INTRAMOLECULAR PHOTOREACTION OF THIOBARBITURATES WITH AN ALKENYL GROUP IN THEIR *N*-SIDE CHAIN. REGIOSELECTIVE SYNTHESIS OF FUSED PYRIMIDINE DERIVATIVES THROUGH PHOTOCYCLOADDITION OF MONO- AND DI-THIOBARBITURATES[1]

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Abstract - Upon irradiation, thiobarbiturates (**1** and **2**) with an alkenyl group in their *N*-side chain give bi- and tri-cyclic fused pyrimidine derivatives through regioselective [2+2] photocycloaddition.

Although the photochemistry of barbiturates has been studied extensively,[2] little is known about that of thiobarbiturates (sulfur analogues). As part of a continuing study on the photochemistry of the nitrogen-thiocarbonyl systems, i.e., thioamide[3] and thioimide,[4] we recently reported that thiobarbiturates undergo efficient intermolecular [2+2] photocycloaddition (Paterno-Büchi reaction) with olefins to give the thietane derivatives.[5] The cycloaddition of monothiobarbiturate (1,3,5,5-tetramethyl-4,6-dioxohexahydropyrimidine-2-thione) occurred only at the 2-position affording the thietane derivatives (1-thia-5,9-diazaspiro[3,5]nonane derivatives), whereas with the 2,4-di- and 2,4,6-tri-thiobarbiturates, the cycloaddition occurred at the 4-position to give the corresponding thietane derivatives (1-thia-5,7-diazaspiro[3,5]nonane derivatives).[5] As a synthetic application of these regioselective photocycloadditions for the construction of various diaza-heterocycles, we now wish to report the intramolecular photocycloaddition of thiobarbiturates (**1** and **2**) with an alkenyl group [-$(CH_2)_nCR=CH_2$; n=2,3] in their *N*-side chain.

Photolyses of thiobarbiturates (**1** and **2**) were performed in acetonitrile (10 mM) using a 1 kW high-pressure mercury lamp through a Pyrex filter under a nitrogen atmosphere at room temperature. The results are

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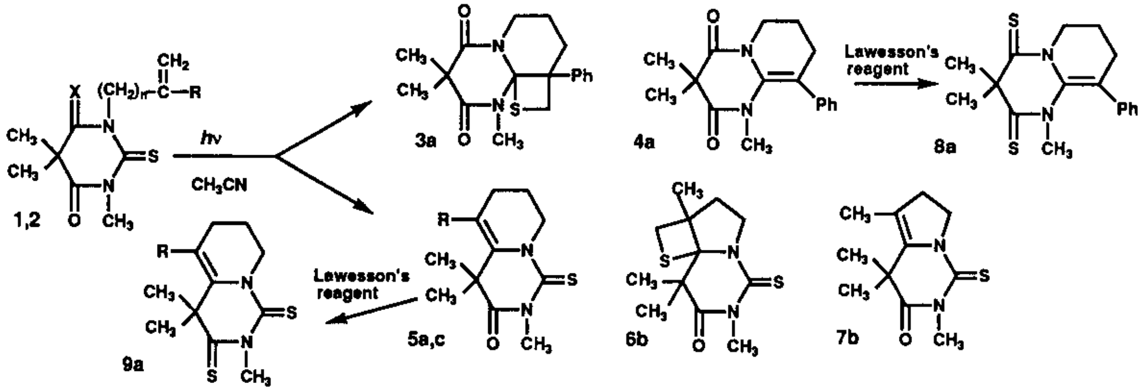
This paper is dedicated to the memory of the late Professor Yoshio Ban.

listed in Table 1. In the photoreaction of *N*-(4-phenyl-4-pentenyl)monothiobarbiturate (**1a**), the cycloaddition of olefin moiety, as expected, occurred at the 2-thiocarbonyl (C=S) in preference to the 4-carbonyl (C=O),[5] giving the corresponding tricyclic thietane (**3a**) in 34% yield, accompanied by the dethioformylated compound (**4a**) in 26% yield. Probably, the compound (**4a**) arises from the initially formed **3a** through photochemical fission (cycloreversion) of the thietane ring.[4,5] In the case of dithiobarbiturate (**2a**), an analogue of **1a**, photocycloaddition occurred at the 4-position to give only the dethioformylated compound (**5a**) in 37% yield. Similarly upon irradiation of **2c**, the bicyclic compound (**5c**) having 6-6-ring system was obtained. Further in the case of *N*-(3-methyl-3-butenyl)dithiobarbiturate (**2b**), both of tricyclic thietane (**6b**) and bicyclic compound (**7b**) having 6-5-ring system were obtained in 18 and 46% yields, respectively, while photoreaction of monothiobarbiturate (**1b**), an analogue of **2b**, gave a complex mixture of inseparable products.



Scheme

Table 1. Photoreactions of **1** and **2**

Compounds	X	n	R	Time (h)	Products	Yield (%)	mp (°C)
1a	O	3	Ph	1.1	**3a**	34	125-127
					4a	26	112-114
1b	O	2	CH_3	0.5	-	-	-
2a	S	3	Ph	1.7	**5a**	37	126-127
2b	S	2	CH_3	0.3	**6b**	18	174-176
					7b	46	68-69.5
2c	S	3	H	0.8	**5c**	21	89-90.5

The structures of all products were determined on the basis of the spectral and analytical data.[6] To confirm the site of photocycloaddition, the products (**4a** and **5a**) were treated with Lawesson's reagent, respectively. The thionation product (**8a**) derived from **4a** was not identical with the dithio-compound (**9a**) from **5a**.[7] This indicated that the photocycloaddition occurred at the 2-position in monothiobarbiturate (**1a**), and at the 4-position in dithiobarbiturate (**2a**), respectively.

