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Cycloaddition of New *N*-Unsubstituted Azomethine Ylides Generated from *N*-(Trimethylsilylmethyl)thioureas to Electron-Deficient Olefins, Acetylenes and Aldehydes, Synthetic Equivalents of Nonstabilized Aminonitrile Ylides[1]

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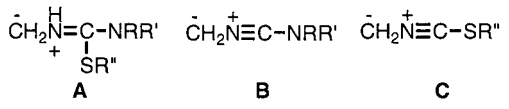
Abstract—The *S*-methylation of *N*-(trimethylsilylmethyl)thioureas and the subsequent desilylation of the silylmethyl group generates *N*-unsubstituted azomethine ylides having both methylthio and amino groups at the ylide carbon. These azomethine ylides undergo successful cycloaddition to electron-deficient olefins, acetylenes and aldehydes. As the methylthio group is eliminated under the reaction conditions to produce the corresponding pyrrolines, pyrroles and 2-oxazolines bearing the amino group at 2-position, these azomethine ylides can be synthetic equivalents of nonstabilized aminonitrile ylides that are otherwise relatively inaccessible.

Introduction

The importance of 1,3-dipoles such as azomethine ylides in organic synthesis has grown rapidly by the development of mild and versatile methods for the generation.[2] A particularly mild method for the generation of nonstabilized azomethine ylides involves the desilylation, usually under the influence of fluoride, of *N*-(silylmethyl)iminium salts.[3] The resultant azomethine ylides can be trapped with electron-deficient olefins and acetylenes to give a variety of pyrrolidines, pyrrolines, and pyrroles.

Water-induced desilylation of *N*-(trimethylsilylmethyl)-imines,[4,5] or thioimidates,[6] and fluoride-mediated desilylation after the in situ *S*- or *N′*-alkylation of *N*-(trimethylsilylmethyl)thioamides[7] or amidines,[7,8] are synthetically valuable since they can lead to novel 1,3-dipoles, *N*-unsubstituted azomethine ylides. It should be emphasized that the *N*-unsubstituted azomethine ylides carrying a leaving group such as alkylthio[6,7] or amino moiety[7,8] at the ylide carbon can be synthetic equivalents of nonstabilized nitrile ylides. This is important because such azomethine ylides directly afford cycloaddition products which are one oxidation state higher than those expected from simple azomethine ylides.



The present research is aiming at opening a new and general route to *N*-unsubstituted azomethine ylides **A** carrying alkylthio and amino moieties, both of which serve as a leaving group, at the ylide carbon and also aiming at establishing their utility as synthetic equivalents of nonstabilized nitrile ylides. Our approach to azomethine ylides **A** consists of initial *S*-alkylation of *N*-(trimethylsilylmethyl)thioureas leading to *N*-(trimethylsilylmethyl)iminium salts, and subsequent desilylation with fluoride. Elimination of the leaving alkylthio group or amino group from the cycloadducts of azomethine ylides **A** gives formal cycloadducts of nonstabilized aminonitrile ylides **B**[9] or alkylthionitrile ones **C**[10], whose generation is little known heretofore, respectively. The most important step in this sequence is regioselective alkylation at the sulfur atom, not at the thiourea nitrogen.

N-(Trimethylsilylmethyl)thioureas were chosen as starting compounds, and cycloadditions of the resulting ylides to electron-deficient olefins, acetylenes, and aldehydes are described.

Keywords: azomethine ylides; 1,3-dipolar cycloadditions; nonstabilized aminonitrile ylide.
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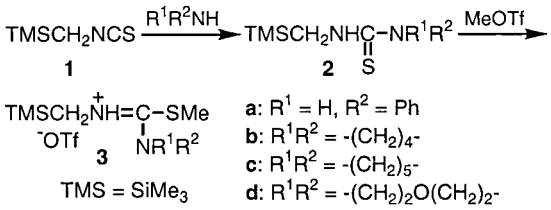
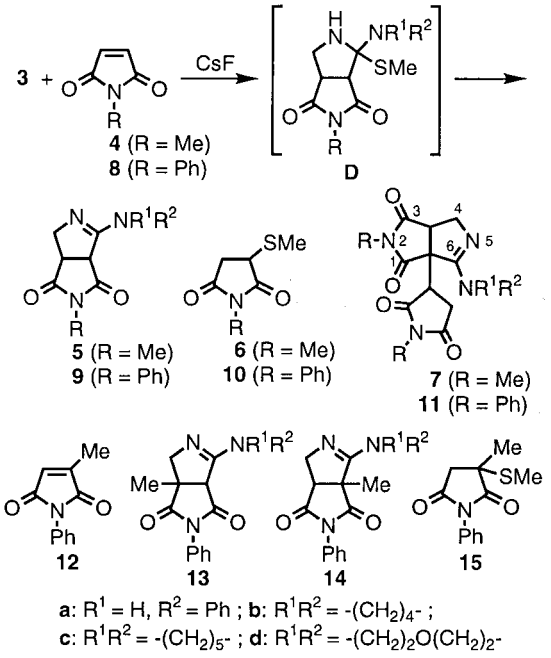


Scheme 1.



Scheme 2.

Results and Discussion

Preparation of *N*-(trimethylsilylmethyl)thioureas and their *S*-methylation

The reaction of (trimethylsilyl)methyl isothiocyanate (**1**)[11] with aniline or cyclic secondary amines such as pyrrolidine, piperidine and morpholine in benzene under reflux furnished the corresponding *N*-(trimethylsilylmethyl)thioureas **2a**–**2d** in excellent yields. The next step is selective *S*-alkylation of thioureas **2** leading to *N*-(trimethylsilylmethyl)-iminium salts. In analogy with *N*-(trimethylsilylmethyl)thioamides,[7] the selective *S*-methylation of **2** with methyl triflate proceeded smoothly to give the corresponding *N*-(trimethylsilylmethyl)iminium triflates **3a**–**3d** as precursors of azomethine ylides **A** (Scheme 1).

Generation of *N*-unsubstituted azomethine ylides and their cycloaddition to maleimides

Although 2-azaallyl anions[9] generated from certain *N*-(silylmethyl)isothioureas can be viewed as synthetic equivalents of aminonitrile ylides, little has been investigated on their reactions with electron-deficient olefins, except for the reaction with dimethyl fumarate in which a Michael adduct was formed but not formal [3+2] cycloadduct.[9a] Thus, generation of *N*-unsubstituted azomethine ylides **A** by desilylation of precursors **3** and subsequent cycloaddition to *N*-methylmaleimide (**4**) as an electron-deficient olefin were first investigated (Scheme 2). The reaction of *N*-(trimethylsilylmethyl)iminium triflate **3a** with **4** was examined in the presence of cesium fluoride (CsF) under a variety of conditions, some of which are listed in Table 1 (entries 1–3,9,10). In all cases the initial cycloadduct **D** (R=Me, R^1=H, R^2=Ph) could not be isolated, but instead methanethiol

Table 1. Cycloaddition with maleimides **4**, **8** and **12** (The reactions were carried out in dry solvent at room temperature (entries 1-3, 9,10, 17-23) or at reflux (entries 4-8, 11-16) for 10 h under nitrogen or argon.)

Entry	Precursor	Maleimide	Solvent[a]	Molar ratio[b]	Product: yield/%
1	**3a**	**4**	DME	1/1/1	**5a** (83)
2	**3a**	**4**	AN	1/1/1.2	**5a** (75)
3	**3a**	**4**	THF	1/1/1.2	**5a** (74)
4	**3b**	**4**	DME	1/1/1	**5b** (24), **6** (2)
5	**3c**	**4**	DME	1/1/1	**5c** (51), **6** (26)
6	**3c**	**4**	AN	1/1/1	**5c** (39), **6** (41)
7	**3c**	**4**	THF	1/1/1	**5c** (45), **6** (27)
8	**3d**	**4**	DME	1/1/1	**5d** (49), **6** (7)
9	**3a**	**4**	DME	1/2/1.2	**5a** (90)
10	**3a**	**4**	THF	1/2/1.2	**5a** (90)
11	**3b**	**4**	DME	1/2/1.2	**5b** (41), **6** (60), **7b** (14)
12	**3b**	**4**	DME	1/2.5/1.2	**6** (52), **7b** (48)
13	**3c**	**4**	DME	1/2/1.2	**5c** (45), **6** (65), **7c** (17)
14	**3c**	**4**	DME	1/2.5/1.2	**6** (30), **7c** (60)
15	**3d**	**4**	DME	1/2/1.2	**5d** (32), **6** (49), **7d** (17)
16	**3d**	**4**	DME	1/2.5/1.2	**6** (43), **7d** (51)
17	**3a**	**8**	DME	1/1/1	**9a** (59), **10** (23)
18	**3d**	**8**	DME	1/1/1.2	**9d** (41), **10** (23), **11d** (6)
19	**3d**	**8**	DME	1/2/1.3	**9d** (8), **11d** (38)
20	**3a**	**12**	DME	1/1/1.3	**13a** + **14a** (70)[c], **15** (26)
21	**3c**	**12**	DME	1/1/1.3	**13a** + **14a** (58)[c], **15** (36)
22	**3d**	**12**	DME	1/1/1.3	**13c** + **14c** (62)[c], **15** (34)
23	**3d**	**12**	DME	1/2/1.3	**13d** + **14d** (54)[c], **15** (37)

[a] DME: 1,2-dimethoxyethane; AN: acetonitrile; THF: tetrahydrofuran.
[b] Molar ratio of **3**/maleimide/CsF.
[c] In all cases the ratio **13/14** was determined to be ca. 2.3/1 by ^{1}H NMR.

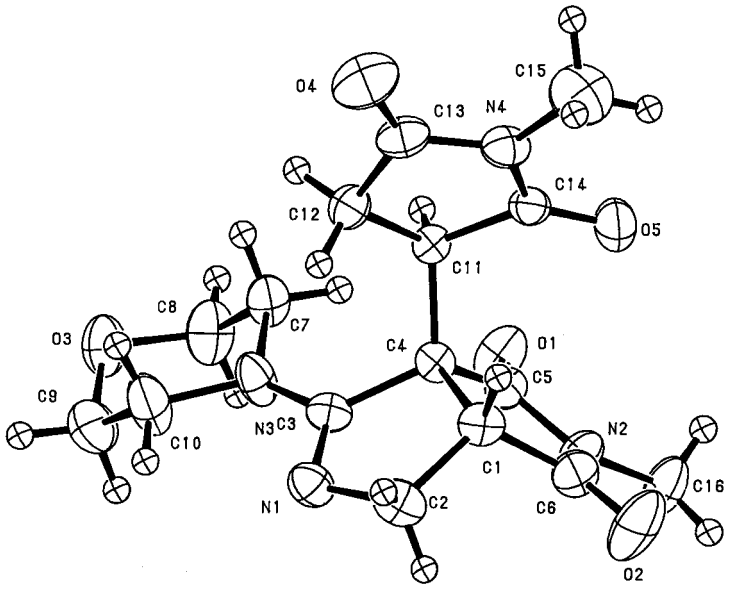
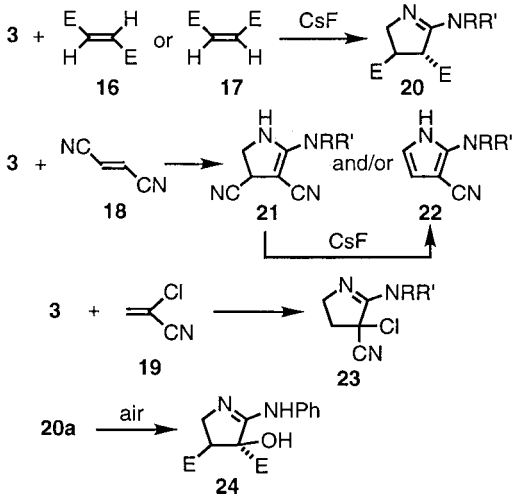


Figure 1.



