

Copper-Catalyzed Intermolecular Generation of Ammonium Ylides with Subsequent [2,3]Sigmatropic Rearrangement. Efficient Synthesis of Bifunctional Homoallylamines#

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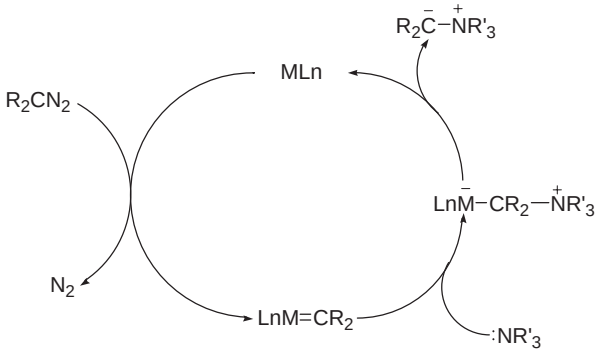
The [2,3]sigmatropic rearrangement of allylic ammonium ylides generated by the reaction of *N*,*N*-dimethyl-1-alkyl-2-methylallylamines derived from terpene alcohols with diazo compounds in the presence of copper catalysts gave trisubstituted *E*-olefins in one-pot. In addition, a cyano substituent at the 2-position of *N*,*N*-dimethylallylamine increased the occurrence of the catalytic [2,3]sigmatropic rearrangement to give the corresponding bifunctional homoallylamines.

[2,3]Sigmatropic rearrangement is used widely in the regio- and stereocontrolled synthesis of carbon frameworks in natural products.[1,2] In general, the treatment of a quaternary ammonium salt with a base can cause the formation of an ammonium ylide species, followed by a spontaneous [2,3]sigmatropic rearrangement to give 3-butenylamines (hereafter named homoallylamines).[3] We have reported the [2,3]sigmatropic rearrangement of ammonium methylides[4a] and ethoxycarbonyl-substituted ammonium ylides[4b–4d] to give *Z*- and *E*-olefins with high stereoselectivity, respectively. Some quaternary ammonium salts are highly hygroscopic and difficult to handle, and undesirable side reactions, including Hofmann elimination and [1,2]rearrangement, may occur when strong bases are used to generate ammonium ylides.[5]

The catalyzed decomposition of diazo compounds to form ammonium ylide is a useful alternative to the widely employed base-promoted methodology (Scheme 1).[6,7] Because of their basicity, amines or imines are good ligands for catalytically active transition-metal compounds, and reaction temperatures required for diazo decomposition in the presence of amines or imines are higher than for reactions in the presence of substrates that possess other heteroatoms. Rhodium carboxylates and homogenous copper complexes have emerged as highly efficient catalysts for the generation of metal-stabilized oxonium ylides. The use of rhodium carboxylates for diazo decomposition made possible the generation of metal carbenes at more moderate temperatures than were previously possible with most copper catalysts.[8] Doyle and co-workers have reported several examples of intermolecular ammonium ylide generation from ethyl diazoacetate (EDA) in the presence of $[Rh_6(CO)_{16}]$ or $[Rh_2(OAc)_4]$. These intermediates undergo [2,3]sigmatropic rearrangement to produce homoallylamine[7a] and alleneamine.[7b] Hata and Watanabe have reported the treatment of 1-benzylazetidine with EDA in the presence of $[Cu(acac)_2]$ underwent ring expansion to give pyrrolidine via Stevens rearrangement.[9] In contrast, Burger and co-workers have claimed that the reaction of 1-benzylazetidine with



Scheme 1.

methyl 3,3,3-trifluoro-2-diazopropanoate, instead of EDA, in the presence of rhodium(II) acetate does not undergo ring enlargement and results in a [1,2]-benzyl migration to give α-(trifluorophenyl)alanine derivative.[6] West and co-workers have carried out an investigation on the intermolecular generation of ammonium ylides, followed by [1,2]-benzyl migration in the presence of Cu metal extensively.[10] The copper-catalyzed intermolecular [2,3]sigmatropic rearrangement of dihydropyridinium ylides has been reported to be a ring-contractive method.[11] The intramolecular version of allylamine possessing diazo moiety has been explored by several groups[12] to provide a general method for the preparation of cyclic amines.

