A New and General Route to *N*-Protonated Azomethine Ylides from *N*-(Silylmethyl)amidines and -thioamides. Cycloaddition of Synthetic Equivalents of Nitrile Ylides

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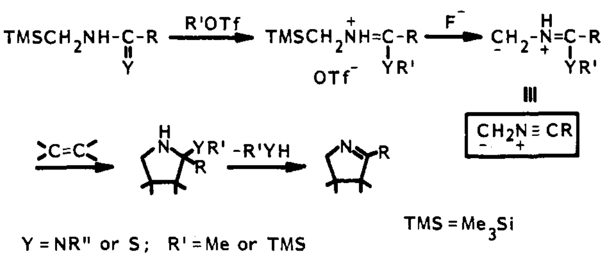
The N- or S-alkylation or -silylation of *N*-(silylmethyl)amidines or -thioamides and the subsequent desilylation of the silylmethyl group generate *N*-protonated azomethine ylides bearing a leaving group. These azomethine ylides undergo successful cycloaddition with electron-deficient olefins, acetylenes, and aldehydes. As the leaving group is eliminated under the reaction conditions, these azomethine ylides can be synthetic equivalents of nonstabilized nitrile ylides which are otherwise relatively inaccessible.

The importance of 1,3-dipoles such as azomethine ylides in organic synthesis has grown rapidly since the discovery that nonstabilized azomethine ylides can be generated by desilylation of *N*-(silylmethyl)iminium salts. These salts can be prepared by N-silylmethylation of imines,[1] quaterization of *N*-(silylmethyl)imines,[2] or *O*- or S-alkylation of *N*-(silylmethyl)amides or -thioamides.[3] Cycloaddition of these ylides with olefins and acetylenes produces a variety of *N*-substituted pyrrolidines, pyrrolines, and pyrroles.

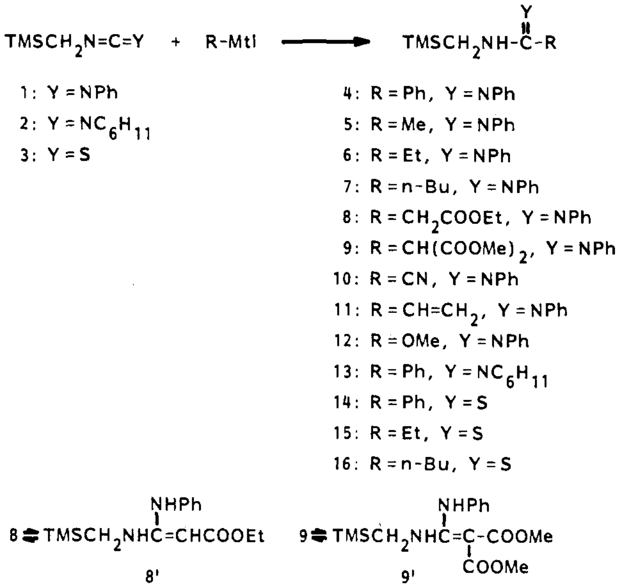
N-Protonated (or *N*-unsubstituted) or *N*-silylated azomethine ylides are accessible through imine–azomethine ylide tautomerism[4] or water-induced desilylation of *N*-(silylmethyl)imines.[5] If a leaving group is added to these imines, the resulting imines can be synthetic equivalents of nitrile ylides by a cycloaddition and elimination sequence.[6,7] This is important because such azomethine ylides directly afford cycloaddition products 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*-protonated azomethine ylides carrying a leaving group at the ylide carbon and also aiming at establishing their utility as synthetic equivalents of nonstabilized nitrile ylides whose direct generation is unknown heretofore. Our approach to the *N*-protonated azomethine ylides consists of initial N- or S-alkylation or -silylation of *N*-(silylmethyl)amidines (Y = NR″) or -thioamides (Y = S) leading to *N*-(silylmethyl)iminium salts. Subsequent attack at the silicon bonded to carbon with a silylophile affords the desired ylides, which undergo cycloaddition with olefins. Elimination of the leaving group from the cycloadducts gives formal nitrile ylide cycloadducts. The most important step in this sequence is regioselective alkylation or silylation on the heteroatom Y, not on the amidine or thioamide nitrogen (Scheme I).

Scheme I



Scheme II



N-(Silylmethyl)-*N*′-phenylamidines and *N*-(silylmethyl)thioamides were chosen as starting compounds. Cycloadditions of the resulting ylides with olefins, acetylenes, and aldehydes are described.

Results and Discussion

Preparation of *N*-(Silylmethyl)amidines and -thioamides. As a preliminary work, a general method for the preparation of a variety of *N*-(silylmethyl)amidines and -thioamides as precursors of *N*-protonated azomethine ylides has to be established. Nucleophilic addition to *N*-((trimethylsilyl)methyl)carbodiimides **1**–**2** and (trimethylsilyl)methyl isothiocyanate (**3**) is our route of choice

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[1] Vedejs, E.; Martinez, G. R. *J. Am. Chem. Soc.* **1979**, *101*, 6452; **1980**, *102*, 7993. Vedejs, E.; Larsen, S.; West, F. G. *J. Org. Chem.* **1985**, *50*, 2170.

[2] Achiwa, K.; Sekiya, M. *Chem. Lett.* **1981**, 1213. Achiwa, K.; Sekiya, M. *Tetrahedron Lett.* **1982**, *23*, 2589. Livinghouse, T.; Smith, R. *J. Chem. Soc., Chem. Commun.* **1983**, 210. Achiwa, K.; Imai, N.; Inaoka, T.; Sekiya, M. *Chem. Pharm. Bull.* **1984**, *32*, 2878.

[3] (a) Vedejs, E.; West, F. G. *J. Org. Chem.* **1983**, *48*, 4773. (b) Padwa, A.; Haffmanns, G.; Tomas, M. *Tetrahedron Lett.* **1983**, *24*, 4303. (c) Padwa, A.; Haffmanns, G.; Tomas, M. *J. Org. Chem.* **1984**, *49*, 3314.

[4] Grigg, R.; Kemp, J. *J. Chem. Soc., Chem. Commun.* **1977**, 125; **1978**, 109. Tsuge, O.; Ueno, K.; Oe, K. *Chem. Lett.* **1979**, 1407. Grigg, R. *Bull. Soc. Chim. Belg.* **1984**, *93*, 593.

[5] Tsuge, O.; Kanemasa, S.; Hatada, A.; Matsuda, K. *Chem. Lett.* **1984**, 801.

[6] Tsuge, O.; Kanemasa, S.; Yorozu, K.; Ueno, K. *Chem. Lett.* **1985**, 1601.

[7] Tsuge, O.; Kanemasa, S.; Matsuda, K. *Chem. Lett.* **1985**, 1411. Tsuge, O.; Kanemasa, S.; Yamada, T.; Matsuda, K. *Heterocycles* **1985**, *23*, 2489.

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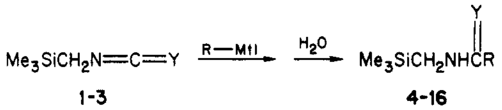
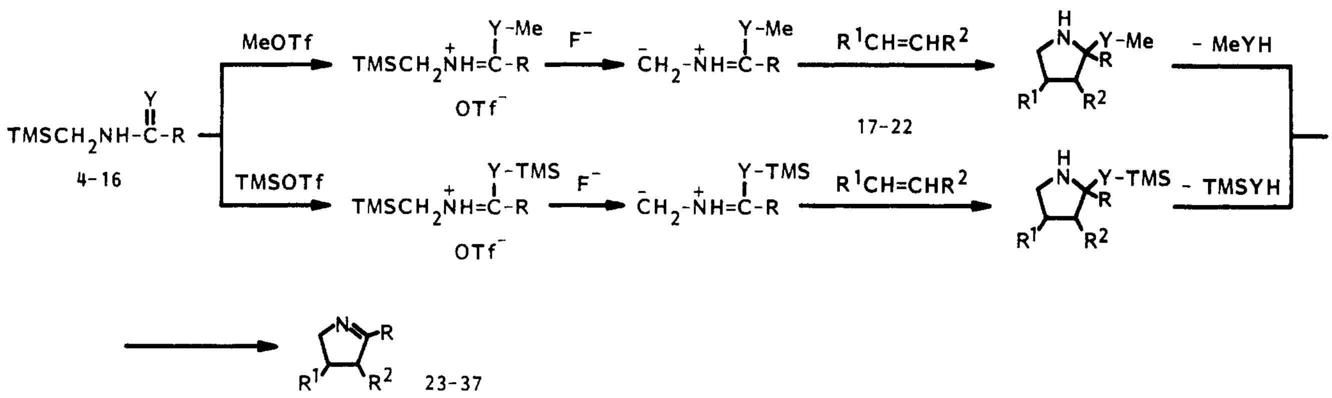
Table I. *N*-(Silylmethyl)amidines 4–13 and -thioamides 14–16



heterocumulene	R-Mtl	reaction conditions				prod.	yield[b] (%)
		solv	R-Mtl/heterocumulene[a]	temp	time (h)		
1	PhLi	THF	1.1	rt	1	4	98
1	MeMgI	ether	1.2	rt	1	5	92
1	EtLi	ether	2	rt	0.5	6	95
1	*n*-BuLi	ether	2.5	rt	1	7	90
1	$LiCH_2COOEt$	THF	1	−78 °C then rt	1	8 + 8′ (7:3)	97
1	$NaCH(COOMe)_2$	THF	1	rt	1	9	59
1	$Me_3SiCN-AlCl_3$[c]	neat	1.2	rt	5	10	97
1	$CH_2=CHLi$	THF	1.1	−78 °C then rt	1	11	94
1	$MeOH-CuCl_2$[d]	MeOH		rt	1	12	82
2	PhLi	THF	1.1	rt	1	13	88
3	PhLi	THF	1.1	rt	0.5	14	98
3	EtLi	ether	1.2	rt	0.5	15	97
3	*n*-BuLi	ether	1.2	rt	0.5	16	93

[a] Molar ratio. [b] Isolated yield based on the heterocumulene. [c] 5 Mol %. [d] 20 Mol %.

