Two- and Three-Component Reactions Leading to New Enamines Derived from 2,3-Dicyanobut-2-enoates

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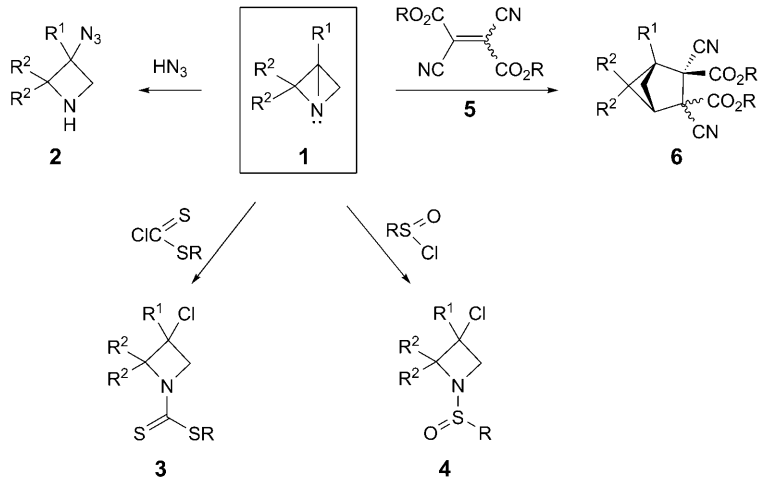
Dedicated to Professor *Peter Stanetty* on the occasion of his 65th birthday

The three-component reactions of 1-azabicyclo[1.1.0]butanes **1**, dicyanofumarates (*E*)-**5**, and MeOH or morpholine yielded azetidine enamines **8** and **9** with the *cis*-orientation of the ester groups at the C=C bond ((*E*)-configuration; *Schemes 3* and *4*). The structures of **8a** and **9d** were confirmed by X-ray crystallography. The formation of the products is explained *via* the nucleophilic addition of **1** onto (*E*)-**5**, leading to a zwitterion of type **7** (*Scheme* 2), which is subsequently trapped by MeOH or morpholine (**10a**), followed by elimination of HCN. Similarly, two-component reactions between secondary amines **10a**–**10c** and (*E*)-**5** gave products **12** with an (*E*)-enamine structure and (*Z*)-oriented ester groups. On the other hand, two-component reactions involving primary amines **10d**–**10f** or NH_3 led to the formation of the corresponding (*Z*)-enamines, in which the (*E*)-orientation of ester groups was established.

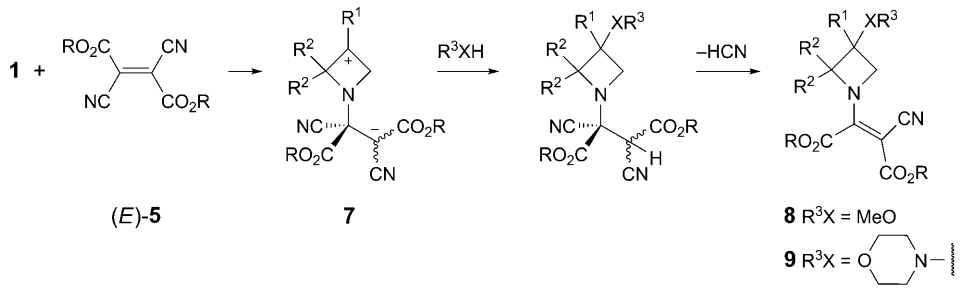
1. Introduction. – In a series of recent articles, new reactions of strained 1-azabicyclo[1.1.0]butanes **1** with diverse electrophiles such as hydrazoic acid [1], dithiochloroformates, and thiophosgene [2], as well as with sulfenyl and sulfinyl chlorides [3], were reported. In all these reactions, azetidine derivatives **2**–**4** were formed *via* 1,3-addition, resulting in the cleavage of the weak N(1)–C(3) bond (*Scheme 1*).

On the other hand, the reaction of the electron-deficient 2,3-dicyanobut-2-enoates **5** (dicyanofumarates and maleates) with 3-phenyl-1-azabicyclo[1.1.0]butane (**1a**; R^1 = Ph, R^2 = H) yielded mixtures of stereoisomeric 1-azabicyclo[2.1.1]hexane dicarboxylates **6** [4] (*Scheme 1*). The mechanism of this ring-enlargement reaction was shown to involve a zwitterionic species, which could be trapped by MeOH [5]. Whereas the ring enlargement leading to **6** depends on steric and electronic effects of the substituents R^1, R^2, and R, the trapping reactions with MeOH were successfully performed regardless of the nature of the substituents. In a preliminary experiment, the zwitterions **7** were also trapped with morpholine instead of MeOH [4] (*Scheme 2*). The products, which were isolated after the trapping experiments, were shown to be enamines of type **8** and **9** with an azetidine residue, *i.e.*, 1:1:1 adducts after elimination of HCN.

Scheme 1



Scheme 2

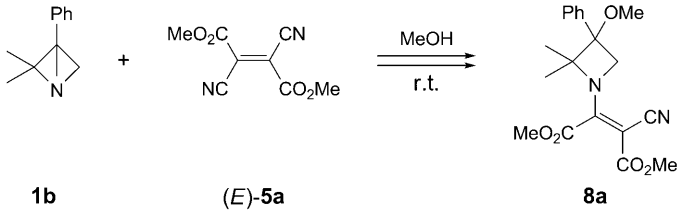


Due to the importance of enamines in organic synthesis (for a recent review, see [6]), we studied the three-component reactions involving **1**, **5**, and secondary amines to obtain more information on the structure and properties of the new class of enamines of type **8** and **9**, which bear three electron-withdrawing groups. In extension of this study, the two-component reactions of (*E*)-**5** and (*Z*)-**5** with differently substituted primary and secondary amines, as well as with NH_3, are described.

2. Results and Discussion. – 2.1. *Three-Component Reactions.* The product isolated from the three-component reaction of **1b** (R^1 = Ph, R^2 = Me), dimethyl dicyanofumarate ((*E*)-**5a**), and MeOH was described tentatively as the (*E*)-isomer **8a** [5] (*Scheme 3*).

In the meantime, single crystals suitable for an X-ray crystal-structure determination were obtained, and the proposed (*Z*)-orientation of the ester groups was unambiguously confirmed (*Fig. 1*,*a*).

Scheme 3



1b (*E*)-**5a** **8a**

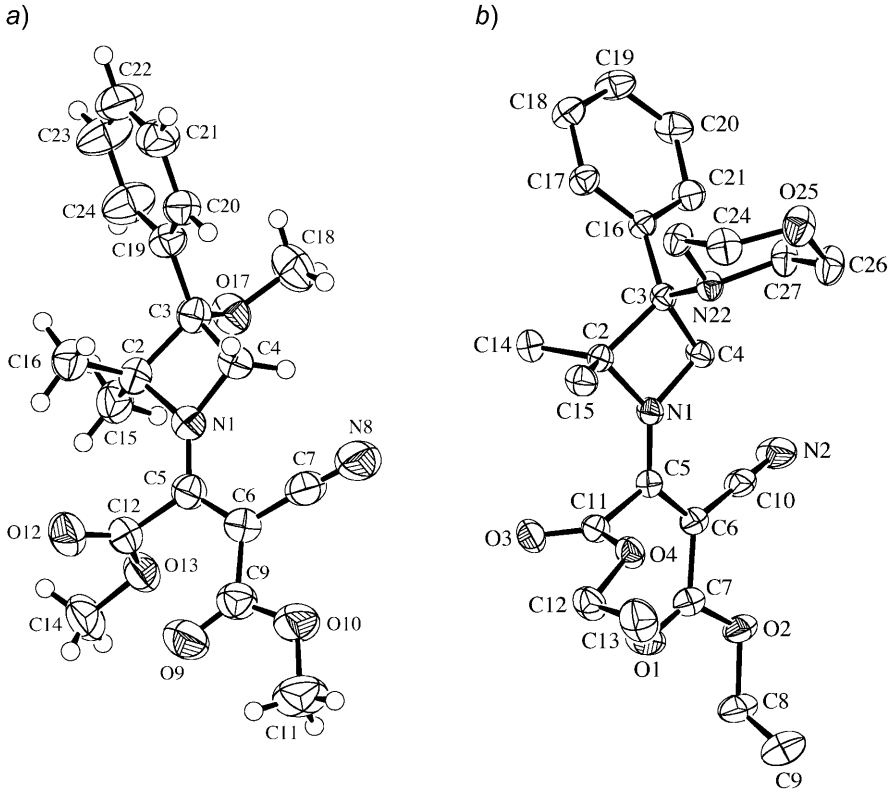


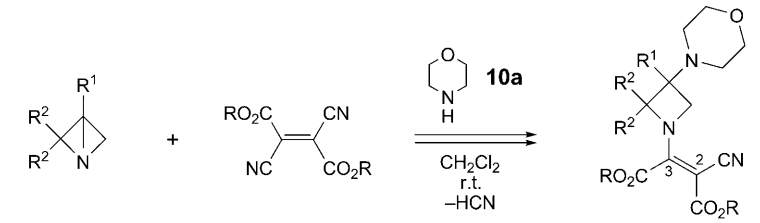
Fig. 1. *ORTEP Plots* [7] *of the molecular structures of* a) **8a** *and* b) **9d** (50% probability ellipsoids, arbitrary numbering of the atoms)

The sequence of reaction steps leading to **8a** and analogous products of type **8** [5] ($R^3X = MeO$; *Scheme* 2) was obvious, as MeOH does not react with (*E*)-**5a**.

On the other hand, in three-component reactions of **1**, (*E*)-**5a**, and secondary amines, both nucleophilic reagents could compete in the addition initiating the reaction. It is worth mentioning that some reactions of NH_3 and diverse amines with

dicyanofumarates have already been described [8][9]. However, the reported structures of the isolated products are contradictory with respect to the (*E*)/(*Z*)-configuration, and, in none of the cases, X-ray crystallography was applied for the determination of the structure. The reactions between differently substituted 1-azabicyclo[1.1.0]butanes **1a**–**1c** and dicyanofumarates (*E*)-**5a**–**5c** in the presence of excess morpholine (**10a**; 1.5 mol-equiv.) gave, in all cases, products of type **9** exclusively (*Scheme 4*). The spectroscopic data were in accordance with these structures, and the most remarkable features were the striking differences of the chemical shifts for the C-atoms of the C=C bond (*e.g.*, in the case of **9d**: δ(C(3)) 156.5, δ(C(2)) 70.8 ppm).