However, there has been few reports on the stereocontrolled synthesis of trisubstituted olefins through [2,3]sigmatropic rearrangement of ammonium ylides induced by allylamines and reactive electrophilic metal carbene intermediates. Intermolecular ylide formation with subsequent [2,3]sigmatropic rearrangement offers a potentially versatile method for the stereoselective synthesis of quaternary centers flanked by useful functional groups. Since the reaction proceeds under non-basic mild conditions, a catalytic protocol can be adopted for elaboration to highly functionalized complex compounds. Herein,

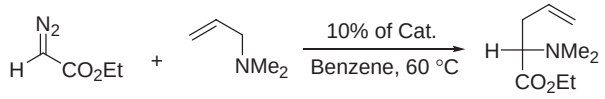
Published on the web January 10, 2008; doi:10.1246/bcsj.81.142

we report the efficient stereoselective synthesis of *E*-trisubstituted olefins via copper-catalyzed generation of ammonium ylides. In addition, we report the substituent effect at the 2-position of *N*,*N*-dimethylallylamine derivatives on the catalytic [2,3]sigmatropic rearrangement.

Results and Discussion

Copper-Catalyzed Intermolecular Formation of Ammonium Ylides and Subsequent [2,3]Sigmatropic Rearrangement. The copper-catalyzed intermolecular generation of ammonium ylides, followed by [2,3]sigmatropic rearrangement, was carried out using EDA **1a** and *N*,*N*-dimethylallylamine (**2a**) (Table 1). When [Cu(OTf)$_2$] was used, both the rearrangement product **3a** and a cyclopropane compound were obtained in 11% and 12% yields, respectively (Entry 2). Thus, it is suggested that [Cu(OTf)$_2$] interacted with a double bond as well as an amino group in an allylamine due to the strong Lewis acidity of [Cu(OTf)$_2$]. The effectiveness of the ylide formation of the carbenoid intermediate can be determined by the competition between [2,3]sigmatropic rearrangement of the generated ylide and the cyclopropanation of the carbon–carbon double bond.[13] However, the use of [Cu(hfacac)$_2$] or [Cu(acac)$_2$] gave the single product without cyclopropane derivative (Entries 4 and 5). As has been previously observed with the use of the rhodium catalysts,[7a] increasing the initial concentration of the allylamine relative to that of the diazo compound resulted in higher yields of the ylide rearrangement products. Thus, the potential drawbacks of this approach include the requirement of a large excess of the amine.

Table 1. Catalytic [2,3]Sigmatropic Rearrangement Using Copper Salts[a)]



1a **2a** **3a**

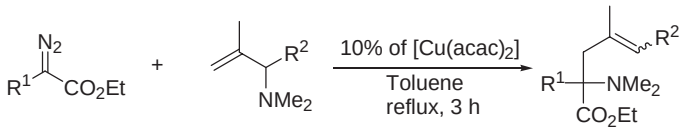
Entry	Cu-cat.	Time/h	Yield/%[b)]
1	[CuBr]	13	16
2	[Cu(OTf)$_2$]	6	11[c)]
3	[Cu$_2$(OAc)$_4$]	20	23
4	[Cu(hfacac)$_2$]	20	31
5	[Cu(acac)$_2$]	22	35

a) The reaction was carried out by using 5.0 molar equivalent of allylamine **2a** unless otherwise noting. b) Yield was calculated on the basis of the amount of the diazo compound. c) The cyclopropane derivative was obtained concomitantly.

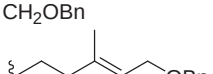
Copper-Catalyzed Intermolecular Formation of Ammonium Ylides and Subsequent Stereoselective [2,3]Sigmatropic Rearrangement of *N*,*N*-Dimethyl-1-alkyl-2-methylallylamines. The copper-catalyzed intermolecular generation of ammonium ylides, followed by [2,3]sigmatropic rearrangement, was applied to the stereoselective synthesis of trisubstituted olefin. The use of *N*,*N*-dimethylallylamine derivatives induced from terpene alcohols afforded the corresponding trisubstituted olefins in one-pot.

At first, we examined the reaction of *N*,*N*-dimethyl-2-methylallylamine (**2b**) with **1a** in the presence of copper catalyst (Table 2). When the reaction was carried out at 60 °C in benzene in the presence of [Cu(hfacac)$_2$], the rearrangement product **3b** was obtained in 23% yield along with the cyclopropane derivative in 19% yield. When [Cu(acac)$_2$] was used at 60 °C in benzene, product **3b** was obtained in 22% yield without

Table 2. Reaction of Diazo Compounds **1a**–**1d** with Allylamines **2b**–**2d**[a)]



