2-Azabuta-1,3-diene-4-carbonitriles: stereoselective synthesis and nucleophilic substitution at the carbon–nitrogen double bond

Antonio Lorente, Marta Casillas, Pilar Gomez-Sal, and Antonio Manzanero

Abstract: The synthesis of (*E*)-1-methoxy-2-azabuta-1,3-diene-4-carbonitriles was performed by methylation of N-alkenylamides **9** and **11**. The *Z* isomers were obtained by treatment of (*E*)-1-methylthio-2-azabuta-1,3-diene-4,4-dicarbonitriles with sodium methoxide in methanol. We also describe the reactions of (*E*)-1-methylthio-2-azabuta-1,3-diene-4,4-dicarbonitriles with pyrrolidine, which afforded 1-(1-pyrrolidinyl) derivatives **20**, **21**, and **23**. X-ray crystallographic analyses of **21** and **23** established the *E* stereochemistry of the C—N double bond.

Key words: 2-azabuta-1,3-diene-4-carbonitriles: stereoselective synthesis, nucleophilic substitution and X-ray diffraction; N-alkenylamides: methylation.

Résumé : On a effectué la synthèse des (*E*)-1-méthoxy-2-azabuta-1,3-diène-4-carbonitriles en effectuant la méthylation des N-alkénylamides **9** et **11**. On a obtenu les isomères *Z* en traitant les (*E*)-1-méthylthio-2-azabuta-1,3-diène-4,4-dicarbonitriles avec du méthylate de sodium dans le méthanol. On décrit aussi les réactions des (*E*)-1-méthylthio-2-azabuta-1,3-diène-4,4-dicarbonitriles avec la pyrrolidine qui conduisent aux dérivés 1-(1-pyrrolidinyle) **20**, **21** et **23**. On a déterminé la stéréochimie *E* de la double liaison C—N par une analyse cristallographique par diffusion des rayons X.

Mots clés : 2-azabuta-1,3-diène-4-carbonitriles : synthèse stéréosélective, substitution nucléophile, diffraction des rayons X; méthylation de N-alkénylamides.

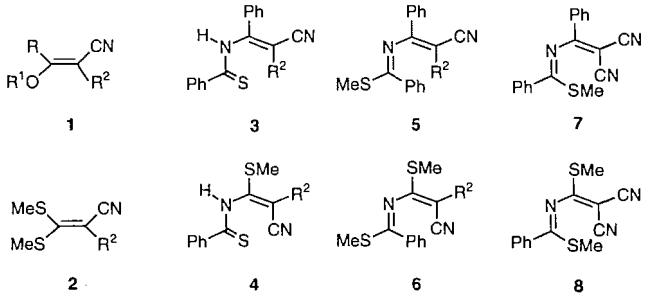
[Traduit par la rédaction]

Introduction

The synthesis of imidates (1–3) or thioimidates (3–5) by alkylation of amides or thioamides is a process that is well documented. In a previous paper (6) we described a stereoselective synthesis of (*E*)-1-methylthio-2-azabuta-1,3-diene-4-carbonitriles (N-alkenyl thioimidates) **5** and **6** by methylation of adducts **3** and **4**, which were formed from addition of thioamides to methoxymethylene compounds **1** or ketene dithioacetals **2**. Treatment of **5***a* and **6***a* with sodium methanethiolate affords *Z* isomers **7** and **8**, respectively.

To gain further insight into the stereoselectivity of these alkylation processes we examined the methylation of adducts **9–11** to afford the 1-methoxy-1-phenyl-2-azabuta-1,3-dienes **12–14**. There are several studies (7–17) on nucleophilic substitutions at the C—N double bond. A nucleophilic addition–elimination mechanism or a pathway involving a nitrilium ion intermediate has been suggested. Herein we describe the reactions of 2-azabuta-1,3-dienes with sodium methoxide or pyrrolidine and their stereochemical results.

Scheme 1.



Results and discussion

The adducts **9–11** were obtained from benzamide and the unsaturated compounds **1** or **2** using NaH as the base. Methylation of adducts **9–11** with diazomethane occurs stereoselectively, affording (*E*)-1-methoxy-1-phenyl-2-azabuta-1,3-dienes **12–14**.

Stereoselective formation of 2-azabuta-1,3-dienes **5** and **6** and **12–14** cannot be explained by assuming an *E* conformation for the adducts because a radiocrystallographic study (18) of **3***b* showed it to have a *Z* conformation. The stereochemical

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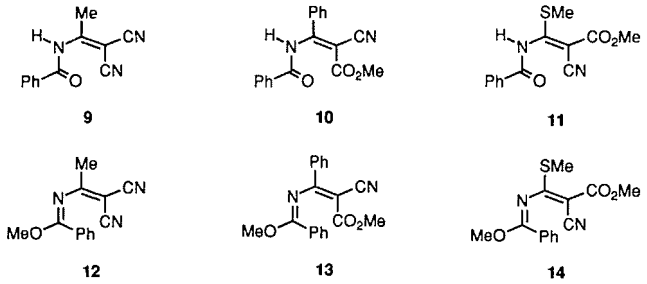
Scheme 2.

