CYCLOADDITION REACTIONS OF 1,3-BENZOTHIAZINES II.[1-3] REACTIONS OF 6,7-DIMETHOXY-2H-1,3-BENZOTHIAZINE WITH DIMETHYL ACETYLENEDICARBOXYLATE AND OTHER DIPOLAROPHILES

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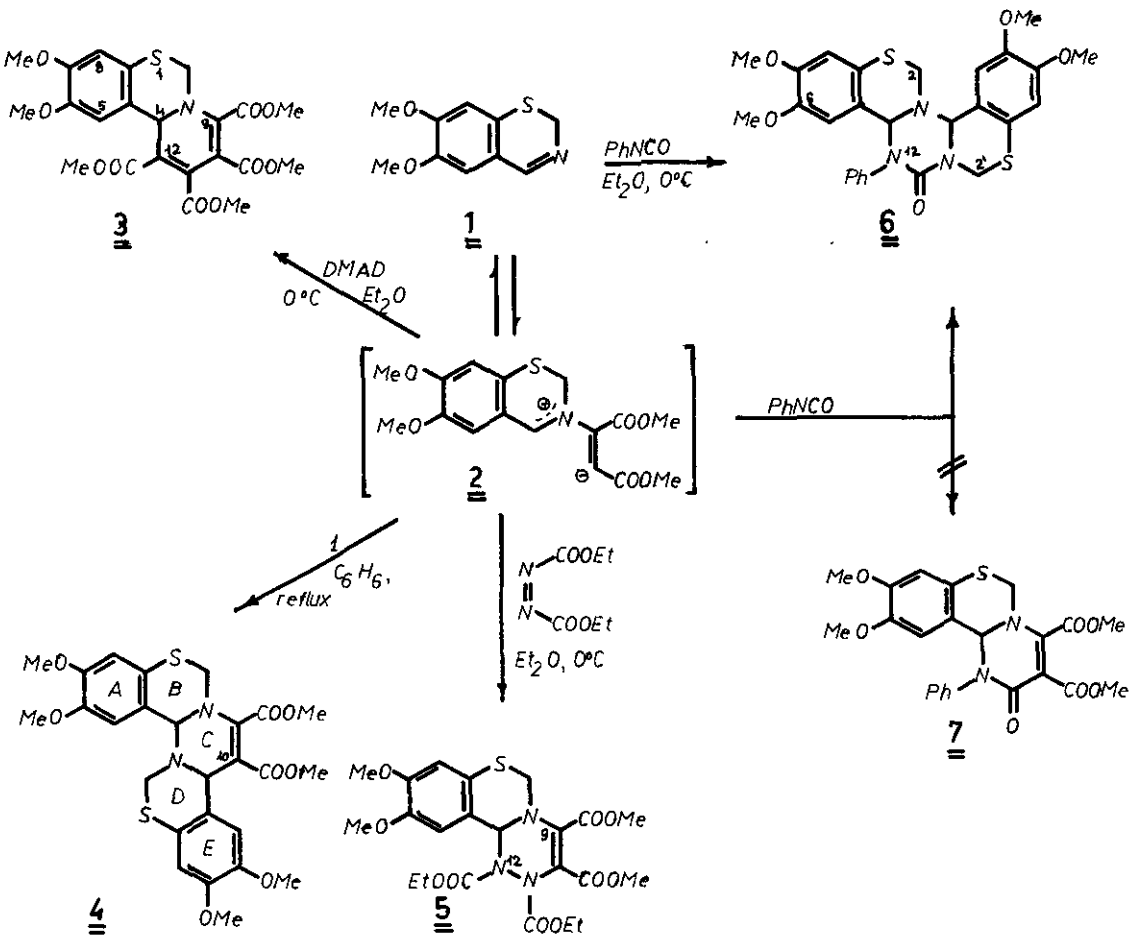
Abstract — New heterocyclic ring systems containing sulfur and nitrogen (3-6) have been synthesized by the reactions of 6,7-dimethoxy-2H-1,3-benzothiazine with dimethyl acetylenedicarboxylate and other dipolarophiles.

In the past 15 years several authors[4-8] have investigated 1,4-dipolar cycloaddition reactions between dimethyl acetylenedicarboxylate (DMAD) and various heterocycles containing the C=N linkage. In this paper we report similar cycloaddition reactions of 6,7-dimethoxy-2H-1,3-benzothiazine (1)[9], which allowed the construction of new heterocyclic ring systems.