Scheme III



because these heterocumulenes 1–3 are readily prepared in high yields from commercially available (chloromethyl)trimethylsilane via (trimethylsilyl)methyl azide.[8,9]

The reaction of 1–3 with a variety of organometallic reagents smoothly occurred at room temperature in dry ether or THF providing excellent yields of *N*-((trimethylsilyl)methyl)amidines 4–13 and -thioamides 14–16 (Scheme II and Table I). Amidine 8, which was produced from 1 and ethyl lithioacetate, was found to be a 7:3 mixture of tautomers 8 and 8′ in chloroform solution. The product formed from 1 and dimethyl sodiomalonate was an enediamine (9′) rather than an amidine (9). The other amidines and thioamides were found to be free from their tautomeric isomers in solution. Tautomers of 4–12 with a double bond to the nitrogen attached to the silylmethyl moiety will lack the stabilization provided by extended conjugation through the phenyl.

Generation of *N*-Protonated Azomethine Ylides and Cycloaddition with Olefinic Dipolarophiles. The next step is selective alkylation of the amidines 4–13 and thioamides 14–16 with an alkylating agent leading to *N*-protonated iminium salts. Desilylation of the salt has to be carried out after the formation of the salt is complete in order to avoid undesired desilylation of the starting amidines and thioamides. Therefore, use of a highly reactive alkylating agent with a nonnucleophilic or nonsilylophilic leaving group is required.

Fortunately, the alkylation is completed in a few minutes at room temperature when amidine 4 or 5 (Y = NPh, R = Ph or Me) was treated with methyl triflate in dry acetonitrile (Scheme III). The amidinium triflates so formed were found to be very soluble in acetonitrile and quite stable to these reaction conditions. No spontaneous desilylation was observed. Similarly, amidine 4 was successfully silylated with trimethylsilyl triflate within 5 min at room temperature (checked on TLC).

With the above results in hand, generation of *N*-protonated azomethine ylides by desilylation at the silylmethyl moiety of the salts formed from 4–16 and subsequent cycloaddition with olefins were investigated (Scheme III). A one-pot alkylation–desilylation-cycloaddition (or silylation–desilylation-cycloaddition) procedure was used: methyl triflate or trimethylsilyl triflate was added to the solution of an amidine or a thioamide in a dry solvent, and the resulting solution was stirred at room temperature for 5 min under nitrogen in order to complete the alkylation or silylation. An olefin and then a fluoride were added, and the mixture was allowed to stir at room temperature until no further reaction was observed by TLC.

Electron-deficient olefins such as *N*-methylmaleimide (17), dimethyl fumarate (18), maleate (19), fumaronitrile (20), methyl acrylate (21), and 3-propen-2-one (22) were employed as dipolarophiles. In all cases, the intial cycloadducts could not be isolated. Instead, the leaving group was eliminated, and cycloadducts 23–37 were obtained after chromatography (Schemes III and IV). The results

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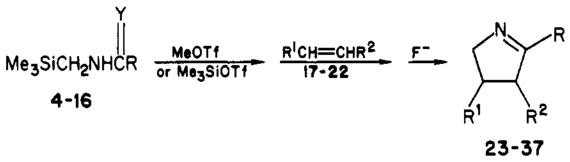
(8) Tsuge, O.; Kanemasa, S.; Matsuda, K. *Chem. Lett.* **1983**, 1131.

(9) Tsuge, O.; Kanemasa, S.; Matsuda, K. *J. Org. Chem.* **1984**, *49*, 2688.

Table II. Cycloaddition with Olefinic Dipolarophiles[a]



entry	olefin	precursor	R′OTf	fluoride	solv[b]	mol ratio[d]	time (h)	prod.	yield[c] (%)
1	17	4	Me_3SiOTf	CsF	AN	1:1:1:1	12	23	63
2			MeOTf	CsF	AN	1:3:1:1	13		74
3		13	Me_3SiOTf	CsF	AN	1:1:1:2	13		25
4		14	MeOTf	CsF	DME	1:1:1:1	13		87
5		5	MeOTf	CsF	AN	1:1:1:1	12	24	56
6			MeOTf	CsF	AN	1:3:1:1	12		82
7			MeOTf	CsF	AN	1:2:0.3:0.3	13		25
8			MeOTf	TBAF	AN	1:1:1:1	14		40
9		6	MeOTf	CsF	AN	1:2:1:1	13	25	77
10		15	MeOTf	CsF	DME	1:1:1:1	13		59
11		7	MeOTf	CsF	AN	1:3:1:1	13	26	70
12		16	MeOTf	CsF	DME	1:1:1:1	14		71
13		8	MeOTf	CsF	AN	1:3:1:1	12	27	36
14	18	4	Me_3SiOTf	CsF	AN	1:1:1:2	15	28	67
15		5	MeOTf	CsF	AN	1:3:1:1	12	29	73
16		6	MeOTf	CsF	AN	1:3:1:1	12	30	63
17		7	MeOTf	CsF	AN	1:3:1:1	13	31	53
18		16	MeOTf	CsF	DME	1:1:1:1	13		68
19	19	16	MeOTf	CsF	DME	1:1:1:1	13		21
20	20	4	TMSOTf	CsF	AN	1:1:1:2	14	32	69
21		14	MeOTf	CsF	DME	1:1:1:1	14		95
22		5	MeOTf	CsF	AN	1:2:1:1	13	33	51
23		6	MeOTf	CsF	AN	1:3:1:1	12	34	51
24		15	MeOTf	CsF	DME	1:1:1:1	13		70
25		7	MeOTf	CsF	AN	1:3:1:1	13	35	58
26	21	14	MeOTf	CsF	DME	1:1:1:1	14	36	48
27	22	14	MeOTf	CsF	DME	1:1:1:1	14	37	63

[a] All reactions were carried out at room temperature under nitrogen. [b] AN: acetonitrile; DME: 1,2-dimethoxyethane. [c] Isolated yield based on the amidine or thioamide. [d] Molar ratio of precursor:olefin:R′OTf:fluoride.

are summarized in Table II.

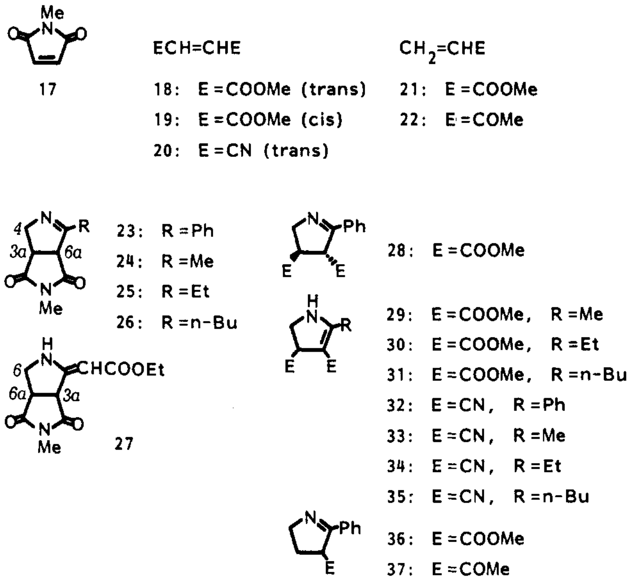
At an early stage of the present work, the cycloaddition using amidine **4** or **5** with *N*-methylmaleimide (**17**) was examined under a variety of conditions, some of which are listed in Table II (entries 1, 2, and 5–8). When acetyl chloride or benzoyl fluoride was used in place of MeOTf or TMSOTf, only a very poor yield of cycloadduct was formed. The desilylation step leading to *N*-protonated azomethine ylide could be achieved more fruitfully with cesium fluoride than with tetrabutylammonium fluoride. A stoichiometric amount of the fluoride is needed.

In the reactions using MeOTf, *N*-methylaniline was obtained in a yield comparable to that of eliminated cycloadduct. This amine was found to add to electron-deficient olefins as dipolarophiles present in the reaction mixture causing decreased yields of cycloadducts. These results indicate that elimination of *N*-methylaniline occurs rapidly as soon as initial cycloadducts are formed. Consequently, better yields of cycloadducts are obtained when more than 1 equiv of dipolarophile is used (entries 5 and 6).

Cycloaddition of the thioamide precursor **14** with *N*-methylmaleimide (**17**) in 1,2-dimethoxyethane proceeded very cleanly to give an excellent yield of eliminated cycloadduct **23** (entry 4). Unlike the amidine cases, addition of methanethiol to **17** did not compete with cycloaddition, so the use of excess of the dipolarophile is not needed.

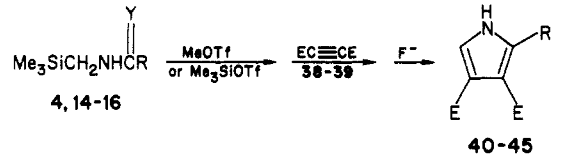
Most of the amidines and thioamides in Table II afforded similar cycloadducts. Amidines **10–12** and enediamine **9′**, however, are entirely useless in this process. *N*-(Silylmethyl)thioamides **14–16** appear to be better precursors for the generation of *N*-protonated azomethine ylides than the corresponding *N*-(silylmethyl)amidines. This is especially true in the case of cycloaddition with unsymmetrically substituted dipolarophiles. Thioamide **14** underwent successful cycloaddition with **21** and **22** giving regioselective products **36** and **37**, respectively. No trace of cycloadducts were obtained from **21** and **22** when amidine **4** was used.