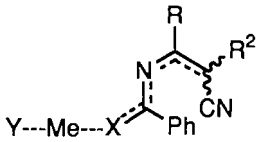


9 **10** **11**

12 **13** **14**

results obtained in the synthesis of these 2-azabuta-1,3-dienes can be accounted for by the lower steric hindrance in the transition state for the formation of the *E* isomers.

Scheme 3.



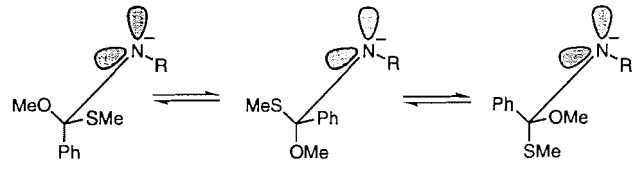
It is well established (19) that the *E* form of imidate or thioimidate esters is more stable than the *Z* form and *E*–*Z* interconvention can proceed by nitrogen inversion or by tautomerization and rotation about the C—N single bond. As we described in a previous paper (6), the 2-azabuta-1,3-dienes **5** and **6** retain their stereochemistry in solution but isomerization of the C—N double bond was achieved by treatment of **5***a* and **6***a* with sodium methanethiolate to afford the *Z* isomers **7** and **8**, respectively. We now report the conversion of (*E*)-1-methylthio-2-azabuta-1,3-diene-4,4-dicarbonitriles **5***a* and **6***a* to (*Z*)-1-methoxyderivatives **15** and **16** by treatment with sodium methoxide in methanol.

Scheme 4.

15 **16**

These results can be rationalized on the basis of the principle of stereoelectronic control. If we assume that an addition–elimination mechanism is followed, the reaction of methoxide ion on **5***a* and **6***a* gives the intermediate **17**, which can rotate to give other conformations with two lone pairs antiperiplanar to SMe, one of which (**18**) gives the *E* product and the other one (**19**) the *Z* product. The fact that only *Z* isomers were obtained can be explained by the greater unfavourable steric hindrance of intermediates **17** and **18**.

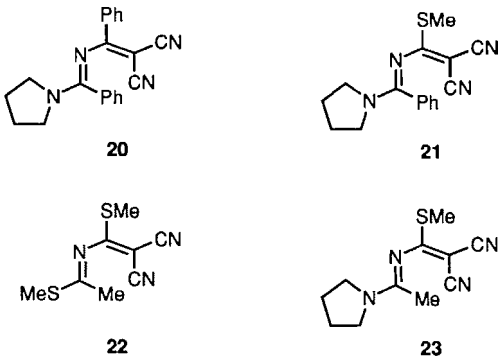
Scheme 5.



18 **17** **19**

The stereochemistry and mechanisms of amine substitution reactions at the C—N double bond have been studied (7–11, 16, 17). In a previous paper (20) were reported the reactions of **5***a* and **6***a* with nitrogen nucleophiles to afford different heterocyclic systems. We describe here the reactions of (*E*)-1-methylthio-2-azabuta-1,3-dienes **5***a* and **6***a* with pyrrolidine in propan-2-ol at room temperature to give (*E*)-1-(1-pyrrolidinyl)-2-azabuta-1,3-dienes **20** and **21**. In a similar manner the reaction of (*E*)-2-azabuta-1,3-diene **22** with pyrrolidine affords (*E*)-1-(1-pyrrolidinyl)-2-azabuta-1,3-diene **23**.

Scheme 6.

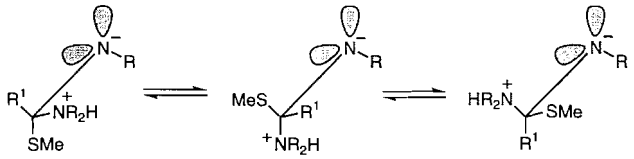


20 **21**

22 **23**

The stereochemical results of these reactions cannot be satisfactorily explained by an addition–elimination pathway because addition of pyrrolidine to **5***a* and **6***a* produces intermediate **24**, which can stereomutate to intermediates **25** and **26**. Both of these have one antiperiplanar electron pair set up for stereoelectronically controlled elimination of methanethiolate ion to afford (*E*)- or (*Z*)-1-(1-pyrrolidinyl)-2-azabuta-1,3-diene, respectively. However, the steric requirements of these intermediates could not account for the stereoselectivity of the reaction.

Scheme 7.



26 **24** **25**

It is possible that the reactions of 1-methylthio-2-azabuta-1,3-dienes with pyrrolidine proceed by an S_N2 or ion-pair (IP) mechanism (21). Additions of nucleophiles to nitrilium ions are known to occur so that the nucleophile and the electron pair on nitrogen are *anti* to each other (22–24), which could account for the observed stereochemical results. Another possibility is the synchronous displacement of the methanethiolate ion without formation of a tetrahedral intermediate (9, 25–27).

Structural study

In previous papers (6, 28) radiocrystallographic studies of 1-methylthio-2-azabuta-1,3-dienes were reported. We describe here the structure of 3-methylthio-1-(1-pyrrolidinyl)-2-azabuta-1,3-diene-4,4-dicarbonitriles **21** and **23**.