1a-d **3b-h**

2b: R^2 = H
2c: R^2 = CH_2OBn
2d: R^2 = 

Entry	Diazo compound	R^1	Amine	Product	Yield/%[b)]	Ratio of *E*/*Z*[c)]
1[d)]	**1a**	H	**2b**	**3b**	50	—
2	**1a**	H	**2c**	**3c**	20	91/9
3	**1b**	Ph	**2c**	**3d**	45	71/29
4	**1b**	Ph	**2d**	**3e**	67	64/36
5	**1c**	Ac	**2c**	**3f**	23	94/6
6[e)]	**1d**	CO_2Et	**2c**	**3g**	64	93/7
7[f)]	**1d**	CO_2Et	**2d**	**3h**	65	90/10
8[d)]	**1d**	CO_2Et	**2d**	**3h**	32	94/6

a) The reaction was carried out by using 3.0 molar equivalent of allylamines **2b**–**2d** unless otherwise noting. b) Yield was calculated on the basis of the amount of the diazo compounds. c) Determined by ^{1}H NMR spectroscopy. d) Reaction was carried out in benzene at reflux for 3 h. e) The reaction was carried out by using 1.0 molar equivalent of allylamines. f) Reaction was carried out in the presence of MS4A.

a cyclopropane compound, and in refluxing benzene, it was obtained in 50% yield (Entry 1).

Notably, the reaction of *N*,*N*-dimethyl-1-alkyl-2-methylallylamines, induced from terpene alcohols, with diazo compounds in the presence of [Cu(acac)$_2$] underwent the catalytic [2,3]sigmatropic rearrangement to give the desired *E*-trisubstituted olefins (Entries 2–8). Whereas the treatment of **2c** with **1a** at reflux in benzene gave a trace amount of the product, *E*-olefin **3c** was obtained in refluxing toluene in 20% yield with $E/Z = 91:9$ (Entry 2). The reaction of **2c** and **2d** with diazo compounds possessing two electron-withdrawing groups, **1c** (R^1 = Ac) or **1d** (R^1 = CO_2Et), afforded bifunctional *E*-olefins **3f**–**3h** (Entries 5–8). It should be noted that the reaction did not need a large amount of amine. Thus, the reaction was performed by using 1 molar equivalent of amine **2c** to give product **3g** in 64% yield (Entry 6).

The reaction of **2d** with **1d** afforded product **3h** in good yield (65%) with $E/Z = 90:10$ (Entry 7). In refluxing benzene instead of toluene, product **3h** was obtained with high *E*-stereoselectivity (Entry 8). Treatment of allylamine **2c** to a catalytic amount of [$Rh_2(OAc)_4$] in benzene at reflux did not produce product **3c**.

A stable ylide may undergo [2,3]sigmatropic rearrangement to give *E*-olefins via a concerted transition state involving a double suprafacial mode, in which R^4CH_2 on the allyl moiety takes a pseudoequatorial conformation to avoid synclinal repulsion with the methyl substituent and 1,3-diaxial interaction with a hydrogen atom[14] (Fig. 1). As the phenyl group may prefer a pseudoaxial alignment in the transition state to some degree, the corresponding rearrangement afforded an E/Z mixture of products **3d** and **3e** (Entries 3 and 4). It has been reported that [2,3]sigmatropic rearrangement of allylic sulfoxides possessing a phenyl group at the 1-position gives *Z*-olefins predominatly.[15]

The Substituent Effect at 2-Position of *N*,*N*-Dimethylallylamine Derivatives. The reaction was carried out by using diazo compounds **1a**–**1d**, *N*,*N*-dimethylallylamine derivatives **2e**–**2g** and [Cu(acac)$_2$] in order to investigate the substituent effect of the functional group R^3 at the 2-position (Table 3). Treatment of allylamines bearing an electron-withdrawing group (R^3 = Cl and CO_2Et) with **1a** gave rearrangement products **3i** and **3j** in moderate yields (Entries 1 and 2). When allylamine **2g** possessing the cyano group at the 2-position was used (Entry 4), we found that [2,3]sigmatropic rearrangement occurred more readily. Next, we investigated the reaction using allylamine **2g** under milder conditions. Among the possible solvents (e.g. benzene, toluene, THF, chloroform, dichloromethane, dichloroethane, and chlorobenzene) for the reaction at low temperature, we found dichloromethane to be

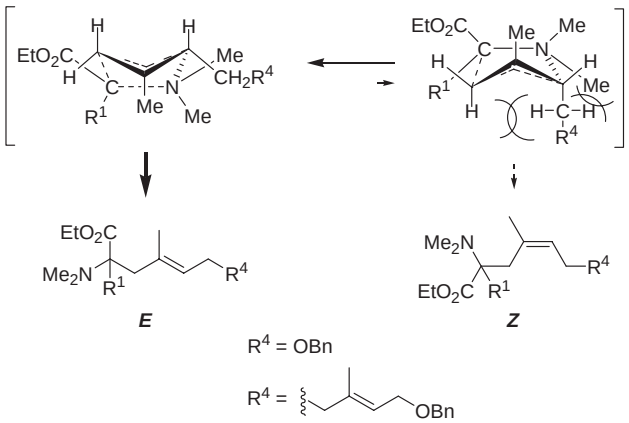
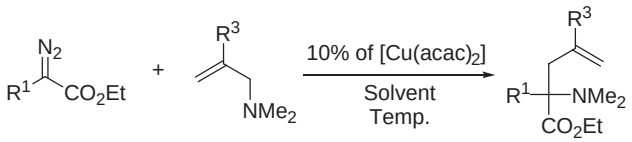