Scheme IV



Structures of the cycloadducts **23–37** were determined on the basis of the spectral data and elemental analyses. Position of double bond in each cycloadduct was found to depend upon the electronic nature and steric size of the substituents. The double bond presumably migrates to the thermodynamically most stable location. This facile

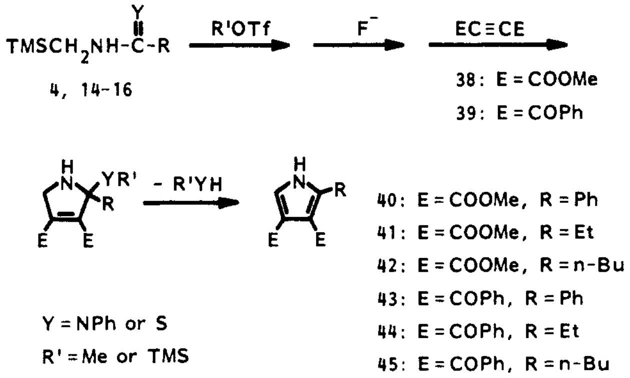
Table III. Cycloaddition with Acetylenic Dipolarophiles[a]



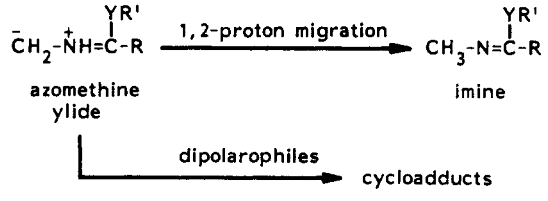
entry	acetylene	precursor	R′OTf	fluoride	solv[b]	mol ratio[d]	time (h)	prod.	yield[c] (%)
1	38	4	Me_3SiOTf	CsF	AN	1:1:1:2	16	40	64
2		14	MeOTf	CsF	DME	1:1:1:1	14		96
3		15	MeOTf	CsF	DME	1:1:1:1	13	41	61
4		16	MeOTf	CsF	DME	1:1:1:1	14	42	63
5	39	4	Me_3SiOTf	CsF	AN	1:1:1:2	14	43	44
6		14	MeOTf	CsF	DME	1:1:1:1	14		87
7		15	MeOTf	CsF	DME	1:1:1:1	13	44	48
8		16	MeOTf	CsF	DME	1:1:1:1	13	45	45

[a] All reactions were carried out at room temperature under nitrogen. [b] AN: acetonitrile; DME: 1,2-dimethoxyethane. [c] Isolated yield based on the precursor. [d] Molar ratio of precursor:acetylene:R′OTf:CsF.

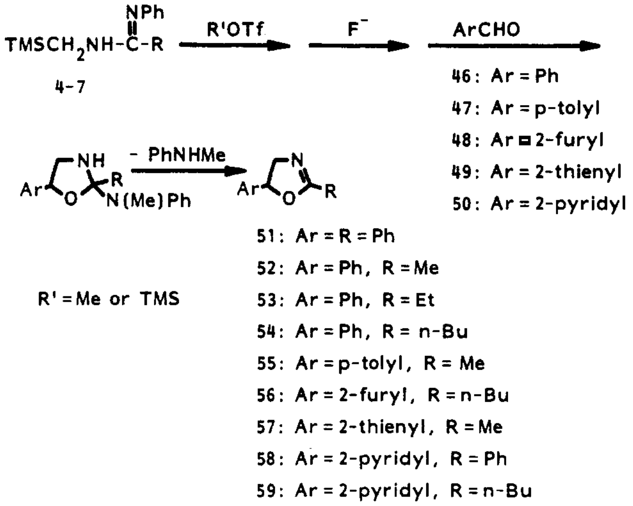
Scheme V



Scheme VI



Scheme VII



migration can result in epimerization of eliminated cycloadducts. For example, concerted cycloaddition[10] between the ylide derived from **16** and cis dipolarophile **19** should produce a cis cycloadduct. The only product isolated, however, was trans cycloadduct **28** (which was also obtained from trans dipolariphile **18**).

Cycloaddition with Acetylenic Dipolarophiles. The above studies clearly show that *N*-(silylmethyl)amidines and -thioamides serve as synthetic equivalents of nonstabilized nitrile ylides through a cycloaddition and elimination sequence. Cycloaddition of these reagents with acetylenic dipolarophiles is, therefore, expected to be a convenient route to *N*-unsubstituted pyrroles bearing a variety of substituents at the 2-, 3-, and 4-positions.

Unfortunately, phenyl-substituted azomethine ylide precursor **4** was the only amidine to produce the expected pyrroles **40** and **43** in fair yields in the reactions with dimethyl acetylenedicarboxylate (**38**) and dibenzoylacetylene (**39**), respectively (Scheme V and Table III). On the other hand, phenyl-substituted thioamide precursor **14** afforded an azomethine ylide which reacted with these acetylenes to give excellent yields of the same products **40** and **43**. The alkyl-substituted derivatives **15** and **16** also produced cycloadducts albeit in lower yields. However, neither precursor gave cycloadducts with unsymmetrically substituted acetylenes such as methyl propynoate and 3-phenylpropynoate. In the cases of reactions leading to no cycloadduct, major products obtained were imines which were probably derived from *N*-protonated azomethine ylides through a 1,2-proton migration (Scheme VI).

These results indicate that *N*-protonated azomethine ylides undergo cycloaddition when they are stabilized by conjugation or when the dipolarophiles used are highly reactive. It seems most likely that the ylides (Y = S) derived from thioamide precursors are more stabilized than those (Y = NPh) from amidine precrursors. When these *N*-protonated azomethine ylides are not sufficiently stabilized or the dipolarophiles are rather inactive, the ylides isomerize into the imines through a 1,2-proton migration.

Cycloaddition with Aldehydes. Nitrile ylides generated by the photolysis of azirines undergo cycloaddition with aldehydes to give 3-oxazolines,[11,12] and similar reactions of azomethine ylides leading to oxazolidines are also known.[3c,13] *N*-Protonated azomethine ylides exhibited

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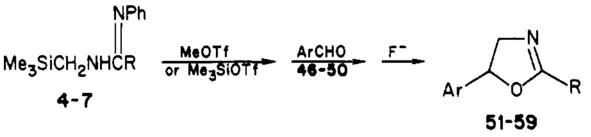
[10] Huisgen, R. *Angew Chem.* **1963**, *75*, 604 and 742. Houk, K. N.; Sims, J.; Duke, Jr., R. E.; Strozier, R. W.; George, J. K. *J. Am. Chem. Soc.* **1973**, *95*, 7287. Houk, K. N.; Sims, J.; Watts, C. R.; Luskus, L. J. *J. Am. Chem. Soc.* **1973**, *95*, 7301.

[11] Giezendanner, H.; Heimgartner, H.; Jackson, B.; Winkler, T.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta* **1973**, *56*, 2611. Padwa, A.; Smolanoff, J.; Wetmore, Jr., S. I. *J. Org. Chem.* **1973**, *38*, 1333.

[12] As reviews: Padwa, A. *Acc. Chem. Res.* **1976**, *9*, 371. Gilgen, P.; Heimgartner, H.; Schmid, H.; Hansen, H.-J.; *Heterocycles* **1977**, *6*, 143.

[13] Lown, J. W.; Akhtar, M. H. *Can. J. Chem.* **1972**, *50*, 2236. Lown, J. W.; Maloney, T. W.; Dallas, G. *Can J. Chem.* **1970**, *48*, 584. Lown, J. W.; Dallas, G.; Moser, J. P. *J. Chem. Soc. C* **1970**, 2383.

Table IV. Cycloaddition with Aldehydes[a]



entry	aldehyde	precursor	R′OTf	fluoride	mol ratio[c]	time (h)	prod.	yield[b] (%)
1	**46**	**4**	Me_3SiOTf	CsF	1:5:1:1	13	**51**	52
2		**5**	MeOTf	CsF	1:5:1:1	12	**52**	65
3		**6**	MeOTf	CsF	1:2:1:1	12	**53**	50
4		**7**	MeOTf	CsF	1:5:1:1	13	**54**	54
5	**47**	**5**	MeOTf	CsF	1:5:1:1	12	**55**	44
6	**48**	**7**	MeOTf	CsF	1:5:1:1	13	**56**	46
7	**49**	**5**	MeOTf	CsF	1:5:1:1	13	**57**	20
8	**50**	**4**	Me_3SiOTf	CsF	1:5:1:1	13	**58**	62
9		**7**	MeOTf	CsF	1:5:1:1	13	**59**	64

[a] All reactions were carried out at room temperature in acetonitrile under nitrogen. [b] Isolated yield based on the precursor. [c] Molar ratio of precursor:aldehyde:R′OTf:CsF.

high regioselectivity in cycloadditions with unsymmetrically substituted olefins. If high regioselectivity is also found in the cylcoadditions with aldehydes, a regioselective route to 2,5-disubstituted 2-oxazolines would become available. The azomethine ylides generated from *N*-(silylmethyl)amidines **4–7** reacted with aromatic **46–47** and heteroaromatic aldehydes **48–50** under reaction conditions listed in Table IV (Scheme VII). The expected 2,5-disubstituted 2-oxazolines **51–59** were obtained in fair yields. However, similar reactions with aliphatic and α,β-unsaturated aldehydes were all unsuccessful. Amidine precursors were found to be much better than thioamide precursors for the synthesis of 2-oxazolines. For example, sequential treatment of thioamide precursor **16** with MeOTf, aldehyde **46**, and cesium fluoride afforded oxazoline **54** in only 11%. The reason for the low yields with thioamide precursors in this case is not understood.

Experimental Section

General Methods. Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were taken with a JASCO A-702 spectrometer. ^1H NMR spectra were recorded on a Hitachi R-40 or a JEOL FX-100 instrument and ^{13}C NMR on a JEOL FX-100 spectrometer at 25.05 MHz. Chemical shifts are expressed in parts per million downfield from tetramethylsilane. Mass spectra were measured with a JEOL JMS-01SG-2 spectrometer at 70 eV of ionization energy. Elemental analyses were performed on a Hitachi 026 CHN analyzer. Thin-layer chromatography (TLC) was accomplished on 0.2 precoated plates of silica gel 60 F-254 (Merck). Visualization was accomplished with ultraviolet light (254 and 365 nm) and iodine. Silica gel 60 (Merck) was used for preparative column chromatography. Micro vacuum distillation was performed with a Shibata GTO-250R Kugelrohr distilling apparatus. Solvents were evaporated with a Tokyo Rikakikai rotary evaporator type V.

