s)
5bb	2	87	b.p. 145°/2	$C_{14}H_{14}N_2S$ (242.3)	2560, 2240, 1595, 1560, 1505, 1445, 760	1.70 (X of ABX, 1H, J = 8.3, 9.8 Hz); 1.86 (s, 3H); 2.70 (d, 3H, J = 1.0 Hz); 3.28 (AB of ABX, 2H, J = 8.3, 9.8 Hz); 7.44–7.77 (m, 3H); 7.90–8.08 (m, 2H)	18.8 (q); 26.0 (q); 34.0 (t); 48.0 (s); 119.6 (d); 122.2 (s); 123.6 (d); 127.0 (d); 127.2 (s); 129.6 (d); 129.9 (d); 146.0 (s); 147.3 (s); 156.5 (s)
5be	12	59	m.p. 52–53.5	$C_{15}H_{17}NS$ (243.3)	2550, 1600, 1505, 1445, 760	1.26 (d, 1H, J = 6.3 Hz); 1.25–2.46 (m, 8H); 2.63 (s, 3H); 3.26 (dt, 1H, J = 3.4, 11.7 Hz); 3.88–4.01 (m, 1H); 7.15 (br. s, 1H); 7.25–8.09 (m, 4H)	18.8 (q); 20.3 (t); 24.2 (t); 26.0 (t); 34.5 (t); 42.1 (d); 49.6 (d); 120.7 (d); 123.5 (d); 125.5 (d); 126.9 (s); 128.8 (d); 129.5 (d); 143.7 (s); 147.4 (s); 163.0 (s)

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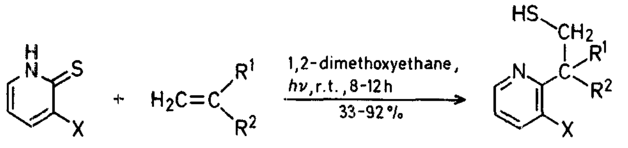
[a] Temperature of Kugelrohr distillation apparatus.

[b] The microanalysis were in satisfactory agreement with the calculated values: C ±0.27, H ±0.12, N ±0.33. Exception: compound **3ac**.

[c] Liquid products as film, solid products as KBr discs.

[d] Compound **3ac** decomposed during attempted purification by distillation. A satisfactory analysis could not be obtained.



1a X = H
1b X = OH

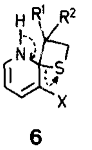
2	R¹	R²
a	CH_3	$COOCH_3$
b	CH_3	$-CN$
c	H	$-CN$
d	H	$-C_6H_5$

3	X	R¹	R²
aa	H	CH_3	$COOCH_3$
ab	H	CH_3	$-CN$
ac	H	H	$-CN$
ad	H	H	C_6H_5
ba	OH	CH_3	$COOCH_3$

The structure of all products **3** was elucidated on the basis of spectral data and element analyses. Thus, the microanalysis of product **3aa** indicated the addition of methyl methacrylate (**2a**) to 2-thiopyridone (**1a**). The I.R. spectrum of **3aa** showed absorption bands at $\nu = 2575\ \text{cm}^{-1}$ characteristic of thiols and at $\nu = 1725\ \text{cm}^{-1}$ due to ester carbonyl. The ^{1}H-N.M.R. spectrum of **3aa** displayed a triplet at $\delta = 1.36$ ppm (assigned to SH), two singlets at $\delta = 1.71$ (assigned to CH_3) and 3.70 ppm (assigned to OCH_3), a doublet at $\delta = 2.23$ ppm (assigned to CH_2), and signals of the pyridine protons. The ^{13}C-N.M.R. spectrum of **3aa** showed signals at $\delta = 33.0$ ($\underline{C}H_2$), 21.5 and 52.3 (2 $\underline{C}H_3$), 55.0 ($C_{\text{quaternary}}$), and 174.5 ppm ($\underline{C}$=O) in addition to signals of the pyridine C-atoms.

Irradiation of pyridine-2-thione (**1a**) in the presence of methyl acrylate and 1,2-disubstituted ethylenes such as crotononitrile and stilbene under the same conditions did not give the corresponding 2-substituted pyridines and **1a** was recovered quantitatively.

The formation of the 2-substituted pyridines **3** can be best explained by assuming an initial photochemical [2 + 2]cycloaddition of the thiocarbonyl group of **1** to the C=C group of the alkene **2** to give an unstable thietane intermediate **6** which undergoes ring cleavage with aromatization of the pyridine ring to yield the final products **3**. The regiochemistry of the cycloaddition is in accord with previously published work on thioamide photochemistry[3a].



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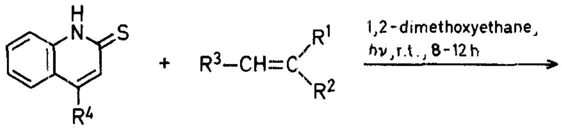
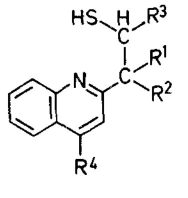
In a similar manner, the 2-substituted quinolines **5** were obtained in high yields when a mixture of 2-quinolinethiones (**4**) and substituted alkenes (**2**) was irradiated under the same conditions.



4a R⁴ = H
4b R⁴ = CH_3

2	R¹	R²	R³
a	CH_3	$COOCH_3$	H
b	CH_3	$-CN$	H
e	H	$-(CH_2)_4-$	



5	R¹	R²	R³	R⁴
aa	CH_3	$COOCH_3$	H	H
ab	CH_3	$-CN$	H	H
ba	CH_3	$COOCH_3$	H	CH_3
bb	CH_3	$-CN$	H	CH_3
be	H	$-(CH_2)_4-$		CH_3

In this case, the reaction also proceeds with cyclohexene (**2e**), a non-terminal alkene, to give 2-(2-mercaptocyclohexyl)-4-methylquinoline (**5be**) in 53 % yield[4].

In conclusion, the photoaddition of certain alkene derivatives provides a preparative route to 2-(2-mercaptoalkyl)-pyridines and -quinolines.

2-(2-Mercaptoalkyl)-pyridines (3) and 2-(2-Mercaptoalkyl)-quinolines (5); General Procedure:

A solution of a 2-thioxo-1,2-dihydropyridine (**1**) or a 2-thioxo-1,2-dihydroquinoline (**4**) (200 mg) in 1,2-dimethoxyethane (60 ml) containing an excess of the alkene derivative **2** (~ 1 ml) in a Pyrex vessel under argon is irradiated with a high-pressure mercury lamp (HALös EHP 300 W, Eikosha) for 2–12 h at room temperature. After removal of the solvent, the residue is chromatographed on a silica gel (Wakogel C-300, flash chromatography) column with benzene/ethyl acetate (19/1–4/1) as eluent to yield product **3** or **5**, respectively.

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[3] For photoreactions of thiocarboxamides and alkenes, see:
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(b) Das, B. C., Fourrey, J. L., Marazano, C., Merrien, A., Palonsky, J. *J. Chem. Res.* [S] **1978**, 370.
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[4] This result is not consistent with the reported photochemical formation of 2-cyclohexylthio-4-methylquinoline from **4b** and cyclohexene: Suzuki, K., Hoshino, M., Oguchi, S. *Tokyo Gakugei Daigaku Kiyo, Dai-4-Bu* **1977**, *29*, 149; *C. A.* **1978**, *88*, 190565.