Fig. 1. Concerted transition state of *E*-selective [2,3]sigmatropic rearrangement.

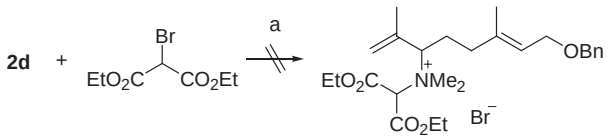
Table 3. Reaction of Diazo Compounds **1a**–**1d** with Allylamine **2e**–**2g**[a)]



1a-d **2e-g** **3i-n**

Entry	Diazo compound	R^1	Amine	R^3	Solvent	Time	Temp /°C	Product	Yield /%[b)]
1	**1a**	H	**2e**	Cl	Benzene	20 min	Reflux	**3i**	56
2	**1a**	H	**2f**	CO_2Et	Benzene	1 h	Reflux	**3j**	45
3	**1a**	H	**2g**	CN	Benzene	20 min	Reflux	**3k**	76
4[c)]	**1a**	H	**2g**	CN	Benzene	20 min	Reflux	**3k**	84
5	**1a**	H	**2g**	CN	Benzene	12 h	60	**3k**	49
6	**1a**	H	**2g**	CN	THF	23 h	60	**3k**	37
7[d)]	**1a**	H	**2g**	CN	DCM	5 h	rt	**3k**	43
8	**1a**	H	**2g**	CN	DCM	18 h	Reflux	**3k**	53
9	**1b**	Ph	**2g**	CN	Toluene	2 h	Reflux	**3l**	88
10	**1c**	Ac	**2g**	CN	Toluene	2 h	Reflux	**3m**	63
11	**1d**	CO_2Et	**2g**	CN	Benzene	4 h	Reflux	**3n**	87

a) The reaction was carried out by using 3.0 molar equivalent of allylamines **2e**–**2g** unless otherwise noting. b) Yield was calculated on the basis of the amount of the diazo compound. c) Six molar equivalent of **2g** was used. d) The reaction was carried out at room temperature using 1.2 molar equivalent of **2g** in the presence of Cu^I species induced from Cu(dpm)$_2$ with phenylhydrazine.



Scheme 2. Reagents and conditions: (a) MeCN, rt, 2 d or ether, rt, 2 d or $CHCl_3$, reflux, 6 h.

the best (Entries 5–8). By controlling the concentration of amine, we found that the reaction proceeded in dichloromethane at ambient temperature. When using 1.2 molar equivalent of **2g**, product was obtained in 34% yield. When the reaction was carried out in the presence of a more active copper(I) species[16] generated from [Cu(dpm)$_2$] and phenylhydrazine,[17] the product was obtained in 43% yield in a short time (Entry 7). When the process was carried out in dichloromethane at room temperature with [$Rh_2(OAc)_4$], the desired product was obtained in 18% yield. In addition, the use of **2g** with diazo compounds **1b–1d** afforded bifunctional homoallylic amines **3l–3n** efficiently (Entries 9–11).

Though we tried to prepare the bifunctional homoallylamines **3f–3h**, **3m**, and **3n** from allylic *tert*-amines and alkylhalides having two electron-withdrawing groups, the corresponding ammonium salts were not obtained owing to the decomposition of alkylhalides by allylic *tert*-amines themselves (Scheme 2). It should be noted that bifunctional homoallylamines **3f–3h**, **3m**, and **3n**, which could not be obtained by the general base-promoted methodology, could be obtained effectively by using the copper-catalyzed carbenoid protocol.

Conclusion

We demonstrated the reaction of *N*,*N*-dimethylallylamine derivatives with diazo compounds in the presence of bisacetylacetonatocopper(II), which may undergo the generation of ammonium ylides species, followed by the spontaneous [2,3]-sigmatropic rearrangement, to give rearrangement products in one-pot. The reaction of *N*,*N*-dimethyl-1-alkyl-2-methylallylamines, derived from terpene alcohols, with diazo compounds afforded the trisubstituted *E*-homoallylamines. A cyano substituent at the 2-position of *N*,*N*-dimethylallylamine derivatives caused the [2,3]sigmatropic rearrangement to occur more readily. Bifunctional homoallylamines, which could not be obtained by using the general base-promoted [2,3]rearrangement, were obtained efficiently using our catalytic carbenoid protocol.