Materials and Solvents. The heterocumulenes **1–3** were prepared according to the reported method.[8,9] Methyl trifluoromethanesulfonate was prepared from the reaction of trifluoromethanesulfonic acid with dimethyl sulfate.[14] Trimethylsilyl trifluoromethanesulfonate is commercially available. Cesium fluoride was dried under vacuum prior to its use. Acetonitrile and 1,2-dimethoxyethane were distilled over P_2O_5 and CaH_2, respectively, and stored on 5-Å molecular sieves. Vinyllithium was generated in situ from dibutyldivinyltin and butyllithium.[15] Other reagents are commercially available or can be prepared by the known method.

General Procedure for the Preparation of *N*-((Trimethylsilyl)methyl)amidines 4–13 and -thioamides 14–16. The mixture of a freshly prepared nucleophile and a heterocumulene (5 mmol) in a dry solvent (10–25 mL) was allowed to react under the conditions summarized in Table I. After the completion of reaction, the mixture was poured into saturated aqueous ammonium chloride and extracted with ether (30 mL × 2). The combined extracts were dried over anhydrous magnesium sulfate and evaporated in vacuo. The amidines **4–13** and thioamides **14–16** obtained above were pure enough, in most cases, to be used for the following reactions without further purification. For the authentic samples, the crude products were purified by a vacuum distillation or chromatography through a short column packed with silica gel by using hexane–ethyl acetate (2:1). The solvent, ratio of reactants, reaction temperature, reaction time, and the yield of product are listed in Table I.

4: yellow oil; IR (neat) 3440 (NH), 1620 (C=N), 1250, and 850 cm^{-1} (Me_3Si); ^1H NMR ($CDCl_3$) δ 0.12 (s, 9 H, Me_3Si), 2.95 (s, 2 H, CH_2), 4.68 (br, 1 H, NH), and 6.63–7.55 (m, 10 H, Ph); MS, *m/e* (relative intensity) 282 (M^+, 34), 267 (52), 180 (51), 154 (89), 135 (76), 94 (100), and 77 (79); HRMS calcd for $C_{17}H_{22}N_2Si$ 282.1551, found 282.1540.

5: pale yellow oil; IR (neat) 3280 (NH), 1630 (C=N), 1250, and 850 cm^{-1} (Me_3Si); ^1H NMR ($CDCl_3$) δ 0.10 (s, 9 H, Me_3Si), 1.75 (s, 3 H, Me), 2.78 (s, 2 H, CH_2), 4.19 (br, 1 H, NH, exchanged with D_2O), and 6.65–7.32 (m, 5 H, Ph); MS, *m/e* (relative intensity) 220 (M^+, 30), 205 (87), 118 (76), 77 (100), and 73 (63); HRMS calcd for $C_{12}H_{20}N_2Si$ 220.1395, found 220.1405.

6: colorless oil; IR (neat) 3290 (NH), 1620 (C=N), 1250, and 850 cm^{-1} (Me_3Si); ^1H NMR ($CDCl_3$) δ 0.11 (s, 9 H, Me_3Si), 1.03 (t, 3 H, CH_2CH_3), 2.14 (q, 2 H, CH_2CH_3), 2.75 (s, 2 H, CH_2Me_3Si), 4.03 (br, 1 H, NH), and 6.53–7.28 (m, 5 H, Ph); MS, *m/e* (relative intensity) 234 (M^+, 9), 219 (47), 132 (69), 77 (100), and 73 (57); HRMS calcd for $C_{13}H_{22}N_2Si$ 234.1551, found 234.1561.

7: pale yellow oil; IR (neat) 3290 (NH), 1620 (C=N), 1250, and 850 cm^{-1} (Me_3Si); ^1H NMR ($CDCl_3$), δ 0.10 (s, 9 H, Me_3Si), 0.72–2.35 (m, 9 H, *n*-Bu), 2.74 (s, 2 H, CH_2Me_3Si), 3.96 (br, 1 H, NH), 6.53–7.24 (m, 5 H, Ph); MS, *m/e* (relative intensity) 262 (M^+, 42), 247 (100), 160 (45), 77 (51), and 73 (39); HRMS calcd for $C_{15}H_{26}N_2Si$ 262.1864, found 262.1866.

8 + **8′** (7:3): pale yellow oil; IR (neat) 3420, 3260 (NH), 1730 (C=O), 1630 (C=N), 1250, and 850 cm^{-1} (Me_3Si); ^1H NMR ($CDCl_3$) δ 0.00 (s, 2.7 H, Me_3Si of **8′**), 0.10 (s, 6.3 H, Me_3Si of **8**), 1.08–1.33 (m, 3 H, CH_2CH_3), 2.32 (d, 0.6 H, CH_2Me_3Si of **8′**), 2.79 (s, 1.4 H, CH_2Me_3Si of **8**), 3.11 (s, 1.4 H, CH_2COOEt of **8**), 3.91–4.24 (m, 2.3 H, CH_2CH_3 and =CH), 5.17 (br, 1 H, NH), 6.56–7.28 (m, 5 H, Ph), and 10.09 (br, 0.3 H, NH of **8′**); MS, *m/e* (relative intensity) 292 (M^+, 63), 277 (100), 91 (54), 77 (55), and 73 (75); HRMS calcd for $C_{15}H_{24}N_2O_2Si$ 292.1606, found 292.1554.

9′: colorless prisms (hexane); mp 89–90 °C; IR (KBr) 3240, 3140 (NH), 1740, 1730 (C=O), 1240, and 850 cm^{-1} (Me_3Si); ^1H NMR ($CDCl_3$) δ 0.04 (s, 9 H, Me_3Si), 2.32 (d, J = 4.8 Hz, 2 H, CH_2Me_3Si changed into a doublet with D_2O), 3.70 (s, 6 H, COOMe), 6.93–7.37 (m, 5 H, Ph), 9.80 (br, 1 H, NH, exchanged with D_2O), and 10.84 (s, 1 H, NH, exchanged with D_2O); MS, *m/e* (relative intensity) 336 (M^+, 100), 321 (32), 189 (31), and 73 (34).

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[14] Beard, C. D.; Baum. K.; Grakauskas, V. *J. Org. Chem.* **1973**, *38*, 3637.

[15] The generation method of vinyllithium from tetravinyltin and phenyllithium[16] was applied to didutyldivinyltin and butyllithium.

[16] Seyferth, D.; Weiner, M. A. *J. Am. Chem. Soc.* **1961**, *83*, 3583.

Anal. Calcd for $C_{16}H_{24}N_2O_4Si$: C, 57.12; H, 7.19; N, 8.33. Found: C, 57.32; H, 7.12; N, 8.26.

10: pale yellow oil; IR (neat) 3370 (NH), 2230 (CN), 1250, and 850 cm^{-1} (Me_3Si); ^1H NMR ($CDCl_3$) δ 0.11 (s, 9 H, Me_3Si), 2.92 (s, 2 H, CH_2), 5.10 (br, 1 H, NH), and 6.77–7.40 (m, 5 H, Ph); MS, *m/e* (relative intensity) 231 (M^+, 39), 216 (68), 77 (41), and 73 (100); HRMS calcd for $C_{12}H_{17}N_3Si$ 231.1191, found 231.1209.

11: colorless oil; IR (neat) 3440 (NH), 1640 (C=N), 1250, and 850 cm^{-1} (Me_3Si); ^1H NMR ($CDCl_3$) δ 0.13 (s, 9 H, Me_3Si), 2.83 (s, 2 H, CH_2), 4.37 (br, 1 H, NH), 5.29 (d, *J* = 10.5 Hz, 1 H, $CH{=}C\mathit{H}_2$), 5.52 (d, *J* = 17.2 Hz, 1 H, $CH{=}C\mathit{H}_2$), 6.14 (dd, *J* = 17.2 and 10.5 Hz, $C\mathit{H}{=}CH_2$), and 6.61–7.25 (m, 5 H, Ph); MS, *m/e* (relative intensity) 232 (M^+, 59), 217 (100), 130 (84), 77 (52), and 73 (46); HRMS calcd for $C_{13}H_{20}N_2Si$ 232.1395, found 232.1388.

12: colorless oil; bp_1 85 °C (bulb-to-bulb); IR (neat) 3420 (NH), 1660 (C=N), 1250, and 850 cm^{-1} (Me_3Si); ^1H NMR ($CDCl_3$) δ 0.00 (s, 9 H, Me_3Si), 2.56 (s, 2 H, CH_2), 3.70 (br, 1 H, NH), 3.81 (s, 3 H, OMe), and 6.73–7.32 (m, 5 H, Ph); MS, *m/e* (relative intensity) 236 (M^+, 32), 221 (40), 119 (28), 91 (28), and 73 (100); HRMS calcd for $C_{12}H_{20}N_2OSi$ 236.1344, found 236.1339.

13: colorless oil; bp_1 160 °C (bulb-to-bulb); IR (neat) 3430 (NH), 1630 (C=N), 1250, and 850 cm^{-1} (Me_3Si); ^1H NMR ($CDCl_3$) δ 0.00 (s, 9 H, Me_3Si), 0.98–2.01 (m, 10 H, CH_2 of cyclohexyl), 2.72 (s, 2 H, $C\mathit{H}_2Me_3Si$), 3.28 (m, 1 H, CH of cyclohexyl), 4.92 (br, 1 H, NH), and 7.00–7.43 (m, 5 H, Ph); MS, *m/e* (relative intensity) 288 (M^+, 40), 287 (45), 176 (100), 118 (58), 104 (90), 77 (37), and 73 (66); HRMS calcd for $C_{17}H_{28}N_2Si$ 288.2020, found 288.2025.

