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INTRAMOLECULAR PHOTOCYCLIZATION OF 3-SUBSTITUTED ALICYCLIC DITHIOIMIDES: FACILE SYNTHESIS OF 2-AZABICYCLOALKANES VIA THE NORRISH TYPE II PROCESS[1)]

Kazuaki Oda,[a] Minoru Machida,[*,a] and Yuichi Kanaoka[b]
Faculty of Pharmaceutical Sciences, Higashi-Nippon-Gakuen University,[a]
Ishikari-Tobetsu, Hokkaido 061-02, Japan and Faculty of Pharmaceutical
Sciences, Hokkaido University,[b] Sapporo 060, Japan

Upon irradiation, dithiosuccinimides (1a-c) and dithioglutarimides (1d-f) with an aralkyl group at the α-position of the thiocarbonyl group undergo the Norrish type II reaction to give the cyclized products (2a-e), 2-azabicycloalkanes with varying ring size.

KEYWORDS —— dithiosuccinimide; dithioglutarimide; intramolecular photocyclization; Norrish type II reaction; 2-azabicycloalkane

A new combination of functional groups often leads to a new reaction system, also in excited state pathways. We have recently shown that the change of a key element in the cyclic imide chromophore from oxygen to sulfur leads to unique thioimide photochemistry.[2)] The excited cyclic thioimides react with olefins only by photoaddition. Other photoreactions such as the Norrish type I (α-cleavage) and type II reactions, which are common to the parent thione and imide families, are less important.[2)] For example, although 3-substituted alicyclic imides 1 (Y=O) undergo Norrish type I reaction and subsequent rearrangements,[3)] neither α-cleavage nor the rearrangements are competitive in the thioimide substrates (1; Y=S) in which α is substituted for thiocarbonyl (Chart 1). As a result, such inertness of the thioimides to the Norrish type I reaction gives the alicyclic thioimide system interesting synthetic capacities; side reactions due to photolytic cleavages are negligible during the course of their

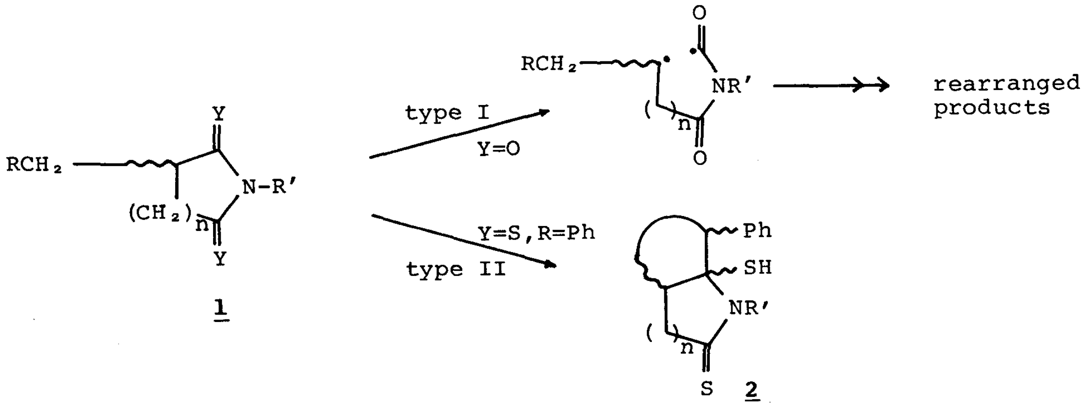
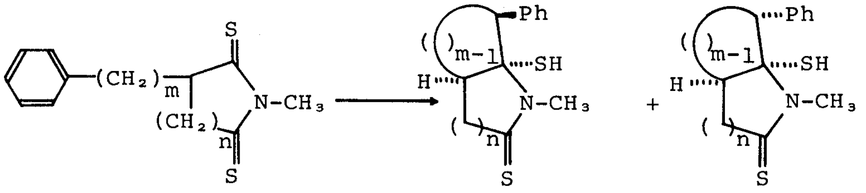


Chart 1

photoadditions.[2)] Indeed, an intramolecular Paterno-Büchi reaction of certain dithiosuccinimides gave rise to a highly strained, fused-ring system.[4)] In the present communication, we wish to report the first example of an intramolecular Norrish type II reaction of the 3-substituted alicyclic thioimides 1 (Y=S). The substrates selected in this work are a series of 3-(ω-phenylalkyl)cyclic dithioimides 1a-e, with which the special reactivity of the excited thiocarbonyl group of the thioimides to abstract benzylic hydrogens[5)] was expected to lead to a facile synthesis of 2-azabicycloalkanes since side reactions such as α-cleavage would be ineffective.

