The Organocopper Route from (2-Propynylidene)morpholinium Triflates to Morpholinoallenes, 1-Morpholino-1,3-butadienes, and 2-Morpholino-1,3-butadienes

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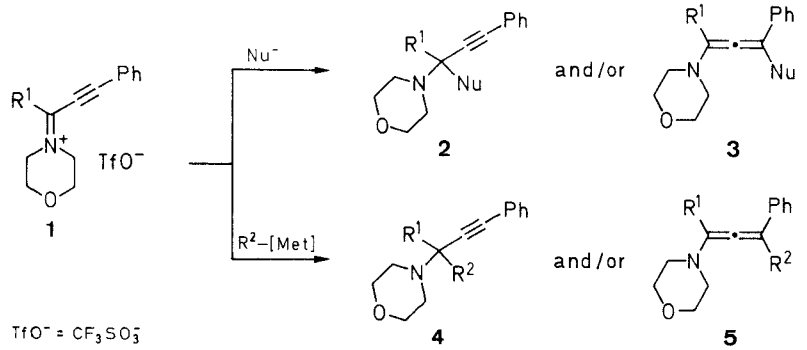
Organocopper reagents undergo conjugate addition to (1,3-diphenyl- and (1-methyl-3-phenyl-2-propynylidene)morpholinium triflates **1a** and **1b**. The resulting morpholinoallenes can be isolated if the allenic unit bears no CH substituent. Allenes bearing a R^1R^2 CH substituent at C-3 can be isolated in some cases; their thermal isomerization yields 4-(1,3-diphenyl-1,3-alkadienyl)morpholines **9**. Allenes resulting from salt **1b** spontaneously isomerize to 2-morpholino-1,3-butadienes **12**. Reaction of allylcopper with **1a** yields 4-[(3*Z* and 3*E*)-1,3-diphenyl-1,3,5-hexatrienyl]morpholine **(8)**.

(3-Phenyl-2-propynylidene)morpholinium triflates **1** (R^1 = Ph, Me) are easily obtained from the appropriate enamino ketone and triflic anhydride in two steps.[1] The resonance-stabilized cations display ambident behavior towards nucleophiles; bond connection can either occur at the iminium carbon atom to form propargylmorpholines **2** or at the acetylenic β-position to form morpholinoallenes **3** (Scheme **1**). Either possibility has been realized with heteronuclophiles such as amines, thiols, and their respective anions.[2] Furthermore, we have already reported in preliminary form that organo-, silyl-, and stannylcuprates add to **1** in a conjugate manner to form morpholinoallenes **5**, whereas organolithium and Grignard reagents yield propargylmorpholines **4** predominantly or exclusively.[3]

So far, dialkylaminoallenes constitute a rather small and little-known subset of the class of electron-rich allenes.[4,5] Presumably, this is due in part to the low stability of the unsubstituted dialkylaminoallenes (such as dimethylamino-,[6,7] diethylamino-,[8] and morpholinoallene[6,7]), which are prone to dimerization and polymerization. Furthermore, dialkylaminoallenes bearing a R^1R^2 substituent at C-1 or C-3 have a tendency to isomerize, by a formal 1,3-hydrogen shift to the central allenic carbon atom, to 2-(or 1-)dialkylamino-1,3-butadienes; this reaction occurs readily in basic media[8] and at elevated temperatures.[9,10]

The conjugate addition of organocopper reagents to 4-(2-propynylidene)morpholinium salts **1** offers the opportunity to synthesize highly substituted and functionalized morpholinoallenes. In this paper, we report on scope and limitation of this novel synthesis.

The 1,4-addition of organocopper reagents [including organocopper compounds (RCu), lower-order and higher-order organocuprates, Grignard reagents in the presence of catalytic or stoichiometric amounts of copper(I) salts] has been widely used in organic synthesis.[11-17] Similarly, the S_N2'-type addition of the same reagents to propargylic compounds ($R^1R^2CX-C\equiv C-$, X being a leaving group) has been used to synthesize a broad range of allenes.[4,5,7,18,19] Since 4-(2-propynylidene)morpholinium cations closely resemble the two organic substrates mentioned except for the full positive charge, a similar reactivity towards organocopper reagents was anticipated. In fact, when salt **1a** is allowed to react with the higher-order cyanocuprates[20] **6a,c,e,f**, prepared in situ from organolithium and copper(I) cyanide in a 2:1 ratio, morpholinoallenes **7a,c,e,f** are obtained as the only isolable products (Scheme **2**, Table 1). Analogously, reaction of **1a** with the lower-order cuprate (s-Bu)$_2$CuLi **(6b)** (a Gilman reagent), prepared from two equivalents of *sec*-butyllithium and one equivalent of copper(I) bromide, or with $(CH_2=CH)_2CuMgBr$ **(6d)** [obtained from two equivalents of vinylmagnesium bromide and one equivalent of copper(I) cyanide], provided morpholinoallenes **7b** and **7d**, respectively. By the same strategy, higher-order silyl- and stannyl(cyano)cuprates **6g–i** were used to synthesize 1-morpholino-3-silyl (or 3-stannyl)allenes **7g–i**;[3] by small variations of the reaction temperature (Table 1), the yields of **7g,h** could be improved as compared to our published[3] procedure. Table 1 illustrates the generality of our synthesis of morpholinoallenes, in that sp^3-, sp^2- and sp-centered carbon nucleophiles as well as silyl and stannyl groups can all be delivered at the β-acetylenic position of salt **1a**. Steric hindrance at the nucleophile does not affect adversely the efficiency of the bond connection **(7c,g–i)**.