14: pale yellow oil; IR (neat) 3220 (NH), 1530 (C=S), 1250, and 850 cm^{-1} (Me_3Si); ^1H NMR ($CDCl_3$) δ 0.16 (s, 9 H, Me_3Si), 3.46 (d, 2 H, CH_2), 7.06–7.65 (m, 5 H, Ph), and 7.70 (br, 1 H, NH); MS, *m/e* (relative intensity) 223 (M^+, 35), 222 (28), 208 (100), 121 (57), and 73 (62); HRMS calcd for $C_{11}H_{17}NSSi$ 223.0850, found 223.0855.

15: yellow oil; IR (neat) 3220 (NH), 1540 (C=S), 1250, and 850 cm^{-1} (Me_3Si); ^1H NMR ($CDCl_3$) δ 0.13 (s, 9 H, Me_3Si), 1.27 (t, 3 H, $CH_2C\mathit{H}_3$), 2.68 (q, 2 H, $C\mathit{H}_2CH_3$), 3.32 (d, 2 H, $C\mathit{H}_2Me_3Si$), and 7.42 (br, 1 H, NH); MS, *m/e* (relative intensity) 175 (M^+, 13), 160 (100), 73 (66), and 70 (36); HRMS calcd for $C_7H_{17}NSSi$ 175.0850, found 175.0827.

16: yellow oil; IR (neat) 3210 (NH), 1540 (C=S), 1250, and 850 cm^{-1} (Me_3Si); ^1H NMR ($CDCl_3$) δ 0.16 (s, 9 H, Me_3Si), 0.90 (t, 3 H, $(CH_2)_3C\mathit{H}_3$), 1.13–1.91 (m, 4 H, $CH_2(C\mathit{H}_2)_2Me$), 2.67 (t, 2 H, $C\mathit{H}_2(CH_2)_2Me$), 3.35 (d, *J* = 6.6 Hz, $C\mathit{H}_2Me_3Si$), and 8.42 (br, 1 H, NH); MS, *m/e* (relative intensity) 203 (M^+, 3), 188 (12), and 73 (100); HRMS calcd for $C_9H_{21}NSSi$ 203.1163, found 203.1163.

General Procedure for the Generation of *N*-Protonated Azomethine Ylides and Their Cycloaddition Reactions with Olefinic Dipolarophiles. Each typical procedure for the reaction using an amidine precursor **4** or a thioamide precursor **14** with *N*-methylmaleimide (**17**) is shown below: (i) To a solution of **4** (0.282 g, 1 mmol) in dry acetonitrile (3 mL) was added methyl trifluoromethanesulfonate (0.11 mL, 1 mmol). After 5 min at room temperature, the olefin **17** (0.333 g, 3 mmol) and then cesium fluoride (0.152 g, 1 mmol) were added, and the resulting mixture was stirred at room temperature under nitrogen for 13 h, poured into water, and extracted with chloroform (30 mL × 2). The combined extracts were dried over anhydrous magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel with a mixture of hexane–ethyl acetate (1:1) to give **23** (0.169 g, 74%). (ii) To a solution of **14** (0.233 g, 1 mmol) in dry 1,2-dimethoxyethane (3 mL) was added methyl trifluoromethanesulfonate (0.11 mL, 1 mmol). After 5 min at room temperature, **17** (0.111 g, 1 mmol) and then cesium fluoride (0.152 g, 1 mmol) were added, and the mixture was stirred at room temperature under nitrogen for 13 h. The same procedure as above gave **23** (0.198 g, 87%).

The reaction conditions applied to the other reactions are listed in Table II.

23: colorless prisms (benzene–petroleum ether); mp 125–126 °C; IR (KBr) 1710 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 2.86 (s, 3 H, NMe), 3.58 (dt, *J* = 8.1, 8.1, and 6.3 Hz, 1 H, 3a-H), 4.28–4.60 (m, 3 H, 4-CH_2 and 6a-H), and 7.28–8.20 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 24.66 (q, NMe), 44.10 (d, 3a-C), 55.65 (d, 6a-C), 62.57 (t, 4-C), 127.92, 128.70, 130.84 (each d), 131.57 (s), 165.88 (s, 6-C), 172.94, and 177.43 (each s, CON); MS, *m/e* (relative intensity) 228 (M^+, 24), 117 (100), and 77 (14). Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.26; H, 5.33; N, 12.08.

24: pale yellow oil; IR (neat) 1700 cm^{-1} (C=O); ^1H NMR ($CDCl_3$), δ 2.20 (s, 3 H, 6-Me), 2.93 (s, 3 H, NMe), 3.49 (dt, *J* = 8.7, 6.0, and 6.0 Hz, 1 H, 3a-H), 3.93 (br d, *J* = 8.7 Hz, 1 H, 6a-H), and 4.19 (m, 2 H, 4-CH_2); ^{13}C NMR ($CDCl_3$) δ 17.53 (q, 6-Me), 24.30 (q, NMe), 43.41 (d, 3a-C), 58.77 (d, 6a-C), 62.42 (t, 4-C), 167.36 (s, 6-C), 173.36, and 178.01 (each s, CON); MS, *m/e* (relative intensity) 166 (M^+, 64), 68 (26), and 55 (100); HRMS calcd for $C_8H_{10}N_2O_2$ 166.0742, found 166.0741.

25: pale yellow oil; IR (neat) 1710 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.18 (t, 3 H, $CH_2C\mathit{H}_3$), 2.63 (m, 2 H, $C\mathit{H}_2Me$), 2.89 (s, 3 H, NMe), 3.45 (dt, *J* = 8.3, 6.0, and 6.0 Hz, 1 H, 3a-H), 3.92 (br d, *J* = 8.3 Hz, 1 H, 6a-H), and 4.16 (m, 2 H, 4-CH_2); ^{13}C NMR ($CDCl_3$) δ 10.18 (q, $CH_2\mathit{C}H_3$), 25.00 (q, NMe), 25.24 (t, $\mathit{C}H_2Me$), 43.94 (d, 3a-C), 58.36 (d, 6a-C), 63.12 (t, 4-C), 172.31 (s, 6-C), 174.07, and 178.66 (each s, CON); MS, *m/e* (relative intensity) 180 (M^+, 8), 94 (18), 80 (34), and 69 (100); HRMS calcd for $C_9H_{12}N_2O_2$ 180.0898, found 180.0893.

26: pale yellow oil; IR (neat) 1710 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 0.92 (t, 3 H, $(CH_2)_3C\mathit{H}_3$), 1.16–1.86 (m, 4 H, $CH_2(C\mathit{H}_2)_2Me$), 2.52 (m, 2 H, $C\mathit{H}_2(CH_2)_2Me$), 2.90 (s, 3 H, NMe), 3.45 (dt, *J* = 8.3, 6.3, and 6.3 Hz, 1 H, 3a-H), 3.94 (br d, *J* = 8.3 Hz, 1 H, 6a-H), and 4.17 (m, 2 H, 4-CH_2); ^{13}C NMR ($CDCl_3$) δ 13.33 (q, $(CH_2)_3\mathit{C}H_3$), 21.90 (t, $(CH_2)_2\mathit{C}H_2Me$), 24.48 (q, NMe), 27.48 (t, $CH_2\mathit{C}H_2Et$), 31.06 (t, $\mathit{C}H_2(CH_2)_2Me$), 43.33 (d, 3a-C), 57.89 (d, 6a-C), 62.59 (t, 4-C), 170.61 (s, 6-C), 173.31, and 177.89 (each s, CON); MS, *m/e* (relative intensity) 208 (M^+, 1), 179 (22), 166 (100), and 55 (15); HRMS calcd for $C_{11}H_{16}N_2O_2$ 208.1211. Found 208.1211.

27: pale yellow oil; IR (neat) 3340 (NH) and 1720 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.21 (t, 3 H, $CH_2C\mathit{H}_3$), 2.91 (s, 3 H, NMe), 3.31–3.63 (m, 1 H, 6a-H), 3.85 (m, 2 H, 6-CH_2), 4.01 (q, 2 H, $C\mathit{H}_2Me$), 4.08 (m, 1 H, 3a-H), 4.86 (s, 1 H, $=C\mathit{H}COOEt$), and 7.63 (br, 1 H, NH); ^{13}C NMR ($CDCl_3$) δ 14.50 (q, $CH_2\mathit{C}H_3$), 25.48 (q, NMe), 41.86 (6a-C), 48.44 (t, 6-C), 49.96 (d, 3a-C), 59.00 (t, $\mathit{C}H_2Me$), 80.79 (d, $=\mathit{C}HCOOEt$), 157.87 (s, 4-C), 170.08 (s, $\mathit{C}OOEt$), 173.66, and 177.36 (each s, CON); MS, *m/e* (relative intensity) 238 (M^+, 40), 193 (62), 166 (100), 108 (21), and 80 (35); HRMS calcd for $C_{11}H_{14}N_2O_4$ 238.0953, found 238.0942.

28: pale yellow oil; IR (neat) 1740 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 3.36–3.76 (m, 1 H, 4-H), 3.61, 3.68 (each s, each 3 H, COOMe), 4.38 (m, 2 H, 5-CH_2), 4.63 (m, 1 H, 3-H), and 7.24–7.92 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 47.32 (d, 4-C), 52.48, 52.58 (each q, $COO\mathit{Me}$), 56.53 (d, 3-C), 64.23 (t, 5-C), 127.96, 128.45, 130.84 (each d), 132.69 (s), 168.12 (s, 2-C), 170.99, and 172.99 (each s, $\mathit{C}OOMe$); MS, *m/e* (relative intensity) 261 (M^+, 16), 201 (69), 117 (100), and 99 (52); HRMS calcd for $C_{14}H_{15}NO_4$ 261.1000, found 261.0990.

