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FACILE INTRAMOLECULAR CYCLOADDITIONS OF 2-(N-ACYLAMINO)-1-THIA-1,3-DIENES

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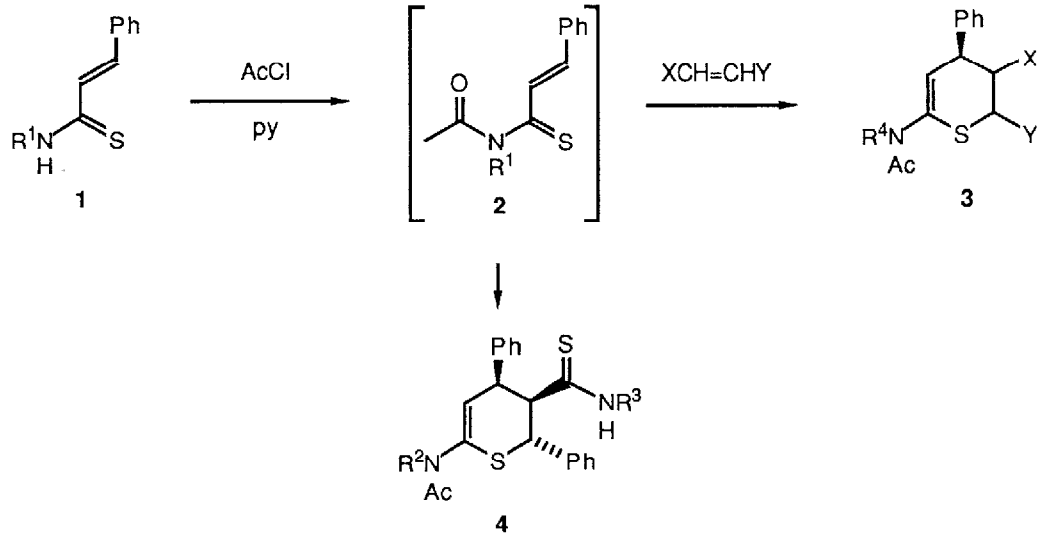
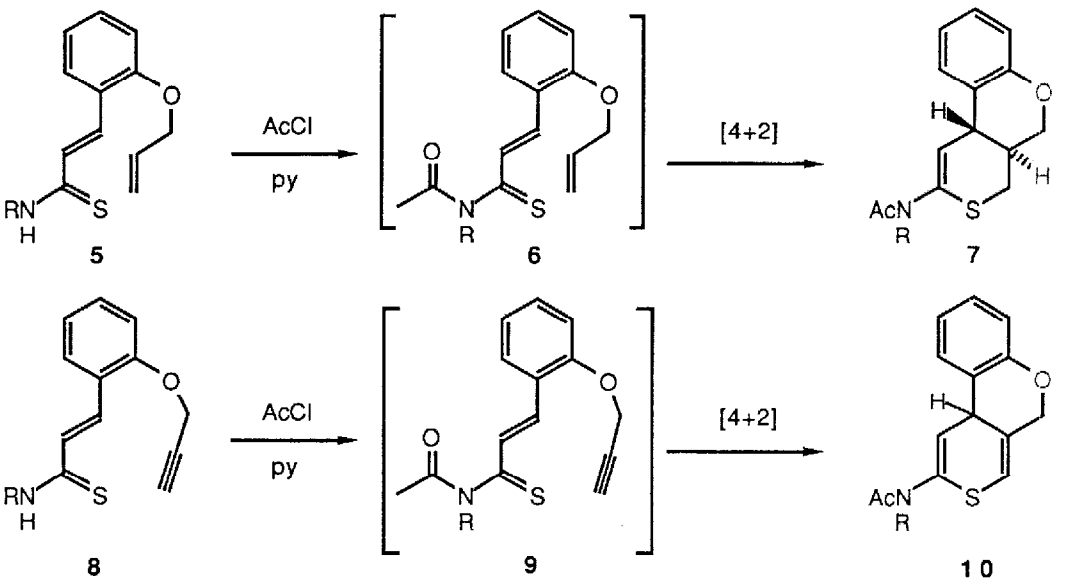
Summary: 2-(N-Acylamino)-1-thia-1,3-dienes, generated via acylation of readily available α,β–unsaturated thioamides, undergo regio- and stereospecific intramolecular Diels-Alder cycloaddition with unactivated olefinic and acetylenic dienophiles to yield polycyclic dihydrothiopyrans.

