Published on 01 January 1986. Downloaded by University of Western Ontario on 31/10/2014 15:55:47.

Intramolecular 1,3-Dipolar Cycloadditions with Thiocarbonyl Ylides

Kevin T. Potts* and Maurice O. Dery

Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12180, U.S.A.

anhydro-2-(2-Allyloxyphenyl)-3,5-diphenyl-4-hydroxythiazolium hydroxide and related alkenic systems, together with the corresponding prop-2-ynyloxy and cyanomethyloxy derivatives, undergo ready thermal intramolecular 1,3-dipolar cycloadditions giving stable 1 : 1-cycloadducts, substituted 4*H*-thieno[3,2-*c*]-, and 4*H*-thiazolo[4,5-*c*]-chromenes, respectively; the structure of one of these has been determined by X-ray crystallography.

Inter- and intra-molecular 1,3-dipolar cycloadditions continue to provide ready access to a variety of structures and also entry to polycyclic ring systems.¹ However, the thiocarbonyl ylide has received little attention in intramolecular cycloadditions, principally owing to difficulties in constructing suitable precursors. A convenient approach would be to utilize the 'masked' thiocarbonyl ylide present in a mesoionic thiazole system, and our results in this area, described in this communication, complement those reported² using the mesoionic 1,3-dithiole system.

(2-Allyloxy)thiobenzanilide³ (1; n = 1) and α -bromophenyl acetyl chloride (2) in benzene and Et₃N at room temperature readily gave a deep-red precipitate of *anhydro-2*-(2-allyloxyphenyl)-3,5-diphenyl-4-hydroxythiazolium hydroxide (3; n = 1) which underwent partial cycloaddition on attempted recrystallization from hot solvents. When the mesoionic system (3; n = 1) was kept in dry benzene at room temperature (36 h), a ready regio- and stereo-selective cycloaddition occurred giving a single pair of stereoisomers (4) and (5).

The major isomer [colourless prisms,[†] EtOH, 66%, m.p. 212-213 °C; v_{CO} 1695 cm⁻¹; (M + 1) 386 (100%)] was shown to be (4), with the configuration of 6-H *endo* to the sulphur bridge, by a single crystal X-ray determination (Figure 1).[‡] The *exo* isomer (5) [colourless prisms, EtOH, 10%, m.p. 140-142 °C, v_{CO} 1695 cm⁻¹; (M + 1) 386 (100%)] was readily

^{\dagger} All new compounds reported had satisfactory analytical data ($\pm 0.4\%$) for C, H, and N.

‡ Crystal data: C₂₄H₁₉NO₂S, M = 385, space group $P\overline{1}$ (no. 2), a = 6.942(1), b = 11.176(2), c = 13.340(3) Å, $\alpha = 68.44(2)$, $\beta = 80.08(2)$, $\gamma = 82.08(2)^\circ$, U = 945.0(3) Å³, Z = 2, $D_c = 1.35$ g cm⁻³, crystal size $0.26 \times 0.42 \times 0.6$ mm, Mo- K_{α} radiation, $\lambda = 0.71069$ Å, $\mu = 1.9$ cm⁻¹. ω -scan range = 2° + [20(K_{\alpha1}) - 20(K_{\alpha2})], 20_{max} = 48°, 3202 observed reflections, 2591 with $I > 3\sigma(I)$ used in the structure refinement to obtain R = 3.59, $R_w = 4.18\%$.

Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1, 1986.

Table 1. ¹H N.m.r. chemical shifts, δ , and coupling constants, J (in Hz) (CDCl₃, 200 MHz) for the intramolecular cycloadducts.

Chemical shift/ð							J/Hz					
Compound	i endo 5-H	exo 5-H	endo 6-H	<i>exo</i> 6-H	endo 7-H	exo 7-H	5-H gem	5-H endo, 6-H	5-H <i>exo</i> , 6-H	7-H endo, 6-H	7-H exo, 6-H	OCH ₂ gem
(4)	2.28 (dd)	2.94 (dd)	3.42 (m)		4.31 (dd)	4.60 (dd)	12.9	4.2	7.9	11.5	4.5	11.1
(5)	2.30 (dd)	3.06 (dd)		3.60 (m)	4.48 (dd)	4.75 (dd)	12.8	5.7	10.3	12.3	4.9	11.1
(6)	2.33-2.45 (m) ^a	3.11 (dd)	3.77 (m)		2.09 (dd)	2.33-2.45 (m)	12.2	3.8	7.9	ь	ь	b
(9)		3.34 (q)	_	3.60(t)		4.74 (m)			8.2		2.1	

^a Overlaps with CH₂CH₂O. ^b Not resolved.



separated from (4; n = 1) by preparative layer chromatography (silica gel, CHCl₃). The two stereoisomers (4; n = 1) and (5; n = 1) were not interconvertible in boiling xylene over 48 h. When (3; n = 1) was heated in boiling toluene (4 h), the ratio of (4):(5) was found to be 7:1 [by ¹H n.m.r. spectroscopy (200 MHz)]. We attribute the preferred formation of (4; n = 1) to a lower conformational energy requirement§ in its transition state when compared to that of cycloadduct (5).