With substituted allylamines and diazoketones in the presence of Cu catalyst, generation of the ammonium ylides occurred almost exclusively, and the subsequent [2,3]sigmatropic rearrangement products were afforded with a high degree of stereocontrol, favoring the *E*-isomer. These results can be explained by steric and/or electronic influences in the transition states for the [2,3]sigmatropic rearrangement.

Experimental

General. IR spectra were recorded on a Perkin-Elmer Paragon 1000 Fourier transform IR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-ALS 400 (400 MHz) spectrometer. Unless otherwise stated, deuterated chloroform was used as the solvent, and tetramethylsilane was used as the internal standard. Chemical shifts in ^{1}H NMR spectra are reported in parts per million downfield from tetramethylsilane, and ^{13}C NMR spectra are reference to the internal solvent standard. Coupling constants (J) are quoted in hertz. Thin-layer chromatography (TLC) was performed on precoated Merck TLC plates with silica gel 60 F-254. Column chromatography was carried out with Cica-Merck Silica gel 60 (Kanto Chemical Industries). All reagents were obtained from commercial suppliers and were used as received unless otherwise indicated. The diazo compounds (**1b–1d**) were prepared by diazo-transfer reaction.[18] Amines **2b**,[19a] **2c** and **2d**,[4,19b,19c] and **2e**[19d] were prepared by using previously reported methods. Amines **2f** and **2g** were prepared from paraformaldehyde and dimethylamine hydrochloride with cyanoacetic acid or ethyl malonate under Mannich reaction conditions, respectively.[19e]

General Procedure for the Reaction of EDA with *N*,*N*-Dimethylallylamine in the Presence of Copper-Catalyst (Table 1). Catalyst (0.1 mmol) was added to a stirred solution of *N*,*N*-dimethylallylamine (5 mmol) in benzene (10 mL) under an atmosphere of argon. The reaction mixture was heated to 60 °C, a solution of EDA (1 mmol) in benzene (2 mL) was added using a syringe pump. After the addition of EDA, the reaction mixture was stirred for 6–22 h. When the reaction mixture was cooled, diethyl ether was added, and the suspension was filtered. The solvent was then removed in vacuo, and the residue was purified by column chromatography on silica gel with hexane/EtOAc (3:1) to give homoallylamines as pale yellow oil. The yield was calculated on the basis of the amount of the diazo compound.

General Procedure for the Copper-Catalyzed [2,3]Sigmatropic Rearrangements (Table 2). Unless otherwise noted, the reaction was performed with Cu(acac)$_2$ (0.1 mmol), allylamine (3 mmol) in toluene (7 mL), and diazo compound (1 mmol) in toluene (2 mL) under an atmosphere of argon. After the addition of the diazo compound using a syringe pump, the reaction mixture was stirred for 3 h at reflux. When the reaction mixture was cooled, diethyl ether was added, and the suspension was filtered. The solvent was then removed in vacuo, and the residue was purified by column chromatography on silica gel with hexane/EtOAc (3:1) to give *E*/*Z* mixture of homoallylamines as pale yellow oil. The yield was calculated on the basis of the amount of the diazo compounds except for the Entry 6. In Entry 6, the yield was based on the recovery of the starting material (allylamine **2c**). The *E* stereochemistry was confirmed by the ^{1}H NMR spectrum.

Ethyl 2-(Dimethylamino)-4-methyl-4-pentenoate (3b): IR (neat): 2979, 2938, 2871, 2832, 2789, 1731, 1650, 1455, 1371, 1262, 1173, 1098, 1029, 891 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.28 (t, J = 7.3 Hz, 3H), 1.76 (s, 3H), 2.30–2.53 (m, 2H), 2.36 (s, 6H), 3.36 (dd, J = 6.4, 8.9 Hz, 1H), 4.17 (q, J = 7.3 Hz, 2H), 4.75 (d, J = 1.0 Hz, 1H), 4.80 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.4, 22.2, 37.9, 41.7, 60.3, 65.9, 112.9, 141.8, 171.7. Anal. Calcd for $C_{10}H_{19}NO_2$: C, 64.83; H, 10.34; N, 7.56%. Found: C, 65.01; H, 10.35; N, 7.34%.