Scheme 4



1a R^1 = Ph, R^2 = H
1b R^1 = Ph, R^2 = Me
1c R^1 = Et, R^2 = H

(*E*)-**5a** R = Me
(*E*)-**5b** R = Et
(*E*)-**5c** R = i-Pr

	R^1	R^2	R
9a	Ph	H	Me
9b	Ph	H	Et
9c	Ph	Me	Me
9d	Ph	Me	Et
9e	Ph	Me	i-Pr
9f	Et	H	Me

In the framework of the present study, the structure **9d** of the product of the reaction of **1b**, (*E*)-**5b**, and **10a** was determined by X-ray crystallography, and the (*E*)-configuration of the C=C bond was established (*Fig. 1,b*)[1]).

The exclusive formation of products **9** indicated that the rate-determining step of the reaction is the nucleophilic attack of **1** onto the C=C bond of **5** *via* a *Michael*-type addition to give the reactive zwitterion of type **7** (*Scheme 2*). The subsequent reaction with **10a** is faster than the alternative ring closure to yield the corresponding ring-enlarged product **6**. As already pointed out [4], the efficiency of the ring closure is strongly dependent on steric and electronic effects of the substituents R^1 and R^2 in **1**, and could be observed only with **1a** (R^1 = Ph, R^2 = H). The successful trapping experiments with morpholine (**10a**) evidenced that, in all cases, independent of the substitution pattern, the zwitterion **7** was formed. The final products **9** are formed *via* elimination of HCN. However, it is not clear which intermediate is responsible for the expulsion of the CN group, although the earlier described formation of the bicyclic

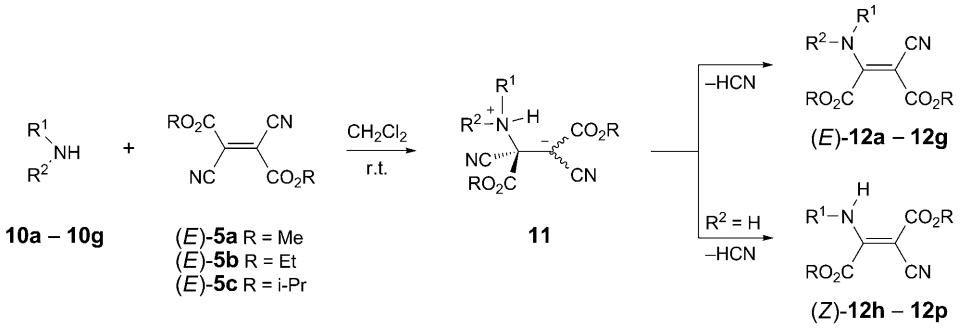
[1]) In [4], the inadequate (*Z*)-configuration of the C=C bond of **10a** was proposed tentatively.

products **6** indicates that the expulsion does not occur in the zwitterion **7**, but only after the addition of **10a**[2]).

In an additional experiment with **1a**, (*E*)-**5a** was replaced by dimethyl dicyanomaleate ((*Z*)-**5a**). The reaction in the presence of **10a** under the conditions described above led to the same product **9a** in a comparable yield. A plausible explanation of this result is based on the assumption that the addition of **10a** occurs onto the zwitterion **7**, which possesses the same stereochemical structure regardless of the configuration of the starting electrophile **5a**.

2.2. *Two-Component Reactions.* Morpholine (**10a**), pyrrolidine (**10b**), dicyclohexylamine (**10c**), cyclohexylamine (**10d**), aniline (**10e**), and (*R*)-1-phenylethylamine (**10f**) were used as nucleophiles (1.5 mol-equiv.) in the reactions with dicyanofumarates (*E*)-**5**. Additionally, the reaction of dimethyl dicyanofumarate ((*E*)-**5a**) with excess NH_3 was performed. In all cases, the reactions in CH_2Cl_2 occurred smoothly at room temperature and yielded selectively a single product. After usual workup and chromatographic purification, most of the products **12** were obtained as crystalline, colorless solids (*Scheme 5* and *Table 1*). The sterically most crowded dicyclohexylamine (**10c**) gave the product **12g** also in a satisfactory yield (43%)[3]).

Scheme 5



The elemental analyses and mass spectra confirmed that the products **12** correspond to 1:1 adducts after elimination of HCN. The spectroscopic data (IR and ^{13}C-NMR) were in good agreement with those of compounds of type **8** and **9**. Again, the C-atoms of the C=C bond show the characteristic chemical shifts of 'push-pull' substituted alkenes (*e.g.*, for **12d**: δ(C(3)) 165.5, δ(C(2)) 70.2 ppm). The structure of **12d** was established by X-ray crystallography, and the (*Z*)-orientation of the ester groups ((*E*)-configuration) was confirmed (*Fig. 2*). Therefore, the configuration of the enamine **12d** corresponded with that established for **8a** and **9d**.

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[2]) In the experiments with **1b** and **1c**, which did not lead to 1-azabicyclo[2.1.1]hexanes **6**, elimination products were not observed.

[3]) This product could not be obtained in analytically pure form because of decomposition during the attempted purification processes and during the storage in $CDCl_3$ solution.

Table 1. *Enamines* **12** *from the Reaction of Amines* **10** *and* NH_3 *with* (*E*)-**5a**–**5c**

10	R^1	R^2	R	(*E*)-**12**	(*Z*)-**12**	Yield [%]
a	$-(CH_2)_2O(CH_2)_2-$		Me	**a**	–	62
			Et	**b**	–	66
			i-Pr	**c**	–	55
b	$-(CH_2)_4-$		Me	**d**	–	61
			Et	**e**	–	34
			i-Pr	**f**	–	67
c	Cyclohexyl	Cyclohexyl	Me	**g**	–	43
d	Cyclohexyl	H	Me	–	**h**	40
			Et	–	**i**	82
			i-Pr	–	**k**	60
e	Ph	H	Me	–	**l**	97
			Et	–	**m**	67
			i-Pr	–	**n**	45
f	Me(Ph)CH (*R*)	H	Me	–	**o** (*R*)	76
	Me(Ph)CH (*S*)	H	Me	–	**o** (*S*)	80
g	H	H	Me	–	**p**	76
	H	H	Et	–	**q**	85

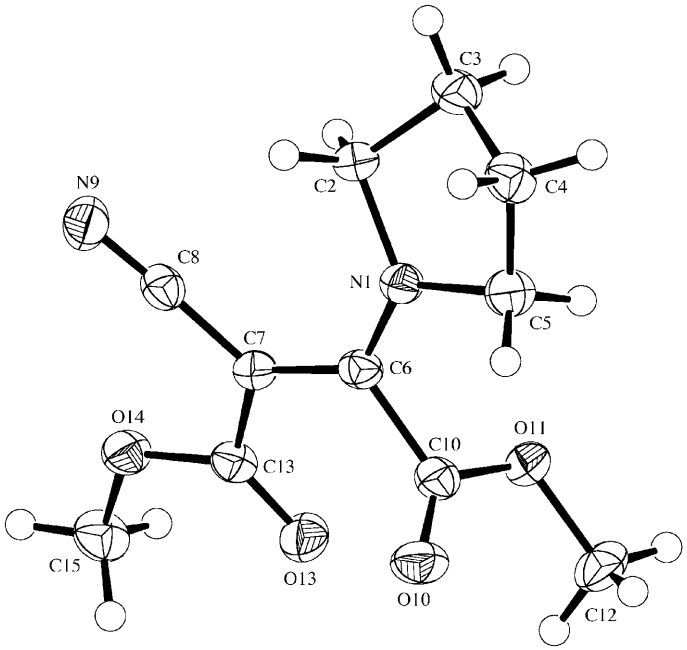


Fig. 2. *ORTEP Plot* [7] *of the molecular structure of* **12d** (50% probability ellipsoids, arbitrary numbering of the atoms)

The comparison of the ^{13}C-NMR data of the products **12a**–**12c** and those of **12d**–**12f** showed a remarkable difference regarding the absorptions of the heterocyclic rings.

Whereas, in the 'morpholine series' **12a**–**12c**, only two signals for four CH_2 groups appear, suggesting a fast rotation about the C(2)–N bond, the spectra of the products **12d**–**12f**, containing the pyrrolidine ring, revealed four separated signals for the four CH_2 groups. An analogous non-equivalency of CH_2 signals was observed for the azetidine ring in **9a** and **9b**.

It is interesting to note that the attempted reactions of (*E*)-**5a** with *N*-methylaniline or diphenylamine under standard conditions (CH_2Cl_2 solution, room temperature, 1.5 mol-equiv. of the amine) did not provide the expected 1:1 product of type **12** even after 4 d. Similarly, the attempted reaction of *N*-methylaniline with (*E*)-**5a** in boiling MeOH was in vain, and, after 8 h, only the starting materials were identified in the ^{1}H-NMR spectrum of the crude mixture.

To examine a possible influence of the configuration of the starting material **5**, an experiment with dimethyl dicyanomaleate ((*Z*)-**5a**) and pyrrolidine (**10b**) was carried out under conditions analogous to those described for the reaction with (*E*)-**5a**. The product obtained in almost the same yield was identical to **12d**. This observation suggests that, after the *Michael*-type addition, the subsequent elimination of HCN occurs from the same intermediate, regardless of the configuration of **5**.

In the series of enamines **12h**–**12n**, which were prepared from fumarates (*E*)-**5a**–**5c** and the primary amines **9d**–**9e**, the spectroscopic data, in general, were in agreement with those observed for **12a**–**12g**. For instance, in the case of **12m**, the IR-absorption bands (KBr) of the ester C=O groups appeared at 1747 and 1671 cm^{-1}, and the most intense band at 1599 cm^{-1} was attributed to the C=C bond. Furthermore, the ^{13}C-NMR spectrum revealed the absorptions of the same group at 167.7 (C(3)) and 74.5 ppm (C(2)). Unexpectedly, the X-ray crystal-structure determination, which was carried out with **12l**, showed that, in this case, the ester groups are (*E*)-oriented, *i.e.*, the enamine is (*Z*)-configured (*Fig. 3*, *a*).

There are two symmetry-independent molecules in the asymmetric unit. The molecules have the same configuration, but differ slightly in the rotational conformations of the Ph rings and the adjacent ester group. In each molecule, the amine H-atom forms an intramolecular H-bond with the O-atom of the ester C=O group at the other end of the C=C bond. This interaction forms a six-membered ring, which can be described by a graph set motif [10] of *S*(6). The amine H-atom in molecule A also forms an intermolecular H-bond with the same ester C=O group of a neighboring molecule B, while molecule B interacts in the same way with molecule A. These interactions thereby link molecules A and B into non-symmetric dimers. Based on the intermolecular interactions alone, the graph set descriptor for this motif is $R_2^2(12)$. A smaller ring with an $R_2^2(4)$ motif is formed *via* the path involving a combination of the intra- and intermolecular interactions.