Description of the structure of compound ***21***

Positional parameters for non hydrogen atoms are given in Table 1. Figure 1 displays the structural formula with the labelling scheme and Tables 2 and 3 show selected geometric parameters. The azadiene framework deviates from coplanarity (C(1)-N(2)-C(3)-C(4)) but to a lesser extent than that found

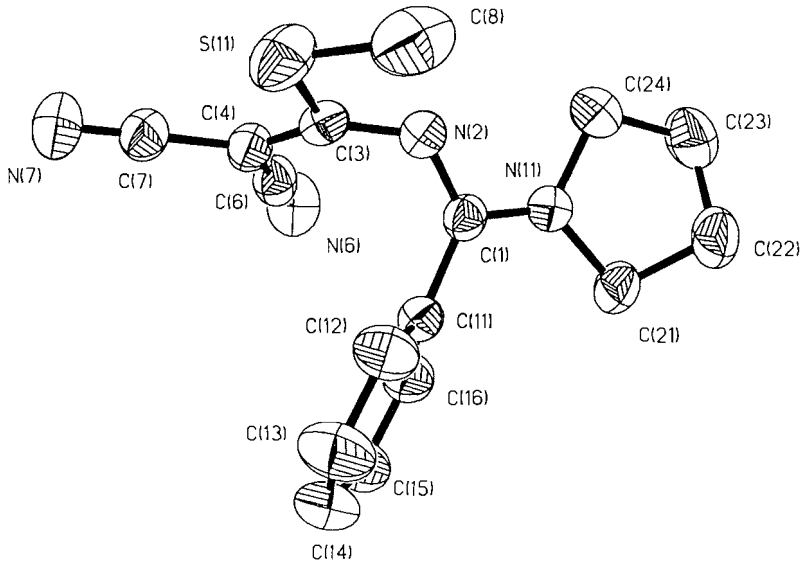
Table 1. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **21**. U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	*y*	*z*	U_{eq}
S(11)	1699(1)	5208(1)	843(1)	68(1)
C(1)	1731(2)	6429(2)	−1004(2)	40(1)
N(2)	1237(2)	6034(2)	−431(1)	48(1)
C(3)	1565(2)	5281(2)	−135(2)	43(1)
C(4)	1718(2)	4516(2)	−540(2)	45(1)
N(11)	1143(2)	7040(1)	−1359(1)	45(1)
N(6)	1282(3)	4441(2)	−1954(2)	71(1)
N(7)	2387(3)	3102(2)	86(2)	74(1)
C(6)	1482(2)	4479(2)	−1322(2)	49(1)
C(7)	2081(3)	3727(2)	−191(2)	52(1)
C(8)	1507(4)	6311(3)	1127(2)	84(1)
C(11)	2942(2)	6250(2)	−1226(2)	42(1)
C(12)	3777(3)	6243(2)	−673(2)	60(1)
C(13)	4905(3)	6040(4)	−859(2)	80(1)
C(14)	5188(3)	5841(3)	−1594(3)	77(1)
C(15)	4364(3)	5850(2)	−2142(2)	65(1)
C(16)	3244(3)	6060(2)	−1963(2)	54(1)
C(21)	1608(3)	7700(2)	−1879(2)	56(1)
C(22)	813(3)	8466(2)	−1746(2)	68(1)
C(23)	−333(3)	8052(3)	−1596(2)	76(1)
C(24)	−33(3)	7261(2)	−1120(2)	60(1)

Table 2. Selected bond lengths (Å) and angles (°) for **21**.

S(11)—C(3)	1.749(3)	S(11)—C(8)	1.779(4)
C(1)—N(2)	1.318(3)	C(1)—N(11)	1.321(3)
C(1)—C(11)	1.492(4)	N(2)—C(3)	1.325(4)
C(3)—C(4)	1.388(4)	C(4)—C(6)	1.418(4)
C(4)—C(7)	1.426(4)	N(11)—C(21)	1.475(4)
N(11)—C(24)	1.476(4)	N(6)—C(6)	1.148(4)
N(7)—C(7)	1.134(4)	C(11)—C(12)	1.383(4)
C(11)—C(16)	1.387(4)	C(12)—C(13)	1.392(5)
C(13)—C(14)	1.382(6)	C(14)—C(15)	1.369(6)
C(15)—C(16)	1.383(5)	C(21)—C(22)	1.515(5)
C(22)—C(23)	1.504(6)	C(23)—C(24)	1.519(5)
C(3)-S(11)-C(8)	102.1(2)	N(2)-C(1)-N(11)	117.9(2)
N(2)-C(1)-C(11)	122.3(2)	N(11)-C(1)-C(11)	119.7(2)
C(1)-N(2)-C(3)	125.5(2)	N(2)-C(3)-C(4)	124.5(3)
N(2)-C(3)-S(11)	118.5(2)	C(4)-C(3)-S(11)	116.8(2)
C(3)-C(4)-C(6)	121.2(3)	C(3)-C(4)-C(7)	122.0(3)
C(6)-C(4)-C(7)	116.8(3)	C(1)-N(11)-C(21)	126.5(2)
C(1)-N(11)-C(24)	120.6(2)	C(21)-N(11)-C(24)	111.3(2)
N(6)-C(6)-C(4)	179.2(3)	N(7)-C(7)-C(4)	179.0(3)
C(12)-C(11)-C(16)	119.3(3)	C(12)-C(11)-C(1)	118.7(3)
C(16)-C(11)-C(1)	121.9(3)	C(13)-C(12)-C(11)	119.9(3)
C(14)-C(13)-C(12)	120.0(3)	C(15)-C(14)-C(13)	120.1(3)
C(14)-C(15)-C(16)	120.2(3)	C(15)-C(16)-C(11)	120.4(3)
N(11)-C(21)-C(22)	102.1(2)	C(23)-C(22)-C(21)	104.2(3)
C(24)-C(23)-C(22)	103.3(3)	N(11)-C(24)-C(23)	103.8(3)