Scheme 3.

was eliminated from **D** and formal aminonitrile ylide cycloadduct **5a** was obtained in good yield.

The reaction of *N*-(trimethylsilylmethyl)iminium triflates **3b**–**3d** bearing cyclic amine moiety with an equivalent of **4** in the presence of CsF was next investigated (entries 4–8). In contrast with **3a**, the corresponding aminonitrile ylide cycloadduct **5b**–**5d** (hereinafter abbreviated as 1:1 adduct) was formed in low to moderate yield, together with *N*-methyl-2-methylthiosuccinimide (**6**) whose structure corresponds to the Michael adduct of eliminated methanethiol to the unreacted **4**. The formation of **6** indicates that the reactivity of azomethine ylides generated from **3b**–**3d** toward **4** is lower than that of the ylide from **3a** and elimination of methanethiol occurs rapidly as soon as initial cycloadducts **D** (R=Me) are formed.[12] Thus, the reactions of **3b**–**3d** with excess **4** were investigated. In contrast to the reaction of **3a** giving a high yield of **5a** as the sole product (entries 9, 10), interestingly, the reactions of **3b**–**3d** gave a

Table 2. Cycloaddition with acyclic olefins **16**–**19**

Entry	Precursor	Olefin	Molar ratio[a]	Temp.	Time/h	Product: Yield/%
1	**3a**	**16**	1/1/1	r.t.	20	**20a** (71)
2	**3c**	**16**	1/1/1	r.t.	20	**20c** (38)
3	**3c**	**16**	1/1/1	reflux	10	**20c** (52)
4	**3d**	**16**	1/1/1	reflux	10	**20d** (57)
5	**3a**	**17**	1/1/1	r.t.	20	**20a** (52)
6	**3c**	**17**	1/1/1	reflux	10	**20c** (35)
7	**3d**	**17**	1/1/1	reflux	10	**20d** (30)
8	**3a**	**18**	1/1/1	r.t.	10	**21a** (61)
9	**3b**	**18**	1/1/1	r.t.	10	**21b** (48)
10	**3c**	**18**	1/1/1	r.t.	10	**21c** (46)
11	**3d**	**18**	1/1/1	r.t.	10	**21d** (48)
12	**3a**	**18**	1/1/2	reflux	10	**21a** (35), **22a** (23)
13	**3c**	**18**	1/1/2	reflux	10	**21c** (24), **22c** (25)
14	**3d**	**18**	1/1/2	reflux	10	**22d** (46)
15	**3a**	**19**	1/1/1.2	reflux	5	**23a** (31)
16	**3a**	**19**	1/5/1.2	reflux	10	**23a** (42)

[a] Molar ratio of **3**/olefin/CsF.

mixture of the corresponding 1:1 adduct **5**, Michael adduct **6** and/or novel product **7b–7d** whose relative yields depended on the reaction conditions (entries 11–16).

On the basis of spectral data and X-ray crystallographic analysis of **7d** whose ORTEP drawing is shown in Fig. 1, the structure of **7** corresponded to an addition product of **5** to **4**, and was determined as 6-amino-2-methyl-6a-[3-(1-methyl-2,5-dioxopyrrolidinyl)]-1,2,3,3a,4,6a-hexahydropyrrolo[3,4-*c*]pyrrole-1,3-dione; the product **7** is hereinafter abbreviated as 1:2 adduct. However, no 1:2 adducts **7b–7d** were formed in the reaction of the corresponding 1:1 adduct **5** with **4** in the presence or absence of CsF in refluxing 1,2-dimethoxyethane (DME). The reaction pathway for the formation of **7** is not clear yet.

The reaction of **3** with *N*-phenylmaleimide (**8**) under similar conditions afforded a mixture of the corresponding aminonitrile ylide 1:1 cycloadduct **9**, Michael adduct, 2-methyl-*N*-phenylsuccinimide (**10**), and/or 1:2 adduct **11**, whose relative yields depended on the nature of **3** as well as reaction conditions. The 1:2 adduct **11d** was formed even in the reaction of **3d** with an equivalent of **8**. The results are listed in entries 17–19 in Table 1.

In order to study the regioselectivity of cycloaddition, the reaction with 2-methyl-*N*-phenylmaleimide (**12**) expected to suppress the formation of 1:2 adduct was investigated (entries 20–23 in Table 1). Although the formation of 1:2 adduct such as type **7** or **11** was completely inhibited, azomethine ylides generated from **3** did not exhibited high regioselectivity in cycloaddition reaction with **12**. In all the reactions the less crowed 3a-methyl-substituted 1:1 adduct **13** was more formed than the crowed 6a-methyl-substituted one **14** (**13/14**=ca. 2.3/1) along with Michael adduct, 2-methyl-2-methylthio-*N*-phenylsuccinimide (**15**).

Cycloadditions to acyclic olefins

Next, the reaction of precursors **3** with electron-deficient acyclic olefins such as dimethyl fumalate (**16**), dimethyl maleate (**17**), fumaronitrile (**18**), and 2-chloroacrylonitrile (**19**) in the presence of CsF in dry DME (Scheme 3, Table 2). Although these acyclic dipolarophiles were somewhat less reactive than the cyclic dipolarophile **4**, the corresponding aminonitrile ylide cycloadducts were obtained in all cases.

The reaction of *cis*-olefin **17** gave the thermodynamically stable *trans*-bis(methoxycarbonyl)-1-pyrroline **20**, which was identical with the cycloadduct from *trans*-olefin **16**. Exclusive formation of 3,4-*trans*-1-pyrroline **20** from both **16** and **17** is due to a ready imine/enamine tautomerism (or a 1-pyrroline/2-pyrroline isomerization).[7] On the other hand, **3** reacted with **18** to give a mixture of 2-pyrroline **21**[13] and 3-cyanopyrrole **22** whose relative yields depended upon reaction conditions: when **21a** or **21c** was heated with CsF in DME for 24 h, **22a** or **22c** was obtained in good yield. The reaction of **3a** with unsymmetrically substituted olefin **19** furnished exclusively the 1-pyrroline **23a** with electron-withdrawing groups in 3-position, though its yield was low.

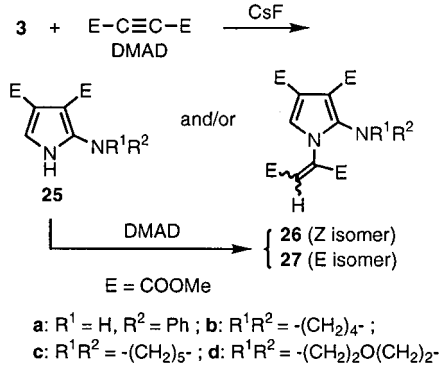
It should be noted that azomethine ylides generated from **3** reacted with acyclic olefins to give the formal [3+2] cycloadduct of amino nitrile ylides, since it has been reported that the 2-azaallyl anion generated from an *N*-(silylmethyl)isothiourea reacted with **16** to form Michael adduct in low yield.[9a]

It has been found that 1-pyrroline **20a** underwent air-oxidation to give 3-hydroxy-1-pyrroline **24**; such air oxidation of 1-pyrrolines has been observed previously.[14]

Cycloadditions to dimethyl acetylenedicarboxylate (DMAD)

The above results clearly show that the azomethine ylides generated from precursors **3** serve as synthetic equivalents of nonstabilized aminonitrile ylides through a cycloaddition and elimination sequence. Cycloaddition of these azomethine ylides to acetylenic dipolarophiles is, therefore, expected to be a convenient route to *N*-unsubstituted 2-aminopyrroles. Unfortunately, the reactivity of diaroyl- and aroylarylacetylenes toward azomethine ylides generated from **3** was low and the reaction under more forced conditions resulted in the formation of intractable materials. The reaction of **3** with DMAD under the influence of CsF, however, furnished the corresponding 1:1 adduct, 2-aminopyrrole **25**, and a mixture of two isomeric 1:2 adducts **26** and **27** whose relative yields depended on the amount of used DMAD (Scheme 4, Table 3)

The reaction of **25** with DMAD in the presence of a base gave a mixture of two isomers **26** and **27** in good yield. On the basis of spectral data and X-ray crystallographic analysis of **26d** whose ORTEP drawing is shown in Fig. 2, the compounds **26** and **27** were assigned as stereoisomeric Michael adducts of **25** to DMAD; **26d** was determined as



Scheme 4.

Table 3. Cycloaddition with DMAD (The reactions were carried out in dry DME at room temperature for 6 h)

Entry	Precursor	Molar ratio[a]	Products (yield, %)
1	**3a**	1/1/1	**25a** (71)
2	**3b**	1/2/1.2	**26b** + **27b** (34)
3	**3c**	1/1/2	**25c** (41), **26c** + **27c** (14)
4	**3c**	1/2/1	**25c** (7), **26c** + **27c** (34)
5	**3d**	1/1/1	**25d** (41), **26d** + **27d** (16)
6	**3d**	1/2/1	**25d** (10), **26d** + **27d** (32)

[a] Molar ratio of **3**/DMAD/CsF.

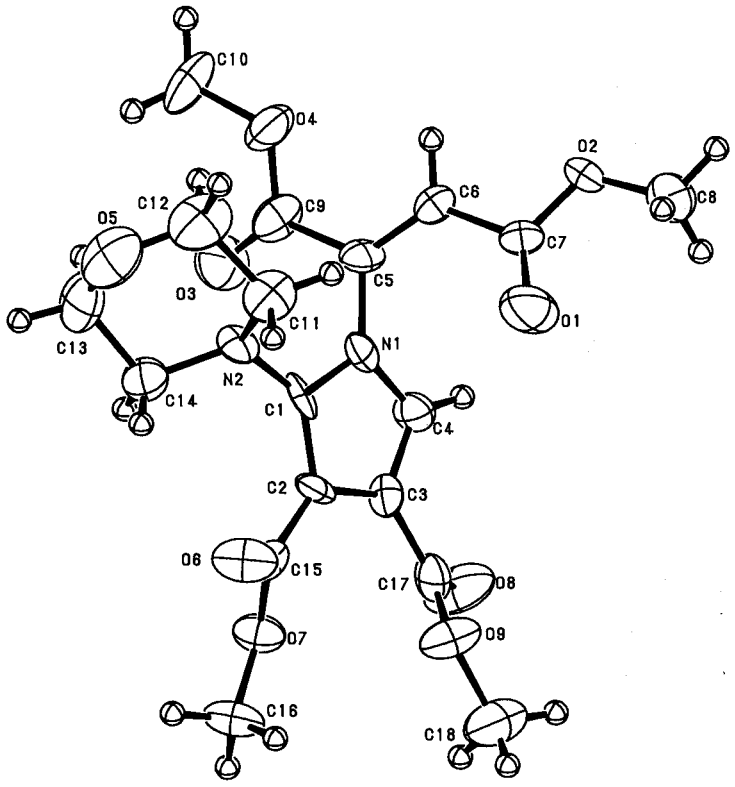
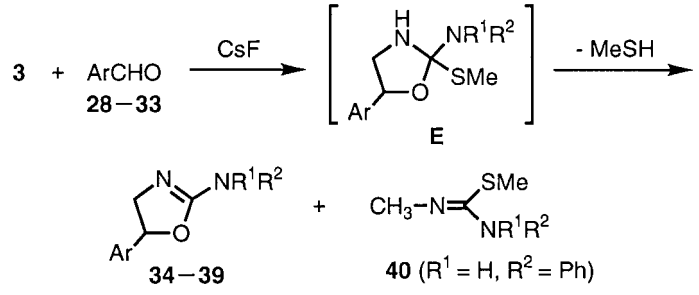


Figure 2.



