Cycloaddition Reactions of Heteroazadienes. The First Intramolecular Diels–Alder Reaction of 1-Thia-3-azabutadienes

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Substituted 1-thia-3-azabutadienes undergo intramolecular [4 + 2] cycloadditions to unactivated carbon–carbon double bonds in high yields.

Cycloaddition reactions of heterodienes,[1] in particular azadienes,[2,3] have been shown to be of great potential in heterocyclic synthesis. The use of hetero-2-azadienes in organic synthesis has been demonstrated recently by Weinreb *et al.* in the case of both inter- and intra-molecular [4 + 2] cycloadditions of *N*-acyl imines (1-oxa-3-aza-1,3-dienes);[4] however, reports concerning [4 + 2] cycloadditions of the analogous 1-thia-3-aza-1,3-dienes are rare[5] and their intramolecular cycloadditions are unknown, to the best of our knowledge. Here, we report that substituted 2-amino-1-thia-3-aza-1,3-dienes, a new type of 1-thia-3-azadienes, smoothly undergo intramolecular [4 + 2] cycloaddition to unactivated alkenes as outlined in Scheme 1.

Heterodienes (**2**) were not isolated, but formed *in situ*† from trimethylsilylimine (**1**)[2] and isothiocyanates. Thus, when (**1**) and phenyl or cyclohexyl isothiocyanate were heated in toluene at 90 °C for 10 h, the cycloadducts (**3**) were obtained in high yields, after column chromatography (silica gel; toluene–ether, 5:1), [(**3a**) 88%; (**3b**) 81%];‡ interestingly, solely the *trans*-fused stereoisomers [J(4a-H–10b-H) 10.3 Hz],[7] derived

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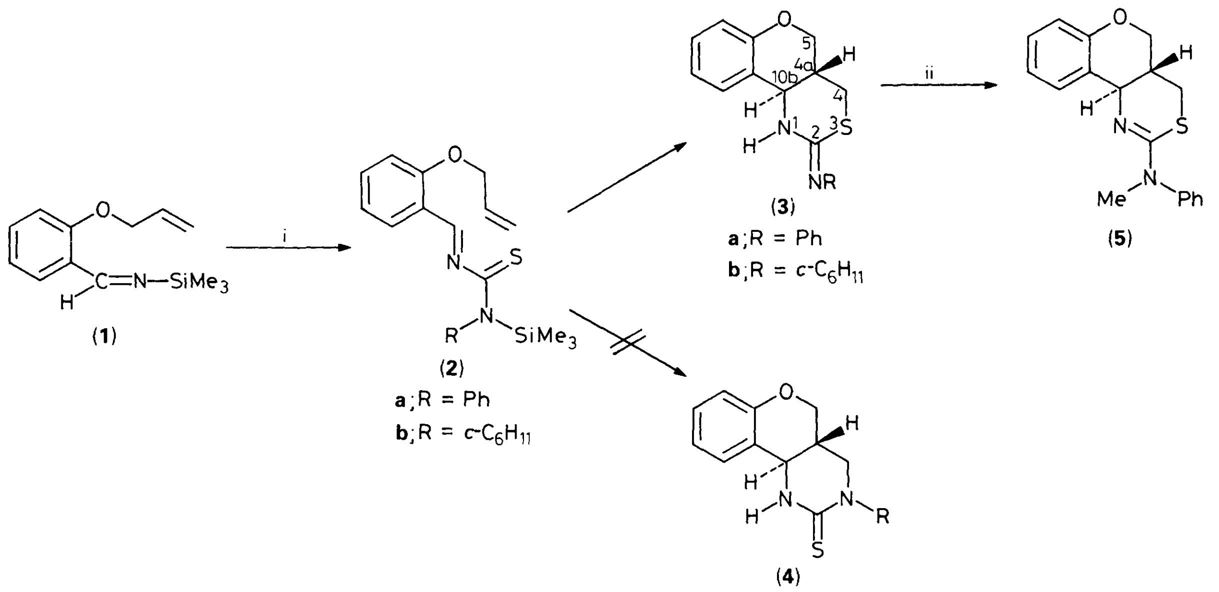
† The preparation and characterization of dienes of type (**2**) has been published already.[6]

