Tetrahedron Letters,Vol.25,No.4,pp 409-410,1984
Printed in Great Britain

0040-4039/84 $3.00 + .00

PHOTOCYCLOADDITION OF ARYLCARBOTHIOAMIDES WITH UNSATURATED SYSTEMS. SYNTHESIS OF 3,5-DIARYL-1,2,4-THIADIAZOLES AND 3-ARYL-4,4,5,5-TETRAMETHYLISOTHIAZOLINES VIA PHOTOGENERATED NITRILE SULFIDES1)

Minoru Machida* and Kazuaki Oda
Faculty of Pharmaceutical Sciences, Higashi-Nippon-Gakuen University,
Ishikari-Tobetsu, Hokkaido, 061-02

Yuichi Kanaoka*
Faculty of Pharmaceutical Sciences, Hokkaido University,
Sapporo 060, Japan

Summary: On irradiation arylcarbothioamides (1) undergo, in the absence of oxygen, the Paterno-Büchi reaction with olefins followed by cleavage, whereas under aerobic conditions the photoreaction proceeds to give 4 and 5 probably via nitrile sulfide intermediates.

Although the photochemistry of thione has been extensively studied,2) few reports have dealt with the photochemical properties of thioamides: namely, thiobenzanilides3) and 4-thiouracils4) have been major subjects in literature, and little is known of photoreactions of arylcarbothioamides. As a logical extension of our photochemical studies of the nitrogen-carbonyl systems,5) we now report the photoreactions of arylcarbothioamides, particularly on their photocycloaddition with multiple linkage systems, which suggests also some synthetic possibilities.

Irradiation of arylcarbothioamides (1) was carried out in the presence of 2,3-dimethyl-2-butene 2 both in a nitrogen atmosphere and under aerobic conditions, and the results are listed in the Table I. In a nitrogen atmosphere, 1 gave isobutyrophenone (3a) (Exp. 1,2). By contrast, under aerobic conditions (in the air), 3,5-diphenyl-1,2,4-thiadiazole (4a) and 3-phenyl-4,4,5,-5-tetramethylisothiazoline (5a) were obtained accompanying small amounts of 3a (Exp. 3). Similarly, with a series of heteroaromatic thioamides (1b-e), the corresponding 3-aryl-4,4,5,5-tetramethylisothiazolines (5b-e) were obtained.

Formation of 4 is always accompanied by concomitant appearance of sulfur, suggesting photogeneration of a nitrile sulfide species (9) as an intermediate.6) This inference was in fact supported by a trapping experiment with ethynylbenzene, which afforded an isothiazole 10, the expected addition product of 9. Although the 1,3-dipolar addition of nitrile sulfide is known to lead to isothiazoles and thiadiazoles,6a,7) convenient methods for the formation of nitrile sulfide seem unknown. Although elucidation of the detailed mechanisms of these reactions awaits further studies, possible pathways for the photoreactions of the arylcarbothioamides are outlined in Chart 1. In parallel to the known photochemical behavior of thioanilides,3) arylcarbothioamides 1 undergo, in the absence of oxygen, the Paterno-Büchi reaction to form a thietane (6), which suffers subsequent photolysis leading ultimately to 3. Under aerobic conditions, by contrast, formation of nitrile sulfide by way of photooxidation through extrusion of the amide hydrogens predominantly proceeds (8→9), competing with formation of the thietane, and the intermediate nitrile sulfide (9) undergoes either 1,3-dipolar cycloaddition with a dipolarophile in a solution or decomposes to sulfur and a nitrile, which will participate in the secondary reaction with 9 giving rise to 4.