28: Ar = Ph ; **29**: Ar = p-ClC_6H_4 ; **30**: Ar = p-$NO_2C_6H_4$;
31: Ar = 2-pyridyl ; **32**: Ar = 3-pyridyl ; **33**: Ar = 4-pyridyl ;
34a: Ar = Ph, R^1 = H, R^2 = Ph ; **35a**: Ar = p-ClC_6H_4, R^1 = H, R^2 = Ph ;
36a: Ar = p-$NO_2C_6H_4$, R^1 = H, R^2 = Ph ; **36c**: Ar = p-$NO_2C_6H_4$, R^1R^2 = -$(CH_2)_5$- ;
36d: Ar = p-$NO_2C_6H_4$, R^1R^2 = -$(CH_2)_2O(CH_2)_2$- ; **37a**: Ar = 2-pyridyl, R^1 = H, R^2 = Ph ;
38a: Ar = 3-pyridyl, R^1 = H, R^2 = Ph ; **39a**: Ar = 4-pyridyl, R^1 = H, R^2 = Ph

Scheme 5.

Table 4. Cycloaddition with aldehydes **28**–**33**

Entry	Precursor	Aldehyde	Molar ratio[a]	Product (yield, %)
1	**3a**	**28**	1/1/1.2	**34a** (15), **40** (30)
2	**3a**	**28**	1/5/1.2	**34a** (39), **40** (48)
3	**3a**	**29**	1/1/1.2	**35a** (30), **40** (46)
4	**3a**	**29**	1/5/1.2	**35a** (54), **40** (29)
5	**3a**	**30**	1/5/1.2	**36a** (70)
6	**3c**	**30**	1/5/1.2	**36c** (90)
7	**3d**	**30**	1/5/1.2	**36d** (77)
8	**3a**	**31**	1/5/1.2	**37a** (71)
9	**3a**	**32**	1/5/1.2	**38a** (63)
10	**3a**	**33**	1/5/1.2	**39a** (76)

[a] Molar ratio of **3**/Aldehyde/CsF.

(*Z*)-1,2-bis(methoxycarbonyl)-1-[3,4-bis(methoxycarbonyl)-2-(morpholino)pyrrolyl]ethene.

It has been reported that the nitrile ylide generated from *N*-(tosylmethyl)methylthioimidoyl chloride reacted with DMAD under severe conditions (in refluxing THF, 40 h) to lead to the formation of a mixture of two isomeric *N*-vinyl pyrroles such as **26** and **27**.[15]

Cycloadditions to aldehydes

Nitrile ylides generated by the photolysis of azirines undergo cycloaddition with aldehydes to give 3-oxazolines,[16,17]

and similar reactions of related ylides generated from the dehydrochlorination of imidoyl chlorides leading to 3-oxazolines, with a few exceptions,[18] are also known.[19] In contrast to the above observations, azomethine ylides generated from the desilylation of *N*-(trimethylsilyl)-methyl-*N*′-methyl-*N*′-phenylamidinium triflates show fairly high reactivity toward aromatic and heteroaromatic aldehydes to give moderate yields of 2,5-disubstituted 2-oxazolines by a sequence of cycloaddition and spontaneous elimination of *N*-methylaniline.[7] By contrast, related azomethine ylides generated by the action of water on *N*-(trimethylsilylmethyl)thioimidates are totally inert to carbonyl compounds.[6] Instead, on treatment with fluoride ion, the thioimidates generate 2-azaallyl anions, which are highly reactive to aromatic aldehydes and produce 2-oxazolines. More recently, two research groups[9] have found that 2-azaallyl anions generated by desilylation of certain *N*-(silylmethyl)isothioureas served as synthetic equivalent of aminonitrile ylides and reacted with carbonyl compounds to produce 2-amino-2-oxazolines.

If the cycloaddition of azomethine ylides generated from **3** to carbonyl compounds occurs in the same manner as those from amidinium salts,[7] the route to 2-amino-substituted 2-oxazolines via the elimination of methanethiol from initial cycloadducts, 2-amino-5-aryl-2-methylthiooxazolidines **E**, would become available. In fact, the azomethine ylides generated from **3a** reacted with aromatic and heteroaromatic aldehydes **28**–**33** in a regioselective manner to give the expected 2-anilino-5-aryl(heteroaryl)-2-oxazolines **34a**–**39a** in low to high yields depending on the nature of aldehydes (Scheme 5, Table 4).

In the reaction with rather inactive dipolarophiles such as benzaldehyde **28** and *p*-chlorobenzaldehyde **29** (entries 1–4 in Table 4),[20] the imine **40** which was probably derived from the azomethine ylide through a 1,2-proton migration was obtained as the by-product. Similar reactions of **3c** and **3d** with *p*-nitrobenzaldehyde **29** afforded the corresponding 2-oxazolines **36c** and **36d** in good yield, respectively.

In conclusion, azomethine ylides readily generated by the desilylation of *N*-(trimethylsilylmethyl)iminium triflates **3** react with electron-deficient olefins, acetylenes and aromatic and heteroaromatic aldehydes to give formal nonstabilized aminonitrile ylides cycloadducts, novel 2-amino-pyrrolines, 2-amino-pyrrole, and 2-amino-2-oxazolines, which are otherwise relatively inaccessible.

Experimental

General procedures

Melting points were determined on a hot-plate microscope apparatus and are not corrected. IR spectra were measured as KBr pellets unless otherwise noted. ^{1}H and ^{13}C NMR spectra were recorded at 270 and 67.5 MHz, respectively, in $CDCl_3$ unless otherwise mentioned. Chemical shifts are expressed in parts per million downfield from TMS. ^{13}C NMR resonance assignments were aided by the use of the DEPT technique to determine number of attached hydrogens. Mass spectra were measured at 70 eV of ionization energy. (Trimethylsilyl)methylisothiocyanate (**1**) was prepared according to the reported method.[10] Cesium fluoride was dried under vacuum prior to its use. Acetonitrile and 1,2-dimethoxyethane were distilled over P_2O_5 and CaH, respectively, and stored on molecular sieves 5A. Other reagents are commercially available. Column chromatography was carried out on silica gel BW 200, BW 300 or NH DM-1020 (Fuji Silisya Chem. Ltd.).

General procedure for the preparation of *N*-(trimethylsilylmethyl)thioureas 2a–2d

The typical procedure is given with an example for the synthesis of 1-phenyl-3-(trimethylsilylmethyl)thiourea (**2a**). A solution of aniline (1.89 g, 20 mmol) and (trimethylsilyl)methylisothiocyanate (**1**) (2.91 g, 20 mmol) in dry benzene (30 mL) was refluxed under argon for 3 h. The solvent was evaporated in vacuo and the residue was recrystallized from cyclohexane to give 4.46 g (93%) of **2a** as colorless needles.

2a. Mp 125–126°C; IR 3288, 1251, 857 cm^{-1}; ^{1}H NMR δ 0.05 (s, 9H), 3.15 (d, J=5.4 Hz, 2H), 5.99 (br s, 1H), 7.21–7.46 (m, 5H), 8.39 (br s, 1H); ^{13}C NMR δ −2.55, 35.71, 125.14, 125.21, 127.04, 130.06, 181.26; MS *m*/*z* (relative intensity) 238 (M^+, 66), 223 (100). Anal. Calcd for $C_{11}H_{18}N_2SSi$: C, 55.41; H, 7.61; N, 11.75. Found: C, 55.16; H, 7.63; N, 11.47.

1-[*N*-(Trimethylisilylmethyl)thiocarbamoyl]pyrrolidine (2b). Yield 98%; colorless needles (hexane); mp 58.5–59°C; IR 3342, 1247, 853 cm^{-1}; ^{1}H NMR δ 0.12 (s, 9H), 1.9–2.1 (m, 4H), 3.18 (d, J=5.1 Hz, 2H), 3.59 (br s, 4H), 5.05 (br s, 1H); ^{13}C NMR δ −2.55, 25.41, 35.83, 49.38, 179.98; MS *m*/*z* (relative intensity) 216 (M^+, 37), 70 (100). Anal. Calcd for $C_9H_{20}N_2SSi$: C, 49.95; H, 9.31; N, 12.94. Found: C, 49.71; H, 9.35; N, 12.89.

1-[*N*-(Trimethylsilylmethyl)thiocarbamoyl]piperidine (2c). Yield 97%; colorless needles (cyclohexane); mp 73–74°C; IR 3352, 1253, 857 cm^{-1}; ^{1}H NMR δ 0.12 (s, 9H), 1.6–1.8 (m, 6H), 3.09 (d, J=2.5 Hz, 2H), 3.65 (br s, 4H), 5.34 (br s, 1H); ^{13}C NMR δ −2.39, 24.31, 25.39, 36.50, 48.95, 182.84; MS *m*/*z* (relative intensity) 230 (M^+, 13), 84 (100). Anal. Calcd for $C_{10}H_{22}N_2SSi$: C, 52.12; H, 9.62; N, 12.12. Found: C, 52.24; H, 9.44; N, 12.14.

1-[*N*-(Trimethylsilylmethyl)thiocarbamoyl]morpholine (2d). Yield 97%; colorless needles (hexane); mp 73–74°C; IR 3376, 1249, 843 cm^{-1}; ^{1}H NMR δ 0.12 (s, 9H), 3.23 (d, J=5.3 Hz, 2H), 3.55–4.02 (m, 8H), 6.50 (br s, 1H); ^{13}C NMR δ −2.35, 36.59, 47.53, 66.14, 184.24; MS *m*/*z* (relative intensity) 232 (M^+, 37), 86 (100). Anal. Calcd for $C_9H_{20}N_2OSSi$: C, 46.51; H, 8.67; N, 12.05. Found: C, 46.49; H, 8.54; N, 12.02.

General procedure for the *S*-methylation of thioureas (2)

The typical procedure is given with an example for the preparation of *N*-(trimethylsilylmethyl)iminium triflate **3a**. To a solution of the thiourea **2a** (2.38 g, 10 mmol) in dry dichloromethane (30 mL) was added methyltriflate (1.80 g, 11 mmol). The reaction mixture was refluxed for 2 h under

argon. The solvent was evaporated in vacuo and recrystallization of the residue from benzene gave 3.83 g (95%) of **3a** as colorless plates.

3a. Mp 122–123°C; IR 3268, 1620, 1257, 859 cm^{-1}; ^1H NMR (a mixture of *E* and *Z* isomers) δ 0.12 (s, 2.25H), 0.17 (s, 6.75H), 2.46 (s, 2.25H), 2.54 (0.75H), 3.01 (d, *J*=5.9 Hz, 0.5H), 3.31 (d, *J*=6.7 Hz, 1.5H), 7.2–7.47 (m, 5H), 7.88 (br s, 0.25H), 8.19 (br s, 0.75H), 9.57 (br s, 0.75H), 9.90 (br s, 0.25H); ^{13}C NMR δ −2.61, −2.53, 14.00, 14.70, 36.62, 36.78, 124.87, 127.13, 128.75, 128.98, 129.45, 130.47, 134.32, 134.77, 166.92, 169.95. Anal. Calcd for $C_{13}H_{21}N_2O_3F_3S_2Si$: C, 38.78; H, 5.26; N, 6.96. Found: C, 38.83; H, 5.20; N, 6.93.