Fig. 1. ORTEP view of compound **21** showing the crystallographic numbering.



in 1-methylthio-2-azabuta-1,3-dienes (6). This allows better conjugation between the pyrrolidine nitrogen and the azadiene framework that produces a shortening of the N(11)—C(1) and N(2)—C(3) bonds and a lengthening of the C(1)—N(2) and C(3)—C(4) double bonds. The phenyl ring is twisted with respect to the plane defined by C(1), N(11), C(11), and N(2) atoms (torsion angle C(12)-C(11)-C(1)-N(2)), which restrains the conjugation. The N(2)-C(3)-C(4) bond angle is expanded whereas S(11)-C(3)-C(4) and S(11)-C(3)-N(2) are correspondingly contracted. These deviations can be considered a consequence of steric effects between the phenyl and dicyanomethylene groups. The stereochemistry of the C(1)—N(2) double bond is *E*. The methylthio group is almost coplanar with the C(3)—C(4) double bond and adopts a *syn* conformation.

Description of the structure of compound ***23***

Positional parameters are given in Table 4 and Fig. 2 displays the structural formula. Tables **5** and **6** show selected geometric parameters, which are similar to those found for compound **21**. The azadiene framework deviates from coplanarity and the stereochemistry of the C(1)—N(2) double bond is *E*. The methylthio group adopts a *syn* conformation.

Table 3. Selected torsion angles (°) for **21**.

C(1)-N(2)-C(3)-C(4)	−53.5(4)	C(24)-N(11)-C(1)-N(2)	−0.6(4)
C(21)-N(11)-C(1)-N(2)	163.9(3)	C(21)-N(11)-C(1)-C(11)	−11.9(4)
C(8)-S(11)-C(3)-N(2)	−7.8(3)	C(4)-C(3)-S(11)-C(8)	177.6(2)
C(7)-C(4)-C(3)-N(2)	179.5(3)	C(6)-C(4)-C(3)-S(11)	171.7(2)
C(6)-C(4)-C(3)-N(2)	−2.5(4)	C(7)-C(4)-C(3)-S(11)	−6.3(4)
C(3)-N(2)-C(1)-N(11)	162.3(3)	C(12)-C(11)-C(1)-N(11)	128.2(3)
C(12)-C(11)-C(1)-N(2)	−47.5(4)		

Table 4. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **23**. U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
S(11)	228(1)	2146(1)	651(1)	65(1)
C(1)	1790(2)	2546(2)	−1597(2)	46(1)
N(2)	1014(2)	2212(1)	−1077(2)	54(1)
C(3)	429(2)	2677(2)	−457(2)	47(1)
C(4)	−125(2)	3510(2)	−635(2)	49(1)
N(11)	2126(2)	2016(1)	−2302(2)	50(1)
N(6)	−87(2)	4232(2)	−2295(2)	74(1)
N(7)	−1367(2)	4232(2)	598(2)	89(1)
C(6)	−98(2)	3922(2)	−1545(2)	53(1)
C(7)	−808(2)	3913(2)	51(2)	60(1)
C(8)	1019(3)	1104(3)	559(3)	102(1)
C(11)	2353(2)	3451(2)	−1385(2)	65(1)
C(21)	1638(2)	1102(2)	−2529(2)	61(1)
C(22)	2274(3)	745(3)	−3354(4)	96(1)
C(23)	3206(3)	1293(3)	−3406(3)	120(2)
C(24)	3076(2)	2185(2)	−2870(2)	68(1)

Table 5. Selected bond lengths (Å) and angles (°) for **23**.