29: pale yellow oil; IR (neat) 3360 (NH) and 1740 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.92 (s, 3 H, 2-Me), 3.37 (t, 1 H, *J* = 8.7 Hz, 4-H), 3.61, 3.70 (each s, each 3 H, COOMe), 4.06 (m, 2 H, 5-CH_2), and 4.50 (br, 1 H, NH, exchanged with D_2O); ^{13}C NMR ($CDCl_3$) δ 14.71 (q, 2-Me), 51.95, 53.06 (each s, $COO\mathit{Me}$), 55.47 (d, 4-C), 59.95 (t, 5-C), 88.06 (s, 3-C), 170.66, 171.60 (each s, COOMe), and 173.01 (s, 2-C); MS, *m/e* (relative intensity) 199 (M^+, 24), 174 (25), 140 (26), 127 (29), 99 (100), 87 (33), and 55 (77); HRMS calcd for $C_9H_{13}NO_4$ 199.0844, found 199.0852.

30: pale yellow oil; IR (neat) 3360 (NH) and 1740 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.18 (t, 3 H, $CH_2C\mathit{H}_3$), 2.33 (q, 2 H, $C\mathit{H}_2CH_3$), 3.45 (t, *J* = 8.7 Hz, 1 H, 4-H), 3.71, 3.77 (each s, each 3 H, COOMe), 4.10 (m, 2 H, 5-CH_2), and 4.21 (br, 1 H, NH, exchanged with D_2O); MS, *m/e* (relative intensity) 213 (M^+, 5), 179 (21), 87 (41), and 55 (100); HRMS calcd for $C_{10}H_{15}NO_4$ 213.1000, found 213.1004.

31: pale yellow oil; IR (neat) 3380 (NH) and 1750 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 0.88 (t, 3 H, $(CH_2)_3C\mathit{H}_3$), 1.10–1.76 (m, 4 H, $CH_2(C\mathit{H}_2)_2Me$), 2.23 (m, 2 H, $C\mathit{H}_2(CH_2)_2Me$), 3.36 (t, *J* = 8.7 Hz, 1 H, 4-H), 3.65, 3.71 (each s, each 3 H, COOMe), and 4.09 (m, 3 H, 5-CH_2 and NH); ^{13}C NMR ($CDCl_3$) δ 13.62 (q, $(CH_2)_3\mathit{C}H_3$), 22.25 (t, $(CH_2)_2\mathit{C}H_2Me$), 27.59 (t, $CH_2\mathit{C}H_2Et$), 28.53 (t, $\mathit{C}H_2(CH_2)_2Me$), 52.02, 53.19 (each s, $COO\mathit{Me}$), 55.72 (d, 4-C), 59.36 (t, 5-C), 87.83 (s, 3-C), 170.50, 171.96 (each s, $\mathit{C}OOMe$), and 175.66 (s, 2-C); MS, *m/e* (relative intensity) 241 (M^+, 2), 215 (40), 140 (32), 87 (50), and 55 (100); HRMS calcd for $C_{12}H_{19}NO_4$ 241.1313, found 241.1313.

32: colorless prisms (benzene); mp 143–145 °C; IR (KBr) 3280 (NH) and 2280 cm^{-1} (CN); ^{1}H NMR (Me$_2$SO-d_6) δ 3.55 (br, 1 H, NH), 3.86 (d, *J* = 9.0 Hz, 2 H, 5-CH$_2$), 4.48 (t, *J* = 9.0 Hz, 1 H, 4-H), and 7.33–7.76 (m, 5 H, Ph); ^{13}C NMR (Me$_2$SO-d_6) δ 32.57 (d, 4-C), 49.46 (t, 5-C), 69.34 (s, 3-C), 119.09, 120.21 (each s, CN), 127.25 (d), 128.41 (s), 129.05, 131.73 (each d), and 164.16 (s, 2-C); MS, *m/e* (relative intensity) 195 (M$^+$, 69), 169 (17), 117 (100), 104 (12), and 77 (26). Anal. Calcd for C$_{12}$H$_9$N$_3$: C, 73.83; H, 4.65; N, 21.53. Found: C, 73.85; H, 4.70; N 21.32.

33: pale yellow oil; IR (neat) 3340 (NH) and 2290 cm^{-1} (CN); ^{1}H NMR (CDCl$_3$) δ 2.00 (s, 3 H, 2-Me), 3.66–4.08 (m, 3 H, 4-H and 5-CH$_2$), and 4.85 (br, 1 H, NH, exchanged with D$_2$O); ^{13}C NMR (CDCl$_3$) δ 13.04 (q, 2-Me), 31.84 (d, 4-C), 50.15 (t, 5-C), 71.53 (s, 3-C), 117.92, 119.14 (each s, CN), and 166.06 (s, 2-C); MS, *m/e* (relative intensity) 133 (M$^+$, 10), 77 (19), and 55 (100); HRMS calcd for C$_7$H$_7$N$_3$ 133.0640, found 133.0640.

34: yellow oil; IR (neat) 3350 (NH) and 2290 cm^{-1} (CN); ^{1}H NMR (CDCl$_3$) δ 1.18 (t, 3 H, CH$_2$C*H*$_3$), 2.37 (q, 2 H, C*H*$_2$CH$_3$), 3.70–4.11 (m, 3 H, 4-H and 5-CH$_2$), and 5.08 (br, 1 H, NH, exchanged with D$_2$O); ^{13}C NMR (CDCl$_3$) δ 11.52 (q, CH$_2$*C*H$_3$), 21.24 (t, *C*H$_2$Me), 32.32 (d, 4-C), 50.44 (t, 5-C), 70.61 (s, 3-C), 118.16, 119.48 (each s, CN), and 171.43 (s, 2-C); MS, *m/e* (relative intensity) 147 (M$^+$, 6), 105 (10), 69 (100), and 54 (30); HRMS calcd for C$_8$H$_9$N$_3$ 147.0789, found 147.0790.

35: yellow oil; IR (neat) 3320 (NH) and 2290 cm^{-1} (CN); ^{1}H NMR (CDCl$_3$) δ 0.91 (t, 3 H, (CH$_2$)$_3$C*H*$_3$), 1.15–1.78 (m, 4 H, CH$_2$(C*H*$_2$)$_2$Me), 2.32 (t, 2 H, C*H*$_2$(CH$_2$)$_2$Me), 3.68–4.08 (m, 3 H, 4-H and 5-CH$_2$), and 5.04 (br, 1 H, NH, exchanged with D$_2$O); ^{13}C NMR (CDCl$_3$) δ 13.64 (q, (CH$_2$)$_3$*C*H$_3$), 22.12 (t, (CH$_2$)$_2$*C*H$_2$Me), 27.44 (t, CH$_2$*C*H$_2$Et), 29.14 (t, *C*H$_2$(CH$_2$)$_2$Me), 32.31 (d, 4-C), 50.39 (t, 5-C), 71.44 (s, 3-C), 117.93, 119.24 (each s, CN), and 169.97 (s, 2-C); MS, *m/e* (relative intensity) 175 (M$^+$, 13), 146 (24), 133 (100), 119 (21), 105 (41), 93 (30), 68 (28), and 55 (75); HRMS calcd for C$_{10}$H$_{13}$N$_3$ 175.1109, found 175.1110.

36: pale yellow oil; IR (neat) 1740 cm^{-1} (C=O); ^{1}H NMR (CDCl$_3$) δ 2.25 (dd, *J* = 13.2 and 6.9 Hz, 2 H, 4-CH$_2$), 3.52 (s, 3 H, COOMe), 3.95–4.25 (m, 3 H, 3-H and 5-CH$_2$), and 7.15–7.85 (m, 5 H, Ph); ^{13}C NMR (CDCl$_3$) δ 29.36 (t, 4-C), 52.30 (q, COO*Me*), 53.30 (d, 3-C), 61.06 (t, 5-C), 128.01, 128.65, 130.83 (each d), 133.48 (s), 169.36 (s, 2-C), and 172.89 (s, *C*OOMe); MS, *m/e* (relative intensity) 203 (M$^+$, 3), 117 (90), 104 (100), 77 (51), and 56 (67); HRMS calcd for C$_{12}$H$_{13}$NO$_2$ 203.0946, found 203.0950.

37: pale yellow oil; IR (neat) 1710 cm^{-1} (C=O); ^{1}H NMR (CDCl$_3$) δ 1.95–2.32 (m, 2 H, 4-CH$_2$), 2.02 (s, 3 H, COMe), 3.96–4.31 (m, 3 H, 3-H and 5-CH$_2$), and 7.17–7.85 (m, 5 H, Ph); MS, *m/e* (relative intensity) 187 (M$^+$, 22), 160 (14), 144 (100), and 117 (52); HRMS calcd for C$_{12}$H$_{13}$NO 187.0996, found 187.0992.

General Procedure for the Cycloaddition Reactions of *N*-Protonated Azomethine Ylides with Acetylenic Dipolarophiles. As a typical example, the reaction of an amidine precursor **4** with dimethyl acetylenedicarboxylate **38** is shown below: To a solution of **4** (0.282 g, 1 mmol) in dry acetonitrile (3 mL) was added trimethylsilyl trifluoromethanesulfonate (0.19 mL, 1 mmol). After 5 min at room temperature, the acetylene **38** (0.142 g, 1 mmol) and then cesium fluoride (0.304 g, 2 mmol) were added, and the mixture was stirred at room temperature under nitrogen for 16 h, poured into water, and extracted with chloroform (30 mL × 2). The combined extracts were dried over anhydrous magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel by using hexane–ethyl acetate (2:1) to give **40** (0.165 g, 64%).

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

40: yellow oil; IR (neat) 3320 (NH) and 1730 cm^{-1} (C=O); ^{1}H NMR (CDCl$_3$) δ 3.72 (s, 6 H, COOMe), 7.17 (s, 1 H, 5-H), 7.15–7.44 (m, 5 H, Ph), and 10.04 (br, 1 H, NH, exchanged with D$_2$O); ^{13}C NMR (CDCl$_3$) δ 51.47, 52.24 (each s, COO*Me*), 113.42, 115.71 (each s, 3- and 4-C), 125.01 (d, 5-C), 127.42, 128.30, 128.72 (each d), 131.01 (s), 134.54 (s, 2-C), 164.83, and 167.83 (each s, *C*OOMe); MS, *m/e* (relative intensity) 259 (M$^+$, 24), 228 (52), 114 (59), and 77 (100); HRMS calcd for C$_{14}$H$_{13}$NO$_4$ 259.0844, found 259.0874.