1-Pyrrolidinyl-substituted *N*-(trimethylsilylmethyl)iminium triflate 3b. Yield 98%; colorless oil; IR (neat) 3244, 1611, 1257, 857 cm^{-1}; ^1H NMR δ 0.15 (s, 9H), 2.0–2.2 (m, 4H), 2.59 (s, 3H), 3.26 (d, *J*=5.9 Hz, 2H), 3.70–3.84 (m, 4H), 8.27 (br s, 1H); ^{13}C NMR δ −2.53, 16.28, 25.18, 39.01, 52.08, 163.88 Anal. Calcd for $C_{11}H_{23}N_2O_3F_3S_2Si$: C, 34.74; H, 6.05; N, 7.37. Found: C, 34.89; H, 5.98; N, 7.29.

Piperidino-substituted *N*-(trimethylsilylmethyl)iminium triflate 3c. Yield 95%; colorless prisms (benzene–hexane (1:1)); mp 87–88°C; IR 3236, 1609, 1249, 855 cm^{-1}; ^1H NMR δ 0.15 (s, 9H), 1.74 (br s, 6H), 2.54 (s, 3H), 3.29 (d, *J*=5.9 Hz, 2H), 3.73 (br s, 4H), 8.93 (br s, 1H); ^{13}C NMR δ −2.41, 17.09, 23.53, 25.82, 39.26, 52.27, 169.13. Anal. Calcd for $C_{12}H_{25}N_2O_3F_3S_2Si$: C, 36.52; H, 6.40; N, 7.10. Found: C, 36.73; H, 6.56; N, 6.98.

Morpholino-substituted *N*-(trimethylsilylmethyl)iminium triflate 3d. Yield 96%; colorless prisms (benzene); mp 65.5–66°C; IR 3226, 1607, 1245, 857 cm^{-1}; ^1H NMR δ 0.16 (s, 9H), 2.57 (s, 3H), 3.32 (d, *J*=5.9 Hz, 2H), 3,82 (br s, 8H), 9.17 (br s, 1H); ^{13}C NMR δ −2.39, 17.11, 39.68, 51.21, 66.14, 169.59. Anal. Calcd for $C_{11}H_{23}N_2O_4F_3S_2Si$; C, 33.22; H, 5.85; N, 7.06. Found: C, 33.36; H, 5.87; N 6.97.

General procedure for the generation of azomethine ylides from *N*-(trimethylsilylmethyl)iminium triflates 3 and their cycloaddition reactions with *N*-methylmaleimide (4)

Each typical procedure for the reaction of iminium triflate **3a** with an equivalent of **4** or **3b** with an excess of **4** is shown below: (i) to a suspension of CsF (76 mg, 0.5 mmol) in dry DME (3 mL) was added a solution of **3a** (201 mg, 0.5 mmol) and **4** (55.5 mg, 0.5 mmol) in dry DME (5 mL), and the resulting mixture was stirred at room temperature under nitrogen for 10 h, and then concentrated in vacuo. The residue was extracted with dichloromethane (15 mL) and organic layer was washed with water (5 mL), dried over anhydrous $MgSO_4$, and evaporated in vacuo. The residue was recrystallized from benzene to give 101 mg (83%) of 1:1 adduct **5a** as colorless needles (entry 1 in Table 1). (ii) To a suspension of CsF (608 mg, 4.0 mmol) in dry DME (10 mL) was added a solution of **3b** (1.52 g, 4.0 mmol) and **4** (890 mg, 8.0 mmol) in dry DME (10 mL), and the resulting mixture was refluxed for 10 h under nitrogen. The mixture was concentrated in vacuo and extracted with dichloromethane (50 mL). The organic layer was washed with water, dried over anhydrous $MgSO_4$, and evaporated in vacuo. The residue was chromatographed (NH DM-1020) to give Michael adduct **6** (382 mg, 60%), 1:1 adduct **5b** (362 mg, 41%) and 1:2 adduct **7b** (184 mg, 14%) from elution of hexane–benzene (1:1), benzene–ethyl acetate (1:4) and ethyl acetate, respectively (entry 11 in Table 1).

The other reactions were carried out under the conditions summarized in Table 1.

Anilino-substituted 1:1 adduct 5a. Mp 190–190.5°C, IR 3278, 1702, 1601 cm^{-1}; ^1H NMR δ 2.97 (s, 3H), 3.45–4.30 (m, 4H), 6.9–7.6 (m, 6H); ^{13}C NMR δ 25.18, 43.44, 54.21, 59.70, 118.46, 122.83, 129.00, 139.97, 154.66, 174.69, 178.41; MS *m/z* (relative intensity) 243 (M^+, 41), 242 (100). Anal. Calcd for $C_{13}H_{13}N_3O_2$: C, 64.17; H, 5.40; N, 17.28. Found: C, 63.96; H, 5.38; N, 17.06.

1-Pyrrolidinyl-substituted 1:1 adduct 5b. Colorless viscous oil; IR (neat) 1696, 1618 cm^{-1}; ^1H NMR δ 1.85–2.20 (m, 4H), 2.97 (s, 3H), 3.2–4.3 (m, 8H); ^{13}C NMR δ 25.06, 25.48, 45.45, 48.57, 53.11, 58.67, 158.65, 173.92, 178.37; MS *m/z* (relative intensity) 221 (M^+, 7), 137 (100). Anal. Calcd for $C_{11}H_{15}N_3O_2$: C, 59.71; H, 6.83; N, 18.99. Found: C, 59.54; H, 6.97; N, 19.06.

Piperidino-substituted 1:1 adduct 5c. Colorless plates (cyclohexane), mp 127–128°C; IR 1688, 1607 cm^{-1}; ^1H NMR δ 1.62 (br s, 6H), 2.97 (s, 3H), 3.40–4.30 (m, 8H); ^{13}C NMR δ 24.36, 25.09, 25.51, 45.30, 48.09, 51.51, 58.18, 160.69, 173.71, 178.32; MS *m/z* (relative intensity) 235 (M^+, 100). Anal. Calcd for $C_{12}H_{17}N_3O_2$: C, 61.26; H, 7.28; N, 17.86. Found: C, 61.54; H, 7.41; N, 17.81.

Morpholino-substituted 1:1 adduct 5d. Colorless prisms (cyclohexane), mp 142–143°C, IR 1694, 1613 cm^{-1}; ^1H NMR δ 2.98 (s, 3H), 3.25–4.28 (m, 12H); ^{13}C NMR δ 25.15, 45.16, 47.15, 51.41, 58.27, 66.47, 160.80, 173.57, 178.04; MS *m/z* (relative intensity), 237 (M^+, 60), 236 (100). Anal. Calcd for $C_{11}H_{15}N_3O_3$: C, 55.68; H, 6.37; N, 17.71. Found: C, 55.61; H, 6.39; N, 17.86.

***N*-Methyl-2-methylthiosuccinimide (6).** Pale yellow oil; IR (neat) 1702 cm^{-1}; ^1H NMR δ 2.32 (s, 3H), 2.55 (dd, *J*=3.6, 18.6 Hz, 1H), 3.01 (s, 3H), 3.17 (dd, *J*=8.9, 18.6 Hz, 1H), 3.77 (dd, *J*=3.6, 8.9 Hz, 1H); ^{13}C NMR δ 14.65, 25.05, 35.76, 40.63, 174.82, 176.46; MS *m/z* (relative intensity) 159 (M^+, 29), 113 (100). Anal. Calcd for $C_6H_9NO_2S$: C, 45.28; H, 5.70; N, 8.80. Found: C, 45.06; H, 5.86; N, 8.58.

1-Pyrrolidinyl-substituted 1:2 adduct 7b. Colorless needles, mp 255–256°C; IR 1696, 1609 cm^{-1}; ^1H NMR δ 1.7–2.0 (m, 4H), 2.98, 3.06 (each s, 3H), 3.70–4.05 (m, 4H), 2.0–4.25 (m, 6H); ^{13}C NMR δ 25.11, 25.61, 25.33, 31.24, 41.87, 48.56, 49.75, 56.72, 63.12, 158.02, 174.37, 174.71, 175.97, 176.73; MS *m/z* (relative intensity) 332 (M^+, 58), 221 (100). Anal. Calcd for $C_{16}H_{20}N_4O_4$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.93; H, 5.87; N, 17.04.

Piperidino-substituted 1:2 adduct 7c. Colorless needles (ethyl acetate), mp 249–250°C; IR 1702, 1603 cm^{-1}; ^1H NMR (pyridine-d_5) δ 1.3–1.8 (m, 6H), 2.87, 3.04 (each s, 3H), 2.25–4.50 (m, 6H,), 3.78 (br s, 4H); ^{13}C NMR (pyridine-d_5) δ 24.61, 24.76, 24.55, 26.12, 32.13, 43.81, 48.03, 50.81, 56.63, 63.88, 160.31, 175.28, 175.65, 177.10, 177.56; MS *m/z* (relative intensity) 346 (M^+, 82), 235 (100). Anal. Calcd for $C_{17}H_{22}N_4O_4$: C, 58.94; H, 6.41; N, 16.18. Found: C, 58.83; H, 6.32; N, 15.97.

Morpholino-substituted 1:2 adduct 7d. Colorless needles (DME), mp>300°C; IR 1694, 1605 cm^{-1}; ^1H NMR δ 2.05–3,70 (m, 6H), 2.98, 3.08 (each s, 3H), 3.50–3.70 (m, 4H), 3.85–4.05 (m, 4H); ^{13}C NMR δ 25.12, 25.79, 31.40, 42.84, 47.27, 50.05, 56.22, 63.43, 66.65, 160.35, 174.04, 175.58, 176.16; MS *m/z* (relative intensity) 348 (M^+, 72), 347 (100). Anal. Calcd for $C_{16}H_{20}N_4O_5$: C, 55.16; H, 5.79; N, 16.08. Found: C, 55.35; H, 5.88; N, 16.09.

Crystallography of 7d

A single crystal (0.18×0.38×0.80 mm^3) grown from a mixture of hexane–benzene (1/1) was used for the unit-cell determinations and the data collections of a Rigaku AFC5S four-circle diffractometer, with graphite-monochromated MoKα radiation (λ=0.71069 Å). This crystal was monoclinic, space group $P2_1$ (#4), a=10.375 (1) Å, b=6.482 (1) Å, c=12.292 (1) Å, β=102.304 (8)°, V=807.6 (2) $Å^3$, Z=2, D_{calcd}=1.432 g/cm^3. All calculations were performed using TEXSAN program.[21] The structure was solved by a direct method (MITHRIL).[22] The non-hydrogen atoms were refined anisotropically and the hydrogen atoms were refined anisotropically and the hydrogen atoms isotoropically. The final *R*-factors after full-matrix least-squares refinements were 0.045 for 1487 observed reflections.