Based on this result, we attributed also the (*Z*)-configuration ((*E*)-orientation of the ester groups) to all enamines **12h**–**12o** derived from primary amines (*Table 1*). The same conclusion was drawn by *Kudo* for the enamines, which he obtained from the reaction of diethyl 2,3-dicyanofumarate (**5b**) with aromatic amines [9]. His arguments were based on a comparison of the IR absorption of the ester C=O groups in enamines of type **12m** with that of model compounds containing only one ester group, in which no intramolecular H-bonding influences the C=O absorption.

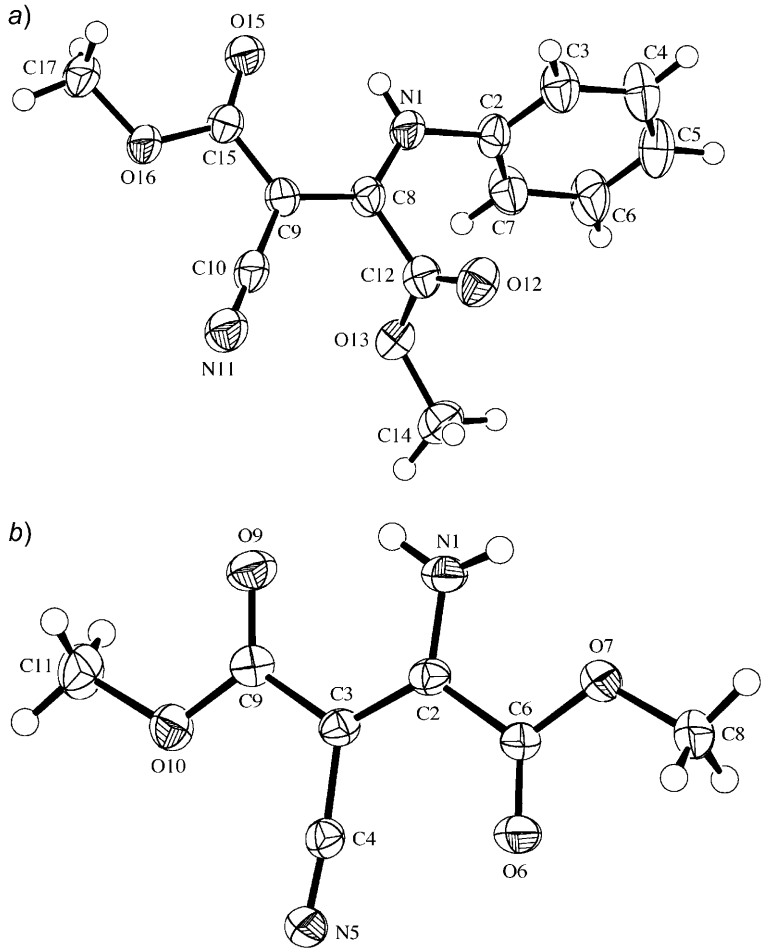


Fig. 3. *ORTEP Plot* [7] *of the molecular structure of* a) *one of the two symmetry-independent molecules of* **12l** *and* b) **12p** (50% probability ellipsoids, arbitrary numbering of the atoms)

With respect to the potential exploration of enamines of type **12** in heterocyclic synthesis, it was of interest to prepare a model compound of this type with a chiral amino group. For this reason, (*E*)-**5a** was reacted with (*R*)- or (*S*)-1-phenylethylamine (**9f**) under the usual conditions. The pure products (*R*,*Z*)-**12o** and (*S*,*Z*)-**12o**, obtained after chromatography and crystallization from MeOH, were optically active.

In an extension of the experiments with secondary and primary amines, fumarates (*E*)-**5a** and (*E*)-**5b**, respectively, were reacted with NH_3 in CH_2Cl_2. A stream of NH_3 gas was bubbled through the suspension at room temperature, until the undissolved (*E*)-**5a** or (*E*)-**5b** completely disappeared. Under this condition, the only product formed was **12p** and **12q**, respectively, and no aminolysis of an ester group was observed. The crystal-structure analysis of **12p** confirmed the expected (*Z*)-config-

(*R*,*Z*)-**12o** (*S*,*Z*)-**12o**

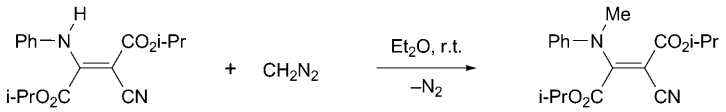
uration of the enamine (*Fig. 3*, *b*). In analogy to the series **12h**–**12o**, this result confirms the decisive influence of the H-bonding on the configuration of the products formed *via Michael* addition and elimination of HCN.

The amine H-atoms are involved in intra- and intermolecular H-bonds. One of these H-atoms forms bifurcated H-bonds. One is an intramolecular interaction with the O-atom of an adjacent ester C=O group to form a six-membered loop, which can be described by a graph set motif [10] of $S(6)$. The other interaction is with the other ester C=O group of a neighboring molecule. This interaction links the molecules into extended chains which run parallel to the [010] direction and can be described by a graph set motif of $C(5)$. The other amine H-atom forms an intermolecular H-bond with the N-atom of the CN group of the same neighboring molecule, also partaking in the same chain formation, and the interaction yields a graph set motif of $C(6)$. The combination of both intermolecular interactions forms another loop with a graph set motif of $R_2^2(9)$.

It is well-established that enamines efficiently undergo [2 + 3] cycloadditions with different 1,3-dipoles [6][11]. In contrast to 2,3-dicyanofumarates (*E*)-**5**, which easily react with thiocarbonyl *S*-methanides [12], the enamines **12** turned out to be inert towards 2,2,4,4-tetramethyl-3-thioxocyclobutanone *S*-methanide. Similarly, the reactions of **12a** and **12h** with CH_2N_2 in Et_2O at room temperature were in vain. Unexpectedly, the analogous reaction with **12l** led to the formation of a new product, of which the ^{1}H-NMR spectrum showed a *singlet* at 3.67 ppm, attributed to a MeN group[4]). The IR spectrum of this product was very similar to the corresponding spectra of the products **12a**–**12g**, confirming the presence of the enamine structure. Based on all spectroscopic evidences, the structure of the enamine (*Z*)-**12r** was proposed (*Scheme 6*).

The observed *N*-methylation shows that the presence of three strongly electron-withdrawing substituents enhances the acidity of the PhNH group and thereby enables

Scheme 6



(*Z*)-**12n** (*Z*)-**12r**

[4]) Some preliminary experiments with CH_2N_2 and selected enamines **12** were performed by Dr. *Korany A. Alli* (on leave from the National Research Center, Dokki, Cairo, Egypt).

the reaction with CH_2N_2, resulting in the *N*-methylation, analogous to the *O*-methylation of carboxylic acids and phenols. To the best of our knowledge, this is the first example of the methylation of a secondary amino group with CH_2N_2. However, this reaction is limited to amino groups bearing aromatic residues.

3. Conclusions. – The presented results show that electron-deficient dicyanofumarates (*E*)-**5** and dicyanomaleates (*Z*)-**5** easily react as *Michael* acceptors with different types of amines. In the case of primary and secondary amines, spontaneous elimination of HCN from the initially formed *Michael* adducts leads to only one isomer of the corresponding enamines of type **12** in a non-stereospecific but stereoselective manner. On the other hand, the highly nucleophilic 1-azabicyclo[1.1.0]butanes **1** form intermediate zwitterions of type **7**, which either undergo ring closure to 1-azabicyclo[2.1.1]hexane derivatives **6** or, in the presence of MeOH or morpholine (**10a**), are trapped to yield azetidine-derived enamines of type **8** or **9**, respectively. In both reaction types, *i.e.*, three- or two-component reactions with secondary amines, only (*E*)-configured enamines (*i.e.*, **9** and **12a**–**12g**), bearing the ester groups in (*Z*)-orientation, are formed. On the other hand, the two-component reactions with primary amines and NH_3 yield the corresponding (*Z*)-configured enamines **12h**–**12q**, which are thermodynamically favored because of the presence of an intramolecular H-bond. The described procedure opens an easy access to a less known type of enamines, which are potentially useful building blocks for the formation of diverse heterocycles. In this context, the recently published synthesis of a fused (2-oxopyridazin-3-ylidene)cyanoacetate from dicyanofumarates and cyclic 1,2-diamines [13a,b], as well as oxadiazinone and pyrazolone derivatives from carbohydrazides and diethyl dicyanofumarate [13c] are of interest. In both cases, the final products were formed spontaneously without isolation of the initially formed enamines.

On the other hand, this study showed that enamines of type **12** do not undergo 1,3-dipolar cycloadditions with thiocarbonyl ylides and CH_2N_2. In the latter case, however, the unexpected methylation of the Ph-substituted amino group occurred quantitatively.

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Experimental Part

1. *General*. M.p.: *Melt-Temp. II* (*Aldrich*); uncorrected. Optical rotations: automatic digital polarimeter *Krüss P3002RS*. IR Spectra: *NEXUS FT-IR* spectrophotometer; in KBr or as neat; absorptions in cm^{-1}. ^1H- and ^{13}C-NMR spectra: *Tesla BS567A* (80 and 20 MHz, resp.) or *Bruker AC 300* instrument (300 and 75.5 MHz, resp.); in $CDCl_3$; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. The multiplicity of the ^{13}C signals was deduced from DEPT spectra. MS: *Finnigan MAT-90* or *Finnigan SSQ-700* instruments. HR-MS: *Finnigan MAT-95*. Elemental analyses were performed in the Analytical Laboratory of the University of Zürich or in the Laboratory of the Polish Academy of Sciences (CBMiMM) in Łódź.

2. *Starting Materials*. All solvents and amines **10a**–**10f** are commercially available reagents, and they were purified before usage according to general methods. Dialkyl (*E*)-1,2-dicyanobut-2-enedioates (dicyanofumarates) **5a**–**5c** were obtained from the corresponding alkyl cyanoacetates and $SOCl_2$, according to a known protocol [14]. *Dimethyl (*Z*)-1,2-dicyanobut-2-enedioate* (dicyanomaleate; (*Z*)-**5a**)

was prepared according to the published photolysis protocol [15]. For the syntheses of 1-azabicyclo[1.1.0]butanes **1**, known procedures were applied: *3-phenyl-1-azabicyclo[1.1.0]butane* (**1a**) [16], *2,2-dimethyl-3-phenyl-1-azabicyclo[1.1.0]butane* (**1b**) [16], and *3-ethyl-1-azabicyclo[1.1.0]butane* (**1c**) [17].

