

CYCLOADDITION REACTIONS OF 1,3-BENZOTHAZINES IV.¹ INTERMOLECULAR
1,3-DIPOLAR CYCLOADDITION OF 2H-1,3-BENZOTHAZINES WITH NITRILIMINES

Lajos FODOR

Central Lab., County Hospital, H-5701 Gyula, P.O.B. 46.

Mohamed-Sami EL-GHARIB, János SZABÓ^N, Gábor BERNÁTH

Inst. Pharm. Chem., Univ. Medical School, H-6701 Szeged, P.O.B. 121.

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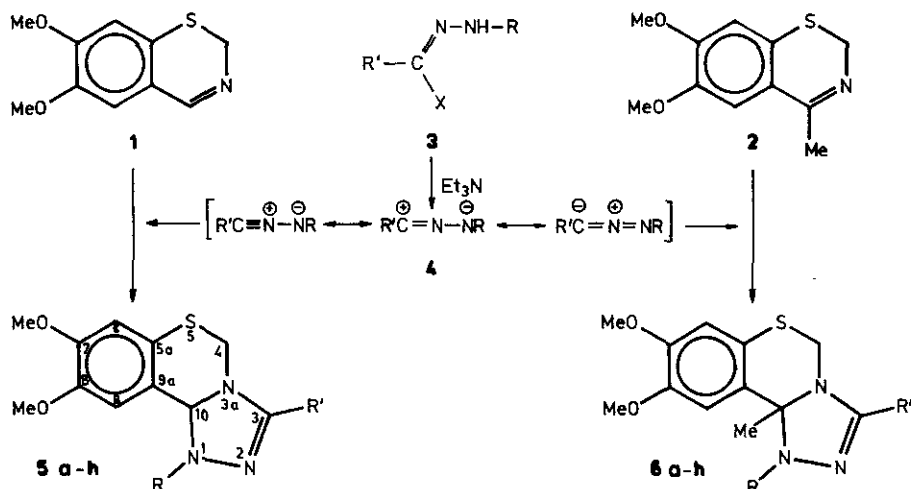
Spectroscopic Dept., EGYT Pharm. Chem. Works, H-1475 Budapest, P.O.B.
100, Hungary

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 base², (b) thermal or photochemical decomposition of tetrazoles^{3,4}, (c) photolysis of sydnone⁵, 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 methods⁸.

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, ¹H and ¹³C 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 (νC=O) and 1270-1245 and 1160-1135 cm⁻¹, respectively (νC-O). νNH and amide-I bands (5h,6h) at about 3370 and



a: R = R' = Ph; X = Cl

b: R = 4-O₂NC₆H₄; R' = Ph; X = Br

c: R = 4-O₂NC₆H₄; R' = 4-ClC₆H₄; X = Br

d: R = Ph; R' = 4-ClC₆H₄; X = Cl

e: R = Ph; R' = CO₂Et; X = Cl

f: R = 4-ClC₆H₄; R' = CO₂Et; X = Cl

g: R = 4-MeC₆H₄; R' = CO₂Et; X = Cl

h: R = Ph; R' = CONHC₆H₄; 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 elsewhere¹⁴, 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 (6g-h) or 3.57-3.89 ppm (5g-h, 6g-d). The H-10 signal of compounds 5g-h appears at 6.11-6.54 ppm, and the corresponding 10-methyl singlet (3H) of compounds 6g-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 (6g-h) or 6.77-7.30 ppm (5g-h, 6g-d). The triplet and quartet (J ≈ 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 6g-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 (5g-h) and the 3-aryl-substituted 10-methyl.

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

Com- pound	Yield %	M.p. °C	Formula M.w.	Analysis/% Calcd./Found			
				C	H	N	S
<u>5a</u>	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
<u>5b</u>	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
<u>5c</u>	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
<u>5d</u>	91	187-189	$C_{23}H_{20}ClN_3O_2S$	63.08	4.60	9.60	-
			437.93	63.46	4.90	9.71	-
<u>5e</u>	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
<u>5f</u>	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
<u>5g</u>	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
<u>5h</u>	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
<u>6a</u>	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
<u>6b</u>	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
<u>6c</u>	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
<u>6d</u>	85	180-181	$C_{24}H_{22}ClN_3O_2S$	63.78	4.91	9.30	-
			451.96	64.00	5.25	9.55	-
<u>6e</u>	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
<u>6f</u>	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
<u>6g</u>	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
<u>6h</u>	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-annellated. 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. ^1H 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 $5a-h$, $6a-h$: $\underline{1}$ or $\underline{2}$ (0.01 mol) was dissolved in benzene (50 ml) and 0.01 mol of $\underline{3}$ 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 $\text{Et}_3\text{N}\cdot\text{HCl}$ 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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