Cycloaddition reaction of azomethine ylides with *N*-phenylmaleimide (8)

Each typical procedure for the reaction of **3a** or **3d** is shown below. (i) A solution of **3a** (1.40 g, 3.5 mmol) and **8** (0.60 g, 3.5 mmol) in dry DME (10 mL) was stirred with CsF (0.53 g, 3.5 mmol) at room temperature for 10 h under argon. The mixture was concentrated in vacuo and extracted with dichloromethane (40 mL). The organic layer was washed with water, dried over anhydrous $MgSO_4$ and evaporated in vacuo. Flash chromatography (BW-300) of the residue gave 1:1 adduct **9a** (0.63 g, 59%) and Michael adduct **10** (0.14 g, 23%) from elution of benzene–ethyl acetate (1:1) (entry 17 in Table 1). (ii) A solution of **3d** (1.2 g, 3.0 mmol) and **8** (1.1 g, 6.0 mmol) in dry DME (10 mL) was refluxed with CsF (0.59 g, 3.9 mmol) for 10 h under nitrogen. Flash chromatography of the reaction mixture obtained by the same procedure as above gave 1:1 adduct **9d** (72 mg, 8%) and 1:2 adduct **11d** (536 mg, 38%) from elution of hexane–benzene (1:1) and benzene–ethyl acetate (1:4), respectively (entry 19 in Table 1).

Anilino-substituted 1:1 adduct 9a. Colorless needles (benzene–cyclohexane (1:1)), mp 140–141°C; IR 3370, 1705 cm^{-1}; ^1H NMR δ 3.70 (ddd, *J*=5.5, 6.7, 8.9 Hz, 1H), 4.11 (d, *J*=8.9 Hz, 1H), 4.33 (d, *J*=6.7 Hz, 2H), 6.86 (s, 1H), 6.99–7.05 (m, 1H), 7.25–7.50 (m, 7H), 7.58 (d, *J*=7.6 Hz, 2H); ^{13}C NMR δ 43.50, 54.29, 60.57, 118.40, 122.91, 126.34, 128.93, 129.04, 129.25, 131.26, 139.64, 154.53, 173.76, 177.39; MS *m/z* (relative intensity) 305 (M^+, 50), 304 (100). Anal. Calcd for $C_{18}H_{15}N_3O_2$; C, 70.80; H, 4.95; N, 13.76. Found: C, 70.81; H, 5.07; N, 13.70.

Morpholino-substituted 1:1 adduct 9d. Colorless needles (hexane–benzene (1:1)), mp 133–134°C; IR 1713 cm^{-1}; ^1H NMR δ 3.45–3.83 (m, 9H), 4.07–4.17 (m, 1H), 4.21 (d, *J*=9.3 Hz, 1H), 4.29 (d, *J*=8.4 Hz, 1H), 7.20–7.29 (m, 2H), 7.37–7.52 (m, 3H); ^{13}C NMR δ 45.14, 47.22, 51.34, 58.81, 66.47, 126.40, 128.86, 129.22, 131.41, 160.77, 172.49, 177.01; MS *m/z* (relative intensity) 299 (M^+, 78), 298 (100). Anal. Calcd for $C_{16}H_{17}N_3O_3$: C, 64.20; H, 5.72, 14.04. Found: C, 64.28; H, 5.87; N, 13.92.

2-Methylthio-*N*-phenylsuccinimide (10). Colorless plates (benzene), mp 95–96°C; IR 1713 cm^{-1}; ^1H NMR δ 2.38 (s, 3H), 2.68 (dd, *J*=3.4, 18.6 Hz, 1H), 3.27 (dd, *J*=8.9, 18.6 Hz, 1H), 3.76 (dd, *J*=3.4, 8.9 Hz, 1H), 7.26–7.37 (m, 2H), 7.37–7.52 (m, 3H); ^{13}C NMR δ 14.91, 35.87, 40.65, 126.41, 128.79, 129.22, 131.61, 173.71, 175.27; MS *m/z* (relative intensity) 221 (M^+, 32), 175 (100). Anal. Calcd for $C_{11}H_{11}NO_2S$: C, 59.72; H, 5.01; N, 6.33. Found: C, 59.58; H, 5.32; N, 6.54.

Morpholino-substituted 1:2 adduct 11d. Colorless needles (EtOH), mp 255–256°C; IR 1715, 1605 cm^{-1}; ^1H NMR δ 2.46 (dd, *J*=7.2, 18.1 Hz, 1H), 3.12 (dd, *J*=9.7, 18.1 Hz, 1H), 3.37 (dd, *J*=3.0, 9.3 Hz, 1H), 3.6–3.8 (m, 8H), 4.07 (dd, *J*=9.3, 15.9 Hz, 1H), 4.20 (dd, *J*=3.0, 9.3 Hz, 1H), 4,26 (dd, *J*=7.2, 9.7 Hz, 1H); 7.25–7.52 (m, 10H); ^{13}C NMR δ 31.50, 43.41, 47.26, 50.01, 56.68, 63.34, 66.63, 126.09, 126.68, 129.16, 129.22, 129.27, 129.41, 130.89, 131.50, 160.14, 172.99, 173.83, 174.86, 175.24; MS *m/z* (relative intensity) 472 (M^+, 100). Anal. Calcd for $C_{26}H_{24}N_4O_5$: C, 66.09; H, 5.12; N, 11.86. Found: C, 65.87; H, 5.31; N, 11.75.

Cycloaddition reaction of azomethine ylides with 2-methyl-*N*-phenylmaleimide (12)

(1) A solution of **3a** (2.01 g, 5.0 mmol) and **12** (0.94 g, 5.0 mmol) in dry DME (10 mL) was stirred with CsF (1.0 g, 6.5 mmol) at room temperature for 10 h under argon. Flash chromatography (BW 300, benzene–ethyl acetate (9:1)) of the reaction mixture obtained by the same procedure as above gave 0.31 g (26%) of Michael adduct **15** and 1.12 g (70%) of a 2.3:1 mixture of 3a-methyl-substituted **13a** and 6a-methyl substituted 1:1 adduct **14a** (estimated by ^1H NMR), respectively (entry 20 in Table 1). Although chromatographic separation of this mixture of **13a** and **14a** was unsuccessful, the mixture was washed with ethanol (15 mL) to leave 380 mg (24%) of **13a** as an insoluble compound.

13a+14a (2.3:1). Colorless viscous oil; IR (neat) 3380, 1715, 1664 cm^{-1}; ^1H NMR δ 1.62 (s, 2.1H), 1.73 (s, 0.9H), 3.34 (t, *J*=5.5 Hz, 0.3H), 3.75 (s, 0.7H), 3.92 (d, *J*=15.2 Hz, 0.7H), 4.32 (d, *J*=5.5 Hz, 0.6H), 4.43 (d, *J*=5.5 Hz, 0.7H), 6.63–6.75 (m, 11H); MS *m/z* (relative intensity) 319 (M^+, 52), 318 (100).

3a-Methyl-substituted 1:1 adduct 13a. Colorless needles (cyclohexane), mp 102–103°C; IR (KBr) 3374, 1711, 1644 cm^{-1}; ^1H NMR δ 1.63 (s, 3H), 3.78 (d, J=1.7 Hz, 1H), 3.91 (d, J=15.2 Hz, 1H), 4.42 (dd, J=1.7, 15.2 Hz, 1H), 6.99–7.06 (m, 1H), 7.25–7.57 (m, 10H); ^{13}C NMR δ 21.36, 50.21, 60.56, 67.47, 118.63, 122.98, 126.34, 128.89, 129.05, 129.22, 131.30, 139.84, 154.41, 172.97, 180.190; MS *m/z* (relative intensity) 319 (M^+, 56), 318 (100). Anal. Calcd for $C_{19}H_{17}N_3O_2$: C, 71.46; H, 5.37; N, 13.16. Found: C, 71.20; H, 5.40; N, 13.03.

2-Methyl-2-methylthio-*N*-phenylsuccinimide (15). Colorless needles (cyclohexane); mp 84.5–85.5°C; IR 1705 cm^{-1}; ^1H NMR δ 1.74, 2.29 (each s, 3H), 2.86, 2.99 (each d, J=18.5 Hz, 1H), 7.26–7.52 (m, 5H); ^{13}C NMR δ 12.92, 21.83, 43.61, 45.35, 126.40, 128.68, 129.18, 131.77, 173.03, 176.87; MS *m/z* (relative intensity) 235 (M^+, 25), 189 (100). Anal. Calcd for $C_{12}H_{13}NO_2S$: C, 61.25; H, 5.57; N, 5.95. Found: C, 61.24; H, 5.63; N, 5.98.

(2) A solution of **3c** (1.58 mg, 4.0 mmol) and **12** (750 mg, 4.0 mmol) in dry DME (10 mL) was stirred with CsF (790 mg, 5.2 mmol) at room temperature for 10 h under argon. Flash chromatography of the residue obtained by the same procedure as above gave 338 mg (36%) of Michael adduct **15** and 722 mg (58%) of a 2.3:1 mixture of 3a-methyl-substituted **13c** and 6a-methyl-substituted 1:1 adduct **14c** (estimated by ^1H NMR) (entry 21 in Table 1). Although chromatographic separation of the mixture of **13c** and **14c** was unsuccessful, the mixture was washed with ethyl acetate (5 mL) to leave the minor adduct **14c** (137 mg, 11%).

13c+14c (2.3:1). Colorless viscous oil; IR (neat) 1717, 1615 cm^{-1}; ^1H NMR δ 1.48–1.85 (m, 9H), 3.22 (dd, J=2.1, 8.0 Hz, 0.3H), 3.45–3.65 (m, 4H), 3.76 (d, J=14.8 Hz, 0.7H), 3.93 (d, J=1.3 Hz, 0.7H), 3.95–4.12 (m, 0.6H), 4.17 (dd, J=1.3, 14.8 Hz, 0.7H), 7.26–7.30 (m, 2H), 7.34–7.50 (m, 3H).

6a-Methylated 1:1 adduct 14c. Colorless needles (cyclohexane), mp 197–198°C; IR 1715, 1595 cm^{-1}; ^1H NMR δ 1.42–1.70 (m, 6H), 1.71 (s, 3H), 3.33 (dd, J=2.1, 8.0 Hz, 1H), 3.52–3.66 (m, 4H), 4.01 (dd, J=8.0, 14.8 Hz, 1H), 4.14 (dd, J=2.1, 14.8 Hz, 1H), 7.26–7.30 (m, 2H), 7.36–7.51 (m, 3H); ^{13}C NMR δ 19.60, 24.42, 25.91, 47.78, 54.99, 55.85, 58.11, 126.32, 128.62, 129.13, 131.84, 163.50, 176.53; MS *m/z* 311 (M^+, 100). Anal. Calcd for $C_{18}H_{21}N_3O_2$: C, 69.43; H, 6.80; N, 13.49. Found: C, 69.35; H, 6.85; N, 13.40.

(3) A solution of **3d** (1.58 g, 4.0 mmol) and **12** (751 mg, 4.0 mmol) in dry DME (10 mL) was stirred with CsF (791 mg, 5.2 mmol) at room temperature for 10 h under argon. Flash chromatography of the residue obtained by the same procedure as above gave 319 mg (34%) of **15** and 776 mg (62%) of a 2.3:1 mixture of 3a-methyl-substituted **13d** and 6a-methyl-substituted 1:1 adduct **14d** (estimated by ^1H NMR) (entry 22 in Table 1). Although chromatographic separation of the 1:1 adducts was again unsuccessful, washing of the mixture with ethanol (5 mL) gave the minor adduct **14d** (125 mg, 10%) as an insoluble compound.

13d+14d (2.3:1). Colorless viscous oil, IR (neat) 1717, 1620 cm^{-1}; ^1H NMR δ 1.60 (s, 2.1H), 1.71 (s, 0.9H), 3.21 (dd, J=2.5, 8.1 Hz, 0.3H), 3.45–3.83 (m, 8.7H), 3.91 (d, J=1.3 Hz, 0.7H), 4.02 (dd, J=8.1, 14.8 Hz, 0.3H), 4.14 (dd, J=2.5, 14.8 Hz, 0.3H), 4.22 (d, J=1.3 Hz, 0.7H), 7.20–7.55 (m, 5H).