Ethyl 6-Benzyloxy-2-(dimethylamino)-4-methyl-4-hexenoate (*E*-3c): IR (neat): 2979, 2936, 2863, 2787, 1730, 1453, 1173, 1091, 1070, 1028, 739, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.25 (t, J = 7.1 Hz, 3H), 1.67 (s, 3H), 2.32–2.52 (m, 2H), 2.35 (s, 6H), 3.33 (dd, J = 6.1, 9.1 Hz, 1H), 4.01 (dd, J = 2.8, 6.6 Hz, 2H), 4.14 (dq, J = 1.2, 7.1 Hz, 2H), 4.47 (s, 2H), 5.45 (t, J = 6.83 Hz, 1H), 7.26–7.34 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.5, 16.4, 40.0, 41.8, 60.1, 66.2, 66.3, 71.8, 123.8, 127.4, 127.7, 128.2, 136.3, 138.4, 171.5. Anal. Calcd for $C_{18}H_{27}NO_3$: C, 70.79; H, 8.91; N, 4.59%. Found: C, 70.76; H, 9.01; N, 4.47%.

Ethyl 6-Benzyloxy-2-(dimethylamino)-2-phenyl-4-methyl-4-

hexenoate (3d): Each of rearrangement products were separated carefully from *E*/*Z* mixture to give 13% of *Z*-**3d** and 32% of *E*-**3d**. *E*-**3d**: IR (neat): 2980, 2932, 2865, 2834, 2790, 1718, 1494, 1447, 1384, 1365, 1204, 1092, 1068, 1028, 739, 701. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.21 (s, 3H), 1.33 (t, $J = 7.1$ Hz, 3H), 2.30 (s, 6H), 2.49 (d, $J = 13.2$ Hz, 1H), 3.07 (d, $J = 13.2$ Hz, 1H), 3.81 (d, $J = 6.3$ Hz, 2H), 4.27–4.32 (m, 4H), 5.12 (t, $J = 6.3$ Hz, 1H), 7.08–7.36 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.8, 17.8, 40.4, 47.4, 60.2, 66.4, 71.5, 74.3, 126.3, 126.7, 127.1, 127.3, 127.6, 128.0, 128.2, 128.3, 129.6, 136.0, 138.5, 169.7. Anal. Calcd for $C_{24}H_{31}NO_3$: C, 75.56; H, 8.19; N, 3.67%. Found: C, 75.54; H, 8.28; N, 3.38%.

Ethyl 10-Benzyloxy-4,8-dimethyl-2-(dimethylamino)-2-phenyl-4,8-decadienoate (*E*-3e): IR (neat): 2978, 2937, 2866, 2790, 1719, 1446, 1120, 1094, 1067, 1027, 737, 701 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.18 (s, 3H), 1.32 (t, $J = 6.9$ Hz, 3H), 1.57 (s, 3H), 1.80–1.89 (m, 4H), 2.29 (s, 6H), 2.36 (d, $J = 13.2$ Hz, 1H), 3.02 (d, $J = 13.2$ Hz, 1H), 4.00 (d, $J = 6.6$ Hz, 2H), 4.28 (q, $J = 6.9$ Hz, 2H), 4.49 (s, 2H), 4.80 (t, $J = 6.6$ Hz, 1H), 5.31 (t, $J = 6.6$ Hz, 1H), 7.12–7.35 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.9, 16.6, 17.4, 26.4, 39.1, 40.5, 47.5, 60.1, 66.6, 72.0, 74.4, 120.4, 126.5, 126.9, 127.3, 127.7, 128.2, 128.3, 129.0, 131.1, 138.3, 139.6, 140.2, 169.6. Anal. Calcd for $C_{29}H_{39}NO_3$: C, 77.47; H, 8.74; N, 3.12%. Found: C, 77.30; H, 8.87; N, 2.91%.

Ethyl 2-Acetyl-6-benzyloxy-2-(dimethylamino)-4-methyl-4-hexenoate (*E*-3f): IR (neat): 2930, 2856, 2792, 1717, 1454, 1352, 1206, 1072, 1027, 740, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (t, $J = 7.1$ Hz, 3H), 1.61 (s, 3H), 2.18 (s, 3H), 2.33 (s, 6H), 2.76 (abq, $J = 13.9$, 76.1 Hz, 2H), 3.97 (d, $J = 6.6$ Hz, 2H), 4.24 (q, $J = 7.1$ Hz, 2H), 4.46 (s, 2H), 5.46 (dt, $J = 1.0$, 6.6 Hz, 1H), 7.25–7.35 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.5, 17.0, 28.0, 40.8, 43.1, 60.8, 66.2, 72.0, 79.7, 126.2, 127.4, 127.7, 128.2, 135.6, 138.3, 168.2, 204.1. Anal. Calcd for $C_{20}H_{29}NO_4$: C, 69.14; H, 8.41; N, 4.03%. Found: C, 69.12; H, 8.47; N, 3.82%.