S(11)—C(3)	1.756(3)	S(11)—C(8)	1.786(3)
C(1)—N(2)	1.315(3)	C(1)—N(11)	1.318(3)
C(1)—C(11)	1.495(3)	N(2)—C(3)	1.323(3)
C(3)—C(4)	1.393(3)	C(4)—C(6)	1.413(4)
C(4)—C(7)	1.420(4)	N(11)—C(21)	1.467(3)
N(11)—C(24)	1.467(3)	N(6)—C(6)	1.147(4)
N(7)—C(7)	1.141(3)	C(21)—C(22)	1.505(4)
C(22)—C(23)	1.413(5)	C(23)—C(24)	1.480(4)
C(3)-S(11)-C(8)	101.8(1)	N(2)-C(1)-N(11)	117.5(2)
N(2)-C(1)-C(11)	123.5(2)	N(11)-C(1)-C(11)	118.9(2)
C(1)-N(2)-C(3)	127.7(2)	N(2)-C(3)-C(4)	125.6(2)
N(2)-C(3)-S(11)	117.5(2)	C(4)-C(3)-S(11)	116.7(2)
C(3)-C(4)-C(6)	120.0(2)	C(3)-C(4)-C(7)	121.5(2)
C(6)-C(4)-C(7)	118.2(2)	C(1)-N(11)-C(21)	122.0(2)
C(1)-N(11)-C(24)	126.0(2)	C(21)-N(11)-C(24)	111.6(2)
N(6)-C(6)-C(4)	178.0(3)	N(7)-C(7)-C(4)	179.2(3)
N(11)-C(21)-C(22)	103.8(2)	C(23)-C(22)-C(21)	107.7(3)
C(24)-C(23)-C(22)	110.3(3)	N(11)-C(24)-C(23)	103.5(2)

Structure and stereochemistry of 2-azabuta-1,3-dienes and their precursors

The configuration of the C—C double bond of adduct **10** was established by comparison with the ^1H NMR spectrum of dimethyl 1-benzamido-1-phenylmethylenemalonate (18) taking into account the shielding effect exerted by the phenyl group on the methoxycarbonyl. This configuration can be stabilized by the N-H.....O=C hydrogen bond as in the adduct **3*b*** (18). The *Z* geometry of the C—C double bond in compound **11** was deduced from NOE experiments and can be explained by an attractive nonbonded CH_3S.....O=C interaction similar to that found in compound **6*b*** (6).

The geometry of the C—N double bond of 2-azabuta-1,3-dienes was established on the basis of chemical shifts (Table 7) of the aromatic hydrogens on C1. The deshielding of the *ortho* hydrogens in compounds **15** and **16** indicates a coplanar arrangement of the phenyl and C—N double bond. This fact is similar to that found in (*Z*)-1-methylthio-2-azabuta-1,3-dienes **7** and **8**. On the contrary, the chemical shifts of the *ortho* aromatic hydrogens of compounds **12–14**, **20**, and **21** are similar to those of the corresponding hydrogens in (*E*)-1-methylthio-2-azabuta-1,3-dienes **5** and **6**. This fact allows us to assign an *E* configuration to the carbon–nitrogen double bond and a twisted conformation for the phenyl ring in solution, as found in the solid state for compound **21**.

Experimental

General

Melting points were determined with a Büchi SMP-20 apparatus and are uncorrected. IR were recorded on a Perkin Elmer 883 spectrophotometer. NMR spectra were obtained on a Varian Unity 300 instrument and mass spectra on a Hewlett Packard HP-5988 at 70 eV. Microanalyses were performed on a Heraeus CHN microanalyser. Flash column chromatography was carried out on silica gel SDS (230–400 mesh). Methoxymethylene compounds (**1**) were prepared using previously reported procedures (29, 30). Ketene dithioacetals (**2**) were prepared according to the procedure described by R. Gompper and W. Töpfl (31). The synthesis of methyl (*Z*)-3-benzamido-2-cyano-3-phenylpropenoate (**10**) was described in a previous paper (18) and methyl (*Z*)-3-benzamido-2-cyano-3-methylthiopropenoate (**11**) was prepared according to the reported procedure (32).

X-Ray diffraction

The crystals were mounted in an Enraf–Nonius CAD-4 automatic four-circle diffractometer, with bisecting geometry and graphite-oriented monochromator, using Mo K_α radiation (λ = 0.7107 Å). Unit cell parameters were calculated by least-squares refinement on diffractometer angles for 25 automatically centered reflections. Crystallographic and experimental details are summarized in Table 8.

Fig. 2. ORTEP view of compound **23** showing the crystallographic numbering.

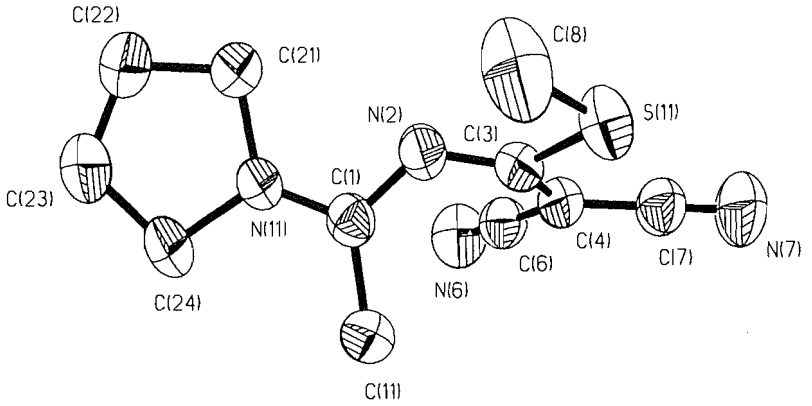


Table 6. Selected torsion angles (°) for **23**.