3. *Three-Component Reactions with* **1a**–**1c**, **10a**, *and* (*E*)-**5a**–**5c**. *General Procedure.* 1-Azabicyclo[1.1.0]butane **1** (1 mmol) and morpholine (**10a**) (87 mg, 1 mmol) were dissolved in 3 ml of CH_2Cl_2 and stirred magnetically at r.t. To this soln., the corresponding (*Z*)-**5** (1 mmol) was added in small portions and, when the addition was complete, stirring was continued at r.t. After 30 min, the solvent was evaporated to dryness, and the residue was analyzed by ^{1}H-NMR spectroscopy. Pure products were obtained after crystallization of the crude mixture; in some cases, column chromatography (CC) or prep. TLC (PLC, SiO_2) was applied prior to crystallization.

*Dimethyl (*E*)-2-Cyano-3-[3-(morpholin-4-yl)-3-phenylazetidin-1-yl]but-2-enedioate* (**9a**). Yield 236 mg (61%). Colorless crystals. M.p. 156–158° (MeOH). IR (KBr): 2206*m* (CN), 1749*s* (C=O), 1702*s* (C=O), 1570v*s* (C=C), 1447*m*, 1437*m*, 1305*s*, 1264v*s*, 1196*m*, 1150*m*, 1133*m*, 1116*m*, 769*m*, 708*m*. ^{1}H-NMR ($CDCl_3$): 7.44–7.33, 7.06–7.03 (2*m*, 5 arom. H); 4.94, 4.91 (*AB*, *J* = 11.6, CH_2(azetidine)); 4.43, 4.39 (*AB*, *J* = 9.6, CH_2(azetidine)); 3.93, 3.72 (2*s*, 2 MeO); 3.73–3.66 (*m*, 2 OC*H*$_2$CH$_2$N); 2.29–2.24 (*m*, 2 OCH$_2$C*H*$_2$N). ^{13}C-NMR ($CDCl_3$): 165.1, 161.8, 158.2 (3*s*, C(3), 2 C=O); 134.5 (*s*, 1 arom. C); 128.3, 127.2 (2*d*, 5 arom. CH); 116.9 (*s*, CN); 70.3 (*s*, C(3′)); 66.8 (*t*, 2 OCH$_2$CH$_2$N); 63.3 (*s*, C(2)); 62.6, 61.8 (2*t*, 2 CH$_2$(azetidine)); 53.7, 52.1 (2*q*, 2 MeO); 46.3 (2*t*, 2 OCH$_2$CH$_2$N). CI-MS: 387 (23), 386 (100, [*M* + 1]$^+$), 189 (9), 188 (6). Anal. calc. for $C_{20}H_{23}N_3O_5$ (385.41): C 62.33, H 6.01, N 10.90; found: C 62.21, H 5.94, N 10.84.

*Diethyl (*E*)-2-Cyano-3-[3-(morpholin-4-yl)-3-phenylazetidin-1-yl]but-2-enedioate* (**9b**). Yield 396 mg (96%). Colorless crystals. M.p. 170–172° (MeOH/CH_2Cl_2). IR (KBr): 2205*m* (CN), 1743*s* (C=O), 1701*s* (C=O), 1567v*s* (C=C), 1448*m*, 1369*w*, 1299*s*, 1259*s* (br.), 1151*m*, 1131*m*, 1116*m*, 1027*m*, 769*m*, 714*m*. ^{1}H-NMR ($CDCl_3$): 7.44–7.33, 7.07–7.04 (2*m*, 5 arom. H); 4.95, 4.87 (*AB*, *J* = 11.4, CH_2(azetidine)); 4.43, 4.39 (*AB*, *J* = 10.6, CH_2(azetidine)); 4.39, 4.17 (2*q*, *J* = 7.1, 2 MeC*H*$_2$O); 3.71–3.67 (*m*, 2 OC*H*$_2$CH$_2$N); 2.31–2.22 (*m*, 2 OCH$_2$C*H*$_2$N); 1.37, 1.27 (2*q*, *J* = 7.1, 2 *Me*CH$_2$O). ^{13}C-NMR ($CDCl_3$): 164.5, 161.3, 158.4 (3*s*, C(3), 2 C=O); 134.6 (*s*, 1 arom. C); 128.3, 127.2 (2*d*, 5 arom. CH); 117.0 (*s*, CN); 70.6 (*s*, C(3′)); 66.8 (*t*, 2 OCH$_2$CH$_2$N); 63.3 (*s*, C(2)); 63.2, 62.6 (2*t*, 2 CH$_2$(azetidine)); 61.6, 61.0 (2*t*, 2 MeCH$_2$O); 46.3 (*t*, 2 OCH$_2$CH$_2$N); 14.3, 13.9 (2*q*, 2 *Me*CH$_2$O). CI-MS: 415 (24), 414 (100, [*M* + 1]$^+$), 189 (8), 188 (6). Anal. calc. for $C_{22}H_{27}N_3O_5$ (413.47): C 63.91, H 6.58, N 10.16; found: C 63.63, H 6.55, N 10.12.

*Dimethyl (*E*)-2-Cyano-3-[2,2-dimethyl-3-(morpholin-4-yl)-3-phenylazetidin-1-yl]but-2-enedioate* (**9c**). CC (SiO_2; CH_2Cl_2/MeOH 98.5:1.5). Yield 217 mg (52%). Colorless crystals. M.p. 198–200° (MeOH/CH_2Cl_2). IR (KBr): 2204*m* (CN), 1749*s* (C=O), 1702*s* (C=O), 1541v*s* (C=C), 1447*m* (br.), 1372*w*, 1290*s*, 1253v*s* (br.), 1145*s*, 1115*s*, 768*m*, 715*m*. ^{1}H-NMR ($CDCl_3$): 7.42–7.31, 7.05–7.03 (2*m*, 5 arom. H); 5.03, 4.88 (*AB*, *J* = 11.8, CH_2(azetidine)); 3.90, 3.72 (2*s*, 2 MeO); 3.81–3.68 (*m*, 2 OC*H*$_2$CH$_2$N); 2.42–2.25, 2.23–2.19 (2*m*, 2 OCH$_2$C*H*$_2$N); 1.75, 1.38 (2*s*, 2 Me). ^{13}C-NMR ($CDCl_3$): 165.3, 162.7, 156.1 (3*s*, C(3), 2 C=O); 132.9 (*s*, 1 arom. C); 128.0, 127.9 (2*d*, 5 arom. CH); 117.9 (*s*, CN); 80.5 (*s*, C(3′)); 70.9 (*s*, C(2′)); 70.5 (*s*, C(2)); 67.1 (*t*, 2 OCH$_2$CH$_2$N); 56.8 (*t*, 2 CH$_2$(azetidine)); 53.4, 52.0 (2*q*, 2 MeO); 49.5 (*t*, 2 OCH$_2$CH$_2$N); 27.7, 23.0 (2*q*, 2 Me). CI-MS: 415 (24), 414 (100, [*M* + 1]$^+$), 189 (8), 188 (6). Anal. calc. for $C_{22}H_{27}N_3O_5$ (413.47): C 63.91, H 6.58, N 10.16; found: C 63.63, H 6.48, N 10.13.

*Diethyl (*E*)-2-Cyano-3-[2,2-dimethyl-3-(morpholin-4-yl)-3-phenylazetidin-1-yl]but-2-enedioate* (**9d**). CC (SiO_2; CH_2Cl_2/MeOH 98.5:1.5). Yield 238 mg (54%). Colorless crystals. M.p. 172–174° (MeOH). IR (KBr): 2203*m* (CN), 1743*s* (C=O), 1702*s* (C=O), 1541v*s* (C=C), 1447*m* (br.), 1368*w*, 1285*m*, 1251v*s* (br.), 1146*s*, 1115*s*, 1027*m*, 767*w*, 713*w*. ^{1}H-NMR ($CDCl_3$): 7.42–7.31, 7.06–7.03 (2*m*, 5 arom. H); 5.04, 4.87 (*AB*, *J* = 11.8, CH_2(azetidine)); 4.36, 4.17 (2*q*, *J* = 7.1, 2 MeC*H*$_2$O); 3.71–3.65 (*m*, 2 OC*H*$_2$CH$_2$N); 2.44–2.39, 2.26–2.21 (2*m*, 2 OCH$_2$C*H*$_2$N); 1.76, 1.38 (2*s*, 2 Me); 1.36, 1.28 (2*q*, *J* = 7.1, 2 *Me*CH$_2$O). ^{13}C-NMR ($CDCl_3$): 164.8, 162.3, 156.5 (3*s*, C(3), 2 C=O); 133.0 (*s*, 1 arom. C); 128.4, 128.0 (2*d*, 5 arom. CH); 118.0 (*s*, CN); 80.4 (*s*, C(3′)); 70.8 (*s*, C(2)); 67.1 (*s*, C(2′)); 67.0 (*t*, 2 OCH$_2$CH$_2$N); 63.1, 60.1 (2*t*, 2 MeCH$_2$O); 56.7 (*t*, CH$_2$(azetidine)); 49.5 (*t*, 2 OCH$_2$CH$_2$N); 27.7, 23.0 (2*q*, 2 Me); 14.4, 13.6 (2*q*, 2 *Me*CH$_2$O). CI-MS: 443 (27), 442 (100, [*M* + 1]$^+$), 189 (10), 188 (8). Anal. calc. for $C_{24}H_{31}N_3O_5$ (441.52): C 65.29, H 7.08, N 9.52; found: C 64.68, H 6.92, N 9.53.