Irradiation of these 3-(ω-phenylalkyl)cyclic dithioimides 1a-e was carried out in benzene (10 mM) using a 1-kW high-pressure mercury lamp (Pyrex filter) in a stream of nitrogen at room temperature for 1-5 h. In all cases a pair of stereoisomers 2-i and 2-ii were obtained as a result of the C-C bond-formation between the thiocarbonyl and the benzylic carbons. The results are listed in Table I.

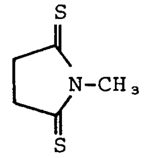
Table I. Photoproducts from 1



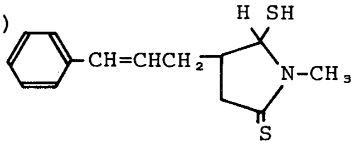
1 2-i 2-ii

1			Time (h)	Hydrogen abstraction	Yield % (mp °C) 2-i	2-ii	
a:	m=2	n=1	1	γ	35(119-122)	29(124-125)	8[a)] (111-112)
b:	m=3	n=1	1	δ	34(131-133)	31(126-127)	4[b)] (oil)
c:	m=4	n=1	5	ε	8[c)]	6[c)]	
d:	m=2	n=2	1	γ	38(135-137)	22(131-133)	
e:	m=3	n=2	5	δ	4[c)]	5[c)]	
f:	m=4	n=2	5	ε	——	——	

a)



b)



c) A mixture of two stereoisomers. Identified by ^{1}H-NMR spectroscopy. The stereochemistry of the ring juncture is unknown.

The structural assignment for all of the products was based on elemental analyses and spectral data. For example, the ^{13}C-NMR spectra of 2-i and 2-ii showed the presence of a newly formed quaternary carbon instead of the disappearance of one thiocarbonyl group. Here the presence of one doublet at 51.3-60.5 ppm indicated the presence of benzylic carbon. The stereochemistry of 2-i and 2-ii was determined on the basis of the ^{1}H-NMR spectra by considering the anisotropic shielding effects of the phenyl ring on the chemical shifts of the

N-methyl group (2a-ii - 2a-i = 0.9 ppm). Thus, 2-i and 2-ii are respectively of trans- and cis-configuration with respect to a thiol and a phenyl group.

As shown in Table I, in the photolysis of a series of thiosuccinimides (n=1; 1a-c) having an aralkyl group at the 3-position of imide ring, hydrogen abstraction took place most effectively at the benzylic position which is γ and δ to the thiocarbonyl group, respectively. But the ability of this abstraction at the benzylic ε-position (1c) strikingly decreased and unchanged 1c was recovered in a 75% yield. Similarly, in the cases of thioglutarimides (n=2; 1d-f), only the γ-hydrogen abstraction reaction at the benzylic carbon proceeded effectively giving the type II products, while 1e with a benzylic δ-hydrogen gave an unseparable mixture of 2e-i and 2e-ii in poor yield, along with recovery of unchanged 1e (73%). Further, when 1f had a benzylic hydrogen available for ε-hydrogen abstraction, no cyclized products due to the Norrish type II reaction were isolated. Instead the substrate 1f was recovered in a 91% yield, even after irradiation for 5 h. In addition, the dithiosuccinimides (1a,b) gave the minor product N-methyl dithiosuccinimide (from 1a) and the reduced thiol (from 1b). This probably results initially from δ-hydrogen abstraction followed by elimination and γ-hydrogen transfer. Apparently the difference in photochemical behavior in these thiosuccinimides and thioglutarimides is due to an unfavorable geometrical distance between the thiocarbonyl group of the latter and the benzylic-hydrogen to be abstracted.

Much attention has been paid to the construction of azabicycloalkane skeletons in view of the biological interest[6] in their 4,5-,[7] 4,6-,[8] and 5,6-[9] ring-fused systems. Very recently 2-azaallyl anion cycloaddition has been reported.[10] This photocyclization also adds a new entry in the synthesis of some 2-azabicycloalkane systems.

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