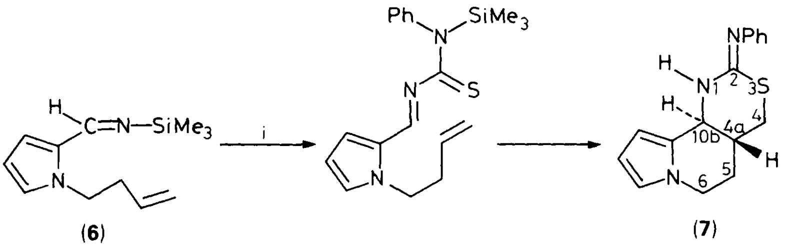
‡ *Spectroscopic data* for compound (**3a**): ^{1}H (300 MHz; $CDCl_3$) δ 2.1 (m, 1H, 4a-H), 2.7 (t, 1H, J 11.5 Hz, 4-H), 2.95 (dd, 1H, J 11.5 and 5.2 Hz, 4-H), 3.75 (t, 1H, J 11.1 Hz, 5-H), 4.2 (dd, 1H, J 11.1 and 1.7 Hz, 5-H), 4.25 (d, 1H, J 10.3 Hz, 10b-H), 5.6 (br. s, NH), 6.8 (dd, 1H, J 8.1 and 1.1 Hz, Ar), 7.0 (m, 2H, Ar), 7.15 (m, 1H, Ar), 7.25 (m, 2H, Ar), 7.4 (d, 2H, J 7.88 Hz, Ar) and 7.6 (d, 1H, J 7.38 Hz, Ar).

For compound (**7**): ^{1}H n.m.r. (300 MHz; $CDCl_3$) δ 1.4—1.8 (m, 3H, 5-H_2, 4a-H), 2.75 (m, 2H, 4-H_2), 3.7 (td, 1H, J 12.1 and 4.3 Hz, 6-H), 3.8 (m, 1H, 6-H), 4.1 (d, 1H, J 9.7 Hz, 10b-H), 6.1 (m, 2H, NH, Ar), 6.4 (br.s, 1H, Ar), 6.9 (t, 1H, J 7 Hz, Ar) and 7.2 (m, 5H, Ar).

Compounds (**3**) and (**7**) exist in solution as the imino tautomers according to the previous ^{13}C n.m.r. studies on related 1,3-thiazines.[10]



Scheme 1. *Reagents and conditions*: i, RNCS, toluene, 90 °C, 10 h; then H_2O; ii, NaH, dimethylformamide, 25 °C; then MeI, 25 °C.



Scheme 2. *Reagents and conditions*: i, see Scheme 1.

from an *exo*-transition state, were detectable in the crude mixture (^{1}H n.m.r., 300 MHz) (Scheme 1); this result is in agreement with previous findings in the case of 2-azabutadienes.[2] The absence of signals in the ^{13}C n.m.r. spectrum above δ 154 rules out structure (**4**), which would result if compounds (**2**) had acted as 1,3-diazabutadienes,§ since the thione carbon resonates at δ >170.[6,9] In addition, (**3a**) (R = Ph) was methylated to give (**5**) (90%, m.p. 143—145 °C), whose structure was confirmed by mass spectrometry [310 (M^+, 32%); 204 (M^+ – *N*-methylaniline, 40%)] and n.m.r. [^{1}H n.m.r. δ 3.3 ($N\text{–}CH_3$); ^{13}C n.m.r. δ 39.52 ($N\text{–}CH_3$)] data.[10] The reaction proved to be applicable to heterocyclic systems (Scheme 2); thus, imine (**6**) was synthesized from *N*-(but-3-enyl)pyrrole-2-carbaldehyde in the usual way,[11] purified by distillation [(**6**), 90%, b.p. 92—95 °C at 0.05 Torr], and then treated with phenyl isothiocyanate (toluene; 90 °C; 10 h) to furnish the *trans*-fused cycloadduct (**7**) [*J*(4a-H–10b-H) 9.7 Hz]‡ in 70% yield after column chromatography (silica gel; toluene–ether, 5 : 1).

In conclusion, this work reveals for the first time that easily available 1-thia-3-azabutadienes suffer intramolecular Diels–Alder cycloadditions with simple alkenes under very mild reaction conditions. This process allows the preparation of structurally complex heterocyclic systems (*e.g.*, functionalized indolizine derivatives) in one simple step starting from silyl imines.¶

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§ This behaviour of (**2**) has been found in reactions with isocyanates[6] and with enamines.[8]

¶ All new compounds isolated gave satisfactory analytical figures and were characterized by spectroscopic means (i.r., mass, ^{1}H and ^{13}C n.m.r.).