*Diisopropyl (*E*)-2-Cyano-3-[2,2-dimethyl-3-(morpholin-4-yl)-3-phenylazetidin-1-yl]but-2-enedioate* (**9e**). CC (SiO_2; CH_2Cl_2/MeOH 99:1). Yield 310 mg (66%). Colorless crystals. M.p. 164–167° (MeOH). IR (KBr): 2202*m* (CN), 1741*s* (C=O), 1698*s* (C=O), 1538v*s* (C=C), 1456*m* (br.), 1374*w*, 1282*m*, 1251v*s* (br.), 1151*s*, 1106*s*, 766*w*, 715*w*. ^{1}H-NMR ($CDCl_3$): 7.44–7.30, 7.06–7.02 (2*m*, 5 arom. H); 5.29–5.11 (*m*, Me_2CHO); 5.04–4.94 (*m*, Me_2CHO); 5.01, 4.88 (*AB*, *J* = 11.9, CH_2(azetidine)); 3.71–3.69 (*m*, 2 OCH_2CH_2N); 2.44–2.34, 2.26–2.22 (2*m*, 2 OCH_2CH_2N); 1.79, 1.40 (2*s*, 2 Me); 1.36, 1.34, 1.27, 1.25 (4*d*, *J* = 7.1, 2 Me_2CHO). ^{13}C-NMR ($CDCl_3$): 164.0, 161.9, 156.8 (3*s*, C(3), 2 C=O); 133.2 (*s*, 1 arom. C); 128.4, 128.0 (2*d*, 5 arom. CH); 118.0 (*s*, CN); 71.6, 68.2 (2*d*, 2 Me_2CH); 71.7 (*s*, C(3′)); 70.8 (*s*, C(2)); 68.3 (*s*, C(2′)); 67.1 (*t*, 2 OCH_2CH_2N); 63.1, 60.1 (2*t*, 2 $MeCH_2O$); 56.6 (*t*, CH_2(azetidine)); 49.5 (*t*, 2 OCH_2CH_2N); 27.9, 23.2 (2*q*, 2 Me); 21.9, 21.4 (2*q*, 2 Me_2CHO). CI-MS: 471 (31), 470 (100, $[M+1]^+$), 189 (7), 188 (4). Anal. calc. for $C_{26}H_{35}N_3O_5$ (469.58): C 66.50, H 7.51, N 8.95; found: C 66.25, H 6.91, N 8.84.

*Dimethyl (*E*)-2-Cyano-3-[3-ethyl-3-(morpholin-4-yl)azetidin-1-yl]but-2-enedioate* (**9f**). PLC (SiO_2; $CHCl_3$/MeOH 99:1). Yield 272 mg (81%). Colorless crystals. M.p. 104–106° (MeOH). IR (KBr): 2205*s*, 1748v*s* (C=O), 1705v*s* (C=O), 1566v*s* (C=C), 1456*s*, 1437*s*, 1293v*s*, 1261v*s* (br.), 1196*m*, 1150*m*, 1117*s* (br.), 1019*m*, 756*s*, 666*m*. ^{1}H-NMR ($CDCl_3$): 4.53, 4.39 (*AB*, *J* = 11.2, CH_2(azetidine)); 4.07, 3.89 (*AB*, *J* = 9.6, CH_2(azetidine)); 3.92, 3.73 (2*s*, 2 MeO); 3.73–3.69 (*m*, 2 OCH_2CH_2N); 2.51 (br. *s*, 2 OCH_2CH_2N); 1.76 (*q*, *J* = 7.4, $MeCH_2$); 1.02 (*t*, *J* = 7.4, $MeCH_2$). ^{13}C-NMR ($CDCl_3$): 165.1, 161.8, 158.4 (3*s*, C(3), 2 C=O); 116.8 (*s*, CN); 70.3 (*s*, C(3′)); 67.1 (*t*, 2 OCH_2CH_2N); 60.5 (*s*, C(2)); 59.9, 59.2 (2*t*, 2 CH_2(azetidine)); 53.6, 52.1 (2*q*, 2 MeO); 45.9 (*t*, 2 OCH_2CH_2N); 24.0 (*t*, $MeCH_2$); 8.3 (*q*, $MeCH_2$). ESI-MS: 360 (100, $[M+Na]^+$). Anal. calc. for $C_{16}H_{23}N_3O_5$ (337.38): C 56.96, H 6.87, N 12.45; found: C 56.98, H 6.83, N 12.18.

4. *Two-Component Reactions with* **10a**–**10f** *and* (*E*)-**5a**–**5c**. *General Procedure.* To a magnetically stirred soln. of the corresponding dialkyl dicyanofumarate **5** (1 mmol) in CH_2Cl_2 (2 ml) at r.t., a soln. of the appropriate amine **10** (1.1 mmol) in CH_2Cl_2 (2 ml) was added dropwise. When the addition was complete, stirring was continued for 15 min, and then the solvent was evaporated to dryness. The residue was analyzed by ^{1}H-NMR spectroscopy, and the crude product was purified either by PLC (SiO_2) or by crystallization from MeOH in the refrigerator. Reported yields refer to products isolated from the crude mixture.

*Dimethyl (*E*)-2-Cyano-3-(morpholin-4-yl)but-2-enedioate* (**12a**). Yield 157 mg (62%). Pale yellow crystals. M.p. 102–104° (MeOH). IR (KBr): 2002*s* (CN), 1755*s* (C=O), 1702*s* (C=O), 1560v*s* (C=C), 1448*s* (br.), 1295*s*, 1281*s*, 1264*s*, 1225*m*, 1195*w*, 1129*s*, 1112*m*, 1032*m*, 1021*m*, 899*w*, 770*w*, 714*w*. ^{1}H-NMR ($CDCl_3$): 4.20–3.60 (*m*, 2 OCH_2CH_2N); 3.92, 3.78 (2*s*, 2 MeO). ^{13}C-NMR ($CDCl_3$): 165.4, 163.2, 159.7 (3*s*, C(3), 2 C=O); 117.1 (*s*, CN); 72.4 (*s*, C(2)); 66.1 (*t*, 2 OCH_2CH_2N); 53.6, 52.2 (2*q*, 2 MeO); 50.5 (*t*, 2 OCH_2CH_2N). EI-MS: 255 (10), 254 (69, M^+), 223 (42), 222 (42), 221 (11), 207 (14), 196 (13), 195 (100), 194 (11), 179 (10), 166 (15), 165 (33), 164 (21), 163 (20), 138 (10), 136 (30), 135 (19), 107 (12), 85 (23), 78 (13). HR-EI-MS: 254.0904 (M^+, $C_{11}H_{14}N_2O_5^+$; calc. 254.0903). Anal. calc. for $C_{11}H_{14}N_2O_5$ (254.24): C 51.97, H 5.55, N 11.02; found: C 51.73, H 5.41, N 11.30.

*Diethyl (*E*)-2-Cyano-3-(morpholin-4-yl)but-2-enedioate* (**12b**). Yield 185 mg (66%). PLC (SiO_2; $CHCl_3$/MeOH 97:3). Colorless, thick oil. IR (KBr): 2003*s* (CN), 1740*s* (C=O), 1702*s* (C=O), 1557v*s* (C=C), 1445*s* (br.), 1389*m*, 1367*m*, 1295*s*, 1287*s*, 1264*s*, 1225*m*, 1128*s*, 1105*s*, 1035*s*, 984*w*, 859*m*, 769*w*, 720*w*. ^{1}H-NMR ($CDCl_3$): 4.38, 4.20 (2*q*, *J* = 7.2, $MeCH_2O$); 3.85–3.66 (*m*, 2 OCH_2CH_2N); 1.37, 1.30 (2*q*, 2 $MeCH_2O$). ^{13}C-NMR ($CDCl_3$): 164.6, 162.5, 159.8 (3*s*, C(3), 2 C=O); 116.9 (*s*, CN); 72.3 (*s*, C(2)); 65.9 (*t*, 2 OCH_2CH_2N); 62.7, 60.7 (2*t*, 2 $MeCH_2O$); 50.2 (*t*, 2 OCH_2CH_2N); 13.7, 13.2 (2*q*, 2 $MeCH_2O$). EI-MS: 283 (7), 282 (41, M^+), 237 (25), 236 (14), 209 (56), 208 (10), 207 (57), 181 (40), 179 (38), 166 (16), 164 (13), 151 (51), 138 (29), 137 (19), 136 (20), 130 (10), 125 (37), 124 (14), 123 (11), 114 (34), 107 (39), 85 (11), 85 (17), 80 (24), 79 (100). HR-EI-MS: 282.1211 (M^+, $C_{13}H_{18}N_2O_5^+$; calc. 282.1216).

*Diisopropyl (*E*)-2-Cyano-3-(morpholin-4-yl)but-2-enedioate* (**12c**). Yield 170 mg (55%). Yellowish crystals. M.p. 130–132° (MeOH). IR (KBr): 2984*m*, 2202*s* (CN), 1742v*s* (C=O), 1702v*s* (C=O), 1549v*s* (C=C), 1440*m*, 1285*s*, 1267*s*, 1235*m*, 1148*m*, 1121*m*, 1102*m*, 1037*m*, 1001*m*, 884*w*, 771*w*, 719*w*. ^{1}H-NMR ($CDCl_3$): 5.22, 4.98 (2 *sept.*, *J* = 7.2, 2 Me_2CHO); 4.00–3.55 (*m*, 2 OCH_2CH_2N); 1.35, 1.25 (2*d*, *J* = 7.2, 2 Me_2CHO). ^{13}C-NMR ($CDCl_3$): 164.2, 162.1, 160.2 (3*s*, C(3), 2 C=O); 117.2 (*s*, CN); 73.1 (*s*, C(2)); 71.1, 68.5 (2*d*, 2 Me_2CHO); 66.2 (*t*, 2 OCH_2CH_2N); 50.1 (*t*, 2 OCH_2CH_2N); 21.5, 21.1 (2*q*, 2 Me_2CHO). EI-

MS: 311 (17), 310 (39, M^+), 226 (10), 225 (75), 210 (14), 209 (100), 208 (41), 207 (69), 182 (23), 181 (83), 179 (10), 166 (14), 153 (11), 151 (16), 138 (42), 137 (30). HR-EI-MS: 310.1528 (M^+, $C_{15}H_{22}N_2O_5^+$; calc. 310.1529). Anal. calc. for $C_{15}H_{22}N_2O_5$ (310.35): C 58.05, H 7.15, N 9.03; found: C 57.98, H 7.09, N 9.04.

*Dimethyl (*E*)-2-Cyano-3-(pyrrolidin-1-yl)but-2-enedioate* (**12d**). Yield 145 mg (61%). Colorless crystals. M.p. 128–130° (MeOH). IR (KBr): 2987*w*, 2198*s* (CN), 1750v*s* (C=O), 1704v*s* (C=O), 1552v*s* (C=C), 1458*m*, 1440*m*, 1287*s*, 1261*m*, 1232*m*, 1196*m*, 1128*s*, 1023*w*, 981*w*, 911*w*, 858*w*, 768*w*, 728*w*. ^{1}H-NMR ($CDCl_3$): 4.20–3.81, 3.79–3.32 (2*m*, CH_2NCH_2); 3.96, 3.75 (2*s*, 2 MeO); 2.30–1.75 (*m*, CH_2CH_2). ^{13}C-NMR ($CDCl_3$): 165.5, 163.0, 157.4 (3*s*, C(3), 2 C=O); 117.7 (*s*, CN); 70.2 (*s*, C(2)); 52.8, 51.4 (2*t*, CH_2NCH_2); 51.0, 50.3 (2*q*, 2 MeO); 24.9, 23.9 (2*t*, CH_2CH_2). ESI-MS: 261 (100, $[M+Na]^+$). EI-MS: 239 (7), 238 (47, M^+), 207 (35), 206 (35), 191 (16), 180 (12), 179 (100), 178 (10), 148 (32), 147 (10), 120 (83), 119 (20), 93 (16). HR-EI-MS: 238.0954 (M^+, $C_{11}H_{14}N_2O_4^+$; calc. 238.0954). Anal. calc. for $C_{11}H_{14}N_2O_4$ (238.25): C 55.46, H 5.92, N 11.76; found: C 55.47, H 5.96, N 11.72.