Scheme **1**

Table 1. Morpholinoallenes **7** Prepared

Product	Cuprate **6**	Reaction Conditions[a]	Yield (%)	mp (°C) (solvent)	Molecular Formula[b]
7a	$Bu_2Cu(CN)Li_2$	−70°C, 0.5 h → −20°C, 1 h, → r.t.	64	61	$C_{23}H_{27}NO$ (333.5)
7b	*s*-Bu_2CuLi	−70°C, 0.5 h → −45°C, 1 h, → r.t.	72	oil	$C_{23}H_{27}NO$ (333.5)
7c	*t*-$Bu_2Cu(CN)Li_2$	−70°C, 0.5 h → 0°C, 1 h, → r.t.	73	71 (MeCN)	$C_{23}H_{27}NO$ (333.5)
7d	$(CH_2{=}CH)_2CuMgBr$	−70°C, 0.5 h → 0°C, 1 h, → r.t.	52	oil	$C_{21}H_{21}NO$ (303.4)
7e	$Ph_2Cu(CN)Li_2$	−70°C, 0.5 h → 0°C, 1 h, → r.t.	53	80 (MeCN)	$C_{25}H_{23}NO$ (353.5)
7f	$(PhC{\equiv}C)_2Cu(CN)Li_2$	−70°C, 0.5 h → 0°C, 1 h, → r.t.	17	oil[c]	$C_{27}H_{23}NO$ (380.0)
7g	$(t\text{-}BuPh_2Si)_2Cu(CN)Li_2$	−70°C, 0.5 h → 0°C, 1 h, → r.t.	67	123 (MeCN)	$C_{35}H_{37}NOSi$ (515.8)
7h	$(Ph_3Si)_2Cu(CN)Li_2$	−70°C, 0.5 h → 0°C, 1 h, → r.t.	52	146	$C_{37}H_{33}NOSi$ (535.8)
7i	$(Ph_3Sn)_2Cu(CN)Li_2$	−70°C, 0.5 h → 0°C, 1 h, → r.t.	31	149	$C_{37}H_{33}NOSn$ (626.4)

[a] Solvent: THF (for **7g–i**); THF/hexane (for **7a–c, f**); THF/Et_2O (for **7d**); THF/cyclohexane/Et_2O (for **7e**).
[b] Satisfactory microanalysis obtained for **7a–g** (C ±0.54, H ±0.06, N ±0.2 (**2e**: −0.46)); for microanalyses of **7g–i**, Ref. 3.
[c] The yellow-greenish oil obtained turns black even when stored under an Ar atmosphere for several hours at 20°C, probably because of polymerization.

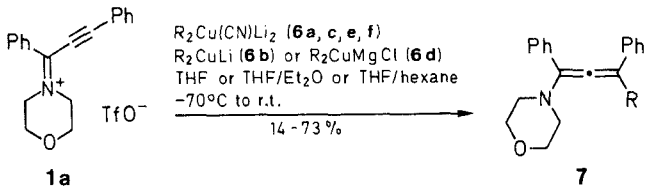
Table 2. Spectral Data for Morpholinoallenes **7a–f**

Product	IR[a] $\nu_{(C=C=C)}$ (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[b], δ, *J* (Hz) NCH_2	OCH_2	Other Signals	^{13}C-NMR ($CDCl_3$/TMS) δ N–C=C=C	C=C=C	N–C=C=C	Other Signals
7a	1927/ 1960	2.78 (mc)	3.75 (pseudo-t)	0.80 (t, CH_3), 1.00–1.80 (m, $CH_2CH_2CH_3$), 2.53 (t, =C–CH_2), 7.00–7.50 (m, Ph)				
7b[c]	1926/ 1960	2.53–2.99 (m)[d]	3.78 (pseudo-t)	0.76–1.90 (m, CH_2CH_3, CH–CH), 7.06–7.60 (m, Ph)	127.64, 127.77	197.93, 197.99	121.10, 121.34	11.87/12.10 (CH_2CH_3), 19.41/ 19.94 (CH–CH_3), 29.13/29.44 (CH_2), 35.86/35.96 ($CHCH_3$), 51.46/51.53 (NCH_2), 67.01/67.04 (OCH_2), 126.3–128.6 (*o*-, *m*-, *p*-C_{arom}), 135.1, 137.36/137.48 (*i*-C_{arom})
7c	1935	2.56–2.75[e]	3.70 (pseudo-t)	1.11 (s, *t*-Bu), 7.10–7.43 (m, Ph)	124.1 or 124.9	195.9	124.9 or 124.1	29.9 (CCH_3), 35.8 (CCH_3), 51.6 (NCH_2), 67.2 (OCH_2), 126.5–128.9 (*o*-, *m*-, *p*-C_{arom}), 135.7, 138.8 (*i*-C_{arom})
7d	1890/ 1945	2.79 (pseudo-t)	3.77 (pseudo-t)	5.25–5.28, 5.39–5.44 (AB part of ABX, $=CH_2$), 6.58 (X-part of ABX, CH=), 7.21–7.50 (m, Ph)	127.1	202.0	116.0	51.3 (NCH_2), 66.9 (OCH_2), 117.2 ($=CH_2$), 127.1–128.8 (*o*-, *m*-, *p*-C_{arom}), 133.7 ($CH{=}CH_2$), 134.5, 136.7 (*i*-C_{arom})
7e	1905/ 1945	2.83 (pseudo-t)	3.76 (pseudo-t)	7.16–7.63 (m, Ph)	130.2	202.2	118.7	51.8 (NCH_2), 66.9 (OCH_2), 125.1–128.9 (*o*-, *m*-, *p*-C_{arom}), 130.2, 135.2, 138.2 (*i*-C_{arom})
7f	1880[f]	2.93 (pseudo-t)	3.83 (pseudo-t)	7.20–7.80 (m, Ph)	122.9	207.1	101.0	48.2 (NCH_2), 66.8 (OCH_2), 83.5, 91.8 (C≡C), 122.9–131.5 (*o*-, *m*-, *p*-C_{arom}), 132.2 (2×), 134.6 (*i*-C_{arom})