We have demonstrated previously [1-3] that treatment of various α,β–unsaturated thioamides **1** with acetyl chloride in the presence of a variety of olefins affords good yields of dihydrothiopyrans **3**. In the absence of added dienophiles, dimeric systems **4** are obtained . These reactions were rationalised as involving N-acylation to yield N-acylamino thiadiene **2** (scheme 1).



Scheme **1**

We now report that these reactive hetereodienes undergo stereo- and regiospecific intramolecular Diels-Alder cycloaddition to olefinic and acetylenic dienophiles to yield tricyclic thiopyrans and dihydrothiopyrans (scheme 2). These reactions appear to be the first reported cases[4] of the intramolecular Diels-Alder cycloaddition of a 1-thia-1,3-butadiene system.



Scheme 2

The precursors **5** and **8** are easily prepared from the known carboxylic acids[5] via the previously described[1-3] amidation/thiation sequence. Thus, in a typical experiment, treatment of the acid chloride derived from 3-(2-allyloxyphenyl)acrylic acid [5] with methylamine yielded the corresponding methyl amide as colourless needles after recrystallisation from ethanol/water (67%, mp, 86-87^{0}C). Treatment of this amide with P_4S_{10} in pyridine[1,2] for 7hrs gave thioamide **5**, R=Me (56%) as a yellow viscous oil after chromatography which solidified on standing (mp, 70-72^{0}C). Heating a solution containing **5** , R=Me (1.6mmol), pyridine (0.26ml) and acetyl chloride (3.2 mmol) in acetone (20ml) at reflux for 16hrs afforded cycloadduct **7**, R=Me (88%) as a yellow viscous oil after chromatography on silica (scheme 2). The results of similar cycloadditions are summarised in the table.

Table. Intramolecular cycloadditions of **6** and **9**

entry	thioamide	product	yield(%)
1	**5** , R = Me	**7** , R = Me	88[a]
2	**5** , R = Et	**7** , R = Et	60[a]
3	**8** , R = Me	**10**, R = Me	48[b]

a: These compounds gave satisfactory nmr, ir, and analytical data consistent with the proposed structures.

b: In this case, due to the instability of this cycloadduct, structural elucidation was based on ^{1}H nmr, ^{13}C nmr and ir data.

As indicated in the table, cycloadditions involving olefinic dienophiles are stereospecific and give cycloadducts which possess a trans ring fusion geometry exclusively (entries 1 and 2). The trans stereochemistry in cycloadducts **7** was readily apparent due to the presence of the large coupling constant (13Hz) in the ^{1}H nmr, between the protons at the ring junction positions [6].

For cycloaddition of dienes **6**, two possible transition state geometries, denoted here as *endo* and *exo* (with respect to the connecting chain between diene and dienophile) are shown below (figure). Inspection of models of these transition states reveals that the *exo* transition state, leading to the observed trans fused systems **7**, is relatively strain free. However, the fully-planar *endo* geometry is highly strained and, infact, would nessecitate a twist out of planarity of the aromatic ring and thus decrease the energy of interaction of diene and dienophile[7] (figure).

Interestingly however, for cycloaddition involving the acetylenic dienophile (entry 3), inspection of models reveals that the aromatic ring must twist out of conjugation with the diene system in order to allow for the approach of diene and dienophile[7] .

