Addition Reaction of Phenyl Isocyanate and Phenyl Isothiocyanate to Partially Cyclic 1,3-Diaza-1,3-butadienes. Synthesis of Annulated 1,3,5-Triazine-2,4(1*H*,3*H*)-diones and -2,4(1*H*,3*H*)-dithiones

Mahmoud A. ABDEL-RAHMAN
Department of Chemistry, Faculty of Science, Sohag University, Egypt
(Received June 22, 1992)

Annulated 1,3,5-triazine-2,4(1*H*,3*H*)-diones and -2,4(1*H*,3*H*)-dithiones (**8** and **9**) are synthesized by a $4\pi+2\pi$ cyclodimerization of heterocyclic heterocumulenes (**6** and **7**). These heterocumulenes are generated from partially cyclic 1,3-diaza-1,3-butadienes (**1a**—**c**) by means of a $2\pi+2\pi$ cycloaddition reaction with phenyl isocyanate or phenyl isothiocyanate and followed by dissociation of the resulting cycloadducts (1,3-diazetidinones (**3**) and 1,3-diazetidithiones (**4**)).

Heterodienes are of large potentiality in the synthesis of heterocyclic compounds.[1,2] Dienes containing two nitrogen atoms have attracted the attention of chemists in recent years because of their importance in natural product synthesis.[3,5] While the chemistry of 1,2- and 1,4-diaza-1,3-butadienes have been extensively investigated, reports on reactions of 1,3-diaza-1,3-butadienes are rare.[1,6] Occasionally these heterodienes have been postulated as reactive intermediates[7,8] and partially cyclic 1,3-diaza-1,3-butadienes have been used as N=C–N=C units in ring closure reaction.[9] Although there exist no general preparation methods of 1,3,5-triazines with oxo or thioxo functions at 2- and 4-positions,[10] some years ago a few 1,3,5-triazine-2,4(1*H*,3*H*)-diones were synthesized from isocyanate adducts.[11,12]

We report here that conveniently substituted 1,3,5-triazine-2,4(1*H*,3*H*)-diones (or 2,4(1*H*,3*H*)-dithiones) are formed from reaction of 2-[*p*-(dimethylamino)benzylideneamino]-benzoxazole (**1a**), -benzothiazole (**1b**) or -benzimidazole (**1c**) with phenyl isocyanate (**2a**) or phenyl isothiocyanate (**2b**). Thus, 1,3-diaza-1,3-butadienes (**1a**—**c**)[13] were refluxed with one equivalent of **2a** or **2b** in benzene for 50—70 h or in xylene for 40—50 h. The resulting products were isolated and characterized on the basis of analytical as well as IR and ^{1}H NMR data.

The formation of 3-(2-benzothiazolyl)-2*H*-1,3,5-triazino[2,1-*b*]benzothiazole-2,4(3*H*)-dione (**8b**) and its analogs (**8b**,**c** and **9a**—**c**) can be regarded as the result from a 1,4-dipolar cycloaddition of the intermediary heterocyclic heterocumulenes **6** and **7** (Scheme 1). The tendency of isocyanate or isothiocyanate of type **6** or **7** to undergo cyclodimerization is known in the cases of 2-isothiocyanato pyridine[14] and 2-isocyanatothiazole,[15] which are isolable only as a dimer of type **8** or **9**. However, the iminoalkyl isocyanate can be isolated as monomer[16]. The reaction may therefore be used for the preparation of novel heterocyclic heterocumulenes.