[a] KBr pellets (for **7a, c, e**) or film (for **7b, d, f**).
[b] 90 MHz (for **7a, b, e, f**) or 400 MHz (for **7c, d**).
[c] Two diastereomers in 1:1 ratio (according to ^{13}C-NMR).
[d] Signal of =C–CH covered by NCH_2.
[e] AB system with each line split into a triplet.
[f] ν (C≡C) = 2180 cm^{-1}.

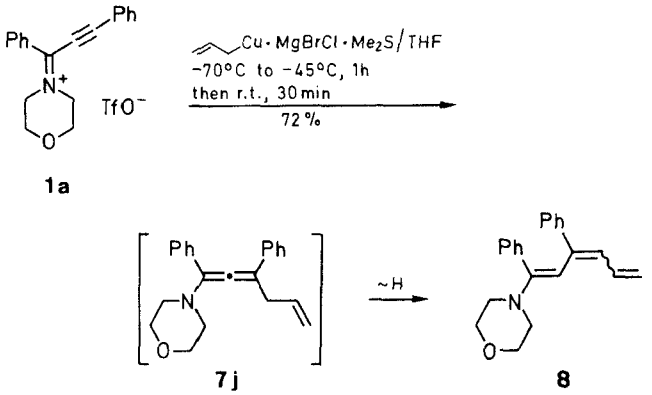
In contrast to unsubstituted dialkylaminoallenes (see introduction), morpholinoallenes **7** (except for **7f**) show no tendency to oligomerize or polymerize. They are, however, sensitive to hydrolysis of their enamine function, and can therefore not be isolated or purified by column chromatography on silica gel. Their isolation is usually achieved by repeated extraction of the reaction mixture with pentane. Whereas the solid products so obtained can be purified by recrystallization, attempts to purify the oily allenes **7b, d, f** by distillation results in thermal isomerization (**7b, d**; see below for **7b**) or polymerizaton (for **7f**); however, the latter allenes are already sufficiently pure according to their spectra and elemental analyses.

In the IR spectrum of **7a–f**, the C=C=C asymmetric stretching vibration appears as a broad, weak or medium-strong absorption at ν = 1935–1890 cm^{-1} (Table 2). In most cases, a distinct, less intense band is observed at higher wavenumbers (ca. 30–55 cm^{-1}), as well as a shoulder at lower wavenumbers. As expected,[21] the



6, 7	R	6, 7	R	6, 7	R
a	Bu	d	$CH=CH_2$	g	$SiPh_2(t\text{-}Bu)$
b	*s*-Bu	e	Ph	h	$SiPh_3$
c	*t*-Bu	f	C≡CPh	i	$SnPh_3$

Scheme 2



Scheme 3

asymmetric stretching vibration of the allenes bearing π substituents, **7d–f**, is shifted to lower wavenumbers. In the ^{13}C-NMR spectra (Table 2), the central allenic carbon atom appears at $\delta = 195.9–207.1$. Since the substituents are such that their influence on the chemical shifts of this carbon atom is small (and in part of opposite sign),[7] the δ values found are not much different from that of dimethylaminoallene ($\delta = 204.2$[7]).

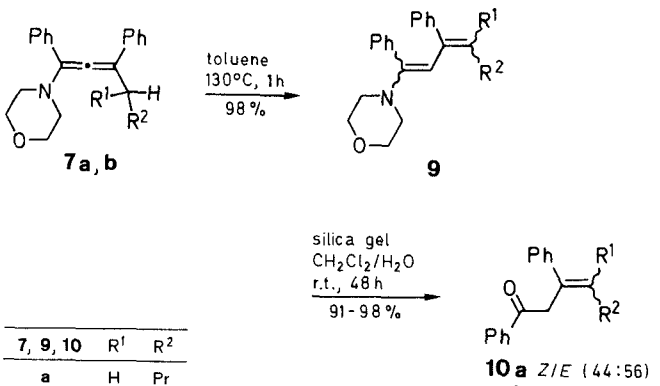
Since the allene moiety of **7a–d,f** is chiral, the NCH_2 protons of the morpholine ring become diastereotopic. Provided that the morpholine ring is freely rotating and inverting, the ^{1}H-NMR signal of NCH_2 is expected to have an AB pattern in which each line is split into a triplet by coupling with the OCH_2 protons (which are too far away from the chiral center to be magnetically inequivalent). This pattern is observed nicely in the spectrum of **7c**.