*Diethyl (*E*)-2-Cyano-3-(pyrrolidin-1-yl)but-2-enedioate* (**12e**). Yield 90 mg (34%). Yellowish crystals. M.p. 69–71° (MeOH). IR (KBr): 2984*w*, 2001*s* (CN), 1741*s* (C=O), 1692*s* (C=O), 1557v*s* (C=C), 1458*w*, 1277*s*, 1254*s*, 1133*m* (br.), 1108*m*, 1029*w*, 769*w*, 736*w*. ^{1}H-NMR ($CDCl_3$): 4.38, 4.20 (2*q*, $J=7.2$, MeCH_2O); 4.20–3.20 (br. *m*, CH_2NCH_2); 2.22–1.70 (br. *m*, CH_2CH_2); 1.38, 1.29 (2*t*, $J=7.2$, 2 *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 165.3, 162.9, 157.9 (3*s*, C(3), 2 C=O); 118.1 (*s*, CN); 71.2 (*s*, C(2)); 62.6, 60.6 (2*t*, CH_2NCH_2); 51.0, 50.6 (2*t*, 2 MeCH_2O); 25.2, 24.3 (2*t*, CH_2CH_2); 14.0, 13.4 (2*q*, 2 *Me*CH_2O). ESI-MS: 289 (100, $[M+Na]^+$). EI-MS: 267 (8), 266 (47, M^+), 237 (16), 221 (27), 220 (27), 194 (12), 193 (87), 192 (22), 191 (100), 165 (52), 164 (11), 148 (11), 137 (13), 121 (24), 120 (47), 119 (12), 79 (14). HR-EI-MS: 266.1267 (M^+, $C_{13}H_{18}N_2O_4^+$; calc. 266.1267). Anal. calc. for $C_{13}H_{18}N_2O_4$ (266.30): C 58.64, H 6.81, N 10.52; found: C 58.57, H 6.81, N 10.64.

*Diisopropyl (*E*)-2-Cyano-3-(pyrrolidin-1-yl)but-2-enedioate* (**12f**). Yield 197 mg (67%). Colorless crystals. M.p. 97–99° (MeOH). IR (KBr): 2980*m*, 2202*m* (CN), 1741v*s* (C=O), 1692v*s* (C=O), 1556v*s* (C=C), 1456*m*, 1343*w*, 1282*s*, 1263*m*, 1180*w*, 1145*m*, 1235*m*, 1106*m*, 769*w*, 736*w*. ^{1}H-NMR ($CDCl_3$): 5.27, 5.01 (2 *sept.*, $J=6.3$, 2 Me_2CHO); 4.05–3.90, 3.60–3.45 (2*m*, CH_2NCH_2); 2.15–1.85 (*m*, CH_2CH_2); 1.35, 1.26 (2*d*, $J=6.3$, 2 *Me*$_2$CHO). ^{13}C-NMR ($CDCl_3$): 164.7, 162.4, 158.1 (3*s*, C(3), 2 C=O); 118.3 (*s*, CN); 71.8 (*s*, C(2)); 70.9, 68.2 (2*d*, 2 Me_2CHO); 50.8 (*t*, CH_2NCH_2); 25.3, 24.5 (2*t*, CH_2CH_2); 21.7, 21.3 (2*q*, 2 *Me*$_2$CHO). EI-MS: 295 (8), 294 (43, M^+), 209 (71), 207 (23), 194 (12), 193 (96), 192 (74), 191 (65), 166 (25), 165 (100), 164 (48), 148 (32), 137 (22), 122 (31), 121 (26), 119 (10), 79 (12). HR-EI-MS: 294.1577 (M^+, $C_{15}H_{22}N_2O_4^+$; calc. 294.1580). Anal. calc. for $C_{15}H_{22}N_2O_4$ (294.35): C 61.21, H 7.53, N 9.52; found: C 60.89, H 7.50, N 9.54.

*Dimethyl (*E*)-2-Cyano-3-(dicyclohexylamino)but-2-enedioate* (**12g**)[5]). Yield 150 mg (43%). Yellowish, viscous oil. IR (KBr): 2941*m*, 2860*m*, 2205*m* (CN), 1737*s* (C=O), 1690v*s* (C=O), 1541v*s* (C=C), 1440v*s*, 1315*m*, 1238*s*, 1186*m*, 1126*s*, 1025*m*, 775*w*, 751*w*. ^{1}H-NMR ($CDCl_3$): 3.84, 3.69 (2*s*, 2 MeO); 3.11 (br. *m*, 2 CHN); 2.15–1.10 (br. *m*, 10 CH_2(cyclohexyl)). ^{13}C-NMR ($CDCl_3$): 168.1, 167.5, 164.1 (3*s*, C(3), 2 C=O); 121.9 (*s*, CN); 73.1 (*s*, C(2)); 53.9 (*d*, 2 CHN); 52.2, 51.1 (2*q*, 2 MeO), 29.3 (*t*, 4 CH_2(cyclohexyl)); 24.8 (*t*, 2 CH_2(cyclohexyl)); 24.6 (*t*, 4 CH_2(cyclohexyl)).

*Dimethyl (*Z*)-2-Cyano-3-(cyclohexylamino)but-2-enedioate* (**12h**). Yield 115 mg (40%). Colorless crystals. M.p. 100–104° (MeOH). IR (KBr): 3256*m* (br.), 2946*m*, 2204*m* (CN), 1751v*s* (C=O), 1704v*s* (C=O), 1588v*s* (C=C), 1446*m* (br.), 1370*w*, 1300*s*, 1245*s*, 1191*m*, 1133*s*, 1087*w*, 773*w*, 734*w*. ^{1}H-NMR ($CDCl_3$): 9.50 (br. *s*, NH); 3.95, 3.76 (2*s*, 2 MeO); 3.25 (br. *m*, CHN); 2.10–1.05 (br. *m*, 5 CH_2(cyclohexyl)). ^{13}C-NMR ($CDCl_3$): 168.4, 161.4, 160.3 (3*s*, C(3), 2 C=O); 116.5 (*s*, CN); 69.4 (*s*, C(2)); 56.2 (*d*, CHN); 55.6, 51.6 (2*q*, 2 MeO); 33.3 (*t*, 2 CH_2(cyclohexyl)); 24.5 (*t*, 2 CH_2(cyclohexyl)); 23.7 (*t*, CH_2(cyclohexyl)). EI-MS: 267 (13), 266 (73, M^+), 235 (16), 234 (24), 223 (31), 219 (14), 207 (57), 206 (14), 205 (12), 202 (15), 192 (12), 191 (29), 185 (73), 184 (30), 179 (11), 175 (12), 174 (14), 163 (20), 154 (10), 153 (100), 147 (14), 141 (24), 126 (14), 125 (63), 124 (10), 83 (40), 82 (27), 81 (22). HR-EI-MS: 266.1268 (M^+, $C_{13}H_{18}N_2O_4^+$; calc. 266.1267). Anal. calc. for $C_{13}H_{18}N_2O_4$ (266.30): C 58.64, H 6.81, N 10.52; found: C 58.44, H 6.73, N 10.74.

*Diethyl (*Z*)-2-Cyano-3-(cyclohexylamino)but-2-enedioate* (**12i**). Yield 241 mg (82%). PLC (SiO_2; $CHCl_3$). Colorless crystals. M.p. 75–77° (MeOH). IR (KBr): 2947*m*, 2208*s* (CN), 1749*s* (C=O), 1669*s*

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[5]) Crude material; see *Footnote 3*.

(C=O), 1586*vs* (C=C), 1369*w*, 1279*vs*, 1254*s*, 1147*w*, 1073*w*, 1031*w*, 786*w*. ^{1}H-NMR ($CDCl_3$): 9.50 (br. *s*, NH); 4.45, 4.26 (2*q*, J = 6.3, 2 MeCH_2O); 3.60–3.05 (br. *m*, CHN); 2.10–1.10 (*m*, 5 CH_2(cyclohexyl)); 1.37, 1.31 (2*t*, J = 7.2, 2 *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 168.2, 161.0, 160.4 (3*s*, C(3), 2 C=O); 115.5 (*s*, CN); 69.6 (*s*, C(2)); 63.6, 60.7 (2*t*, Me*C*H_2O); 55.5 (*d*, CHN); 33.4, 24.6, 23.9 (3*t*, 5 CH_2(cyclohexyl)); 14.0, 13.5 (2*q*, 2 *Me*CH_2O). EI-MS: 295 (19), 294 (91, M^+), 265 (18), 251 (24), 249 (20), 248 (37), 239 (18), 222 (15), 221 (100), 220 (24), 219 (80), 213 (40), 212 (12), 205 (15), 202 (22), 193 (15), 184 (11), 182 (12), 177 (28), 175 (18), 174 (14), 167 (33), 149 (13), 148 (10), 147 (21), 141 (63), 140 (26), 139 (80), 113 (20), 112 (17), 111 (34), 83 (41), 82 (24), 81 (30). HR-EI-MS: 294.1576 (M^+, $C_{15}H_{22}N_2O_4^+$; calc. 294.1580). Anal. calc. for $C_{15}H_{22}N_2O_4$ (294.35): C 61.21, H 7.53, N 9.52; found: C 61.24, H 7.57, N 9.68.

