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A NEW UNEXPECTED RING CLOSURE FROM 3-AMINO-1,5-DIARYL-1<u>H</u>-1,2,4-TRIAZOLES[1]

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Abstract - A new unexpected ring closure of 3-amino-1,5-diaryl-1H-1,2,4-triazoles with 2,2'-dithiobis(benzoyl chloride) to a polycondensed system is reported.

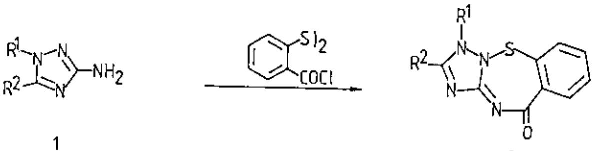
Several methods have been reported to transform α-aminoheterocycles into condensed systems.[2-5] We show here a facile synthesis of a polycondensed ring system starting with 3-amino-1,5-diaryl-1H-1,2,4-triazoles 1.

Compounds 1 react with 2,2'-dithiobis(benzoyl chloride) in benzene in the presence of tributylamine to afford 1,2,4-triazolo[2,3-b][1,2,4]benzothiadiazepines 2a-j with moderate to good yields (Table 1).

Table 1

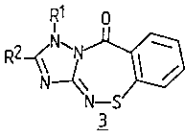
Compound 2			Yield	mp	Formula	Microanalysis data				Selected spectral data[a]	
	R¹	R²	%	°C		Found C H	 N S	Requires C H	 N S	Ir: $\nu_{C=O}$ cm^{-1}	Ms: M^{+} (m/z)
a	4-Cl-Ph	4-Cl-Ph	80	258-261	$C_{21}H_{12}Cl_2N_4OS$	57.23 2.67	12.54 7.18	57.41 2.78	12.75 7.30	1664	438/440/442
b	4-Cl-Ph	4-F-Ph	68	238-240	$C_{21}H_{12}ClFN_4OS$	59.71 2.68	13.06 7.70	59.51 2.85	13.22 7.56	1666	422/424
c	4-F-Ph	4-Cl-Ph	65	237-239	$C_{21}H_{12}ClFN_4OS$	59.38 2.99	13.03 7.63	59.51 2.85	13.22 7.56	1664	422/424
d	4-F-Ph	4-F-Ph	40	217-222	$C_{21}H_{12}F_2N_4OS$	62.16 2.75	13.81 7.82	62.06 2.98	13.89 7.94	1664	406
e	4-F-Ph	Ph	51	194-199	$C_{21}H_{13}FN_4OS$	64.76 3.22	14.27 8.42	69.94 3.37	14.42 8.25	1661	388
f	4-Cl-Ph	4-Me-Ph	78	253-255	$C_{22}H_{15}ClN_4OS$	63.19 3.75	13.25 7.59	63.08 3.61	13.37 7.65	1663	418/420
g	4-Me-Ph	4-Cl-Ph	87	255-257	$C_{22}H_{15}ClN_4OS$	63.24 3.51	13.30 7.76	63.08 3.61	13.37 7.65	1670	418/420
h	4-F-Ph	4-Me-Ph	57	233-234	$C_{22}H_{15}FN_4OS$	65.78 3.54	13.79 7.85	65.66 3.76	13.92 7.97	1663	402
i	4-Cl-Ph	4-MeO-Ph	47	234-238	$C_{22}H_{15}ClN_4O_2S$	60.58 3.31	12.62 7.47	60.76 3.48	12.88 7.37	1663	434/436
j	4-Cl-Ph	4-NO_2-Ph	76	300-302	$C_{21}H_{12}ClN_5O_3S$	56.31 2.83	15.42 7.28	56.07 2.69	15.57 7.13	1670	449/451

a) ^{1}H nmr-data are not characteristic.



1 2

The structure of the products 2 was determined by elementary analysis and by ir, nmr and mass spectroscopy. The isomeric structures 3 and 4 could be excluded on the following basis.