In order to transfer an allyl group to propyne iminium ion **1a**, we decided to utilize allylcopper rather than an allylcuprate. Although alkylcopper reagents in general are rather unreactive in those coupling reactions usually carried out with "ate" complexes,[11] allylcopper has been used repeatedly with good success (e.g. conjugate addition to propargyl esters,[22] addition to imines[23]). Furthermore, allylcopper reagents in the presence of chlorotrimethylsilane have only recently been found to add to α,β-unsaturated ketones cleanly and consistently in the 1,4-mode,[24] in contrast to higher-order diallyl(cyano)cuprates and simple diallylcuprates.

Addition of salt **1a** to a suspension of allylcopper (prepared from equimolar amounts of allylmagnesium chloride and copper(I) bromide–dimethyl sulfide complex at -45 °C) in tetrahydrofuran produced, after work-up, 1-morpholino-1,3,5-hexatriene **8**. According to ^{1}H- and ^{13}C-NMR spectra, only two isomers are present; based on the difference of δ values for 4-H, 5-H, and 2-H ($\Delta\delta$ = 0.22, 0.38, and 0.07 ppm, respectively) it can be concluded, that the 3,4-diastereomers are present (3*Z*/3*E*, 3:1). In the ^{13}C-NMR spectrum, an upfield shift for the olefinic C-2 signal is observed, as expected (γ-effect) for the 3*E*-isomer ($\Delta\delta = -5.5$ ppm).

Obviously, 1,3,5-hexatriene **8** is formed from 1-morpholino-1,2,5-hexatriene **7j** by a spontaneous prototropic shift. The proton-activating influence of the vinyl group is certainly responsible for the reduced stability of **7j** as compared to the other allenes bearing R^1R^2CH substituents at C-3, **7a** and **7b**. However, the latter allenes are isomerized as well under thermal impact, and 1-morpholino-1,3-butadienes **9a,b** are obtained. According to NMR spectra, at least three of the four possible diastereomers are formed for **9a** (isomer ratio 47:42:11), whereas only two isomers are seen for **9b** (67:33).

Mild hydrolysis converts the dienamines into β,γ-unsaturated ketones **10**. Since virtually the same diastereomer ratios are found (Scheme 4) in **10a,b** as in **9a** (two major isomers) or **9b**, respectively, it may be concluded that hydrolysis does not alter the configuration at the C-3–C-4 double bond of dienamines **9** and that only one (or mainly one, for **9a**) C-1–C-2 diastereomer is present. The same conclusion has been reached for hexatriene **8**, as discussed above. The structural assignment of the two isomers of **10a** is based on NMR data, such as NOE experiments (irradiation at the resonance of =CH) and the observation of a significant upfield shift of δ(CO–$\underline{C}H_2$) in (*E*)-**(10a)** (γ-effect). For **10b**, it was assumed that the proton resonance of the olefinic β-substituents is shifted upfield when they are *cis* to the phenyl ring. This was also the case for δ(=CH) in (*E*)-**10a**; it implies that the phenyl ring is tilted against the olefinic plane. The effect of a shift reagent [Eu(dpm)$_3$] on the NMR spectrum of the mixture of isomers confirmed the configurational assignment.

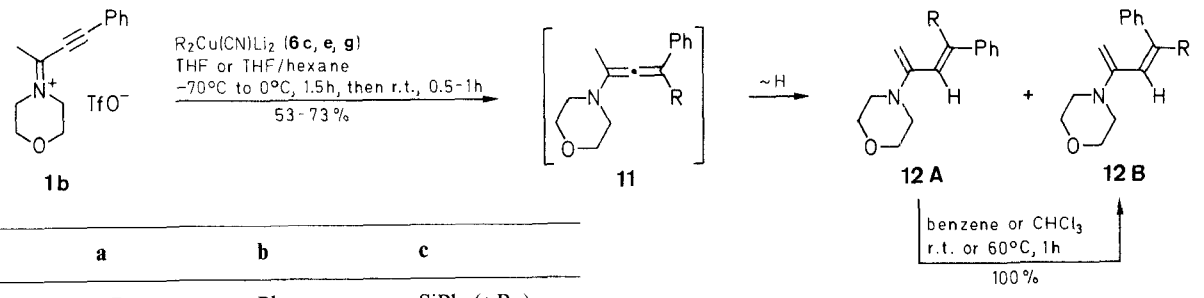


7, 9, 10	R^1	R^2
a	H	Pr
b	Me	Et

Scheme 4

The higher-order cyanocuprates **6c,e,g** also undergo conjugate addition to the 1-methyl-substituted 4-(2-propynylidene)morpholinium salt **1b** (Scheme **5**). However, the expected morpholinoallenes **11** isomerize under the reaction conditions by a prototropic 1,3-shift, and the 2-morpholino-1,3-butadienes **12a–c** are isolated (Table 3). [A minor byproduct, which was detected in the crude products obtained immediately after workup (^{1}H-NMR: δ (Me) = 1.96) but had disappeared a few hours later, may be the allene **11c**]. For **12a** and **12c**, diastereomers are possible; immediately after workup, isomer **A** is the major (for **12a**) or exclusive (for **12c**) diastereomer found.