6a-Methyl-substituted 1:1 adduct 14d. Colorless needles (cyclohexane), mp 186–187°C; IR 1715, 1605 cm^{-1}; ^1H NMR δ 1.72 (s, 3H), 3.36 (dd, J=2.5, 8.0 Hz, 1H), 3.52–3.74 (m, 8H), 4.02 (dd, J=8.0, 15.2 Hz, 1H), 4.14 (dd, J=2.5, 15.2 Hz, 1H), 7.26–7.30 (m, 2H), 7.40–7.51 (m, 3H); ^{13}C NMR δ 19.69, 47.01, 55.26, 55.54, 58.01, 66.72, 126.29, 128.77, 129.18, 131.64, 163.57, 176.31, 176.39; MS *m/z* 313 (M^+, 100). Anal. Calcd for $C_{17}H_{19}N_3O_3$: C, 65.16; H, 6.11; N, 13.41. Found: C, 65.37; H, 6.24; N, 13.16.

Cycloaddition reactions of azomethine ylides with dimethyl fumarate (16) or dimethyl maleate (17)

As a typical example, the reaction of **3a** with **16** is shown below. A solution of **3a** (201 mg, 0.5 mmol) and **16** (72 mg, 0.5 mmol) in dry DME (7 mL) was stirred with CsF (76 mg, 0.5 mmol) at room temperature for 20 h under nitrogen, and then concentrated in vacuo. The residue was extracted with dichloromethane (13 mL) and organic layer was washed with water (5 mL), dried over anhydrous $MgSO_4$ and then evaporated in vacuo. Flash chromatography of the residue on silica gel (BW 300) with a mixture of benzene–ethyl acetate (4:1) gave 98 mg (71%) of aminonitrile cycloadduct **20a** (entry 1 in Table 2).

The reaction of **3a** with **17** under similar reaction conditions furnished the same cycloadduct **20a** in 52% yield (entry 5 in Table 2). The other reactions of **3** with **16** or **17** are listed in Table 2.

(*E*)-2-Anilino-3,4-bis(methoxycarbonyl)-1-pyrroline (20a). Colorless viscous oil, IR (neat) 3378, 1738, 1647 cm^{-1}; ^1H NMR δ 3.64–3.75 (m, 2H), 3.80, 3.83 (each s, 3H), 4.20–4.35 (m, 2H), 6.79–6.88 (m, 1H), 6.97–7.37 (m, 3H), 7.55–7.62 (m, 2H); ^{13}C NMR δ 44.51, 52.47, 53.12, 54.21, 59.35, 118.54, 122.59, 128.96, 139.93, 155.56, 169.83, 173.35; MS *m/z* (relative intensity) 276 (M^+, 60), 275 (100). HRMS Calcd for $C_{14}H_{16}N_2O_4$ 276.1110. Found: 276.1129.

(*E*)-3,4-Bis(methoxycarbonyl)-2-piperidino-1-pyrroline (20c). Colorless oil, IR (neat) 1738 cm^{-1}; ^1H NMR δ 1.57 (br s, 6H) 3.38 (br s, 4H), 3.72, 3.75 (each s, 3H), 3.96–4.24 (m, 4H); ^{13}C NMR δ 24.44, 25.54, 47.78, 47.87, 51.21, 52.41, 52.63, 59.30, 163.09, 170.86, 173.62; MS *m/z* (relative intensity) 268 (M^+, 44), 209 (100). Anal. Calcd for $C_{13}H_{20}N_2O_4$: C, 58.19; H, 7.51; N, 10.44. Found: C, 57.87; H, 7.62, N, 10.58.

(*E*)-3,4-Bis(methoxycarbonyl)-2-morpholino-1-pyrroline (20d). Pale yellow oil, IR (neat) 1738 cm^{-1}; ^1H NMR δ 3.30–3.80 (m, 8H), 3.73, 3.78 (each s, 3H), 3.30–4.30 (m, 4H); ^{13}C NMR δ 47.08, 47.51, 52.05, 52.48, 52.73, 59.39, 66.46, 163.18, 170.41, 173.45; MS *m/z* (relative intensity) 270 (M^+, 60), 211 (100). Anal. Calcd for $C_{12}H_{18}N_2O_5$: C, 53.32; H, 6.71; N, 10.37. Found: C, 53.03; H, 6.83; N, 10.59.

Cycloaddition reactions of azomethine ylides with fumaronitrile (18)

As a typical run, the reaction of **3a** with **18** in DME under reflux is shown below (entry 12 in Table 2). A solution of **3a** (403 mg, 1.0 mmol) and **18** (78 mg, 1.0 mmol) in dry DME (25 mL) was refluxed with CsF (304 mg, 2.0 mmol) for 10 h under nitrogen, and then concentrated in vacuo. Flash chromatography of the residue obtained by the same procedure as above gave **22a** (42 mg, 23%) and **21a** (73.5 mg, 35%) from elution of a mixture of benzene–ethyl acetate (9:1) and AcOEt, respectively.

The other reactions were performed under the conditions listed in Table 2 (entries 8–11, 13 and 14).

2-Anilino-3,4-dicyano-2-pyrroline (21a).[13] Pale yellow viscous oil. IR (neat) 3346, 3146, 2252, 2174, 1656 cm^{-1}; MS *m/z* (relative intensity) 210 (M^+, 10), 77 (100). HRMS Calcd for $C_{12}H_{10}N_4$ 210.0905. Found: 210.0885.

3,4-Dicyano-2-(1-pyrrolidinyl)-2-pyrroline (21b). Colorless needles (benzene–hexane (1:1)), mp 135–136°C; IR 3270, 2242, 2160, 1595 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.75–2.0 (m, 4H), 3.36–3.40 (m, 4H), 3.49 (dd, *J*=2.1, 4.6 Hz, 1H), 3.55 (dd, *J*=2.1, 9.3 Hz, 1H), 4.11 (dd, *J*=4.6, 9.3 Hz, 1H), 6.39 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 24.78, 31.88, 45.61, 47.55, 47.96, 121.58, 122.10, 160.91; MS *m/z* (relative intensity) 188 (M^+, 72), 160 (100). Anal. $C_{10}H_{12}N_4$: C, 63.81; H, 6.43; N, 29.76. Found: C, 63.85; H, 6.33; N, 29.46.

3,4-Dicyano-2-piperidino-2-pyrroline (21c). Colorless needles (cyclohexane), mp 125–126°C; IR (KBr) 3272, 2236, 2166, 1603 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.40–1.70 (m, 6H), 3.32–3.44 (m, 4H), 3.48 (dd, *J*=2.1, 4.6 Hz, 1H), 3.52 (dd, *J*=2.1, 9.7 Hz, 1H), 4.12 (dd, *J*=4.6, 9.7 Hz, 1H), 6.51 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 23.32, 25.07, 32.02, 46.43, 46.61, 47.67, 121.47, 121.69, 162.78; MS *m/z* (relative intensity) 202 (M^+, 7), 175 (100). Anal. Calcd for $C_{11}H_{14}N_4$: C, 65.32; H, 6.98; N, 27.70. Found: C, 65.41; H, 7.05; N, 27.48.

3,4-Dicyano-2-morpholino-2-pyrroline (21d). Colorless prisms (benzene), mp 153–154.5°C; IR (KBr) 3282, 2234, 2170 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.28–3.45 (m, 4H), 3.46–3.67 (m, 6H), 4.16 (dd, *J*=5.1, 9.3 Hz, 1H), 6.64 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 31.90, 46.61, 46.67, 47.39, 65.34, 121.27, 163.27; MS *m/z* (relative intensity) 204 (M^+, 63), 177 (100). Anal. Calcd for $C_{10}H_{12}N_4O$: C, 58.81; H, 5.92; N, 27.44. Found: C, 58.84; H, 5.98; N, 27.27.

2-Anilino-3-cyanopyrrole (22a). Colorless needles (ethyl acetate–hexane (1:1)), mp 92.5–93.5°C; IR (KBr) 3358, 3270, 2216 cm^{-1}; ^1H NMR δ 5.89 (br s, 1H), 6.32, 6.44 (each dd, *J*=2.5, 3.4 Hz, 1H), 6.87–6.92 (m, 2H), 6.95–7.02 (m, 1H), 7.26–7.33 (m, 2H), 8.20 (br s, 1H); ^{13}C NMR δ 80.74, 110.04, 113.51, 116.28, 116.98, 121.63, 129.68, 139.91, 142.50; MS *m/z* (relative intensity) 183 (M^+, 100). Anal. Calcd for $C_{11}H_9N_3$: C, 72.11; H, 4.95; N, 22.94. Found: C, 71.88; H, 5.01; N, 22.77.

3-Cyano-2-(1-pyrrolidinyl)pyrrole (22b). Gray needles (ethyl acetate–hexane (1:1)), mp 172–173°C; IR (KBr) 3258, 2198 cm^{-1}; ^1H NMR δ 1.85–2.15 (m, 4H), 3.4–3.6 (m, 4H), 6.13, 6.17 (each d, *J*=3.4 Hz, 1H), 8.13 (br s, 1H); ^{13}C NMR δ 25.48, 48.55, 68.34, 110.35, 110.69, 120.75, 147.47; MS *m/z* (relative intensity) 161 (M^+, 100). Anal. Calcd for $C_9H_{11}N_3$: C, 67.06; H, 6.88; N, 26.07. Found: C, 66.78; H, 6.82; N, 25.80.

3-Cyano-2-piperidinopyrrole (22c). Colorless needles (ethyl acetate–hexane (1:1)), mp 90–90.5°C; IR (KBr) 3272, 2206 cm^{-1}; ^1H NMR δ 1.42–1.72 (m, 6H), 3.27–3.31 (m, 4H), 6.17, 6.28 (each dd, *J*=2.5, 3.4 Hz, 1H), 8.59 (br s, 1H); ^{13}C NMR δ 23.79, 25.37, 50.53, 73.98, 110.56, 111.89, 119.51, 149.67; MS *m/z* (relative intensity) 175 (M^+, 100). Anal. Calcd for $C_{10}H_{13}N_3$: C, 68.54; H, 7.48; N, 23.98. Found: C, 68.82; H, 7.43; N, 23.99.

3-Cyano-2-morpholinopyrrole (22d). Purple needles (benzene–hexane (1:1)), mp 127–128°C; IR 3276, 2210 cm^{-1}; ^1H NMR δ 3.25–3.35 (m, 4H), 3.80–3.85 (m, 4H), 6.22, 6.34 (each dd, *J*=2.5, 3.3 Hz, 1H), 8.62 (br s, 1H); ^{13}C NMR δ 49.45, 66.31, 75.22, 110.92, 112.47, 113.76, 148.48; MS *m/z* (relative intensity) 177 (M^+, 78), 119 (100). Anal. Calcd for $C_9H_{11}N_3O$: C, 61.00; H, 6.26; N, 23.72. Found: C, 61.07; H, 6.29; N, 23.65.

Dehydrocyanation of pyrroline 21a leading to pyrrole 22a

A solution of **21a** (294 mg, 1.4 mmol) in dry DME (5 mL) was refluxed with CsF (205 mg, 1.4 mmol) under nitrogen for 24 h, and then concentrated in vacuo to leave the residue. Flash chromatography of the residue obtained by the same procedure as above gave 218 mg (85%) of **22a** by using a mixture of benzene–ethyl acetate (1:1) as eluent.