With DMAD, compound 1 gave a 1:2 adduct (3, 52%, mp 201-202°C) or a 2:1 adduct (4, 64%, mp 118-119°C), depending on the reaction conditions. We suggest that these reactions take place via the transition state 2; evidence for this is the formation of the 1:1:1 adduct (5, 68%, mp 194-195°C) in the presence of diethyl azodicarboxylate in ether solution. With another dipolarophile, such as phenyl isocyanate in ether solution, the reaction under varied conditions always gave compound 6 (58%, mp 152-154°C) as the isolable product, instead of compound 7 which would be expected on the basis of the transition state 2. This fact leads to the conclusion that process $1 \rightleftharpoons 2$ is reversible, and phenyl isocyanate actually reacts with 1. Indeed, from the interaction of compound 1 and phenyl isocyanate in ether solution, product 6 could be isolated in the same yield (57%) as from the reaction in the presence of DMAD.



Structures 3-6 have been confirmed by elemental analysis, and IR and ^{1}H-NMR measurements (cf. Table).

Table. IR and ^{1}H-NMR data of compounds 3-6.

	IR bands in KBr pellet (cm^{-1})			
	Methoxy group		Ester group	
	ν CH	ν C-O	ν C=O	ν C-O
3	2840	1270 1180	1745 1700	1250 1150
4	2840	1265 1170	1745,[b] 1690[b]	1220 1090
5	2840	1255[f] 1170	1740 1720[g]	1255[f] 1090
6[h]	2840	1260 1165	1650[i]	-

[a] can be assigned alternatively
[b] ν C=C band
[c] two overlapping singlets
[d] CH_2 group neighboring with the β-enamino nitrogen
[e] δCH_3(ethyl): 1.05 (broad) and 1.35 ppm (sharp), 2x t, (2x3H) δOCH_2: ~ 4.3 ppm, qa (2x2H)
[f] coalesced bands
[g] carbamoyl carbonyl band
[h] phenyl group: 765 and 705 cm^{-1} (IR) 400-440 Hz, m (5H) (^{1}H-NMR at 60MHz)
[i] amide-I band
[j] CH_2 group neighboring with the amide nitrogen

^{1}H-NMR chemical shifts in $CDCl_3$ solution (δ_{TMS}= 0 ppm)										
	δOMe s(3H)		δSCH$_2$N group				δH-4	δH-5	δH-8
			δA	δB	J_{AB}(Hz)	ΔδAB	s(1H)	s(1H)	s(1H)
3	3.60 3.80 3.87	3.75 3.85 3.90	4.90	4.60	11	0.30	5.50	6.70[a]	6.65[a]
4	3.50 3.90	3.85[c] 3.95[c]	3.89[d] 4.56[d]	3.77[d] 4.38[d]	12 12	0.12 0.18	5.45 5.55	7.00[c]	6.75 6.80
5[e]	3.70 3.85	3.80 3.90	5.02	4.58	14	0.44	6.50	7.10	6.85
6[h]	3.30 3.80	3.70 3.85	4.49[j] 5.58[j]	3.58[j] 4.35[j]	12 13	0.91 1.23	5.80 6.00	6.20 7.00	6.50 6.70

Primary evidence for structure 3 is afforded by the ^{1}H-NMR spectrum, which shows the signals of six methoxy groups and methylene group (in Pos. 2), as well as three singlets of 1 H intensity, corresponding to protons in position 4,5 and 8.

The extremely small chemical shift of one of the methoxy signals in compounds 3, 4 and 6 is noteworthy (3.60, 3.50 and 3.30 ppm, respectively). In the case of 3 this signal is due to the C-12 carbomethoxy group, whose protons are shielded by the benzene ring. For similar reasons the C-10 methoxy protons of compound 4 are also strongly shielded, since in the most probable conformations they are situated above the benzene ring E. The same effect is found for the methyl triplet of one of the ethoxy groups (C-12) in compound 5. This triplet appears at 1.05 ppm with an upfield shift of 0.3 ppm, and there is a line broadening due to sterically hindered rotation. The C-6 methoxy group in compound 6 is even more shielded (3.30 ppm) because of the anisotropy from the C-12 phenyl group.

The stronger shielding of H-5 in compound 3 is explained by the anisotropy of the carbonyl group. No such effect is found in 4, and in the case of compound 5 it is compensated by the opposite effect of the neighboring, coplanar nitrogen. On the other hand, the analogous anisotropic effect of the C-12 phenyl ring in compound 6 gives rise to a much greater increase of shielding; compared with compound 4, the upfield shift is 0.3 ppm for 3 and 0.8 ppm, for 6.

It is worth mentioning that in compound 6 the chemical shift difference of both ring-methylene proton pairs is about trebled as compared with the other three cases. The explanation is that the H-2e and H-2'e atoms are coplanar with the benzene ring E and the carbonyl group, respectively, resulting in a considerable downfield shift.

Finally, we note that signals of the two ring-methylene groups in compound 4 have been assigned on the assumption that the chemical shift of the C-2 protons must be greater than that of the C-2' methylene protons, owing to the nearness of the enamine group having -I effect.

All these spectroscopic characteristics, bearing on the steric constitution of the molecules examined, furnish proof of the proposed structures.

Related reactions of the 4-methyl and 4-phenyl derivatives of compound 1 will be reported in a forthcoming paper.

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