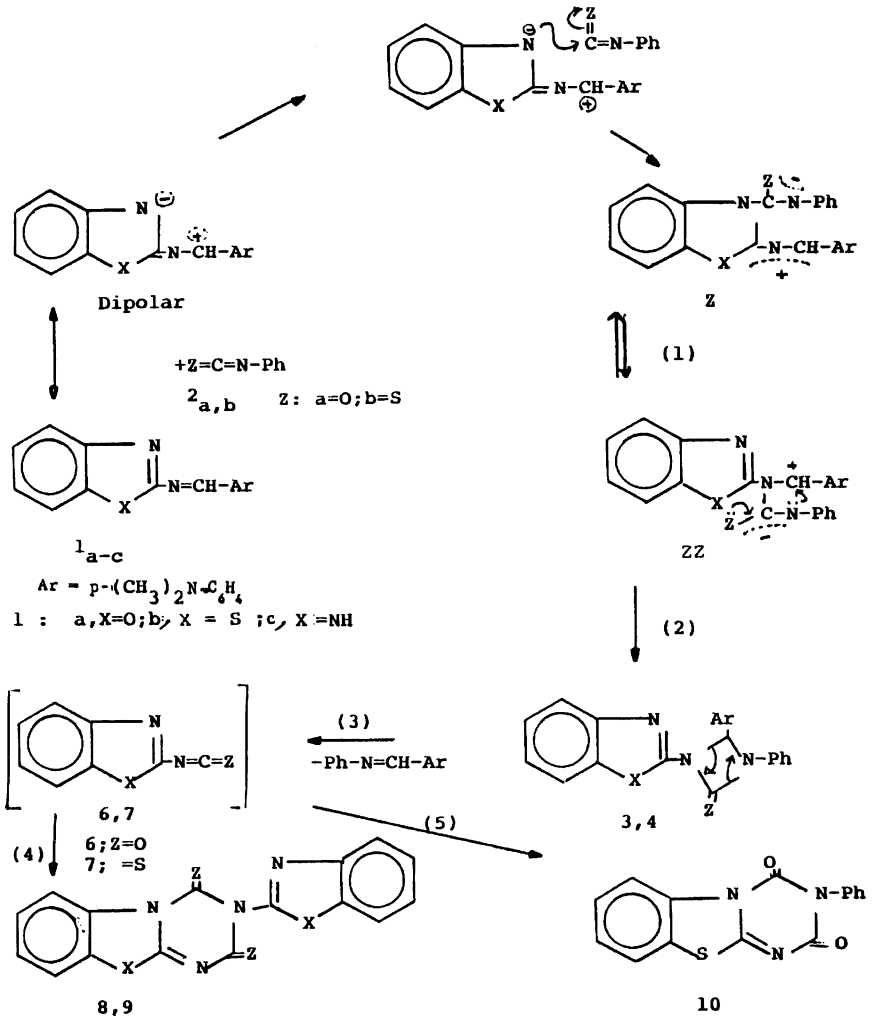
In an attempt to support the formation of the heterocyclic heterocumulene **6a** and its presence as intermediate in the reaction sequence, the reaction of **1a** with 2.0 equivalents of phenyl isocyanate in refluxing toluene for 16 h was carried out. The isolated crystalline product was characterized as known compound **10** on the basis of analytical and IR- and ^{1}H NMR data.[17] The reaction of phenyl isocyanate can occur via a two-step mechanism with the formation of a zwitterionic intermediate from which the compound **10** is formed.[18] Alternatively, the formation of **10** could be regarded as a Diels–Alder like reaction occurring with a one-step mechanism (Scheme 1).

Because of the substantial differences in electronegativity of the reacting atoms we propose a nonsynchronous concerted or even a stepwise mechanism for cycloaddition reaction of heterocumulenes **2a**,**b** to partially cyclic 1,3-diaza-1,3-butadienes (**1a**—**c**). The formation of intermediate cycloadducts **3a**—**c**, **4a**—**c**, and the subsequent synthesis of final products **8**, **9** can be explained through the following two possibilities:

1) The reaction of 1,3-diaza-1,3-butadienes (**1a**—**c**) as dipolar dienes with heterocumulenes **2a**,**b** may lead to the formation of dipolar intermediate (**Z**). At the reaction temperature the intermediate **Z** isomerized[9,19] to zwitterionic intermediate (**ZZ**), which through ring closure lead to 1,3-diazetidinones (**3a**—**c**) or 1,3-diazetidinethiones (**4a**—**c**). These cycloadducts are usually unstable and their disproportion lead to the elimination of (*p*-dimethylaminobenzylidene)aniline and gives the corresponing heterocyclic heterocumulenes (**6**,**7**). They, cyclodimerize to give the crystalline compounds (**8a**—**c**, **9a**—**c**).

Proposal about the formation of zwitterion **Z** and its isomerization at high temperature to **ZZ** was discussed previously by Richter and Ulrich.[9] Where they studied the reaction of some analogous partially cyclic 1,3-diaza-1,3-butadienes with phenyl isocyanate under different conditions.

2) The introduction of an electron-donating group at the *p*-position of benzylidene moiety should increase the possibility of the $2\pi+2\pi$ cycloaddition[20] of 1,3-diaza-1,3-butadienes (**1a**—**c**) with heterocumulenes **2a**,**b** across the 3,4 N=C double bond



Scheme 1.

with heterocumulenes **2a,b**. This leads to the corresponding 1,3-diazetidithiones (**3a—c**) or 1,3-diazetidithiones (**4a—c**) via the zwitterionic intermediate **ZZ** (Scheme 1). The dissociation of these cycloadducts at the reaction temperature followed by cyclodimerization of the resulting heterocyclic heterocumulenes to give the compounds (**8a—c**, **9a—c**) as final products. In an attempt to obtain an experimental evidence for this assumption, the reaction of 1,3-diaza-1,3-butadienes (**1a—c**) with heterocumulenes (**2a,b**) was carried out under mild conditions (room temperature and/or short time). The reaction under these conditions did not proceed the starting materials, being recovered unchanged

The cycloaddition studies of these and other related partially cyclic 1,3-diaza-1,3-butadienes with various dienophiles and heterodienophiles are under way.