The similar dehydrocyanation of **20c** gave a 79% yield of **21c**.

Cycloaddition reaction of azomethine ylide with 2-chloroacrylonitrile (19)

A solution of **3a** (1.2 g, 3.0 mmol) and **19** (1.31 g, 15 mmol) in dry DME (10 mL) was refluxed with CsF (547 mg, 3.6 mmol) for 10 h under argon. Chromatography (BW-200, benzene–ethyl acetate (9:1)) of the reaction mixture obtained by the same procedure as above gave 277 mg (42%) of 2-anilino-3-chloro-3-cyano-1-pyrroline (**23a**) (entry 16 in Table 2).

23a. Pale brown oil, IR (neat) 3360, 2240, 1680 cm^{-1}; ^1H NMR δ 2.68 (dt, *J*=6.4, 14.3 Hz, 1H), 2.84 (dt, *J*=7.2, 14.3 Hz, 1H), 3.91 (br s, 2H), 7.02–7.12 (m, 1H), 7.28–7.38 (m, 4H), 7.48 (br s, 1H); ^{13}C NMR δ 41.31, 58.15, 77.29, 116.15, 123.74, 128.35, 129.23, 155.01; MS *m/z* (relative intensity) 221 (M^+, 25), 220 (40), 219 (M^+, 80), 218 (100). HRMS Calcd for $C_{11}H_{10}N_3Cl$ 219.0564. Found: 219.0560.

Air oxidation of 20a leading to 2-anilino-3,4-bis(methoxycarbonyl)-3-hydroxy-1-pyrroline (24). A solution of **20a** (314 mg, 1.15 mmol) in ethanol (10 mL) was stirred at room temperature under air atmosphere for 10 days. The solvent was evaporated in vacuo and the residue was triturated with

benzene to give solid which was recrystallized from benzene to give 72 mg (22%) of **24** as colorless plates. Mp 71–72°C; IR 3550, 3296, 1738, 1715 cm^{-1}; ^1H NMR δ 3.72, 3.81 (each s, 3H), 3.5–4.1 (m, 4H), 7.05–7.38 (m, 6H); MS *m/z* (relative intensity) 292 (M^+, 60), 291 (100). Anal, Calcd for $C_{14}H_{16}N_2O_5$: C, 57.53; H, 5.52; N, 9.59. Found: C, 57.67; H, 5.42; N, 9.48.

The cycloaddition reactions of azomethine ylides with DMAD

As typical examples, the reactions of entries 1 and 6 in Table 3 are shown, respectively. (i) A solution of **3a** (423 mg, 1.05 mmol) and DMAD (150 mg, 1.05 mmol) in dry DME (3 mL) was stirred with CsF (160 mg, 1.05 mmol) at room temperature for 6 h under argon. The reaction mixture was concentrated in vacuo and the residue was extracted with dichloromethane (20 mL). The organic layer was washed with water, dried over anhydrous $MgSO_4$, and evaporated in vacuo. Flash chromatography (BW 300) of the residue with a mixture of benzene–ethyl acetate (4:1) gave 204 mg (71%) of aminonitrile cycloadduct **25a**. (ii) A solution of **3d** (0.98 g, 2.5 mmol) and DMAD (0.71 g, 5.0 mmol) in dry DME (10 mL) was stirred with CsF (0.38 g, 2.5 mmol) at room temperature for 6 h. Flash chromatography of the residue obtained from the same procedure as above with a mixture of benzene–ethyl acetate (5:1) gave 327 mg (32%) of a 2:1 mixture of **26d** and **27d** (estimated by ^1H NMR) and 68 mg (10%) of **25d**, respectively.

2-Anilino-3,4-bis(methoxycarbonyl)pyrrole (25a). Colorless prisms (benzene), mp 148–149°C; IR 3352, 3296, 1713 cm^{-1}; ^1H NMR δ 3.74, 3.75 (each s, 3H), 6.8–7.4 (m, 6H), 8.32, 9.06 (each br s, 1H); ^{13}C NMR δ 51.09, 51.45, 93.40, 114.19, 118.64, 119.67, 129.93, 139.94, 143.89, 164.63, 166.35; MS *m/z* (relative intensity) 274 (M^+, 44), 210 (100). Anal. Calcd for $C_{14}H_{14}N_2O_4$: C, 61.31; H, 5.15; N, 10.21. Found: C, 61.44; H, 5.28; N, 10.05.

3,4-Bis(methoxycarbonyl)-2-piperidinopyrrole (25c). Pale yellow viscous oil, IR (neat) 3296, 1711 cm^{-1}; ^1H NMR δ 1.45–1.70 (m, 6H), 3.02–3.15 (m, 4H), 3.77, 3.80 (each s, 3H), 6.91 (d, J=3.0 Hz, 1H), 9.30 (br s, 1H); ^{13}C NMR δ 23.95, 25.88, 51.48, 51.52, 100.47, 115.13, 118.83, 147.081, 165.35, 166.68; MS *m/z* (relative intensity) 266 (M^+, 100). HRMS Calcd for $C_{13}H_{18}N_2O_4$ 266.1267. Found: 266.1275.

3,4-Bis(methoxycarbonyl)-2-morpholinopyrrole (25d). Colorless prisms (ethyl acetate–hexane (1:1)), mp 127–128°C; IR 3284, 1711 cm^{-1}; ^1H NMR δ 3.10–3.25 (m, 4H), 3.7–3.8 (m, 4H), 3.78 (d, J=2.9 Hz, 1H), 9.57 (br s, 1H); ^{13}C NMR δ 51.20, 51.60, 51.63, 66.85, 101.70, 115.30, 119.27, 145.48, 165.26, 165.51; MS *m/z* (relative intensity) 268 (M^+, 100). Anal Calcd for $C_{12}H_{16}N_2O_5$: C, 53.72, H, 6.01; N, 10.44. Found: C, 53.80; H, 6.01; N, 10.50.

Reaction of pyrrole 25d with DMAD

A solution of **25d** (172 mg, 0.64 mmol) and DMAD (91 mg, 0.64 mmol) in dry benzene (3 mL) was stirred with triethylamine (72 mg, 0.71 mg) at room temperature for 4 h under nitrogen. The reaction mixture was evaporated in vacuo, and flash chromatography (BW 300) of the residue with a mixture of benzene–ethyl acetate (4:1) gave 205 mg (78%) of a 3:1 mixture of isomeric Michael adducts **26d** and **27d** (estimated by ^1H NMR). Although quantitative separation of the isomers was very difficult, pure **26d** and **27d** were obtained by further chromatography and recrystallization. The structure of (*Z*)-Michael adduct **26d** was determined by the X-ray crystallographic analysis.

(*Z*)-1,2-Bis(methoxycarbonyl)-1-[3,4-bis(methoxycarbonyl)-2-(morpholino)pyrrolyl]ethane (26d). Pale yellow prisms (hexane–benzene (1:1)) mp 147–148°C; IR 1738, 1705 cm^{-1}; ^1H NMR δ 2.97–3.05 (m, 4H), 3.58–3.61 (m, 4H), 3.73, 3.79, 3.84, 3.89 (each s, 3H), 6.91 (s, 1H), 7.01 (s, 1H); ^{13}C NMR δ 51.45, 51.64, 51.91, 52.47, 53.21, 67.22, 107.83, 115.09, 123.02, 123.90, 137.57, 144.63, 163.27, 163.66, 263.75, 165.49. MS *m/z* (relative intensity) 410 (M^+, 60), 319 (100). Anal. Calcd for $C_{18}H_{22}N_2O_9$: C, 52.68; H, 5.40; N, 6.83. Found: C, 52.79; H, 5.49; N, 6.73.

Crystallography of 26d

A single crystal (0.18×0.32×0.36 mm) grown from a mixture of hexane–benzene (1:1) was used for the unit-cell determination and the data collections of a Rigaku AFC5S diffractometer. This crystal was monoclinic, space group $P2_1$ (#14), Z=4 with a=8.20(3) Å, b=8.980(6) Å, c=27.13(1) Å, β=96.64(9)°, V=1985(8) $Å^3$, and D_{calcd}= 1.373 g/cm^3. All calculations were performed using the TEXSAN program,[21] and the structure was solved by a direct method (MITHRIL).[22] The final R-factors after full-matrix least-squares refinement were 0.087 for 1149 observed reflections.

(*E*)-Morpholino isomer 27d. Colorless needles (hexane–benzene (1:1)), mp 104–105°C; IR 1738, 1717 cm^{-1}; ^1H NMR δ 2.90–3.15 (m, 4H), 3.55–3.75 (m, 4H), 3.80, 3.81, 3.88, 3.89 (each s, 3H), 6.25 (s, 1H), 7.14 (s, 1H); ^{13}C NMR δ 50.82, 51.70, 52.30, 52.51, 53.05, 66.69, 111.09, 116.37, 118.59, 121.81, 139.03, 141.61, 162.73, 163.19, 163.89, 165.06; MS *m/z* (relatively intensity) 410 (M^+, 56), 319 (100). Anal. Calcd for $C_{18}H_{22}N_2O_9$: C, 52.68, H, 5.40, N, 6.83. Found: C, 52.79; H, 5.49; N, 6.73.

A similar reaction of pyrrole **25b** or **25c** with DMAD gave a mixture of the corresponding Michael adducts **26b** (*Z* isomer) and **27b** (*E* isomer) or **26c** (*Z* isomer) and **27c** (*E* isomer) in 72 or 74% yield, respectively. However, pure **26b** could not be isolated.

(*E*)-1,2-Bis(methoxycarbonyl)-1-[3,4-bis(methoxycarbonyl)-2-(1-pyrrolidinyl)pyrrolyl]ethene (27b). Colorless needles (hexane–ethyl acetate (1:1)), mp 107–108°C; IR 1720, 1710 cm^{-1}; ^1H NMR δ 1.72–2.12 (m, 4H), 2.96–3.31 (m, 4H), 3.72, 3.78, 3.83, 3.89 (each s, 3H), 6.25 (s, 1H), 7.15 (s, 1H); MS *m/z* (relative intensity) 394 (M^+, 57), 303 (100). Anal. Calcd for $C_{18}H_{22}N_2O_8$: C, 54.82; H, 5.62; N, 7.10. Found: C, 54.75; H, 5.52; N, 6.94.

(*Z*)-1,2-Bis(methoxycarbonyl)-1-[3,4-bis(methoxycarbonyl)-2-(piperidino)-pyrrolyl]ethene (26c). Pale yellow viscous oil; IR (neat) 1734, 1714 cm^{-1}; ^1H NMR δ 1.47 (br

s, 6H), 2.90 (br s, 4H), 3.73, 3.78, 3.82, 3.87 (each s, 3H), 6.84 (s, 1H), 7.01 (s, 1H); ^{13}C NMR δ 23.76, 26.15, 51.64, 51.45, 51.91, 52.47, 53.21, 107.83, 115.09, 123.07, 123.07, 123.90, 137.51, 144.63, 163.27, 163.66, 163.75, 165.50; MS *m/z* (relative intensity) 408 (M^+, 67), 317 (100). HRMS Calcd for $C_{19}H_{24}N_2O_8$ 408.1533. Found: 408.1539.