C(1)-N(2)-C(3)-C(4)	53.4(4)	C(21)-N(11)-C(1)-C(11)	177.6(2)
C(8)-S(11)-C(3)-N(2)	3.4(3)	C(4)-C(3)-S(11)-C(8)	177.6(2)
C(24)-N(11)-C(1)-C(11)	5.5(4)	C(11)-C(1)-N(2)-C(3)	18.2(4)

Table 7. ^{1}H and NMR[a] chemical shifts for 2-azabuta-1,3-dienes at 300 MHz.

	12	**13**	**14**	**15**	**16**	**20**	**21**	**23**
CH_3S			2.36				2.48	2.30
CH_3O	3.99	4.33	4.01	4.22	4.16 (s, 6H)			
CO_2CH_3		3.75	3.63					
Aromatics	7.44–7.60 (m)	7.55–7.93 (m)	7.54–7.63 (m)	7.55–7.65 (m, 6H)	7.54–7.63 (m, 2H)	6.97–7.0 (m, 3H)	7.41–7.44 (m, 2H)	
				8.02–8.07 (m, 2H)	8.42–8.45 (m, 3H)	7.05–7.24 (m, 3H)	7.50–7.57 (m, 3H)	
				8.47–8.53 (m, 2H)		7.27–7.33 (m, 2H)		
						7.42–7.62 (m, 2H)		
Others	2.32 (s, 3H, CH_3)					3.79 (t, J = 6.96, 2H, N-CH_2)	3.61 (t, J = 6.96, 2H, N-CH_2)	3.58 (t, J = 6.59, 2H, N-CH_2)
						3.39 (t, J = 6.77, 2H, N-CH_2)	3.44 (t, J = 6.77, 2H, N-CH_2)	3.43 (t, J = 6.59, 2H, N-CH_2)
						1.98–2.07 (m, 2H, CH_2)	1.95–2.04 (m, 2H, CH_2)	2.15 (s, 3H, CH_3)
						1.82–1.91 (m, 2H, CH_2)	1.82–1.91 (m, 2H, CH_2)	1.86–1.96 m, 4H, 2 CH_2)

[a]All spectra were registered in DMSO-d_6 with the exception of compound **13** ($CDCl_3$).

Data were collected at room temperature, using the $\omega/2\theta$ scan mode. Two check reflections measured every 90 min showed no significant variation. Intensities were corrected for Lorentz and polarization effects in the usual manner. No absorption or extinction corrections were made. The structures were solved by a combination of direct methods and Fourier synthesis and refined by least squares against F^2. All non hydrogen atoms were refined anisotropically. In **21**, the hydrogen atoms were found in the difference Fourier synthesis map and included in further refinement with fixed isotropic temperature factors. In **23** the hydrogen atoms were included from geometrical calculations with thermal parameters equivalent to the carbon to which they were attached. Final R_1 = 0.0664 and wR_2 = 0.1920 were obtained for **21** with a weighting scheme $w = 1/[\sigma^2(F_o^2) + (0.1301P)^2 + 0.6739P]$ and R_1 = 0.0515 and wR_2 = 0.1405 for **23** with a

Table 8. Crystal data and structure refinement for **21** and **23**.

	21	**23**
Empirical formula	$C_{16}H_{16}N_4S$	$C_{11}H_{14}N_4S$
Crystal size	0.25 × 0.3 × 0.2 mm	0.5 × 0.35 × 0.3 mm
Colour	Pale yellow	Pale yellow
Crystal habit	Rhombohedral	Hexagonal
Formula weight	296.39	234.32
Temperature	293(2) K	293(2) K
Wavelength	0.71069 Å	0.71069 Å
Crystal system	Orthorhombic	Orthorhombic
Space group	*Pbca*	*Pbca*
Unit cell dimensions	a = 11.669(1) Å	a = 12.669(1) Å
	b = 15.332(2) Å	b = 14.122(2) Å
	c = 17.770(3) Å	c = 14.150(2) Å
Volume	3179.2(7) Å^3	2531:6(5) Å^3
Z	8	8
Density (calculated)	1.238 g/cm^3	1.230 g/cm^3
Absorption coefficient	2.02 cm^{-1}	2.36 cm^{-1}
F(000)	1248	992
θ range for data collection	2.29–27.02	2.15–28.22
Index ranges	$0 < h < 14$, $0 < k < 19$, $0 < l < 22$	$0 < h < 16$, $0 < k$ 18, $0 < l < 18$
Reflections collected	3530	3179
Independent reflections	3466 (R_{int} = 0.0174)	3119 (R_{int} = 0.0099)
Refl. observed with $I > 2\sigma(I)$	2296	1936
Absorption correction	N/A	N/A
Refinement method	Full-matrix least squares on F^2	
Data/restraints/parameter	3446/0/190	3116/0/145
Goodness of fit on F^2	1.200	1.111
Final R indices ($I > 2\sigma(I)$)	R_1 = 0.0664, wR_2 = 0.1920	R_1 = 0.0515, wR_2 = 0.1405
Largest diff. peak and hole	0.458 and −0.440 e Å^{-3}	0.263 and −0.342 e Å^{-3}
Weighting scheme calcd.	$w = 1/[\sigma^2(F_o^2) + (0.1301P)^2 + 0.6739P]$	$w = 1/[\sigma^2(F_o^2) + (0.0761P)^2 + 1.0989P]$
	In both cases $P = (F_o^2 + 2F_o^2)/3$	

weighting scheme $w = 1/[\sigma^2(F_o)^2 + (0.0761P)^2 + 1.0989P]$ where $P = (F_o^2 + 2F_c^2)/3$ and $R_1 = \Sigma||F_o| - |F_o||/\Sigma|F_o|$ and $wR_2 = [|\Sigma(F_o^2 - F_c^2)^2|/|\Sigma w(F_o^2)^2|]^{1/2}$.