*Diisopropyl (*Z*)-2-Cyano-3-(cyclohexylamino)but-2-enedioate* (**12k**). Yield 194 mg (60%). PLC (petroleum ether/CH_2Cl_2 3:7). Colorless crystals. M.p. 72–74° (MeOH). IR (KBr): 2947*m*, 2213*s* (CN), 1745*s* (C=O), 1660*s* (C=O), 1593*vs* (C=C), 1452*w* (br.), 1351*m*, 1281*vs*, 1244*m*, 1146*w*, 1099*m*, 994*w*, 784*w*. ^{1}H-NMR ($CDCl_3$): 9.50 (br., NH); 5.32, 5.08 (2 *sept.*, J = 6.3, 2 Me_2C*H*O); 3.00–3.50 (br. *m*, CHN); 2.20–1.10 (br. *m*, 5 CH_2(cyclohexyl)); 1.40, 1.30 (2*d*, J = 6.3, 2 *Me*$_2$CHO). ^{13}C-NMR ($CDCl_3$): 167.9, 160.7, 160.6 (3*s*, C(3), 2 C=O); 116.6 (*s*, CN); 69.8 (*s*, C(2)); 71.9, 68.4, 55.5 (3*d*, 2 Me_2*C*HO, CHN); 33.5, 24.6, 24.0 (3*t*, 5 CH_2(cyclohexyl)); 21.6, 21.2 (2*q*, 2 *Me*$_2$CHO). EI-MS: 323 (11), 322 (53, M^+), 279 (15), 238 (22), 237 (100), 235 (27), 221 (41), 220 (45), 219 (46), 207 (35), 195 (10), 194 (10), 193 (52), 192 (13), 157 (25), 156 (11), 155 (16), 153 (15), 139 (40), 120 (83), 113 (44), 112 (23), 111 (41), 83 (47), 82 (23), 81 (22). HR-EI-MS: 322.1892 (M^+, $C_{17}H_{26}N_2O_4^+$; calc. 322.1893). Anal. calc. for $C_{11}H_{14}N_2O_4$ (322.41): C 63.33, H 8.13, N 8.69; found: C 63.48, H 8.08, N 8.72.

*Dimethyl (*Z*)-2-Cyano-3-(phenylamino)but-2-enedioate* (**12l**). Yield 254 mg (97%). Colorless crystals. M.p. 90–92° (MeOH). IR (KBr): 3256 *m* (br.), 2962*w*, 2215*s* (CN), 1755*vs* (C=O), 1679*vs* (C=O), 1582*vs* (br., C=C), 1498*w*, 1435*m*, 1273*vs* (br.), 1155*w*, 1034*m*, 779*m*, 697*w*. ^{1}H-NMR ($CDCl_3$): 11.00 (br., NH); 7.50–7.00, 6.85–6.50 (2*m*, 5 arom. H); 3.85, 3.75 (2*s*, 2 MeO). ^{13}C-NMR ($CDCl_3$): 168.0, 161.3, 158.7 (3*s*, C(3), 2 C=O); 137.0 (*s*, 1 arom. C); 129.7, 127.5, 122.7 (3*d*, 5 arom. CH); 115.7 (*s*, CN); 74.3 (*s*, C(2)); 53.6, 52.3 (2*q*, 2 MeO). EI-MS: 261 (10), 260 (68, M^+), 201 (68), 200 (62), 170 (13), 169 (100), 157 (29), 144 (48), 142 (23), 141 (16), 134 (11), 115 (19), 77 (74). HR-EI-MS: 260.0795 (M^+, $C_{13}H_{12}N_2O_4^+$; calc. 260.0797). Anal. calc. for $C_{13}H_{12}N_2O_4$ (260.25): C 60.00, H 4.65, N 10.76; found: C 60.28, H 4.56, N 11.03.

*Diethyl (*Z*)-2-Cyano-3-(phenylamino)but-2-enedioate* (**12m**). Yield 192 mg (67%). Colorless crystals. M.p. 76–78° (MeOH/dry ice). IR (KBr): 3221*m* (br.), 2983*w*, 2213*m* (CN), 1747*s* (C=O), 1671*s* (C=O), 1599*vs* (br., C=C), 1369*m*, 1278*vs* (br.), 1229*w*, 1038*m*, 780*w*, 699*w*. ^{1}H-NMR ($CDCl_3$): 11.10 (br. *s*, NH); 7.60–6.95 (*m*, 5 arom. H); 4.38, 4.27 (2*q*, J = 6.2, 2 MeCH_2O); 1.45, 1.15 (2*t*, J = 6.2, 2 *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 167.8, 160.9, 159.0 (3*s*, C(3), 2 C=O); 137.0 (*s*, 1 arom. C); 129.6, 127.5, 123.0 (3*d*, 5 arom. CH); 115.8 (*s*, CN); 74.5 (*s*, C(2)); 63.4, 61.5 (2*t*, 2 MeCH_2O); 14.0, 13.3 (2*q*, 2 *Me*CH_2O). EI-MS: 289 (15), 288 (82, M^+), 215 (51), 214 (56), 188 (13), 187 (100), 186 (24), 170 (20), 169 (81), 144 (37), 143 (54), 142 (40), 116 (15), 115 (14), 77 (63). HR-EI-MS: 288.1108 (M^+, $C_{15}H_{16}N_2O_4^+$; calc. 288.1110). Anal. calc. for $C_{15}H_{16}N_2O_4$ (288.31): C 62.49, H 5.59, N 9.72; found: C 62.86, H 5.64, N 9.84.

*Diispropyl (*Z*)-2-Cyano-3-(phenylamino)but-2-enedioate* (**12n**). Yield 143 mg (45%). Colorless crystals. M.p. 82–84° (MeOH). IR (KBr): 2980*m*, 2209*m* (CN), 1742*vs* (C=O), 1674*vs* (C=O), 1560*vs* (C=C), 1583*s*, 1496*w*, 1375*m*, 1353*m*, 1343*w*, 1279*vs*, 1239*m*, 1182*w*, 1168*w*, 1102*s*, 1006*w*, 901*w*, 784*w*, 764*w*, 699*m*. ^{1}H-NMR ($CDCl_3$): 11.05 (br. *s*, NH); 7.05–7.50 (*m*, 5 arom. H); 5.09, 5.11 (2 *sept.*, J = 6.3, 2 Me_2C*H*O); 1.36, 1.22 (2*d*, J = 6.3, 2 *Me*$_2$CHO). ^{13}C-NMR ($CDCl_3$): 167.2, 160.3, 159.2 (3*s*, C(3), 2 C=O); 137.0 (*s*, 1 arom. C); 129.3, 127.3, 123.3 (3*d*, 5 arom. CH); 115.6 (*s*, CN); 74.4 (*s*, C(2)); 71.8, 69.2 (2*d*, 2 Me_2*C*HO); 21.5, 21.4, 20.8, 20.7 (4*q*, 2 *Me*$_2$CHO). EI-MS: 317 (10), 316 (48, M^+), 274 (28), 232 (30), 215 (15), 214 (13), 188 (26), 187 (100), 186 (18), 170 (47), 169 (37), 168 (14), 174 (14), 160 (33), 144 (32), 143 (46), 142 (23), 116 (11), 115 (12), 77 (45). HR-EI-MS: 316.1423 (M^+, $C_{17}H_{20}N_2O_4^+$; calc. 316.1423). Anal. calc. for $C_{17}H_{20}N_2O_4^+$ (316.36): C 64.54, H 6.37, N 8.85; found: C 65.18, H 6.46, N 9.07.

*Dimethyl (*Z*)-2-Cyano-3-{[(*R*)-1-phenylethyl]amino}but-2-enedioate* ((*R*,*Z*)-**12o**). Yield 220 mg (76%). PLC ($CHCl_3$). Colorless, viscous oil. $[\alpha]_D^{20} = -81.5$ (c = 0.2, CH_2Cl_2). IR (neat): 3227*m* (br.), 2955*m*, 2213*s* (CN), 1749*vs* (C=O), 1676*vs* (C=O), 1586*vs* (br., C=C), 1437*m*, 1278*vs* (br.), 1245*m*, 1121*m*, 1026*m*, 784*m*, 765*w*, 700*m*. ^{1}H-NMR ($CDCl_3$): 9.80 (br. *s*, NH); 7.45–7.14 (*m*, 5 arom. H); 4.71

(*dq*, *J* = 6.9, 6.9, MeC*H*); 3.79, 3.74 (2*s*, 2 MeO); 1.61 (*d*, *J* = 6.9, *Me*CH). ^{13}C-NMR ($CDCl_3$): 168.5, 161.4, 160.5 (3*s*, C(3), 2 C=O); 141.3 (*s*, 1 arom. C); 129.1, 128.3, 126.1 (3*d*, 5 arom. CH); 116.3 (*s*, CN); 71.4 (*s*, C(2)); 55.9, 52.1 (2*q*, 2 MeO); 53.5 (*d*, *C*HN); 23.7 (*q*, Me). EI-MS: 288 (8, M^+), 256 (6), 106 (9), 105 (100), 104 (9), 103 (6), 79 (6), 77 (8). HR-EI-MS: 288.1108 (M^+, $C_{15}H_{16}N_2O_4^+$; calc. 288.1110).

Dimethyl (*Z*)*-2-Cyano-3-{[(*S*)-1-phenylethyl]amino}but-2-enedioate* ((*S*,*Z*)-**12o**). Yield 230 mg (80%). PLC ($CHCl_3$). Colorless, viscous oil. $[\alpha]_D^{20} = +80.4$ (*c* = 0.2, CH_2Cl_2). IR (KBr) and ^{1}H-NMR ($CDCl_3$) were identical with those of (*R*,*Z*)-**12o**. EI-MS: 288 (8, M^+), 256 (6), 106 (10), 105 (100), 104 (8), 103 (5), 79 (7), 77 (8). HR-EI-MS: 288.1106 (M^+, $C_{15}H_{16}N_2O_4^+$; calc. (288.1110).

5. *Reaction of* (*E*)-**5a** *and* (*E*)-**5b** *with* NH_3. Through a magnetically stirred suspension of 1 mmol of (*E*)-**5a** or (*E*)-**5b** in CH_2Cl_2 (2 ml), a stream of dry NH_3 gas (produced from aq. NH_3 soln. and KOH pellets) was bubbled at r.t. for 5 min. Then, the soln. was homogeneous, and stirring was continued for another 10 min. The solvent was evaporated *in vacuo*, and the crystalline crude product was purified by crystallization.