Both **12aA** and **12cA** are transformed quantitatively to their respective isomers **12aB** and **12cB** even at room temperature (neat or in solution, see experimental part). For steric reasons, the latter isomers are expected to be more stable. Thus, the prototropic step **11** → **12A** yields mainly the kinetically favored butadiene which is transformed subsequently into the thermodynamically favored diasteromer **12B**. Since the isomerization **11** → **12** is likely to be a base-catalyzed process[9] in which a second allene molecule acts as the base, a proton must be delivered at the central allenic carbon in a bimolecular reaction on the way to **12**. Clearly, approach of the conjugate acid of **11** is less hindered from the side of the phenyl ring which is less bulky than *tert*-butyl or *tert*-butyldiphenylsilyl, and the butadiene isomer **12A** is formed. The ease of the *cis* → *trans* isomerization (**12A** → **12B**) is quite surprising. It is assumed that it occurs by a sequence of two conrotatory electrocyclcic reactions (butadiene → cyclobutene → butadiene); an acid-catalyzed process is excluded based on the observation, that **12aA** isomerizes at the same rate in benzene or chloroform solution. Thermal electrocyclizations of butadienes occur for highly substituted derivatives, and an equilibrium between a substituted butadiene and a cyclobutene maintained at room temperature is even more rare.[25,26] Several monocylic 1-dialkylaminocyclobutenes have been reported to be stable at room temperature and above,[27,28,30] whereas in other cases, electrocyclic ring-opening has been observed at ca. 50–100 °C.[29,30] 2-Morpholino-1,3-butadienes **12A,B** are likely to exist in a configuration close to *s-cis*, since a



11, 12	a	b	c
R	*t*-Bu	Ph	$SiPh_2(t\text{-Bu})$

Scheme **5**

Table 3. 2-Morpholino-1,3-butadienes **12a–c** Prepared

Product	Ratio **A/B** after work-up (after equilibration)	Yield (%)	IR[a] ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[b], δ Isomer **A**	Isomer **B**	^{13}C-NMR ($CDCl_3$/TMS)[c] δ
12a	79 : 21 (< 3 : 97)	73[d]	1635 (sh), 1575, 1445, 1355, 1235, 1110, 690	1.19 (s, *t*-Bu), 2.97 (NCH_2), 3.71 (OCH_2), 3.98, 3.99 (2s, $=CH_2$), 5.68 (pseudo-t, =CH) 6.98–7.23 (m, Ph)	1.12 (s, *t*-Bu), 2.71 (NCH_2), 3.57 (OCH_2), 3.68, 3.78 (2s, $=CH_2$), 6.00 (d, J = 0.8, =CH)	Isomer **A**/Isomer **B**: 31.1/29.6 [$C(\underline{C}H_3)_3$], 36.5/36.5 [$\underline{C}(CH_3)_3$], 48.0/48.7 (NCH_2), 66.62, 66.69 (OCH_2), 86.8/91.2 (CH_2=), 122.6 (d, CH=), 125.8–129.5 (C_{arom}), 145.5/140.0 (i-C_{arom}), 152.1–154.1 (=$\underline{C}$–Ph, =$\underline{C}$–N)
12b		53	1640, 1585, 1550, 1430, 1350, 1245, 1105, 690	2.86 (NCH_2), 3.43 (OCH_2), 4.10, 4.12 (2s, CH_2=), 6.43 (s, CH=), 7.24–7.46 (m, Ph)		48.9 (NCH_2), 66.5 (OCH_2), 92.5 (CH_2=), 126.2–130.3 (CH=, C_{arom}), 140.3, 143.5, 144.5 (=$\underline{C}Ph_2$, i-C_{arom}), 152.5 (N–C=)
12c	> 97 : 3 (< 3 : 97)	59[d]	1655, 1590, 1420, 1118, 1099	0.76 (s, *t*-Bu), 2.53 (NCH_2), 3.20 (s, 1H, $=CH_2$), 3.57 (OCH_2), 3.86 (s, 1H, $=CH_2$), 6.83 (s, 1H, CH=)	0.95 (s, *t*-Bu), 2.73 (NCH_2), 3.40 (OCH_2), 3.90, 3.99 (2s, CH_2=), 6.52 (s, CH=), 6.93–7.60 (m, Ph)	Isomer **B**: 19.0 [$\underline{C}(CH_3)_3$], 28.6 [$C(\underline{C}H_3)_3$], 48.8 (NCH_2), 66.4 (OCH_2), 92.7 (CH_2=), 125.7 (d), 127.5–129.2, 135.0 (s), 136.5 (d), 142.5 (s), 142.7 (d), 143.1 (s), 152.2 (N–C=)

[a] Values are given for **12aB** (film), **12b** (KBr pellet), and **12cB** (film).
[b] 400 MHz spectra. The signals of NCH_2 and OCH_2 are pseudo-triplets in all cases.
[c] 100.6 MHz spectra.
[d] Yield after complete isomerization **12A** → **12B**.

strong steric interaction between the morpholine ring and a substituent at C-4 should disfavor the *s-trans* configuration.[31] Thus, the termini of the 1,3-diene unit are already in a geometrical position suitable for electrocyclic ring closure, a fact which explains the low activation energy for the isomerization process **12A** → **12B**.