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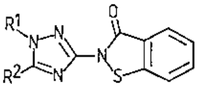

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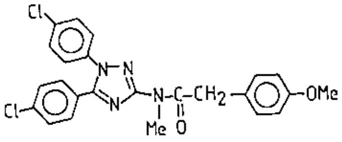
Ir data could not be used to differentiate the five and seven membered rings. 2-R-1,2-Benzisothiazol-3(2*H*)-ones 4 (R=subst. phenyl, pyridyl, pyridazinyl and pyrazinyl) prepared by us with known methods[6] from sulfenyl bromides showed $\nu_{C=O}$ bands in the same intervals (1664-1688 cm^{-1}) as 2a-j. Structure 4 can, however, be ruled out on the basis of the mass spectra. By analogy of the known rearrangement and SO_3-extrusion of saccharin in the mass spectrometer[7] SO-extrusion from compounds 4 was observed, in contrast with compounds 2 where this loss of SO could not be detected. Structure 2 could be proved chemically: acylation of 1 leads only to the exo-acylated compounds which could not be thermally rearranged to endo-acylated ones as it is known in reversed case.[8] Thus 1,5-bis(4-chlorophenyl)-3-(2-methylthiobenzamido)-1*H*-1,2,4-triazole and 1,5-bis(4-chlorophenyl)-3-(4-chlorobenzamido)-1*H*-1,2,4-triazole did not change upon heating to 200 °C with or without solvent. The other fact to support the exo-acylation was the following: 1,5-bis-(4-chlorophenyl)-3-[N-methyl-N-(4-methoxyphenylacetyl)]amino-1*H*-1,2,4-triazole (5) was synthesized (by methylation of the acylamino compound with methyl iodide in DMF in the presence of sodium methoxide, yield 49 %, mp 120-123 °C) and decoupling experiments were accomplished. These investigations showed long-range-coupling of N-C*H*$_3$ and CO-C*H*$_2$-Ar with the carbon atom of the carbonyl group confirming the fact of the exo-acylation.



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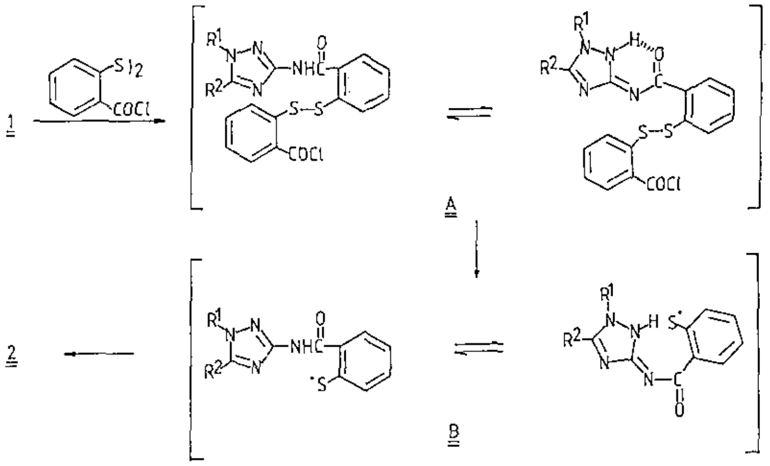
As for the formation of compounds 2 the following mechanism is considered:



In the first step the formation of a benzamide derivative A can be assumed which after homolytic cleavage and H-abstraction (formation of radical B) cyclises to 2. The radical type reaction was supported by the observation that the reaction was very fast in apolar solvents, and slower in polar ones.

Thus reaction time (reaction of 1a with 2,2'-dithiobis(benzoyl chloride) at 40 °C) varied strongly with the solvent as shown below:

Solvent	Reaction time
Benzene	30 min
Chloroform	30 h
Dichloromethane	30 h
Acetone	50 h
DMF	no reaction
Formamide	no reaction

In order to prove this mechanism, we tried to verify the existence of intermediate A: the reaction was carried out in dichlorometane at 40 °C and at definite intervals samples were withdrawn, cooled to -20 °C and analysed by ^{1}H nmr spectroscopy. The spectra unambigously proved the existence of A: the NH-signals appeared at 9.8-10.1 ppm, during the reaction, confirming the ring NH-tautomeric from of A. The esr-measurements, however, failed to confirm our hypothesis on the radical mechanism, presumably, due to the short half-life of the radicals.

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EXPERIMENTAL

Melting points were measured on a Boetius apparatus and uncorrected. Ir spectra were measured (in KBr) on a Bruker IFS-85 spectrophotometer, ^{1}H nmr spectra were obtained on a Varian XL-100 instrument using TMS as internal standard. Mass spectra were recorded on a Varian MAT SM1 double focusing mass spectrometer.

1,2-Bis(subst.phenyl)-1*H*-1,2,4-triazolo[2,3-b][1,2,4]benzothiadiazepines **2a-j**

A mixture of **1a-j**, 2,2'-dithiobis(benzoyl chloride) and tributylamine (10 mmol each) in 70 ml of benzene was refluxed for 30 min. Then the reaction mixture was cooled, the precipitated products were filtered, washed with benzene and dried. The crude products were recrystallized from DMF until homogenous by tlc (except for **2e** which was recrystallized from acetonitrile).

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