In conclusion, thiobarbiturates (**1** and **2**) undergo efficient [2+2] photocycloaddition with the olefinic group in their *N*-side chain, giving tricyclic thietanes and/or its fission-products (bicyclic compounds) in analogous with intermolecular photoreaction of thiobarbiturate with olefins.[5] This regioselective photocycloaddition could provide a useful method for the construction of a variety of fused pyrimidine derivatives containing one nitrogen atom at a ring junction, otherwise inaccessible by conventional thermal reaction.

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6. Selected data of photoproducts are as follows.

3a: Ir (nujol) 1670, 1640 cm^{-1}; ms (*m/z*): 330 (M^+), 284 (M^+-HCHS); ^1H-nmr ($CDCl_3$) δ: 1.58 (3H, s, CH_3), 1.9-2.2 (2H, m, N-$CH_2C\underline{H}_2$-), 2.75 (3H, s, N-CH_3), 2.96 (1H, d, *J* =10 Hz, S-CH_2-), 3.71 (1H, d, *J*=10 Hz, S-CH_2-), 3.4-3.7(2H, m, Ph-C-$C\underline{H}_2$-CH_2-), 4.5-4.9 (2H, m, N-CH_2-), 6.9-7.4 (5H, m, aromatic H); ^{13}C-nmr ($CDCl_3$) δ: 17.9(t), 24.3(q), 25.9(q), 30.2(t), 32.2(q), 41.3(t), 42.2(t), 44.4(s), 64.4(s), 88.4(s), 123.7(d x 2), 127.0(d), 128.8(d x 2), 145.3(s), 172.0(s), 172.3(s).

4a: Ir (nujol) 1695, 1655 cm^{-1}; ms (*m/z*): 284 (M^+); ^1H-nmr ($CDCl_3$) δ: 1.50 (6H, s, CH_3 x 2), 1.8-2.1 (2H, m, N-$CH_2C\underline{H}_2$-), 2.61 (2H, t, *J*=6 Hz, C=C-CH_2-), 2.64 (3H, s, N-CH_3), 3.8-4.0 (2H, m, N-CH_2-), 7.1-7.5 (5H, m, aromatic H); ^{13}C-nmr ($CDCl_3$) δ: 21.2(q x 2), 22.0(t), 29.6(t), 36.3(q), 42.0(t), 47.5(s), 112.3(s), 127.6(d), 128.1(d x 2), 128.9(d x 2), 131.1(s), 139.3(s), 169.6(s), 171.5(s).

6b: Ir (nujol) 1695 cm^{-1}; ms (*m/z*): 270 (M^+), 224 (M^+-HCHS); ^1H-nmr ($CDCl_3$) δ: 1.17 (3H, s, CH_3), 1.55 (3H, s, CH_3), 1.71 (3H, s, CH_3), 1.8-2.1 (2H, m, N-$CH_2C\underline{H}_2$-), 2.71 (1H, d, *J*=9 Hz, S-CH_2-), 3.06 (1H, d, *J*=9 Hz, S-CH_2-), 3.50 (3H, s, N-CH_3), 4.1-4.5 (2H, m, N-CH_2-); ^{13}C-nmr ($CDCl_3$) δ: 20.2(q), 20.6(q), 23.9(q), 30.7(t), 34.2(q), 37.8(t), 47.2(s), 51.1(t), 58.3(s), 80.7(s), 171.0(s), 177.7(s).

7b: Ir (nujol) 1695, 1680, 1655 cm^{-1}; ms (*m/z*): 224 (M^+); ^1H-nmr ($CDCl_3$) δ: 1.57 (6H, s, CH_3 x 2), 1.89 (3H, t, *J*=1.5 Hz, C=C-CH_3), 2.56 (2H, t, *J*=8 Hz, C=C-CH_2-), 3.59(3H, s, N-CH_3), 4.20 (2H, t, *J*=8 Hz, N-CH_2-); ^{13}C-nmr ($CDCl_3$) δ: 14.4(q), 26.2(q x 2), 33.0(t), 34.2(q), 40.9(s), 52.0(t), 121.8(s), 134.6(s), 170.7(s), 171.3(s).

7. **8a**: Ms (*m/z*): 316 (M^+); ^1H-nmr ($CDCl_3$) δ: 1.77 (6H, s, CH_3 x 2), 1.9-2.3 (2H, m, N-$CH_2C\underline{H}_2$-), 2.68 (2H, t, *J*=6 Hz, C=C-$C\underline{H}_2$-), 3.06 (3H, s, N-CH_3), 4.3-4.5 (2H, m, N-$C\underline{H}_2$-), 7.2-7.5 (5H, m, aromatic H).

9a: Ms (*m/z*): 316 (M^+); ^1H-nmr ($CDCl_3$) δ: 1.19 (6H, s, CH_3 x 2), 1.8-2.2 (2H, m, N-$CH_2C\underline{H}_2$-), 2.2-2.5 (2H, m, C=C-CH_2-), 4.10 (3H, s, N-CH_3), 4.3-4.5 (2H, m, N-CH_2-), 7.0-7.4 (5H, m, aromatic H).

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