Calculations were performed with SHELXS-90 (33) and SHELXL-93 (34) programs on an Alpha AXP digital workstation.[2]

3-Benzamido-2-cyano-3-methylpropenenitrile 9

To a suspension of 80% NaH (142 mg, 7.3 mmol) in a mixture of dry benzene (15 mL) and dry *N,N*-dimethylacetamide (15 mL), 2-cyano-3-ethoxy-3-methylpropenenitrile (500 mg, 3.6 mmol) and benzamide (445 mg, 3.6 mmol) were added. The mixture was stirred at room temperature for 42 h and then poured into ice-water (50 mL). The aqueous layer was acidified with 10% hydrochloric acid and the precipitate formed was collected and recrystallized from hexane–benzene; 40% yield, mp 120–122°C; ν_{max} (KBr)/cm^{-1}: 3343, 2222, 1713, 1586 and 1476; δ_H (DMSO-d_6) 3.15 (s, 3H, CH_3), 7.54–7.90 (m, 5H, ArH), and 11.16 (s, 1H, NH); *m/z*: 211 (M$^+$, 15%), 106 (58), 105 (100), 77 (97), and 51 (84). Anal. calcd. for $C_{12}H_9N_3O$: C 68.22, H 4.30, N 19.9; found: C 68.05, H 4.41, N 20.01.

(*E*)-1-Methoxy-3-methyl-1-phenyl-2-azabuta-1,3-diene-4,4-dicarbonitrile 12

A solution of **9** (211 mg, 1 mmol) in dry ethyl acetate (20 mL) was methylated at 0°C with diazomethane (generated from Diazald® (750 mg, 3.5 mmol)). The solvent was removed at reduced pressure to afford the crude product, which was purified by flash column chromatography using hexane – ethyl acetate (5:1) as eluent; yield: 7%, mp 34–35°C (from hexane–benzene); ν_{max} (KBr)/cm^{-1}: 2256, 2226, 1658, and 1494; *m/z*: 225 (M$^+$, 44%), 210 (43), 193 (19), 153 (34), 105 (56), and 77 (100). Anal. calcd. for $C_{13}H_{11}N_3O$: C 69.31, H 4.93, N 18.66; found: C 69.10, H 4.89, N 18.91.

(1*E*, 3*Z*)-Methyl 4-cyano-1,3-diphenyl-2-azabuta-1,3-diene-4-carboxylate 13

A solution of **10** (153 mg, 0.5 mmol) in dry ethyl acetate (25 mL) was methylated at 0°C with diazomethane (generated from diazald (375 mg, 1.75 mmol)). The solvent was evapo-

[2] Tables of hydrogen coordinates and of isotropic and anisotropic displacement parameters for **21** and **23** have been deposited and can be purchased from: The Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, Canada K1A 0S2. The tables of hydrogen coordinates have also been deposited with the Cambridge Crystallographic Data Centre, and can be obtained on request from The Director, Cambridge Crystallographic Data Centre, University Chemical Laboratory, 12 Union Road, Cambridge, CB2 1EZ, U.K.

rated at reduced pressure and the crude product thus obtained was purified by flash column chromatography using hexane – ethyl acetate (6:1) as eluent; yield: 15%, mp 153–154°C (from propan-2-ol); ν_{max} (Nujol)/cm^{-1}: 2221, 1714, 1687, 1605, 1593, and 1462; *m/z*: 320 (M$^+$, 4%), 261 (4), 247 (10), 106 (8), 105 (100), 77 (32), and 51 (6). Anal. calcd. for $C_{19}H_{16}N_2O_3$: C 71.24, H 5.03, N 8.74; found: C 71.01, H 5.15, N 8.92.

(1*E*, 3*Z*)-Methyl 4-cyano-1-methoxy-3-methylthio-1-phenyl-2-azabuta-1,3-diene-4-carboxylate 14

A solution of **11** (200 mg, 0.725 mmol) in dry ether (70 mL) was methylated at 0°C with diazomethane (generated from diazald (550 mg, 2.56 mmol)). The solvent was removed at reduced pressure to afford the crude product, which was purified by flash column chromatography using hexane – ethyl acetate, 5:1 and then 3:1, as eluent; yield: 75%, mp 141–142°C (from propan-2-ol); ν_{max} (Nujol)/cm^{-1}: 2216, 1696, and 1644; *m/z*: 290 (M$^+$, 10%), 249 (15), 118 (5), 105 (100), and 77 (34). Anal. calcd. for $C_{14}H_{14}N_2O_3S$: C 57.92, H 4.86, N 9.65; found: C 57.81, H 4.9, N 9.71.