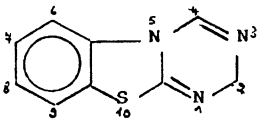
Experimental

Melting points are uncorrected. The infrared spectra are determined with a Univcam SP 200G spectrometer (KBr, cm^{-1}) ^1H NMR spectra are recorded at (60 MHZ) on a Varian A-60 spectrometer. The chemical shifts are reported as δ values in ppm, TMS is used as internal reference standard. Elemental analyses are done by Micro analytical Laboratory, Cairo University, Giza, Egypt.

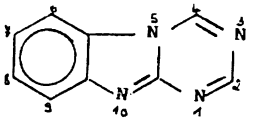
2-[*p*-Dimethylaminobenzylideneamino]benzoxazole, -benzothiazole, and -benzimidazole were prepared by the reported procedures.[13,21]

Synthesis of Substituted 1,3,5-Triazines (8 and 9). General Procedure: To a solution of partially cyclic 1,3-diaza-1,3-butadienes (**1a,c**) [0.01 mol] in dry benzene [30 ml], the heterocumulene (**2a,b**) [0.01 mol] are added. The resulting mixture is refluxed for 50—70 h. The solvent is removed under a reduced pressure. The precipitated product is crystallized from ethanol to give the corresponding product **8a—c** and **9a—c**.

Experimental, IR (KBr, cm^{-1}) and ^1H NMR (DMSO, δ/ppm) Data of Compounds (8a—c) and (9a—c). 8a: Mp 280°C; yield 50%; IR double band 1690, 1740 (ν C=O), 1610 (ν C=N); ^1H NMR δ=8.3—7.2 (m, 8H). Found: C, 60.21; H, 2.41; N, 17.25%. Calcd for



Scheme 2. 2*H*-1,3,5-triazino[2,1-*b*]benzothiazole



Scheme 3. 1,3,5-triazino[1,2-*a*]benzimidazole

$C_{16}H_8N_4O_4$: C, 60; H, 2.5; N, 17.5%.

8b: Mp 304°C; yield 55%; IR double band 1680, 1735 (ν C=O), 1615 (ν C=N); ^{1}H NMR δ=8.6—7.4 (m, 8H). Found: C, 54.44; H, 2.04; N, 15.81%. Calcd for $C_{16}H_8N_4O_2S_2$: C, 54.54; H, 2.27; N, 15.90%.

8c: Mp 169°C; yield 65%; IR double band 1680, 1730 (ν C=O), 1620 (ν C=N); ^{1}H NMR δ=8.7—7.2 (m, 8H), 8.8 (br, 2H, 2NH). Found: C, 60.21; H, 3.01 ; N, 26.31%. Calcd for $C_{16}H_{10}N_6O_2$: C, 60.37; H, 3.14; N, 26.14%.

9a: Mp 228°C; yield 40%; IR 1180 (ν C=S), 1615 (ν C=N); ^{1}H NMR δ=7.8—7.0 (m, 8H). Found: C, 54.49; H, 2.20; N, 15.81%. Calcd for $C_{16}H_8N_4O_2S_2$: C, 54.54; H, 2.27; N, 15.90%.

9b: Mp 190°C; yield 55%; IR 1200 (ν C=S), 1620 (ν C=N); ^{1}H NMR δ=8.5—7.3 (m, 8H). Found: C, 49.89; H, 2.00; N, 2.08%. Calcd for $C_{16}H_8N_4S_4$: C, 50.00; H, 2.08; N, 14.58%.

9c: Mp 148°C; yield 40%; IR 1185 (ν C=S), 1615 (ν C=N); ^{1}H NMR δ=8.0—7.1 (m, 8H), 8.8 (br, 2H, 2NH). Found: C, 54.89; H, 2.80; N, 24.01%. Calcd for $C_{16}H_{10}N_6S_2$: C, 54.85; H, 2.85; N, 24.00%.