The *E* or *Z* configurations of compounds **12a** and **12c** were deduced from ^{1}H-NMR data (Table 3). In all cases, the phenyl ring at C-4 of the butadiene unit must be strongly tilted against the plane containing the C-3–C-4 double bond because of the bulky group R. Thus, 3-H in **12aA** is expected to be shielded with respect to 3-H in **12aB**; this is indeed observed ($\delta = -0.32$). Conversely, since the *s-cis* conformation shown in Scheme **5** is assumed for both isomers and on steric grounds (see above), the olefinic protons at C-1 appear at higher field in **12aB**, where they are in the shielding cone of the phenyl ring at C-1. For the pair **12cA/12cB**, the olefinic proton at C-3 is shielded more when it is *cis* to the *tert*-butyldiphenylsilyl)group **(12cB)** rather than to the phenyl ring. This has been proven on an alkene closely related to **12c**, where the constitution of one diastereomer could be established by X-ray analysis.[32]

In conclusion, we have shown that the reaction of 4-(2-propynylidene)morpholinium triflates with organocopper reagents is a versatile route to highly substituted and functionalized morpholinoallenes. Allenes bearing a methyl group at C-1 cannot be isolated, since they rapidly isomerize to give 2-morpholino-1,3-butadienes. The stability of morpholinoallenes bearing a R^1R^2CH substituent at C-3 towards prototropic isomerization is more balanced; however, quantitative rearrangement to 1-morpholino-1,3-butadienes is only a matter of temperature.

We consider the synthesis of **8, 9**, and **12** as a valuable addition to already existing strategies producing acyclic 1-dienamines [e.g. addition of *sec*-amines to α,β-unsaturated aldehydes[33] or ketones[34] (in the latter case, 2-dienamines may be formed instead), thermal reaction of propargyl alcohols with carboxamide acetals[35]] and 2-dienamines (e.g. mercury(II)-catalyzed addition of *sec*-amines to 3-buten-1-ynes[36]). Because of the incorporated enamine function, all three classes of title compounds are of interest for further synthetic transformations, especially addition of electrophiles and cycloaddition reactions (for reactions of 1- and 2-dienamines, see Ref.[34]; for recent cycloaddition reactions of 2-dienamines, see Ref.[37]).

All reactions (except for the hydrolyses) were carried out in rigourously dried glassware under an Ar atmosphere. THF and Et_2O were dried (KOH), distilled over $LiAlH_4$, and stored under Ar. Petroleum ether (distilled at 40–60 °C) and toluene were refluxed with Na, distilled, and stored over molecular sieves (4 Å) under an Ar atmosphere. Melting points were determined in a copper block and are not calibrated. ^{1}H-NMR spectra: Varian EM 390 (90 MHz) and Bruker AMX 400 (400 MHz), TMS as internal standard. ^{13}C-NMR spectra: Bruker WP 200 (50.3 MHz) and Bruker AMX 400 (100.6 MHz), TMS as internal standard. IR spectra: Perkin-Elmer Infrared Spectrophotometer 397, Beckmann IR 20A. Microanalyses: Perkin-Elmer EA 240 and EA 2400.

Synthesis of Solutions of Organocuprates 6b–f:[38]

Lithium Di-sec-butylcuprate(I) **(6b)**: Two equivalents of a solution of *s*-BuLi in cyclohexane/hexane (98:8, v/v) (1.3 M, 7.6 mL, 9.9 mmol) are added dropwise at −70 °C to a magnetically stirred suspension of CuBr · Me_2S (1 equiv, 1.01 g, 4.9 mmol) in THF (25 mL). The mixture is brought to −45 °C, stirred for 30 min, and recooled to −70 °C for further use.

Lithium Di-tert-butyl(cyano)cuprate(I) **(6c)**:[3] A solution of *t*-BuLi (2 equiv) in hexane (1.5 M, 4.9 mL, 7.4 mmol) is added at −70 °C to a magnetically stirred suspension of CuCN (0.33 g, 3.7 mmol) in THF (30 mL). The yellow mixture is brought to 0 °C within 30 min. After 5 min at 0 °C, a colorless solution has been formed which is cooled to −70 °C for further use.

Magnesium Bromide (Divinyl)cuprate(I) **(6d)**: A solution of (CH_2=CH)MgBr (2 equiv) in THF (1.0 M solution, 11.5 mL, 11.5 mmol) is added dropwise at −70 °C to a magnetically stirred suspension of CuCN (1 equiv, 0.52 g, 5.80 mmol) in Et_2O (10 mL). The mixture is brought to 0 °C within 15 min, stirred for 3 min, and the brown suspension is cooled to −70 °C for further use.

Lithium Cyano(diphenyl)cuprate(I) **(6e)**: A solution of PhLi in cyclohexane/Et_2O (70:30, v/v) (2 equiv, 2 M, 3.1 mL, 6.1 mmol) is added at 0 °C to a magnetically stirred solution of CuCN (0.29 g, 3.2 mmol) in THF (25 mL). After 30 min at 0 °C, a faintly yellow homogeneous solution is obtained, which is cooled to −70 °C for further use.

Lithium Bis(phenylethynyl)cyanocuprate(I) **(6f)**: To a solution of phenylacetylene (0.82 g, 8.0 mmol) in THF (20 mL), BuLi (1.6 M solution in hexane, 5. mL, 8.0 mmol) is added. After 30 min, the solution is cooled to 0 °C, CuCN (3.70 g, 4.10 mmol) is added, and after stirring for 30 min, the solution is cooled to −70 °C for further use.

4-(1,3-Diphenyl-1,2-heptadienyl)morpholine (7a); Typical Procedure:
A solution of BuLi in hexane (1.6 M, 5.88 mL, 9.40 mmol) is added dropwise at −70 °C to a magnetically stirred suspension of CuCN (1.01 g, 4.93 mmol) in THF (25 mL). The mixture is brought to −20 °C within 30 min, stirred for 10 min, and the dark-brown solution is recooled to −70 °C. A suspension of salt **1a**[1] (2.00 g, 4.70 mmol) in THF (25 mL) is gradually added. After additional stirring at −70 °C for 30 min, the mixture is brought to −25 °C, stirred for 1 h, and warmed to r.t. within 30 min. The solvent is removed at 0.003 mbar, and the residue is extracted with petroleum ether (3 × 65 mL). The combined extracts yield, after evaporation of the solvent, a yellow powder; yield: 1.00 g (64%); mp 61 °C.

