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# TRISUBSTITUTED THIAZOLES BY A 6π-ELECTROCYCLIZATION OF IMINOTHIOCARBONYL YLIDES

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Iminothiocarbonyl ylides are generated by a sulfur ligand exchange reaction of sulfonium salts and undergo a 6π-electrocyclic closure and aromatization to trisubstituted thiazoles. Related carbonyl ylides preferred a 4π-electrocyclization.

Electrocyclic closure have become an important entry to heterocyclic compounds[1]. We wish to report here the electrocyclic closure of iminothiocarbonyl ylides which combines high yields of trisubstituted thiazoles with a simple experimental procedure starting from readily available reactants. No similar electrocyclization is described for iminothiocarbonyl ylides.

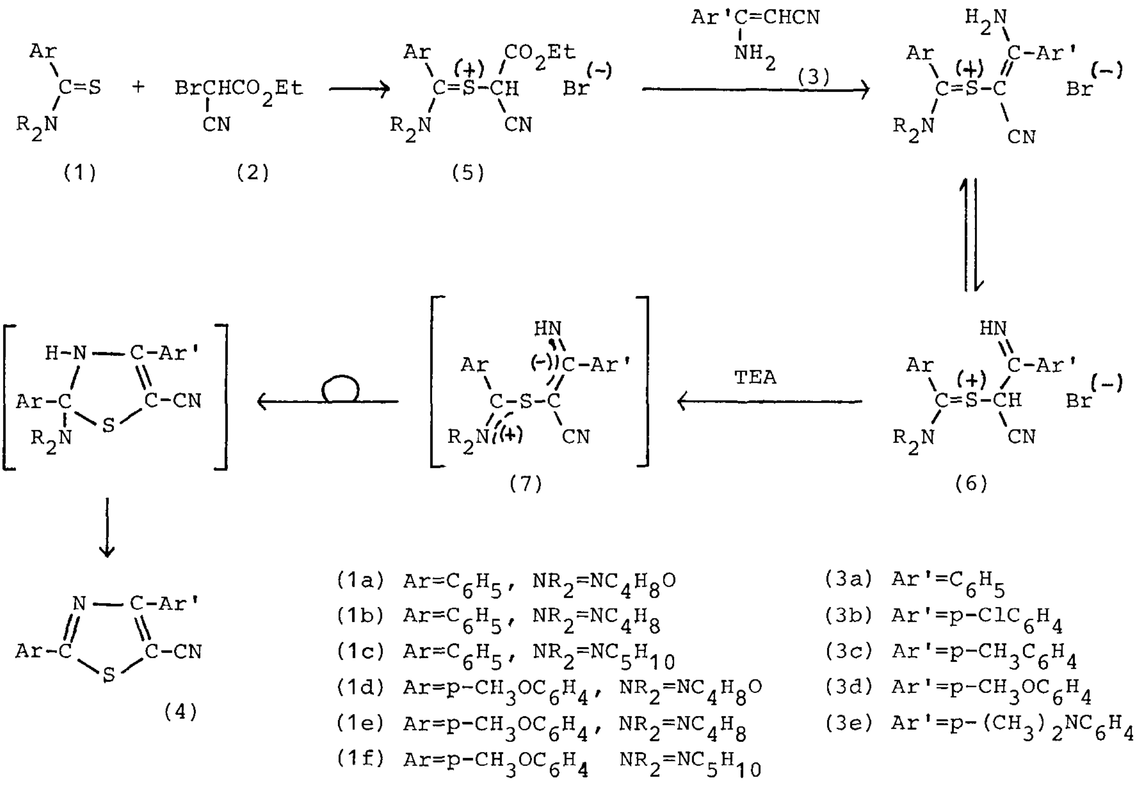
A solution of equimolar amounts of benzothioamides (1a-f), α-bromo-ethyl cyanoacetate (2) and β-aminocinnamonitriles[2] (3a-e) was stirred for 2 h. at room temperature to give a suspension. Upon treatment with triethylamine (TEA) and stirring 24 h. 2,4-diaryl-5-cyano-thiazoles (4a-l) were isolated by column chromatography. Compounds (4) (m.p.s and yields are given in table) were identified on the basis of i.r., $^1$H-n.m.r. and mass spectra[3], and by Hantzsch's synthesis[4].