41: colorless plates (chloroform–petroleum ether); mp 121–122 °C; IR (KBr) 3260 (NH) and 1720 cm^{-1} (C=O); ^{1}H NMR (CDCl$_3$) δ 1.16 (t, 3 H, CH$_2$C*H*$_3$), 2.79 (q, 2 H, C*H*$_2$Me), 3.71, 3.75 (each s, each 3 H, COOMe), 7.10 (d, *J* = 2.1 Hz, 1 H, 5-H), and 10.07 (br, 1 H, NH); ^{13}C NMR (CDCl$_3$) δ 13.94 (q, CH$_2$*C*H$_3$), 20.35 (t, *C*H$_2$Me), 51.42 (q, COO*Me*), 110.89, 115.48 (each s, 3- and 4-C), 124.07 (d, 5-C), 142.07 (s, 2-C), 165.42, and 166.24 (each s, *C*OOMe); MS, *m/e* (relative intensity) 211 (M$^+$, 6), 180 (40), 150 (50), 121 (64), 93 (100), and 79 (42). Anal. Calcd for C$_{10}$H$_{13}$NO$_4$: C, 56.86; H, 6.20; N, 6.63. Found: C, 56.72; H, 6.16; N, 6.69.

42: colorless prisms (benzene–petroleum ether); mp 90–91 °C; IR (KBr) 3290 (NH) and 1700 cm^{-1} (C=O); ^{1}H NMR (CDCl$_3$) δ 0.84 (t, 3 H, (CH$_2$)$_3$C*H*$_3$), 1.05–1.75 (m, 4 H, CH$_2$(C*H*$_2$)$_2$Me), 2.75 (t, 2 H, C*H*$_2$(CH$_2$)$_2$Me), 3.71, 3.74 (each s, each 3 H, COOMe), 7.10 (d, *J* = 2.1 Hz, 1 H, 5-H), and 10.16 (br, 1 H, NH); MS, *m/e* (relative intensity) 239 (M$^+$, 20), 207 (62), 178 (100), and 164 (34). Anal. Calcd for C$_{12}$H$_{17}$NO$_4$: C, 60.24; H, 7.16; N, 5.85. Found: C, 60.43; H, 7.20; N, 6.01.

43: colorless prisms (chloroform–ethanol); mp 224–225 °C; IR (KBr) 3260 (NH) and 1650 cm^{-1} (C=O); ^{1}H NMR (CDCl$_3$) δ 6.70–7.90 (m, 15 H, Ph), 7.13 (s, 1 H, 5-H), and 10.62 (br, 1 H, NH); MS, *m/e* (relative intensity) 351 (M$^+$, 8), 189 (23), 105 (51), 77 (100), and 51 (62). Anal. Calcd for C$_{24}$H$_{17}$NO$_2$: C, 82.03; H, 4.88; N, 3.99. Found: C, 82.02; H, 4.96; N, 4.00.

44: colorless needles (chloroform–ethanol); mp 205–206 °C; IR (KBr) 3200 (NH) and 1650 cm^{-1} (C=O); ^{1}H NMR (Me$_2$SO-d_6) δ 1.16 (t, 3 H, CH$_2$C*H*$_3$), 2.65 (q, 2 H, C*H*$_2$Me), 7.10–7.72 (m, 11 H, Ph and 5-H), and 11.73 (br, 1 H, NH); MS, *m/e* (relative intensity) 303 (M$^+$, 84), 302 (100), 105 (65), and 77 (90). Anal. Calcd for C$_{20}$H$_{17}$NO$_2$: C, 79.18; H, 5.65; N, 4.62. Found: C, 79.30; H, 5.62; N, 4.84.

45: colorless needles (ethanol–petroleum ether); mp 119–120 °C; IR (KBr) 3220 (NH) and 1660 cm^{-1} (C=O); ^{1}H NMR (CDCl$_3$) δ 0.6–1.6 (m, 7 H, CH$_2$(C*H*$_2$)$_2$C*H*$_3$), 2.55 (t, 2 H, C*H*$_2$(CH$_2$)$_2$Me), 6.78 (d, *J* = 2.1 Hz, 1 H, 5-H), 7.02–7.92 (m, 10 H, Ph), and 10.58 (br, 1 H, NH); MS, *m/e* (relative intensity) 331 (M$^+$, 45), 330 (41), 288 (36), 210 (30), 105 (88), and 77 (100). Anal. Calcd for C$_{22}$H$_{21}$NO$_2$: C, 79.73; H, 6.39; N, 4.23. Found: C, 79.79; H, 6.32; N, 4.50.

General Procedure for the Cycloaddition Reactions of *N*-Protonated Azomethine Ylides with Aldehydes. As a typical example, the reaction of **4** with benzaldehyde (**46**) is shown below: To a solution of **4** (0.282 g, 1 mmol) in dry acetonitrile (3 mL) was added trimethylsilyl trifluoromethanesulfonate (0.19 mL, 1 mmol). After 5 min at room temperature, **46** (0.51 mL, 5 mmol) and then cesium fluoride (0.152 g, 1 mmol) were added, and the mixture was stirred at room temperature under nitrogen for 13 h, poured into water, and extracted with chloroform (30 mL × 2). The combined extracts were dried over anhydrous magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel by using hexane–ethyl acetate (3:1) to give **51** (0.117 g, 52%).

The other reactions were performed under the conditions listed in Table IV.

51: pale yellow oil; IR (neat) 1650 cm^{-1} (C=O); ^{1}H NMR (CDCl$_3$) δ 3.90 (dd, *J* = 15.0 and 9.0 Hz, 1 H, one of 4-CH$_2$), 4.41 (dd, *J* = 15.0 and 10.5 Hz, 1 H, the other of 4-CH$_2$), 5.55 (dd, *J* = 10.5 and 9.0 Hz, 1 H, 5-H), and 7.20–7.96 (m, 10 H, Ph); ^{13}C NMR (CDCl$_3$) δ 63.06 (t, 4-C), 80.84 (d, 5-C), 125.58, 128.16, 128.28, 128.63, 129.10 (each d), 131.28 (s), and 163.08 (s, 2-C); MS, *m/e* (relative intensity) 223 (M$^+$, 5), 117 (100), 105 (36), 77 (98), and 51 (55); HRMS calcd for C$_{15}$H$_{13}$NO 223.0996, found 223.1000.

52: pale yellow oil; IR (neat) 1680 cm^{-1} (C=O); ^{1}H NMR (CDCl$_3$) δ 2.02 (s, 3 H, 2-Me), 3.67 (dd, *J* = 14.1 and 8.4 Hz, 1 H, one of 4-CH$_2$), 4.15 (dd, *J* = 14.1 and 9.9 Hz, 1 H, the other of 4-CH$_2$), 5.35 (dd, *J* = 9.9 and 8.4 Hz, 5-H), and 7.22 (s, 5 H, Ph); MS, *m/e* (relative intensity) 161 (M$^+$, 19) and 55 (100); HRMS calcd for C$_{10}$H$_{11}$NO 161.0840, found 161.0839.

53: pale yellow oil; IR (neat) 1670 cm^{-1} (C=O); ^{1}H NMR (CDCl$_3$) δ 1.22 (t, 3 H, CH$_2$C*H*$_3$), 2.35 (q, 2 H, C*H*$_2$Me), 3.68 (dd, *J* = 14.7 and 8.4 Hz, 1 H, one of 4-CH$_2$), 4.17 (dd, *J* = 14.7 and 9.6 Hz, 1 H, the other of 4-CH$_2$), 5.34 (dd, *J* = 9.6 and 8.4 Hz, 1 H, 5-H), and 7.18 (s, 5 H, Ph); MS, *m/e* (relative intensity) 175 (M$^+$, 1), 105 (51), 91 (33), 77 (67), 69 (100), and 54 (46); HRMS calcd for C$_{11}$H$_{13}$NO 175.0996, found 175.0995.

54: pale yellow oil; IR (neat) 1670 cm^{-1} (C=O); ^{1}H NMR (CDCl$_3$) δ 0.91 (t, 3 H, (CH$_2$)$_3$C*H*$_3$), 1.15–1.85 (m, 4 H, CH$_2$(C*H*$_2$)$_2$Me), 2.32 (t, 2 H, C*H*$_2$(CH$_2$)$_2$Me), 3.65 (dd, *J* = 14.1 and 7.8 Hz, 1 H, one of 4-CH$_2$), 4.15 (dd, *J* = 14.1 and 10.2 Hz, 1 H, the other of 4-CH$_2$), 5.32 (dd, *J* = 10.2 and 7.8 Hz, 1 H, 5-H), and 7.17 (s, 5 H, Ph); ^{13}C NMR (CDCl$_3$) δ 13.74 (q, (CH$_2$)$_3$*C*H$_3$), 22.37

(t, $(CH_2)_2CH_2Me$), 27.83 (t, CH_2CH_2Et), 28.06 (t, $CH_2(CH_2)_2Me$), 62.59 (t, 4-C), 80.55 (d, 5-C), 125.58, 128.11, 128.69 (each d), 141.20 (s), and 168.03 (s, 2-C); MS, *m/e* (relative intensity) 203 (M^+, 5), 161 (96), 118 (32), 97 (65), 68 (39), and 55 (100); HRMS calcd for $C_{13}H_{17}NO$ 203.1309, found 203.1309.