Dimethyl (Z)*-3-Amino-2-cyanobut-2-enedioate* (**12p**). Yield 140 mg (76%). Colorless crystals. M.p. 143–145° (MeOH). IR (KBr): 3395*s* (br.), 3281*s*, 3226*m*, 2207*s* (CN), 1757*s* (C=O), 1690*s* (C=O), 1623v*s* (br., C=C), 1528*m*, 1442*s*, 1266v*s* (br.), 1182*w*, 1090*s*, 994*w*, 869*w*, 781*m*, 660*m* (br.). ^{1}H-NMR ($CDCl_3$): 9.20, 6.77 (2 br. *s*, 2 NH); 4.01, 3.84 (2*s*, 2 MeO). ^{13}C-NMR ($CDCl_3$): 168.1, 161.3, 154.3 (3*s*, 2 C=O, C(3)); 116.0 (*s*, CN); 75.2 (*s*, C(2)); 54.2, 52.5 (2*q*, 2 MeO). EI-MS: 185 (8), 184 (84, M^+), 153 (100), 152 (12), 126 (15), 125 (66), 124 (34), 93 (20), 82 (12), 81 (21). HR-EI-MS: 184.0481 (M^+, $C_7H_8N_2O_4^+$; calc. 184.0484). Anal. calc. for $C_7H_8N_2O_4 \cdot 0.5\ H_2O$ (193.16): C 43.53, H 4.70, N 14.50; found: C 43.53, H 4.31, N 14.49.

Diethyl (Z)*-3-Amino-2-cyanobut-2-enedioate* (**12q**). Yield 180 mg (85%). Colorless crystals. M.p. 75–77° (hexane/CH_2Cl_2) ([9]: m.p. 78–79°). IR (KBr): 3404*m*, 3287*s* (br.), 3223*m* (br.), 2982*w*, 2209*s* (CN), 1752*m* (C=O), 1683*s* (C=O), 1620v*s* (br., C=C), 1533*w*, 1368*m*, 1270v*s* (br.), 1085*s*, 1024*w*, 778*w*, 649*m* (br.). ^{1}H-NMR ($CDCl_3$): 9.25, 6.73 (2 br. *s*, 2 NH); 4.46, 4.28 (2*q*, *J* = 7.2, 2 MeCH_2O); 1.43, 1.34 (2*t*, *J* = 7.2, 2 *Me*CH_2O). EI-MS: 213 (12), 212 (82, M^+), 184 (25), 167 (20), 140 (43), 139 (100), 138 (12), 112 (57), 111 (56), 110 (14), 96 (13), 95 (27), 93 (15). HR-EI-MS: 212.0794 (M^+, $C_9H_{12}N_2O_4^+$; calc. 212.0797).

6. N-*Methylation of* (*Z*)-**12n** *with* CH_2N_2. A small portion of (*Z*)-**12n** (80 mg, 0.25 mmol) was dissolved in Et_2O (0.5 ml), and a cold soln. of CH_2N_2 in Et_2O was added dropwise in excess at r.t. The yellow soln. was stored in a closed flask at r.t. for 48 h. Then, AcOH was added in small portions in order to destroy the excess CH_2N_2. When the evolution of N_2 was complete, the mixture was evaporated to dryness. The crude product was analyzed by ^{1}H-NMR spectroscopy, which indicated that the starting material had completely been converted to a new product. The thick, yellowish oil was purified by prep. TLC (SiO_2; $CHCl_3$/MeOH 98 :2) to yield 66 mg of a viscous yellow oil. Subsequent crystallization from MeOH gave a crystalline product.

Diisopropyl (Z)*-2-Cyano-3-[(methyl)(phenyl)amino]but-2-enedioate* ((*Z*)-**12r**). Yield 264 mg (80%). Yellow crystals (MeOH). M.p. 94–96°. IR (KBr): 2984*m*, 2205*m* (CN), 1742v*s* (C=O), 1694*s* (C=O), 1537v*s* (C=C), 1301*m*, 1261*s*, 1234*s*, 1103*s*, 1038*w*, 1002*w*, 770*w*, 750*w*, 702*w*. ^{1}H-NMR ($CDCl_3$): 7.44–7.33, 7.29–7.24 (2*m*, 5 arom. H); 5.01, 4.94 (2 *sept.*, *J* = 6.3, 2 Me_2C*H*O); 3.67 (*s*, MeN); 1.27, 1.60 (2*d*, *J* = 6.3, 2 *Me*$_2$CHO). ^{13}C-NMR ($CDCl_3$): 164.2, 161.9, 160.8 (3*s*, C(3), 2 C=O); 116.4 (*s*, CN); 76.4 (*s*, C(2)); 70.9, 68.9 (2*d*, 2 Me_2*C*HO); 44.4 (*q*, MeN); 21.8, 21.1 (2*q*, 2 *Me*$_2$CHO). EI-MS: 330 (21, M^+), 270 (13), 229 (36), 202 (10), 201 (59), 200 (11), 184 (12), 183 (60), 158 (25), 157 (100), 156 (24), 142 (16), 106 (11), 77 (19). HR-EI-MS: 330.1577 (M^+, $C_{18}H_{22}N_2O_4^+$; calc. 330.1580).

7. *X-Ray Crystal-Structure Determination of* **8a**, **9d**, **12d**, **12l**, *and* **12p** (*Table 2* and *Figs. 1–3*)[6]). All measurements were performed on a *Nonius KappaCCD* diffractometer [18] using graphite-monochromated MoK_α radiation (λ 0.71073 Å) and, in the cases of **9d**, **12d**, **12l**, and **12p**, an *Oxford Cryosystems Cryostream* 700 cooler. The data collection and refinement parameters are given in *Table 2*, and views of the molecules are shown in *Figs. 1–3*. Data reduction was performed with *HKL Denzo* and *Scalepack*

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[6]) CCDC-717505–717509 contain the supplementary crystallographic data for this article. These data can be obtained free of charge from the *Cambridge Crystallographic Data Centre via* http://www.ccdc.cam.ac.uk/data_request/cif.

Table 2. *Crystallographic Data of Compounds* **8a**, **9d**, **12d**, **12l**, *and* **12p**

	8a	**9d**	**12d**	**12l**	**12p**
Crystallized from	MeOH	MeOH	MeOH	MeOH	MeOH
Empirical formula	$C_{19}H_{22}N_2O_5$	$C_{24}H_{31}N_3O_5$	$C_{11}H_{14}N_2O_4$	$C_{13}H_{12}N_2O_4$	$C_7H_8N_2O_4$
Formula weight [g mol^{-1}]	358.39	441.52	238.24	260.25	184.15
Crystal color, habit	colorless, prism	colorless, prism	colorless, prism	colorless, prism	colorless, prism
Crystal dimensions [mm]	$0.32 \times 0.38 \times 0.43$	$0.25 \times 0.28 \times 0.35$	$0.12 \times 0.15 \times 0.30$	$0.08 \times 0.10 \times 0.20$	$0.20 \times 0.20 \times 0.28$
Temp. [K]	293(1)	160(1)	160(1)	160(1)	160(1)
Crystal system	orthorhombic	monoclinic	monoclinic	triclinic	monoclinic
Space group	$Pca2_1$	$P2_1/c$	$P2_1/c$	$P\bar{1}$	$P2_1/c$
Z	4	4	4	4	4
Reflections for cell determination	1921	7192	2183	4415	2552
2θ Range for cell determination [°]	4–50	4–60	4–50	4–50	4–60
Unit cell parameters					
a [Å]	8.2208(1)	10.0947(2)	10.6701(5)	9.0771(7)	8.2123(2)
b [Å]	10.9262(2)	10.2121(1)	8.2743(5)	10.1227(7)	12.1096(3)
c [Å]	20.9095(4)	23.2509(4)	13.1335(6)	14.538(1)	9.0786(2)
α [°]	90	90	90	101.003(4)	90
β [°]	90	101.8165(9)	92.790(3)	93.427(4)	110.718(1)
γ [°]	90	90	90	100.934(4)	90
V [Å^3]	1878.14(5)	2346.10(7)	1158.2(1)	1281.1(2)	844.46(4)
D_x [g cm^{-3}]	1.267	1.250	1.366	1.349	1.448
μ(MoK_α) [mm^{-1}]	0.0923	0.0880	0.105	0.102	0.121
Scan type	ϕ and ω	ϕ and ω	ω	ω	ω
$2\theta_{(max)}$ [°]	50	60	50	50	60
Total reflections measured	19731	53556	16990	19962	25559
Symmetry-independent reflections	1698	6859	2035	4502	2464
Reflections with $I > 2\sigma(I)$	1475	5379	1538	2628	1900
Reflections used in refinement	1698	6853	2035	4502	2463
Parameters refined; restraints	241; 1	294; 0	157; 0	355; 0	128; 0
Final $R(F)$ ($I > 2\sigma(I)$ reflections)	0.0330	0.0614	0.0403	0.0741	0.0454
$wR(F^2)$ (all data)	0.0854	0.1684	0.1120	0.2139	0.1383
Weights [a; b][a])	0.0519; 0.1370	0.0718; 1.1177	0.0592; 0.0879	0.0772; 0.7436	0.0746; 0.1488
Goodness-of-fit	1.043	1.058	1.046	1.099	1.061
Secondary extinction coefficient	0.038(6)	0.133(6)	0.007(2)	–	–
Final Δ_{max}/σ	0.001	0.001	0.001	0.016	0.001
$\Delta\rho$ (max; min) [e Å^{-3}]	0.12; −0.11	0.51; −0.28	0.20; −0.20	0.25; −0.25	0.28; −0.26

[a]) $w = [\sigma^2(F_o^2) + (aP)^2 + bP]^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$.

[19]. The intensities were corrected for *Lorentz* and polarization effects, but not for absorption. Equivalent reflections were merged. The structures were solved by direct methods using SIR92 [20] for **8a**, **9d**, and **12d**, and SHELXS97 [21] for **12l** and **12p**, which revealed the positions of all non-H-atoms. In the case of **12l**, the asymmetric unit contains two symmetry-independent molecules. The coordinates of the two molecules were tested carefully for a relationship from a higher symmetry space group using the program PLATON [22], but none could be found. The non-H-atoms were refined anisotropically. The amine H-atoms of **12l** and **12p** were placed in the positions indicated by a difference electron-density map, and their positions were allowed to refine together with individual isotropic displacement parameters. All other H-atoms in all of the structures were placed in geometrically calculated positions and refined using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to 1.2 U_{eq} of its parent C-atom (1.5 U_{eq} for Me groups). The refinement of each structure was carried out on F^2 using full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2 - F_c^2)^2$. A correction for secondary extinction was applied in the cases of **8a**, **9d**, and **12d**. In the cases of **9d** and **12p**, six and one reflections, resp., whose intensities were considered to be extreme outliers, were omitted from the final refinement. Neutral-atom-scattering factors for non-H-atoms were taken from [23a], and the scattering factors for H-atoms were taken from [24]. Anomalous dispersion effects were included in F_c [25]; the values for f' and f'' were those of [23b]. The values of the mass attenuation coefficients are those of [23c]. All calculations were performed using the SHELXL97 [26] program.

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