(*E*)-Piperidino isomer 27c. Colorless needles (hexane); mp 109–110°C; IR 1751, 1721 cm^{-1}; ^{1}H NMR δ 1.50 (br s, 6H), 2.89–2.92 (m, 4H), 3.79, 3.81 (each s, 3H), 3.87 (s, 6H), 6.24 (s, 1H), 7.12 (s, 1H); ^{13}C NMR δ 23.45, 25.51, 51.82, 51.64, 52.20, 52.47, 52.87, 110.21, 116.06, 117.99, 121.42, 139.33, 143.56, 162.60, 163.39, 164.11, 165.55; MS *m/z* (relative intensity) 408 (M^+, 70), 317 (100). Anal. Calcd for $C_{19}H_{24}N_2O_8$: C, 55.87; H, 5.92; N, 6.86. Found: C, 55.82; H, 6.04; N, 6.76.

Cycloaddition reactions of azomethine ylides with aldehydes 28–33

(i) Reaction with benzaldehyde (**28**). After a solution of **3a** (1.5 g, 3.73 mmol) and **28** (1.98 g, 18.7 mmol) in dry DME (10 mL) was stirred with CsF (679 mg, 4.5 mmol) at room temperature for 10 h under argon, the reaction mixture was concentrated in vacuo. The residue was extracted with ether (30 mL) and flash chromatography (BW-300) of the extract furnished imine **40** (324 mg, 48%) and 2-oxazoline **34a** (342 mg, 39%) from elution of a mixture of benzene–ethyl acetate (9:1) and ethyl acetate, respectively (entry 2 in Table 4).

The similar reaction of **3a** with *p*-chlorobenzaldehyde (**29**) gave a mixture of 2-oxazoline **35a** and imine **40** (entries 3 and 4 in Table 4).

2-Anilino-5-phenyl-2-oxazoline (34a). Colorless needles (cyclohexane), mp 127–128°C. IR 3240, 1657 cm^{-1}; ^{1}H NMR δ 3.78 (dd, *J*=7.6, 11.8 Hz, 1H), 4.24 (dd, *J*=8.9, 11.8 Hz, 1H), 5.55 (dd, *J*=7.6, 8.9 Hz, 1H), 6.79 (br s, 1H), 6.94–7.01 (m, 1H), 7.21–7.38 (m, 9H); ^{13}C NMR δ 58.76, 80.86, 119.19, 122.35, 125.86, 128.48, 128.82, 128.96, 140.02, 140.64, 157.19; MS *m/z* (relative intensity) 238 (M^+, 40), 134 (100). Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.59; H, 5.93; N, 11.76. Found: C, 75.81; H, 6.05; N, 11.46.

2-Anilino-5-(*p*-chlorophenyl)-2-oxazoline (35a). Colorless needles (benzene), mp 156–157°C, IR 3240, 1651 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 3.62 (dd, *J*=6.7, 12.2 Hz, 1H), 4.24 (dd, *J*=9.3, 12.2 Hz, 1H), 5.58 (dd, *J*=6.7, 9.3 Hz, 1H), 6.88–6.94 (m, 1H), 7.40, 7.47 (each d, *J*=8.4 Hz, 2H), 7.51 (d, *J*=7.2 Hz, 2H), 9.13 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 60.65, 77.67, 117.48, 121.00, 127.40, 128.50, 128.64, 132.52, 140.14, 140.64, 155.59; MS *m/z* (relative intensity) 274 (M^+, 5), 272 (M^+, 17), 134 (100), 132 (47). Anal. Calcd for $C_{15}H_{13}N_2OCl$: C, 66.03; H, 4.81; N, 10.27. Found: C, 66.31; H, 4.87; N, 10.35.

2,3-Dimethyl-1-phenylisothiourea (40). Colorless needles (hexane); mp 59.5–60.5°C; IR 3342, 1603 cm^{-1}; ^{1}H NMR δ 2.25 (s, 3H), 2.91 (s, 3H), 4.40 (br s, 1H), 6.89–6.91 (m, 2H), 6.97–7.03 (m, 1H), 7.22–7.29 (m, 2H); ^{13}C NMR 13.87, 30.01, 122.32, 122.60, 128.95, 149.63, 154.57. Anal. $C_9H_{12}N_2S$: C, 59.97; H, 6.71; N, 15.54. Found: C, 60.09; H, 6.82; N, 15.50.

(ii) As a typical example of the reaction with *p*-nitrobenzaldehyde (**30**), the reaction of **3c** is shown (entry 6 in Table 4). A solution of **3c** (1.5 g, 3.8 mmol) and **30** (2.87 g, 19.0 mmol) in dry DME (15 mL) was stirred with CsF (703 mg, 4.6 mmol) at room temperature for 10 h under argon. The reaction mixture was concentrated in vacuo and the residue was extracted with chloroform (30 mL). Flash chromatography of the extract on silica gel (BW-300) with a mixture of ethyl acetate–ethanol (10:1) gave 943 mg (90%) of 2-oxazoline **36c**.

Reactions of **3a** and **3d** with **30** under similar conditions gave the corresponding 2-oxazolines **36a** and **36d**, respectively (entries 5 and 7 in Table 4).

2-Anilino-5-(*p*-nitrophenyl)-2-oxazoline (36a). Colorless prisms (benzene), mp 189.5–190°C, IR 3236, 1657, 1518, 1354 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 3.34 (dd, *J*=6.7, 12.7 Hz, 1H), 4.34 (dd, *J*=9.3, 12.7 Hz, 1H), 5.76 (dd, *J*=6.7, 9.3 Hz, 1H), 6.90–6.96 (m, 1H), 7.23–7.30 (m, 2H), 7.63–7.67 (m, 4H), 8.29 (d, *J*=8.9 Hz, 2H); 9.45 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 60.95, 77.07, 117.45, 121.15, 123.90, 126.47, 128.55, 140.38, 147.04, 148.87, 155.54; MS *m/z* (relative intensity) 283 (M^+, 81), 119 (100). Anal. Calcd for $C_{15}H_{13}N_3O_3$: C, 63.59; H, 4.63; N, 14.83. Found: C, 63.62; H, 4.67; M, 14.76.

5-(*p*-Nitrophenyl)-2-piperidino-2-oxazoline (36c). Colorless needles (hexane), mp 86–87°C, IR 1649, 1522, 1340 cm^{-1}, ^{1}H NMR δ 1.62 (br s, 6H), 3.44 (br s, 4H), 3.65 (dd, *J*=7.2, 12.2 Hz, 1H), 4.28 (dd, *J*=9.3, 12.2 Hz, 1H), 5.57 (dd, *J*=7.2, 9.3 Hz, 1H), 7.45–7.51 (m, 2H), 8.21–8.27 (m, 2H); ^{13}C NMR δ 24.19, 25.37, 46.68, 61.28, 79.99, 123.99, 126.14, 147.56, 148.68, 161.22; MS *m/z* (relative intensity) 275 (M^+, 36), 84 (100). Anal. Calcd for $C_{14}H_{17}N_3O_3$: C, 61.08; H, 6.22; N, 15.26. Found: C, 60.89; H, 6.28; N, 15.42.

2-Morpholino-5-(*p*-nitrophenyl)-2-oxazoline (36d). Colorless needles (benzene–hexane (1:1)), mp 89–90°C; IR 1663, 1521, 1344 cm^{-1}; ^{1}H NMR δ 3.40–3.52 (m, 4H), 3.68 (dd, *J*=7.6, 12.7 Hz, 1H), 4.29 (dd, *J*=9.3, 12.7, 1H), 5.62 (dd, *J*=7.6, 9.3 Hz, 1H), 5.70–5.80 (m, 4H), 7.49 (d, *J*=8.9 Hz, 2H), 8.22–8.27 (m, 2H); ^{13}C NMR δ 45.88, 61.06, 66.32, 80.38, 124.06, 126.20, 147.69, 148.03, 160.95; MS *m/z* (relative intensity) 277 (M^+, 34), 86 (100). Anal. Calcd for $C_{13}H_{15}N_3O_4$: C, 56.31; H, 5.45; N, 15.15. Found: C, 56.20; H, 5.41; N, 15.18.

(iii) Reaction of **3a** with 2-pyridinecarboxaldehyde (**31**). After a solution of **3a** (1.5 g, 3.73 mmol) and **31** (1.99 g, 18.6 mmol) in dry DME (10 mL) was stirred with CsF (673 mg, 4.4 mmol) at room temperature for 10 h under argon, the reaction mixture was concentrated in vacuo. The residue was extracted with ether (30 mL), and flash chromatography of the extract on silica gel (BW-300) with ethyl acetate furnished 635 mg (71%) of 2-oxazoline **37a** (entry 8 in Table 4).

A similar reaction of **3a** with 3-(**32**) or 4-pyridinecarboxaldehyde (**33**) afforded the corresponding 2-oxazolines **38a** or **39a**, respectively (entries 9, 10 in Table 4).

2-Anilino-5-(2-pyridyl)-2-oxazoline (37a). Colorless needles (benzene), mp 138.5–139.5°C, IR 3370, 1688 cm^{-1}; ^1H NMR δ 3.95 (dd, J=6.7, 11.8 Hz, 1H), 4.35 (dd, J=9.3, 11.8 Hz, 1H), 5.67 (dd, J=6.7, 9.3 Hz, 1H), 6.4–7.2 (br s, 1H), 6.99 (t, J=7.6 Hz, 1H), 7.21–7.44 (m, 6H), 7.70 (t, J=7.6 Hz, 1H), 8.59 (d, J=5.1 Hz, 1H); ^{13}C NMR δ 57.32, 80.34, 119.21, 119.82, 122.42, 123.04, 128.98, 137.03, 140.77, 149.49, 156.92, 159.49; MS *m/z* (relative intensity) 239 (M^+, 14), 93 (100). Anal. Calcd for $C_{14}H_{13}N_3O$: C, 70.28; H, 5.48; N, 17.56. Found: C, 70.33; H, 5.56; N, 17.44.

2-Anilino-5-(3-pyridyl)-2-oxazoline (38a). Colorless needles (benzene), mp 127.5–128°C, IR 3238, 1653 cm^{-1}; ^1H NMR δ 3.84 (dd, J=7.6, 12.2 Hz, 1H), 4.35 (dd, J=9.3, 12.2 Hz, 1H), 5.25 (br s, 1H), 5.59 (dd, J=7.6, 9.3 Hz, 1H), 6.99–7.06 (m, 1H), 7.25–7.42 (m, 5H), 7.70–7.73 (m, 1H), 8.59–8.65 (m, 2H); ^{13}C NMR δ 59.42, 78.20, 118.87, 122.55, 123.79, 129.04, 133.42, 135.85, 140.07, 147.49, 149.77, 156.94; MS *m/z* (relative intensity) 239 (M^+, 65), 93 (100). Anal. Calcd for $C_{14}H_{13}N_3O$: C, 70.28; H, 5.48; N, 17.56. Found: C, 70.36; H, 5.54; N, 17.56.

2-Anilino-5-(4-pyridyl)-2-oxazoline (39a). Colorless needles (hexane–benzene (1:1)), mp 134.5–135°C, IR 3254, 1680 cm^{-1}; ^1H NMR δ 3.76 (dd, J=7.2, 12.2 Hz, 1H), 4.36 (dd, J=9.3, 12.2 Hz, 1H), 5.23 (dd, J=7.2, 9.3 Hz, 1H), 6.97–7.05 (m, 1H), 7.20–7.45 (m, 7H), 8.55–8.65 (m, 2H); ^{13}C NMR δ 59.55, 78.62, 118.78, 120.11, 122.64, 129.07, 139.82, 149.32, 150.20, 156.91; MS *m/z* (relative intensity) 239 (M^+, 86), 104 (100). Anal. Calcd for $C_{14}H_{13}N_3O$: C, 70.28; H, 5.48; N, 17.56. Found: C, 70.27; H, 5.55: N, 17.45.

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