$C_{23}H_{27}NO$	calc.	C 82.84	H 8.16	N 4.20
(333.5)	found	82.3	8.1	4.0

Spectral data: Table 2.

Morpholinoallenes **7b–i** are prepared analogously (Table 1). The synthesis of **7c** by this procedure has already been described.[3]

4-[(3*Z* and 3*E*)-1,3-Diphenyl-1,3,5-hexatrienyl]morpholine (8):
A round-bottom flask is placed in an ice bath and charged with Mg turnings (3.85 g, 15.4 mmol), an I_2 crystal, and THF (30 mL). Allyl chloride (0.79 g, 10.4 mmol) is added dropwise. When the exothermic reaction is over, the mixture is filtered into a three-necked round-bottom flask cooled to −70 °C, CuBr · Me_2S (2.13 g, 10.4 mmol) is added in several portions, and the resulting yellow-brown suspension is then stirred at −45 °C for 30 min. After recooling to −70 °C, a suspension of salt **1a**[1] (2.00 g, 4.70 mmol) in THF (25 mL) is added. The mixture is brought to −45 °C, stirred for 1 h, then allowed to come to r.t. within 30 min. The solvent is evaporated at 0.003 mbar, and the residue is extracted with petroleum ether (3 × 65 mL). After removing the solvent from the combined extracts, a viscous orange-colored oil is left, which cannot be purified further by column chromatography (hydrolysis) or distillation (polymerization); yield: 1.06 g (72%); diastereomer ratio: 3*Z*/3*E* = 3:1. A correct microanalysis was not obtained.
IR (film): ν = 1580, 1438, 1257, 1215, 1118, 695 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 2.85/2.93 (NCH_2), 3.69/3.76 (OCH_2), 4.77/4.96 (dd, J = 10.0, 2.0 Hz, 6'-H, *cis* to 5'-H), 4.90/5.08 (dd, J = 16.4, 2.0 Hz, 6'-H, *trans* to 5'-H), 5.38/5.45 (s, 2'-H), 5.90/6.13 (d, J = 11.2 Hz, 4'-H), 6.27/6.65 (ddd, J = 16.4, 11.2 Hz, 5'-H). (The first of the two values separated by a slah refers to the (3'*Z*)-isomer)

^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 49.5/50.0 (NCH_2), 66.9 (OCH_2), 108.6/103.1 (C-2'), 115.0/116.2 (C-6'), 126.3–131.7 (C_{arom}, 1 C_{olefin}), 134.8/134.9 (d, C-4' or C-5'), 137.0/139.5 (s), 140.4/142.4 (s), 152.2/154.0 (C-1').

4-(1,3-Diphenyl-1,3-heptadienyl)morpholine (9a):
A solution of **7a** (0.50 g, 1.50 mmol) in toluene (25 mL) is heated for 1 h at 130 °C in a tightly closed thick-walled Schlenk tube. The solvent is removed at 25 °C/0.003 mbar, and the residual oil is subjected to bulb-to-bulb distillation at 230 °C/0.02 mbar; yellow oil, mixture of at least three diastereomers (isomer ratio determined by ^{1}H-NMR: 47:42:11); yield: 0.49 g (98 %).

$C_{23}H_{27}NO$	calc.	C 82.84	H 8.16	N 4.20
(333.5)	found	82.7	8.0	3.8

IR (film): ν = 1603, 1448, 1120, 695 cm^{-1}.

^{1}H-NMR (benzene-d_6, 400 MHz): δ = 0.82/0.62/0.93–1.02 (t, CH_3), 1.15/0.97/1.49 (mc, CH_2CH_3), 1.80–1.86/2.27/1.80–1.83 (mc, =C–CH_2), 2.78/2.87 (pseudo-t, NCH_2), 3.73/3.66/3.43 (pseudo-t, OCH_2), 5.50/5.17/5.92 (t, ^3J = 7.4 Hz, =CH–C_3H_7), 5.31/5.26 (s, N–C=CH), 7.06–7.56 (m, Ph). (Values are given for each isomer in the order of decreasing percentage; some signals of the third isomer are covered by one of the other two isomers. The following ^{13}C-NMR data are presented in the same way.)

^{13}C-NMR (benzene-d_6, 100.6 MHz): δ = 13.0/12.7 (CH_3), 21.2/21.8/21.6 (CH_3–CH_2), 30.8/30.4/31.3 (=CH–CH_2), 49.2/48.6/48.1 (NCH_2), 66.2/66.0/66.3 (OCH_2), 103.1/108.2/105.0 (N–C=CH), 151.7/149.6/150.0 (N–C=).

4-[(3*Z*- and 3*E*)-4-Methyl-1,3-diphenyl-1,3-hexadienyl]morpholine (9b):
From **7b** (0.50 g, 1.50 mmol) as described for **9a**; yellow oil, 67:33 mixture of diastereomers; yield: 0.49 g (98 %); bp 230 °C/0.02 mbar.

