# CYCLOADDITION REACTIONS OF 1,3-BENZOTHIAZINES IV.[1] INTERMOLECULAR 1,3-DIPOLAR CYCLOADDITION OF 2H-1,3-BENZOTHIAZINES WITH NITRILIMINES

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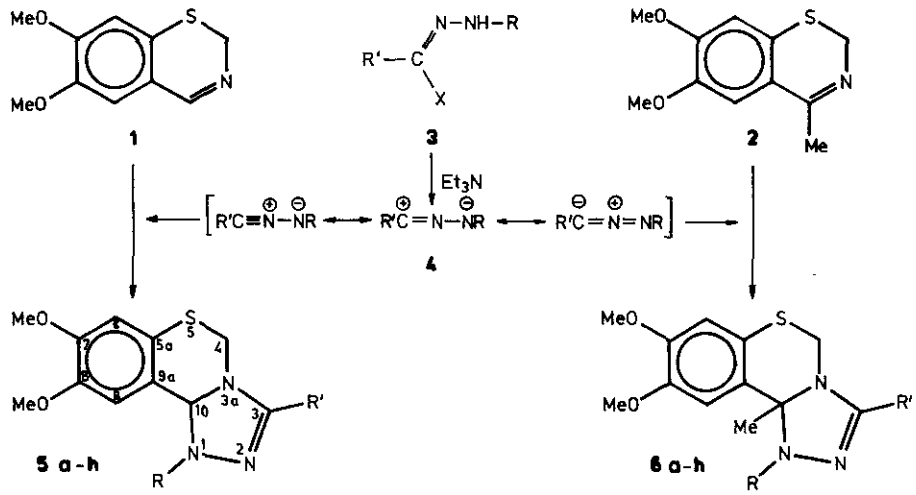
Abstract — Thermal [3+2] intermolecular cycloaddition of nitrilimines to 2H-1,3-benzothiazines (1, 2) gives new fused tricyclic ring systems (5, 6).

1,3-Dipolar cycloaddition is one of the most useful methods for the preparation of five-membered heterocycles. Numerous possibilities for variation are available by changing the structures of both the dipole and the dipolarophile. Nitrilimines are a long-known and thoroughly investigated class of 1,3-dipoles. Access to this group of dipoles can be achieved by (a) treatment of hydrazonyl halides with base[2], (b) thermal or photochemical decomposition of tetrazoles[3,4], (c) photolysis of sydnones[5], and (d) thermal elimination of carbon dioxide from 1,3,4-oxadiazolin-5-ones[6,7]. Inter- and intramolecular cycloaddition of nitrilimines has been widely investigated and in many cases has led to the synthesis of a variety of interesting heterocyclic compounds, some of which would be tedious to synthesize by other methods[8].

Following our studies of the cycloaddition reactions of 1,3-benzothiazines, we now report that the reactions of 6,7-dimethoxy-2H-1,3-benzothiazine (1)[9] and its 4-methyl analogue (2)[9] with hydrazonyl halides (3a-h)[10-13] give the new angularly-condensed triazolobenzothiazines (5a-h, 6a-h). The structures and purity of the new compounds were confirmed by IR, $^{1}H$ and $^{13}C$ NMR measurements.

The most important IR data are as follows: Characteristic nitro bands of compounds 5b,c and 6b,c: 1515-1480, 1325-1295 and 840-825 $cm^{-1}$, respectively. Ester bands of compounds 5e,f,g and 6e,f,g: 1700-1715 ($\nu$C=O) and 1270-1245 and 1160-1135 $cm^{-1}$, respectively ($\nu$C-O). $\nu$NH and amide-I bands (5h,6h) at about 3370 and



a: R = R' = Ph; X = Cl
b: R = 4-$O_2NC_6H_4$; R' = Ph; X = Br
c: R = 4-$O_2NC_6H_4$; R' = 4-$ClC_6H_4$; X = Br
d: R = Ph; R' = 4-$ClC_6H_4$; X = Cl
e: R = Ph; R' = $CO_2Et$; X = Cl
f: R = 4-$ClC_6H_4$; R' = $CO_2Et$; X = Cl
g: R = 4-$MeC_6H_4$; R' = $CO_2Et$; X = Cl
h: R = Ph; R' = $CONHC_6H_4$; X = Cl

3375 $cm^{-1}$ and 1685 and 1680 $cm^{-1}$, respectively. Naturally, all the spectra contain the bands characteristic of methoxy and phenyl and/or para-disubstituted phenyl groups.