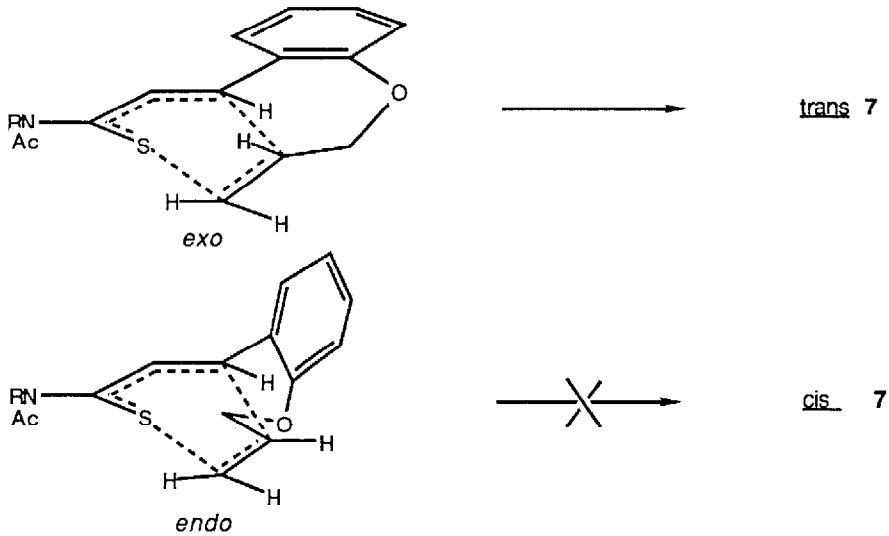


Figure. Possible transition state geometries for intramolecular cycloadditions.

Clearly, intramolecular cycloaddition of these thiadienes to electronically unactivated olefins and acetylenes is a facile process. Further exploration of the scope and potential of these cycloadditions is in progress in these laboratories.

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References and notes.

1. Barnish, I.T.; Fishwick, C.W.G.; Hill , D.R.; Szantay Jr., C. *Tetrahedron Lett.*, **1989**, *30*, 4449.

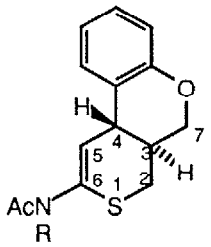
2. Barnish, I.T.; Fishwick, C.W.G.; Hill , D.R.; Szantay Jr., C. *Tetrahedron*, **1989**, *45*, 6771.

3. Barnish, I.T.; Fishwick, C.W.G.; Hill , D.R.; Szantay Jr., C. *Tetrahedron*, **1989**, *45*, 7898.

4. An intramolecular cycloaddition of a 1-thia-3-aza-butadiene system has been reported, see Barluenga, J.; Tomas, M.; Ballesteros, A.; Lopez, L., *J. Chem. Soc., Chem. Commun.*, 1989, 1487.

5. See : Cohen, M.D.; Schmidt, G.M.J.; Sonntag, F.I., *J. Chem. Soc.*, **1964**, 2000.

6. Selected ^{1}H nmr data;



7, R = Me, δ($CDCl_3$, ppm), 7.20-6.65, (4H, m, Ar<u>H</u>); 6.10, (1H, d, J=3Hz,H-5); 4.30, (1H, dd, Hx-7); 3.75, (1H, dd, H_y-7); 3.45, (1H,dd, J=3Hz, 13Hz, H-4); 3.00, (3H, s, C<u>H</u>$_3$N-); 2.90-2.75, (2H, m, H_2-2); 2.30-2.10, (1H, m, H-3); 2.00, (3H, s, C<u>H</u>$_3$CO-).

7, R = Et, δ($CDCl_3$, ppm), 7.15-6.75, (4H, m, Ar<u>H</u>); 6.05, (1H, d, H-5); 4.30, (1H, dd, H_x-7); 3.80, (1H, dd, H_y-7); 3.55-3.35, (3H, m, $CH_3C\underline{H}_2$-, H-4); 2.90-2.75, (2H, m, H_2-2); 2.30-2.10, (1H, m, H-3); 2.05, (3H, s, C<u>H</u>$_3$CO-); 1.10, (3H, t, $C\underline{H}_3CH_2$-).

10, δ($CDCl_3$, ppm), 7.25-6.85, (4H, m, Ar<u>H</u>); 6.30, (1H, m, H-2); 5.80, (1H, d, H-5); 4.65-4.40, (3H, m, H-4, H-7); 3.05, (3H, s, C<u>H</u>$_3$N-); 2.15, (3H, s, C<u>H</u>$_3$CO-).

7. Full details will be published elsewhere.

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