Diethyl 2-(4-Benzyloxy-2-methyl-2-butenyl)-2-(dimethylamino)malonate (*E*-3g): IR (neat): 2981, 2956, 2905, 2871, 2792, 1754, 1726, 1454, 1227, 1072, 1027, 741, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.27 (t, $J = 7.1$ Hz, 6H), 1.68 (s, 3H), 2.38 (s, 6H), 2.82 (s, 2H), 4.00 (d, $J = 6.6$ Hz, 2H), 4.21 (q, $J = 7.1$ Hz, 4H), 4.46 (s, 2H), 5.52 (t, $J = 6.6$ Hz, 1H), 7.27–7.35 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 17.3, 40.8, 43.7, 61.0, 66.3, 71.9, 75.5, 125.6, 127.3, 127.6, 128.1, 135.5, 138.3, 167.9. Anal. Calcd for $C_{21}H_{31}NO_5$: C, 66.82; H, 8.28; N, 3.71%. Found: C, 66.90; H, 8.34; N, 3.57%.

Diethyl 2-(8-Benzyloxy-2,6-dimethyl-2,6-octadienyl)-2-(dimethylamino)malonate (*E*-3h): IR (neat): 2980, 2936, 2857, 2790, 1755, 1726, 1454, 1226, 1098, 1068, 1029, 740, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23 (t, $J = 7.1$ Hz, 6H), 1.63 (s, 6H), 1.99–2.11 (m, 4H), 2.36 (s, 6H), 2.75 (s, 2H), 4.02 (d, $J =$ 6.7 Hz, 2H), 4.20 (q, $J = 7.1$ Hz, 4H), 4.50 (s, 2H), 5.25 (t, $J =$ 6.7 Hz, 1H), 5.39 (dt, $J = 1.0$, 6.7 Hz, 1H), 7.25–7.37 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.5, 16.6, 16.8, 26.5, 39.4, 40.8, 43.9, 60.8, 66.6, 72.0, 75.7, 120.8, 127.3, 127.6, 128.2, 128.5, 131.0, 138.4, 139.9, 168.0. Anal. Calcd for $C_{26}H_{39}NO_5$: C, 70.08; H, 8.82; N, 3.14%. Found: C, 69.90; H, 8.87; N, 3.02%.

General Procedure for the Copper-Catalyzed [2,3]Sigmatropic Rearrangements (Table 3). Unless otherwise noted, the reaction was performed with $Cu(acac)_2$ (0.1 mmol) and allylamine (3 mmol) in the solvents (7 mL) listed in the table and diazo compound (1 mmol) in the appropriate solvent (2 mL) under an atmosphere of argon. After the addition of the diazo compound using a syringe pump, the reaction mixture was stirred for 20 min–18 h listed in the table. When the reaction mixture was cooled, diethyl ether was added, and the suspension was filtered. The solvent was then removed in vacuo, and the residue was purified by column chromatography on silica gel with hexane/EtOAc (3:1) to give corresponding homoallylamines as pale yellow oil. The yield was calculated on the basis of the amount of the diazo compounds.

Ethyl 4-Chloro-2-(dimethylamino)-4-pentenoate (3i): IR (neat): 2980, 2940, 2871, 2834, 2789, 1731, 1637, 1455, 1371, 1246, 1228, 1175, 1098, 1035, 886, 637 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (t, $J = 7.1$ Hz, 3H), 2.37 (s, 6H), 2.65 (ddd, $J = 0.7$, 6.8, 14.4 Hz, 1H), 2.78 (ddd, $J = 0.7$, 7.8, 14.4 Hz, 1H), 3.59 (dd, $J = 6.8$, 7.8 Hz, 1H), 4.19 (dq, $J = 2.4$, 7.1 Hz, 2H), 5.22 (d, $J = 1.2$ Hz, 1H), 5.24 (d, $J = 1.2$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 39.0, 41.5, 60.3, 64.8, 114.7, 139.0, 170.7. Anal. Calcd for $C_9H_{16}ClNO_2$: C, 52.56; H, 7.84; N, 6.81%. Found: C, 52.48; H, 7.80; N, 6.62%.