The NMR data are discussed in detail elsewhere[14], where we also report the conformational analyses of these compounds. The most important $^1H$ NMR characteristics: The non-equivalent protons of the 4-methylene group give an AB multiplet, with chemical shifts at 4.05-4.80 and 4.40-5.80 ppm, respectively, and a coupling constants of 11.5-13.5 Hz. The two singlets methoxy of 3-3H intensity are in the intervals 3.74-3.97 and 3.23-3.27 (6e-h) or 3.57-3.89 ppm (5a-h, 6a-d). The H-10 signal of compounds 5a-h appears at 6.11-6.54 ppm, and the corresponding 10-methyl singlet (3H) of compounds 6a-h at 1.82-2.12 ppm. The H-6 and H-9 singlets can be found in the intervals 6.49-6.89 and 5.93-6.07 (6e-h) or 6.77-7.30 ppm (5a-h, 6a-d). The triplet and quartet ($J \approx 7$ Hz) of the carbethoxy group in compounds 5e,f,g and 6e,f,g are identifiable at 1.36-1.39 and 4.35-4.38 ppm. The multiplets of the aromatic hydrogens are identifiable in all cases with the expected multiplicity and intensity.

The strong shielding of H-9 and the C-8 methoxy group in compounds 6e-h led us to the conclusion of a different conformation for the latter compounds relative to the others. From temperature-dependence of the $^1H$ NMR spectra, we concluded that all compounds unsubstituted on C-10 (5a-h) and the 3-aryl-substituted 10-methyl