These results illustrate examples of the dramatic difference in the photochemical behavior of arylcarbothioamides and arylcarboamides, the latter being incapable of performing these transformations. In addition, these photoreactions may provide, by using a variety of dipolarophiles, a simple route to the synthesis of certain sulfur-containing nitrogen-heterocycles (4 and 5), which would serve as potential candidates for antimicrobial and other biologically active agents.[8)]

Table 1 Photoproducts[a)] from Arylcarbothioamides (1)

Exp.	Subt.	Olefin	(Mole ratio, 2/1)	Conditions[b)]	Time (hr)	Photoproducts (Yield %, mp °C)
1	1a	2	5	N	20	3a(18, oil) 1a(68)
2	1a	2	30	N	2	3a(76) 1a(16)
3	1a	2	5	A	20	3a(8) 5a(48, oil) 4a(22, 88-89.5)
4	1a	2	30	A	1	3a(34)[c)] 5a(52)[c)]
5	1b	2	5	A	25	3b(22)[c)] 5b(24)[c)] (mixture)
6	1c	2	5	A	25	5c(32, oil)
7	1d	2	5	A	20	5d(26, oil) 4d(18, 104-106)
8	1e	2	5	A	20	5e(28, oil) 4e(19, 84-86)
9	1a	ethynylbenzene	2	A	20	5a(18) 10(22, 80-81)

a) All products showed reasonable analytical and spectral data (IR, Mass, ^{1}H-NMR, ^{13}C-NMR).
b) Conditions, N: in nitrogen atmosphere A: in the air.
c) Yields by ^{1}H-NMR spectroscopy.

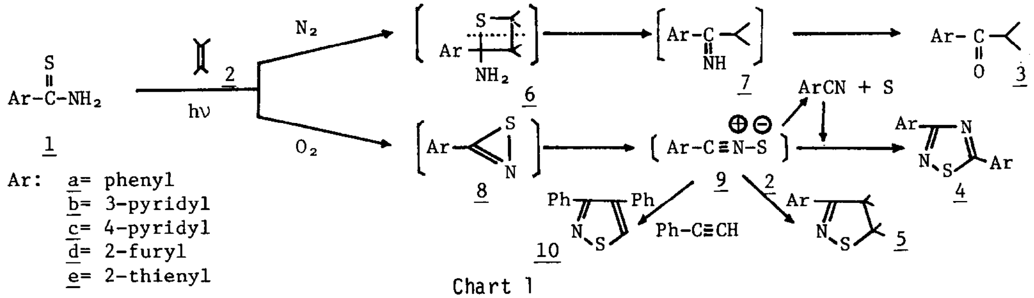

Chart 1

Acknowledgements This work was supported in part by the Grant-in-Aid for Scientific Research No. 56370032 and No. 57570769 (to M. M.), No. 57118006 and No. 58110005 (to Y. K.) from the Ministry of Education, Science and Culture.

References and Notes

1. a) Photochemistry of the Nitrogen-Thiocarbonyl Systems. Part 1; b) Photoinduced Reactions. Part 68. Part 67: M.Machida, K.Oda, and Y.Kanaoka, Chem. Pharm. Bull., in press.
2. a) P.de Mayo, Accounts Chem. Res., 1976, **9**, 52; b) A.Ohno, Int. J. Sulfur Chem. B, 1971, **6**, 183; c) A.Ohno, Y.Ohnishi, and G.Tsuchihashi, J. Am. Chem. Soc., 1969, **91**, 5038.
3. P.de Mayo, L.K.Sydnes, and G.Wenska, J. Org. Chem., 1980, **45**, 1549.
4. J.L.Fourrey, P.Jouin, and J.Moron, Tetrahedron Lett., 1974, 3005.
5. a) Y.Kanaoka, Accounts Chem. Res., 1978, **11**, 407; b) P.H.Mazzocchi, "Organic Photochemistry". Vol. 5, ed. by A.Padwa, Marcel Dekker Inc., N.Y. 1981, p421.
6. a) R.K.Howe, T.A.Gruner, L.G.Carter, L.L.Black, and J.E.Franz, J. Org. Chem., 1978, **43**,3736; b) A.Holm, N.Harrit, and N.H. Toubro, J. Am. Chem. Soc., 1975, **97**, 6197.
7. a) R.K.Howe, T.A. Gruner, and J.E.Franz, J. Org. Chem., 1977, **42**, 1813; b) M.J. Sanders and J.R.Grunwell, J. Org. Chem., 1980, **45**, 3753.
8. T.Noguchi, Y.Hashimoto, T.Mori, S.Kano, and K.Miyazaki, YAKUGAKU ZASSHI, 1968, **88**, 1437.

(Received in Japan 10 October 1983)