Increase in the chain length of (1; n = 2) and reaction with (2) gave (3; n = 2) which was purified by low temperature recrystallization [scarlet needles, CH₂Cl₂-hexane, 42%, m.p. 122—124 °C; v_{CO} 1650 cm⁻¹; (M + 1) 400 (8%)]. On heating (3; n = 2) in boiling xylene for 48 h cycloaddition occurred to (6) in a highly regio- and stereo-selective reaction. N.m.r. data used to assign the configuration at 5-H and 6-H are in Table 1.



Figure 1. Molecular structure of (4). Selected bond lengths (Å) and angles(°): S(1)-C(3), 1.841(2); N(1)-C(11), 1.426(2); N(1)-C(10b), 1.486(3); C(2)-C(3), 1.540(3); C(3)-C(4), 1.545(3); C(4a)-C(5),1.514(4); C(5)-O(6), 1.430(2); C(10a)-C(10b), 1.491(3); S(1)-C(10b), 1.491(3); S(1)-C(10bC(10b), 1.844(2); N(1)-C(2), 1.374(2); C(2)-O(2), 1.218(3); C(3)-C(31), 1.509(2); C(4)-C(4a), 1.543(3); C(4a)-C(10b), 1.541(2); C(3)-S(1)-C(10b), 80.3(1); C(11)-N(1)-C(10b), 124.5(1); N(1)-C(10b), 124.5(1); N(1)-C(10C(4)-C(4a)-C(5), 115.2(2); C(5)-C(4a)-C(10b), 108.9(2); C(5)-C(5)-C(4a)-C(10b), 108.9(2); C(5)-C(5)-C(5)-C(5)O(6)-C(6a), 115.3(1); O(6)-C(6a)-C(10a), 122.6(2); C(6a)-C(7)-C(8), 120.2(2); S(1)-C(10b)-C(4a), 103.7(1); S(1)-C(10b)-C(10a), C(4a)-C(10b)-C(10a), 114.7(2);C(11)-N(1)-C(2),112.5(1);124.0(2); C(2)-N(1)-C(10b), 110.0(1); N(1)-C(2)-C(3), 108.5(2); C(4a), 105.8(1); C(4)-C(4a)-C(10b), 105.5(1); C(4a)-C(5)-O(6), 110.8(2); O(6)-C(6a)-C(7), 116.6(2); S(1)-C(10b)-N(1), 100.7(1); N(1)-C(10b)-C(4a), 106.2(2).

Increase in the chain length of (1) to n = 3 gave, after reaction with (2), the mesoionic system (3; n = 3) which was also obtained by low temperature crystallization. However, when heated in boiling xylene for 8 days, no cycloaddition occurred, the mesoionic system decomposing under these reaction conditions.

The intramolecular cycloaddition of (8) is of particular interest in that the stereochemistry is established at three centres by the facial selectivity shown in the cycloaddition.

[§] Determined by molecular mechanics calculations using a computer program⁴ 'Molecule Builder.'



The mesoionic system (7), on alkylation with 3-bromocyclohexene in hot acetone- K_2CO_3 , gave (8) as deep-red irregular prisms which started to undergo cycloaddition under these reaction conditions. The reaction was completed in boiling xylene giving (9) [colourless needles, EtOH, 23%, m.p. 228-229 °C; (M + 1) 426 (100%)]. The structure of (9) was established from the n.m.r. data in Table 1 with an *exo*-configuration for 5-H and 6-H being assigned on the basis of their chemical shifts. Also, a nuclear Overhauser enhancement of 0.16 was observed between 6-H and 7-H, establishing their *cis*-relationship.

Incorporation of a triple bond into the dipolarophilic side chain also resulted in reactive systems which underwent cycloaddition. On heating (10; X = CH) in benzene for 6 h the cycloadduct (12; X = CH) was isolated, obtained by loss of PhNCO from the 1:1-cycloadduct (11; X = CH) [colourless needles, EtOH, 35%, m.p. 67-68 °C (lit.⁴ m.p. 74-75 °C); (M + 1) 265 (100%)]. The corresponding system (10; X = N), obtained from (7) and chloroacetonitrile, also underwent partial cycloaddition during its preparation, the reaction being completed by refluxing in toluene for 36 h. Loss of PhNCO



from the 1:1-cycloadduct (11; X = N) gave the ring-fused thiazole system (12; X = N) [tan needles, MeOH, 42%, m.p. 127-128 °C; M^{++} 265 (100%)].

The above cycloadditions stand in marked contrast to those reported for this mesoionic ring system carried out in the intermolecular mode⁵ where no cycloaddition occurred with unactivated alkynes, alkenes, and nitriles.

Received, 6th January 1986; Com. 017

References

- 1 For recent reviews of these topics see '1,3-Dipolar Cycloaddition Chemistry,' ed. A. Padwa, vol. 1--2, John Wiley, New York, 1984.
- H. Gotthardt and O. Hues, *Liebigs Ann. Chem.*, 1981, 347.
 K. T. Potts and M. O. Dery, *J. Chem. Soc.*, *Chem. Commun.*, 1986, 1440.
- 4 K. J. Miller, Rensselaer Polytechnic Institute, personal communication.
- 5 K. T. Potts, E. Houghton, and U. P. Singh, J. Org. Chem., 1974, 39, 3627.