PHYSICAL AND ANALYTICAL DATA ON COMPOUNDS 5a-h AND 6a-h

| Compound | Yield % | M.p. °C | Formula M.w. | Analysis/% Calcd./Found C | H | N | S |
|---|---|---|---|---|---|---|---|
| 5a | 89 | 170-171 | $C_{23}H_{21}N_3O_2S$ | 68.46 | 5.25 | 10.41 | 7.95 |
| | | | 403.49 | 68.50 | 5.31 | 10.36 | 7.79 |
| 5b | 91 | 203-205 | $C_{23}H_{20}N_4O_4S$ | 61.59 | 4.50 | 12.49 | 7.15 |
| | | | 448.49 | 61.42 | 4.39 | 12.56 | 7.23 |
| 5c | 90 | 214-216 | $C_{23}H_{19}ClN_4O_4S$ | 57.20 | 3.97 | 11.60 | 6.63 |
| | | | 482.93 | 57.31 | 4.04 | 11.49 | 6.52 |
| 5d | 91 | 187-189 | $C_{23}H_{20}ClN_3O_2S$ | 63.08 | 4.60 | 9.60 | - |
| | | | 437.93 | 63.46 | 4.90 | 9.71 | - |
| 5e | 85 | 139-140 | $C_{20}H_{21}N_3O_4S$ | 60.13 | 5.30 | 10.52 | 8.03 |
| | | | 399.46 | 60.24 | 5.38 | 10.64 | 8.11 |
| 5f | 86 | 180-181 | $C_{20}H_{20}ClN_3O_4S$ | 55.36 | 4.65 | 9.68 | 7.39 |
| | | | 433.90 | 55.47 | 4.72 | 9.67 | 7.43 |
| 5g | 78 | 150-151 | $C_{21}H_{23}N_3O_4S$ | 61.00 | 5.61 | 10.16 | 7.76 |
| | | | 413.48 | 60.91 | 5.76 | 10.37 | 7.89 |
| 5h | 87 | 183-184 | $C_{24}H_{22}N_4O_3S$ | 64.55 | 4.97 | 12.55 | 7.18 |
| | | | 446.52 | 64.46 | 5.01 | 12.31 | 7.21 |
| 6a | 82 | 184-185 | $C_{24}H_{23}N_3O_2S$ | 69.04 | 5.55 | 10.06 | 7.69 |
| | | | 417.51 | 68.92 | 5.63 | 10.06 | 7.75 |
| 6b | 92 | 179-181 | $C_{24}H_{22}N_4O_4S$ | 62.32 | 4.80 | 12.11 | 6.93 |
| | | | 462.54 | 62.19 | 4.86 | 12.04 | 6.78 |
| 6c | 94 | 222-224 | $C_{24}H_{21}ClN_4O_4S$ | 58.00 | 4.26 | 11.27 | 6.45 |
| | | | 496.96 | 58.07 | 4.34 | 11.32 | 6.37 |
| 6d | 85 | 180-181 | $C_{24}H_{22}ClN_3O_2S$ | 63.78 | 4.91 | 9.30 | - |
| | | | 451.96 | 64.00 | 5.25 | 9.55 | - |
| 6e | 84 | 134-135 | $C_{21}H_{23}N_3O_4S$ | 61.00 | 5.61 | 10.16 | 7.76 |
| | | | 413.48 | 60.87 | 5.69 | 10.24 | 7.86 |
| 6f | 88 | 135-136 | $C_{21}H_{22}ClN_3O_4S$ | 56.31 | 4.95 | 9.38 | 7.16 |
| | | | 447.93 | 56.45 | 5.04 | 9.47 | 7.24 |
| 6g | 86 | 129-131 | $C_{22}H_{25}N_3O_4S$ | 61.80 | 5.89 | 9.83 | 7.50 |
| | | | 427.51 | 61.92 | 5.97 | 9.88 | 7.41 |
| 6h | 90 | 169-170 | $C_{25}H_{24}N_4O_3S$ | 65.20 | 5.25 | 12.17 | 6.96 |
| | | | 460.54 | 65.39 | 5.36 | 12.29 | 6.78 |

analogues (6a-d) occur in a rigid conformation. The 10-methyl-3-carbethoxy derivatives are conformationally more flexible systems, where H-9 and the 8-methoxy substituent lie close to the 1-aryl ring in the preferred conformer. Consequently, the heterorings must be *cis*-anellated. By taking up this more strained structure the molecules avoid the steric hindrance of the 10-methyl and 1-aryl groups. This conformation is stabilized probably by a hydrogen-bond. $^{13}C$ NMR spectra gave additional proof of the structures and postulated conformations.[14]

## EXPERIMENTAL

The IR spectra were run on a Specord 75 (JENA) grating spectrometer, in KBr pellets. $^1$H NMR spectra were recorded at room temperature in $CDCl_3$ solution at 250 MHz, on a BRUKER WM-250 FT-spectrometer equipped with a superconducting magnet, using TMS as internal standard. Sweep width: 5 kHz, pulse width: 1 μs (flip angle $\sim 20^\circ$), acquisition time: 1.64 s, number of scans: 8, computer memory 16 K, digital resolution: 0.61 Hz/point.

General procedure for synthesis of 5a-h, 6a-h: 1 or 2 (0.01 mol) was dissolved in benzene (50 ml) and 0.01 mol of 3 was added. The mixture was refluxed, and a solution of $Et_3N$ (0.01 mol) in 30 ml benzene was added dropwise, with stirring, during 1 h. The crystalline $Et_3N.HCl$ was removed by filtration, the benzene solution was evaporated and the residue was then crystallized from EtOH to obtain crystals (cf. Table).

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Received, 31st October, 1983