Synthesis of 3-Phenyl-2*H*-1,3,5-triazino[2,1-*b*]-benzothiazole-2,4(3*H*)-dione (10). A solution of **1a** [0.01 mol] and phenyl isocyanate [0.02 mol] in toluene (30 ml) was heated under reflux. After 16 h the toluene was evaporated off under a reduced pressure and the residue was washed with a small amount of acetone. Crude substance **10** (60%), was crystallized from DMF/ether, mp 280°C (285°C).[9]

The Prepared 1,3,5-Triazinediones (8) and 1,3,5-Triazinedithiones (9) :

8a: 3-(2-Benzoxazolyl)-2*H*-1,3,5-triazino[2,1-*b*]benzoxazole-2,4(3*H*)-dione

8b: 3-(2-(Benzothiazolyl)-2*H*-1,3,5-triazino[2,1-*b*]benzothiazole-2,4(3*H*)-dione

8c: 3-(2-Benzimidazolyl)-3,10-dihydro-1,3,5-triazino[1,2-*a*]-benzimidazole-2,4-dione

9a: 3-(2-Benzoxazolyl)-2*H*-1,3,5-triazino[2,1-*b*]benzoxazole-2,4(3*H*)-dithione

9b: 3-(2-Benzothiazolyl)-2*H*-1,3,5-triazino[2,1-*b*]benzothiazole-2,4(3*H*)-dithione

9c: 3-(2-benzimidazolyl)-3,10-dihydro-1,3,5-triazino[1,2-*a*]-benzimidazole-dithione (Scheme 2 Scheme 3)

References

1) D. L. Boger and S. M. Weinreb, in "Hetero Diels–Alder Cycloddition Reaction in Organic Synthesis," ed by H. H. Wasserman, Academic Press, New York (1987), p. 239.

2) D. L. Boger, *Tetrahedron*, **39**, 2869 (1983).

3) L. E. Overman, C. B. Petty, T. Ban, and G. T. Huang, *J. Am. Chem. Soc.*, **105**, 6335 (1983).

4) M. L. Bremmer and S. M. Weinreb, *Tetrahedron Lett.*, **24**, 261 (1983).

5) D. L. Boger and J. S. Penek, *J. Org. Chem.*, **48**, 261(1983).

6) J. H. Barluenga, M. Tomas, A. Ballesteras, and L. Loper, *Synthesis*, **1984**, 228.

7) C. Grundmann, G. Weisse, and S. Seide, *Justus Liebigs Ann. Chem.*, **17**, 577 (1952).

8) V. M. Cherkasov, N. A. Kapran, and V. N. Zavatskii, *Chem. Heterocycl. Comp. USSR*, **1969**, 266.

9) R. Richter and H. Ulrich, *Chem. Ber.*, **103**, 3525 (1970).

10) J. M. E. Quirke, in Katritzky and Rees "Comprehensive Heterocyclic Chemistry," ed by A. J. Boulton and A. Meckillip, Pergamon Press, Oxford (1984), Vol. 3, p. 457; T. S. Griffin, T. S. Woods, and A. R. Klayman, *Adv. Heterocycl.*, **18**, 130 (1975).

11) I. Matsuda, K. Itoh, and Y. Ishii, *J. Chem. Soc., Perkin Trans. 1*, **1972**, 1678.

12) I. Matsuda, S. Yamamoto, and Y. Ishii, *J. Chem. Soc., Perkin Trans. 1*, **1976**, 1528.

13) H. M. Osman, M. Z. A. Bader, M. M. Mahmoud, and Z. A. Hezien, *J. Indian Chem. Soc.*, **59**, 763 (1982).

14) H. M. Blatter and H. Lukaszewski, *Tetrahedron Lett.*, **1964**, 1087.

15) U. V. Gizycki and G. Oertel, *Angew. Chem., Int. Ed. Engl.*, **7**, 381 (1968).

16) L. J. Samaray, W. A. Bondar, and G. I. Derkatsch, *Angew. Chem., Int. Ed. Engl.*, **6**, 864 (1967).

17) U. V. Gizycki and G. Oertel, *Angew. Chem., Int. Ed. Engl.*, **7**, 380 (1968).

18) R. Gompper, *Angew. Chem., Int. Ed. Engl.*, **8**, 312 (1969).

19) H. Ulrich, B. Tucker, and A. A. R. Saylgh, *Angew. Chem., Int. Ed. Engl.*, **7**, 291 (1968).

20) R. Richter, *Angew. Chem., Int. Ed. Engl.*, **8**, 938 (1969).

21) a) Kh. M. Hassan, A. M. Mahmoud, and H. M. El-Scherief, *Z. Naturforsch.*, **336**, 1005 (1987); b) A. E. Abdel-Rahman, A. M. Mahmoud, G. M. El-Nager, and El-Scherief, *Pharmazie*, **38**, 589 (1983).