55: pale yellow oil; IR (neat) 1680 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 2.01 (s, 3 H, 2-Me), 2.29 (s, 3 H, *p*-Me), 3.65 (dd, J = 14.7 and 8.1 Hz, 1 H, one of 4-CH_2), 4.12 (dd, J = 14.7 and 9.9 Hz, 1 H, the other of 4-CH_2), 5.32 (dd, J = 9.9 and 8.1 Hz, 1 H, 5-H), and 7.06 (m, 4 H, Ar); MS, *m/e* (relative intensity) 175 (M^+, 3), 119 (11), 55 (100), and 54 (60); HRMS calcd for $C_{11}H_{13}NO$ 175.0996, found 175.0994.

56: pale yellow oil; IR (neat) 1670 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 0.88 (t, 3 H, $(CH_2)_3CH_3$), 1.13–1.78 (m, 4 H, $CH_2(CH_2)_2Me$), 2.25 (t, 2 H, $CH_2(CH_2)_2Me$), 3.95 (d, J = 8.7 Hz, 2 H, 4-CH_2), 5.34 (t, J = 8.7 Hz, 1 H, 5-H), 6.24 (br s, 2 H, furyl), and 7.29 (br s, 1 H, furyl); ^{13}C NMR ($CDCl_3$) δ 13.69 (q, $(CH_2)_3CH_3$), 22.27 (t, $(CH_2)_2CH_2Me$), 27.73 (t, CH_2CH_2Et), 27.97 (t, $CH_2(CH_2)_2Me$), 58.43 (t, 4-C), 73.53 (5-C), 108.42, 110.37 (each d, 3- and 4-C of furyl), 143.21 (d, 5-C of furyl), and 167.85 (s, 2-C); MS, *m/e* (relative intensity) 193 (M^+, 12), 152 (60), 94 (38), 68 (37), and 55 (100); HRMS calcd for $C_{11}H_{15}NO_2$ 193.1102, found 193.1085.

57: pale yellow oil; IR (neat) 1670 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.98 (s, 3 H, 2-Me), 3.80 (dd, J = 15.0 and 7.8 Hz, 1 H, one of 4-CH_2), 4.14 (dd, J = 15.0 and 10.2 Hz, 1 H, the other of 4-CH_2), 5.59 (dd, J = 10.2 and 7.8 Hz, 1 H, 5-H), and 6.80–7.25 (m, 3 H, Ar); MS, *m/e* (relative intensity) 157 (M^+, 10), 97 (19), 77 (16), and 55 (100); HRMS calcd for C_8H_9NOS 167.0403, found 167.0407.

58: yellow oil; IR (neat) 1650 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 4.08 (dd, J = 14.4 and 7.5 Hz, 1 H, one of 4-CH_2), 4.45 (dd, J = 14.5 and 10.2 Hz, 1 H, the other of 4-CH_2), 5.63 (dd, J = 10.2 and 7.5 Hz, 1 H, 5-H), and 6.90–8.51 (m, 9 H, Ph and Ar); ^{13}C NMR ($CDCl_3$) δ 61.76 (t, 4-C), 80.67 (d, 5-C), 119.65, 122.76 (each d), 127.40 (s), 128.16, 128.28, 131.33, 136.80, 149.36 (each d), 160.10 (s), and 163.51 (s, 2-C); MS, *m/e* (relative intensity) 224 (M^+, 21), 117 (38), 105 (94), 77 (100), and 51 (50); HRMS calcd for $C_{14}H_{12}N_2O$ 224.0949, found 224.0947.

59: yellow oil; IR (neat) 1670 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 0.92 (t, 3 H, $(CH_2)_3CH_3$), 1.18–1.86 (m, 4 H, $CH_2(CH_2)_2Me$), 2.35 (t, 2 H, $CH_2(CH_2)_2Me$), 3.83 (dd, J = 14.1 and 7.8 Hz, 1 H, one of 4-CH_2), 4.22 (dd, J = 14.1 and 9.9 Hz, 1 H, the other of 4-CH_2), 5.44 (dd, J = 9.9 and 7.8 Hz, 1 H, 5-H), and 7.00–8.53 (m, 4 H, Ar); ^{13}C NMR ($CDCl_3$) δ 13.23 (q, $(CH_2)_3CH_3$), 21.87 (t, $(CH_2)_2CH_2Me$), 27.29 (t, CH_2CH_2Et), 27.54 (t, $CH_2(CH_2)_2Me$), 60.74, (t, 4-C), 80.03 (d, 5-C), 119.48, 122.61, 136.66, 149.22 (each d), 160.01 (s), and 167.62 (s, 2-C); MS, *m/e* (relative intensity) 204 (M^+, 8), 162 (16), 147 (50), 119 (65), 78 (40), 55 (50), and 40 (100); HRMS calcd for $C_{12}H_{16}N_2O$ 204.1262, found 204.1271.

Registry No. **1**, 90606-25-0; **2**, 90606-26-1; **3**, 18293-48-6; **4**, 101402-19-1; **5**, 101402-20-4; **6**, 101402-21-5; **7**, 101402-22-6; **8**, 101402-23-7; **8′**, 101402-56-6; **9**, 101402-24-8; **10**, 101402-25-9; **11**, 101402-26-0; **12**, 101402-27-1; **13**, 101402-28-2; **14**, 101402-29-3; **15**, 101402-30-6; **16**, 101402-31-7; **17**, 930-88-1; **18**, 624-49-7; **19**, 624-48-6; **20**, 764-42-1; **21**, 96-33-3; **22**, 78-94-4; **23**, 101402-32-8; **24**, 101402-33-9; **25**, 101402-34-0; **26**, 101402-35-1; **27**, 101402-36-2; **28**, 101402-37-3; **29**, 101402-38-4; **30**, 101402-39-5; **31**, 101402-40-8; **32**, 41413-77-8; **33**, 101402-41-9; **34**, 101402-42-0; **35**, 101402-43-1; **36**, 101402-44-2; **37**, 101402-45-3; **38**, 762-42-5; **39**, 1087-09-8; **40**, 69640-27-3; **41**, 101402-46-4; **42**, 101402-47-5; **43**, 101402-48-6; **44**, 101402-49-7; **45**, 101402-50-0; **46**, 100-52-7; **47**, 104-87-0; **48**, 98-01-1; **49**, 98-03-3; **50**, 1121-60-4; **51**, 22020-69-5; **52**, 66614-71-9; **53**, 14225-46-8; **54**, 101402-51-1; **55**, 101402-52-2; **56**, 101402-53-3; **57**, 101402-54-4; **58**, 92148-78-2; **59**, 101402-55-5; PhLi, 591-51-5; MeMgI, 917-64-6; EtLi, 811-49-4; BuLi, 109-72-8; $LiCH_2COOEt$, 56267-15-3; $NaCH(COOMe)_2$, 18424-76-5; $CH_2{=}CHLi$, 917-57-7.

Reactions of Enamines of Cyclic Ketones with Methyl Propiolate. Reinvestigation and Application in a Tandem Ring Expansion with Four C Atoms

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Enamines of cyclic ketones **1** with ring sizes ranging from seven to twelve react with methyl propiolate via (2 + 2) cycloaddition and subsequent *conrotatory* ring opening of the cyclobutene moiety in **2**. The resulting *cis,trans*-cycloalkadienes **3** rearrange further via a thermal [1,5] hydrogen shift to the corresponding *cis,cis*-cycloalkadienes **4**. The structures previously described in the literature of several of these cycloalkadienes are shown to be incorrect. For a representative *cis,trans*-cycloalkadiene (**3g**, R = H) and a *cis,cis*-cycloalkadiene (**5a**, R = H) the structures were proven by single-crystal X-ray analysis. The reactive "enamine" moiety in **4** allows a tandem ring-expansion reaction of enamines of cyclic ketones with four C atoms. Reaction of **4** with a second electron-deficient acetylenic ester gives the *cis,cis,trans*-cycloalkatrienes **6**.

Reactions of enamines of cyclic ketones with acetylenic esters in an apolar solvent[2,3] have often been employed for ring enlargement with two C atoms.[4] Examples include the synthesis of medium-sized heterocycles[5-11] and of natural products such as muscone,[12,13] steganone,[14] and velleral.[15] This ring expansion involves a (2 + 2) cyclo-

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(1) (a) Laboratory of Organic Chemistry. (b) Laboratory of Chemical Physics.

(2) Cook, A. G. In *Enamines: Synthesis, Structure and Reactions*; Cook, A. G., Ed.; Marcel Dekker: New York, 1969; p 230.

(3) Fuks, R.; Viehe, H. G. In *Chemistry of Acetylenes*; Viehe, H. G., Ed.; Marcel Dekker: New York, 1969; p 435.

(4) Hickmott, P. W. *Tetrahedron* **1982**, *38*, 3363.

(5) George, M. V.; Khetan, S. K.; Gupta, R. K. *Adv. Heterocycl. Chem.* **1976**, *19*, 279.

(6) Reinhoudt, D. N. *Adv. Heterocycl. Chem.* **1977**, *21*, 253.

(7) Acheson, R. M.; Elmore, N. F. *Adv. Heterocycl. Chem.* **1978**, *23*, 263.

(8) (a) Lamm, B.; Aurell, C.-J. *Acta Chem. Scand., Ser. B* **1981**, *35*, 197. (b) Lamm, B., Aurell, C.-J. *Ibid.* **1982**, *36*, 435.

(9) Schultz, A. G.; Fedynyshyn, T. H. *Tetrahedron* **1982**, *38*, 1761.

(10) Rodrigues, J. A. R.; Verardo, L. I. *J. Heterocycl. Chem.* **1983**, *20*, 1263.

(11) Vieillescazes, C.; Coen, S.; Ragonnet, B.; Roggero, J.-P. *Heterocycles* **1985**, *23*, 927.

(12) Yoshii, E.; Kimoto, S. *Chem. Pharm. Bull.* **1969**, *17*, 629.

(13) (a) Stork, G.; Macdonald, T. L. *J. Am. Chem. Soc.* **1975**, *97*, 1264. (b) Mookherjee, B. D.; et al. International Flavors & Fragrances Inc., U.S. Pat. 4 224 352, 1980.