Diethyl 2-Dimethylamino-4-methyleneglutarate (3j): IR (neat): 2980, 2938, 2871, 2833, 2788, 1728, 1632, 1448, 1370, 1298, 1266, 1243, 1185, 1097, 1033, 937, 817 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.27 (t, $J = 7.1$ Hz, 3H), 1.31 (t, $J = 7.1$ Hz, 3H), 2.35 (s, 6H), 2.64–2.74 (m, 2H), 3.45 (dd, $J = 6.7$, 8.5 Hz, 1H), 4.15 (dq, $J = 2.1$, 7.1 Hz, 2H), 4.22 (q, $J = 7.1$ Hz, 2H), 5.61 (d, $J = 1.3$ Hz, 1H), 6.20 (d, $J = 1.3$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 14.4, 31.9, 41.7, 60.2, 60.7, 66.3, 127.1, 137.1, 166.7, 171.4. Anal. Calcd for $C_{12}H_{21}NO_4$: C, 59.24; H, 8.70; N, 5.76%. Found: C, 59.04; H, 8.73; N, 5.71%.

Ethyl 4-Cyano-2-(dimethylamino)-4-pentenoate (3k): IR (neat): 2981, 2941, 2871, 2836, 2790, 2224, 1729, 1624, 1454, 1370, 1236, 1178, 1097, 1034 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (t, $J = 7.1$ Hz, 3H), 2.36 (s, 6H), 2.55–2.68 (m, 2H), 3.49 (dd, $J = 7.3$, 8.3 Hz, 1H), 4.14–4.26 (m, 2H), 5.80 (d, $J = 0.5$ Hz, 1H), 5.92 (d, $J = 0.5$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.5, 34.3, 41.4, 60.5, 65.2, 118.1, 119.9, 132.3, 170.2. Anal. Calcd for $C_{10}H_{16}N_2O_2$: C, 61.20; H, 8.22; N, 14.27%. Found: C, 60.97; H, 8.29; N, 14.02%.

Ethyl 4-Cyano-2-(dimethylamino)-2-phenyl-4-pentenoate (3l): IR (neat): 2983, 2940, 2836, 2793, 2223, 1721, 1493, 1447, 1297, 1227, 1192, 1068, 1027, 946, 705 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (t, $J = 7.1$ Hz, 3H), 2.38 (s, 6H), 2.91 (dabq, $J = 1.0$, 14.0, 28.0 Hz, 2H), 4.34 (q, $J = 7.1$ Hz, 2H), 5.10 (d, $J = 1.0$ Hz, 1H), 5.68 (d, $J = 1.0$ Hz, 1H), 7.24–7.32 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.8, 40.7, 42.9, 60.8, 74.1, 118.4, 118.6, 127.5, 127.6, 128.1, 135.4, 138.5, 159.5. Anal. Calcd for $C_{16}H_{20}N_2O_2$: C, 70.56; H, 7.40; N, 10.29%. Found: C, 70.33; H, 7.51; N, 10.00%.

Ethyl 2-Acetyl-4-cyano-2-(dimethylamino)-4-pentenoate (3m): IR (neat): 2985, 2843, 2796, 2224, 1718, 1617, 1462, 1356, 1233, 1168, 1050, 952 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33 (t, $J = 7.1$ Hz, 3H), 2.24 (s, 3H), 2.41 (s, 6H), 2.90 (dabq, $J = 1.1$, 14.9, 24.4 Hz, 2H), 4.29 (dq, $J = 1.2$, 7.1 Hz, 2H), 5.85 (s, 1H), 5.99 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 27.9, 36.4, 40.8, 61.6, 79.4, 117.9, 118.2, 135.5, 167.9, 203.3. Anal. Calcd for $C_{12}H_{18}N_2O_3$: C, 60.49; H, 7.61; N, 11.76%. Found: C, 60.38; H, 7.65; N, 11.54%.

Diethyl 2-(2-Cyanoallyl)-2-dimethylaminomalonate (3n): IR (neat): 2984, 2906, 2839, 2795, 2224, 1756, 1728, 1620, 1465, 1448, 1391, 1367, 1303, 1235, 1209, 1094, 1064, 1041, 953, 859 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.31 (t, $J = 7.1$ Hz, 6H), 2.43 (s, 6H), 2.97 (d, $J = 1.2$ Hz, 2H), 4.27 (q, $J = 7.1$ Hz, 4H), 5.90 (d, $J = 0.7$ Hz, 1H), 6.00 (s, 1H). ^{13}C NMR (100 MHz,

$CDCl_3$): δ 14.1, 37.8, 40.6, 61.5, 74.7, 117.8, 118.2, 135.0, 167.5. Anal. Calcd for $C_{13}H_{20}N_2O_4$: C, 58.19; H, 7.51; N, 10.44%. Found: C, 58.01; H, 7.52; N, 10.34%.

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This paper is dedicated to the memory of Professor Yoshihiko Ito.

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