(*Z*)-1-Methoxy-1,3-diphenyl-2-azabuta-1,3-diene-4,4-dicarbonitrile 15

To a solution of sodium (23 mg, 1 mmol) in dry methanol (40 mL) was added **5***a* (151 mg, 0.5 mmol). The reaction mixture was heated at reflux for 2 h and then the solvent was removed at reduced pressure. The crude product thus obtained was purified by flash column chromatography using hexane – ethyl acetate (7:1) as eluent, affording 48 mg (31% yield) of **7**. With the same eluent 1-methoxy-2-azabuta-1,3-diene (**15**) was obtained; 68% yield, mp 151–152°C (from methanol); ν_{max} (KBr)/cm^{-1}: 2216, 1583, 1554, 1529, 1494, 1468, and 1449; δ_H ($CDCl_3$): 4.29 (s, 3H, OCH_3), 7.50–7.60 (m, 6H, ArH), 8.16–8.19 (m, 2H, ArH), and 8.57–8.60 (m, 2H, ArH); *m/z*: 287 (M$^+$, 100%), 257 (21), 256 (26), 184 (52), 156 (22), 155 (33), 129 (25), 128 (13), 127 (40), 104 (46), 103 (38) and 77 (39). Anal. calcd. for $C_{18}H_{13}N_3O$: C 75.23, H 4.56, N 14.63; found: C 75.41, H 4.51, N 14.22.

(*Z*)-1,3-Dimethoxy-1-phenyl-2-azabuta-1,3-diene-4,4-dicarbonitrile 16

To a solution of sodium (92 mg, 4 mmol) in dry methanol (25 mL), was added. **6***a* (110 mg, 0.4 mmol). The mixture was stirred at room temperature for 6 h. The solvent was removed at reduced pressure to afford the crude product, which was purified by flash column chromatography using hexane – ethyl acetate (3:1) as eluent; 27% yield, mp 164–165°C (from hexane–methanol); ν_{max} (KBr)/cm^{-1}: 2224, 1583, 1548, and 1461; *m/z*: 241 (M$^+$, 75%), 214 (27), 196 (26), 186 (27), 170 (18), 118 (53), 104 (100), 92 (69), and 77 (73). Anal. calcd. for $C_{13}H_{11}N_3O_2$: C 64.72, H 4.6, N 17.42; found: C 64.95, H 4.51, N 17.64.

(*E*)-1,3-Diphenyl-1-(1-pyrrolidinyl)-2-azabuta-1,3-diene-4,4-dicarbonitrile 20

To a solution of **5***a* (180 mg, 0.59 mmol) in dry propan-2-ol (20 mL) was added pyrrolidine (74 μL, 0.89 mmol). The mixture was stirred at room temperature for 23 h. The solvent was removed at reduced pressure to afford the crude product, which was washed with hexane and recrystallized from propan-2-ol; 95% yield, mp 170–171°C; ν_{max} (KBr)/cm^{-1}: 2212, 2201, 1581, 1546, 1512, 1486, and 1458; *m/z*: 326 (M$^+$, 26%), 272 (6), 257 (10), 192 (2), 153 (35), 104 (40), 77 (53), and 70 (100). Anal. calcd. for $C_{21}H_{18}N_4$: C 77.28, H 5.56, N 17.17; found: C 77.41, H 5.62, N 17.11.

(*E*)-3-Methylthio-1-phenyl-1-(1-pyrrolidinyl)-2-azabuta-1,3-diene-4,4-dicarbonitrile 21

To a solution of **6***a* (160 mg, 0.59 mmol) in dry propan-2-ol (20 mL) was added pyrrolidine (74 μL, 0.89 mmol). The mixture was stirred at room temperature for 23 h. The solvent was removed at reduced pressure to afford the crude product, which was washed with hexane and recrystallized from ethyl acetate; 83% yield, mp 138–139°C; ν_{max} (KBr)/cm^{-1}: 2205, 1579, 1453, and 1441; *m/z*: 296 (M$^+$, 27%), 249 (36), 207 (10), 180 (44), 153 (26), 146 (26), 123 (15), 104 (87), 91 (31), 77 (87), and 70 (100). Anal. calcd. for $C_{16}H_{16}N_4S$: C 64.84, H 5.44, N 18.9; found: C 64.99, H 5.33, N 19.02.

(*E*)-1-Methyl-3-methylthio-1-(1-pyrrolidinyl)-2-azabuta-1,3-diene-4,4-dicarbonitrile 23

To a solution of **22** (32 mg, 0.15 mmol) in dry propan-2-ol (20 mL) was added pyrrolidine (74 μL, 0.89 mmol). The mixture was stirred at room temperature for 22 h. The solvent was removed at reduced pressure to afford the crude product, which was recrystallized from ethyl acetate – hexane; 83% yield, mp 123–124°C; ν_{max} (KBr)/cm^{-1}: 2203, 1567, and 1424; *m/z*: 234 (M$^+$, 42%), 219 (14), 187 (25), 146 (19), 123 (20), 118 (46), 91 (12), and 70 (100). Anal. calcd. for $C_{11}H_{14}N_4S$: C 56.39, H 6.02, N, 23.91; found: C 56.11, H 6.12, N 24.07.

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