Table

M.p.s and yields of thiazoles (4) from benzothiomorpholide derivatives[5]

| | Ar | Ar' | mp(C) | (%) | | Ar | Ar' | mp(C) | (%) |
|---|---|---|---|---|---|---|---|---|---|
| (4a) | $C_6H_5$ | $C_6H_5$ | 120 | 70 | (4f) | p-$CH_3OC_6H_4$ | $C_6H_5$ | 130-1 | 71 |
| (4b) | $C_6H_5$ | p-$ClC_6H_4$ | 122-4 | 72 | (4g) | p-$CH_3OC_6H_4$ | p-$ClC_6H_4$ | 157-9 | 78 |
| (4c) | $C_6H_5$ | p-$CH_3C_6H_4$ | 140-2 | 73 | (4h) | p-$CH_3OC_6H_4$ | p-$CH_3C_6H_4$ | 125-6 | 74 |
| (4d) | $C_6H_5$ | p-$CH_3OC_6H_4$ | 121-2 | 79 | (4i) | p-$CH_3OC_6H_4$ | p-$CH_3OC_6H_4$ | 137-8 | 76 |
| (4e) | $C_6H_5$ | p-$(CH_3)_2NC_6H_4$ | 125-6 | 65 | (4l) | p-$CH_3OC_6H_4$ | p-$(CH_3)_2NC_6H_4$ | 170-2 | 61 |

The formation of thiazoles (4) could be rationalized as shown in scheme 1.



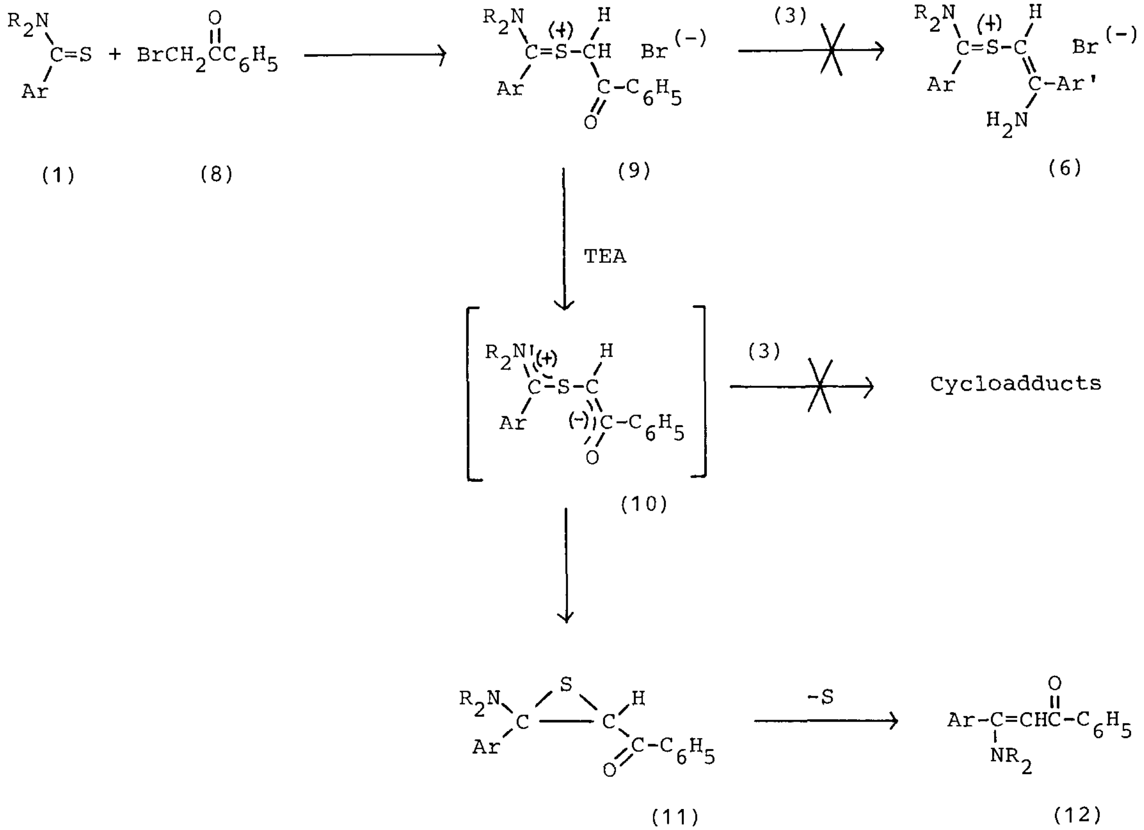
(1a) $Ar=C_6H_5$, $NR_2=NC_4H_8O$
(1b) $Ar=C_6H_5$, $NR_2=NC_4H_8$
(1c) $Ar=C_6H_5$, $NR_2=NC_5H_{10}$
(1d) $Ar=p\text{-}CH_3OC_6H_4$, $NR_2=NC_4H_8O$
(1e) $Ar=p\text{-}CH_3OC_6H_4$, $NR_2=NC_4H_8$
(1f) $Ar=p\text{-}CH_3OC_6H_4$ $NR_2=NC_5H_{10}$

(3a) $Ar'=C_6H_5$
(3b) $Ar'=p\text{-}ClC_6H_4$
(3c) $Ar'=p\text{-}CH_3C_6H_4$
(3d) $Ar'=p\text{-}CH_3OC_6H_4$
(3e) $Ar'=p\text{-}(CH_3)_2NC_6H_4$

Scheme 1

Sulfonium salts (5), which could be isolated upon interaction of benzothioamides and Br-ethylcyanoacetate, readily exchange the ligand in the presence of β-aminocinnamonitriles (3) yielding salts (6), as it was verified by independent experiments. Treatment with TEA of salts (6) generates the iminothiocarbonyl ylides (7) which undergo a 6π-electrocyclic closure to 4-thiazolines, never isolated from the reaction mixtures because of the easy elimination of secondary amine to give the aromatic thiazoles (4).

When α-bromoacetophenone (8) is used instead of (2) the initially formed salts (9) did not react with (3) to give (6). Treatment with TEA generates the corresponding transient carbonylthiocarbonyl ylides (10) which were not trapped by (3), but preferred a 4 π-electrocyclization to thiiranes (11) which are the main reaction products[6] as shown in scheme 2.



Scheme 2

Thiiranes structures are based upon spectral data[7] and sulfur extrusion reaction to afford enaminoketones[8] (12) on treatment with sodium ethoxide at room temperature.

These results show that the nucleophilic substitution at sulfur depends upon the presence of a good leaving group as well as the stability of the forming salt. Furthermore they suggest that 6$\pi$-electrocyclizations besides occurring in the "pull-pull" ylides[9], take place also in the "push-pull" ylides if the terminal center of the "pull" substituent has an adequate nucleophilic character. Further investigations are in progress in this area.

## References and Footnotes

1. R. Huisgen, *Angew.Chem.Int.Ed.Engl.*, **19**, 947 (1980).
2. a) $\beta$-Aminocinnamonitriles (3) show an interesting dipolarophilic and nucleophilic activity. They react with nitrile oxides to give preferentially the cycloadducts at the C≡N triple bond rather than at the C=C double bond[2b,c]. These unexpected results prompted us to extend the study of their reactivity to thiocarbonyl ylides. b) A. Corsaro, U. Chiacchio and G. Purrello, *J.Chem. Soc., Perkin I*, 2154 (1977). c) A. Corsaro, U. Chiacchio, A. Compagnini and G. Purrello, *J.Chem.Soc., Perkin I*, 1635 (1980).
3. I.r. spectra contain bands at 4.59 $\mu$ for C≡N and at 6.50 and 6.57 $\mu$ for thiazole ring. $^1$H-n.m.r. spectra, besides the proton signals of the different phenyl substituents, show only aromatic proton signals. Mass spectra are dominated by the molecular ion (base peak) and the major fragment derived from the cleavage of 1,2 and 3,4 bonds (thiirenium ion).
4. a) Thiazoles yields isolated from Hantzsch's synthesis[4b] are much lower, about 30%. b) *Organic Reactions*, **6**, 378 (1951).
5. Similar yields have been obtained from benzothiopyrrolidide and benzothiopiperidide and their p-methoxy derivatives.
6. a) It is worthy mentioning that no thiiranes and enaminoketones have been isolated from a similar reaction with the corresponding tetramethylthiouronium salt[6b]. b) S. Mitamura, M. Takaku and H. Nozaki, *Tetrahedron Letters*, 3651 (1969).
7. I.r. spectra show a strong carbonyl band at 6.0 $\mu$. $^1$H-n.m.r. spectra display an aromatic multiplet at $\delta$ 7.0-7.9 and a multiplet at higher fields for the protons of the amine fragment and thiirane. Mass spectra exhibit a very weak molecular ion and a strong $(M-S)^+$ fragment (base peak).
8. a) Identified by mixture melting point and/or i.r. and mass spectra comparison with authentic samples obtained according to the literature[8b]. b) G. Purrello and A. Lo Vullo, *Tetrahedron Letters*, 4515, (1970).
9. K. Oka, A. Dobashi and S. Hara, *Tetrahedron Letters*, 3579 (1980).

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