$C_{23}H_{27}NO$	calc.	C 82.84	H 8.16	N 4.20
(333.5)	found	82.7	8.1	3.8

IR (film): ν = 1600, 1445, 1118, 695 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 0.77/0.98 (t, CH_2–CH_3), 1.53 (s, =C–CH_3), 1.88/2.15 (=C–CH_2), 2.81 (pseudo-t, NCH_2), 3.70 (pseudo-t, OCH_2), 5.37/5.52 (s, N–C=CH), 6.84–7.26 (m, Ph). (The first of the two values separated by a slash refers to the major isomer).

^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 12.9/11.9 (CH_2–CH_3), 19.0/18.8 (=C–CH_3), 28.0/28.2 (CH_2–CH_3), 50.0/50.1 (NCH_2), 67.0 ($OCHC_2$), 108.3/107.6 (N–C=CH), 132.1, 124.8–129.7, 132.1, 134.6, 138.2, 143.4 (C_{arom}, C=C(Me)Et), 151.4 (N–C=). (The first of the two values separated by a slash refers to the major isomer).

(*Z*)- and (*E*)-1,3-Diphenyl-3-hepten-1-one (10a):
To a solution of **9a** (0.49 g, 1.47 mmol) in non-dried CH_2Cl_2 is added silica gel (5.0 g). After stirring for 48 h, the mixture is filtered, the solvent is removed from the filtrate, and the residue is subjected to bulb-to-bulb distillation at 153 °C/0.02 mbar to give a colorless oil (mixture of diastreomers; *Z*/*E*, 44:56) yield: 0.36 g (91 %).

$C_{19}H_{20}O$	calc.	C 85.73	H 7.57	
(266.2)	found	85.8	7.8	

IR (film): ν = 1680 (s, C=O), 1203 (s), 688 cm^{-1} (s).

^{1}H-NMR ($CDCl_3$, 90 MHz): *E* -isomer: δ = 0.82 (s, Me), 3.93 (br s, CO–CH_2), 5.53 (tt, ^3J = 7.5 Hz, $|^4J|$ = 1.5 Hz); *Z*-isomer: δ = 0.94 (s, Me), 4.13 (s, CO–CH_2), 5.93 (t, ^3J = 7.5 Hz, =CH); common signals: δ = 1.14–1.66 (m, CH_3-CH_2), 1.83–2.30 (m, =C–CH_2), 7.00–8.20 (m, Ph).

^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 13.9/13.6 (Me), 22.5/22.8 (CH_2–CH_3), 31.2/31.1 (=CH–CH_2), 40.6/48.7 (CO–CH_2); 122.2, 123.5, 125.9–132.9, 134.2, 136.8, 140.4, 142.8 (C=C, C_{arom}). (Where two values are given, the first one refers to the more intense signal, which is attributed to (*E*)-**10a**).

(*Z*)- and (*E*)-4-Methyl-1,3-diphenyl-3-hexen-1-one (10b):
From **9b** (0.49 g, 1.47 mmol) as described above for **10a**; colorless oil, mixture of diastereomers (*Z*/*E*, 66:34); yield: 93 %; bp 173 °C/0.05 mbar.

$C_{19}H_{20}O$	calc.	C 85.73	H 7.57	
(266.2)	found	85.9	7.5	

IR (film): ν = 1680 (s, C=O), 1205 (s), 700 cm^{-1} (s).

^{1}H-NMR ($CDCl_3$, 400 MHz): (*Z*)-**10b**: δ = 0.96 (t, CH_2–CH_3), 1.79 (s, =C–CH_3), 1.96 (q, CH_2–CH_3), 4.03 (s, CO–CH_2). (*E*)-**10b**: δ = 1.06 (t, CH_2–CH_3), 1.63 (s, =C–CH_3), 2.16 (q, CH_2–CH_3), 4.06 (s, CO–CH_2).

^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 13.1/12.5 (CH_2–CH_3), 17.7/19.2 (=C–CH_3), 28.4/27.6 (CH_2–CH_3), 45.0/44.2 (CO–CH_2), 126.–132.7 (C=C, C_{arom}), 137.8/137.2 (CO–C_{arom}), 143.6/143.8 (=C–C_{arom}), 197.4/197.7 (C=O). (The first of the two values separated by a slash refers to the *Z*-isomer).

5,5-Dimethyl-2-morpholino-4-phenyl-1,3-hexadiene (12a):
To a magnetically stirred solution of **6c**, prepared as described above from *t*-BuLi [24.9 mL (42.4 mmol) of a 1.7 M solution in hexane] and CuCN (2.00 g, 22.2 mmol) in THF (25 mL), is added gradually at – 70 °C a suspension of salt **1b**[1] (7.69 g, 21.2 mmol) in THF (25 mL). The dark-red suspension is brought to – 10 °C within 30 min, stirred for 1 h, brought to r.t. (30 min) and stirred for 30 min. The solvent is removed at 0.003 mbar, and the residue is extracted with petroleum ether (3 × 65 mL). After removal of the solvent from the combined extracts at 0.003 mbar, a yellow-orange oil is left which consists of **12aA** and **12aB** (73:27). In solution (benzene or $CHCl_3$, 24 h, r.t. or 60 °C, 1 h), this mixture is quantitatively transformed into the (3*Z*)-isomer **12aB**; by bulb-to-bulb distillation at 170 °C/0.03 mbar, isomerization is incomplete. Yield of **12aB**: 4.20 g (73 %).

$C_{18}H_{25}NO$	calc.	C 79.66	H 9.28	N 5.16
(271.4)	found	79.8	9.3	5.1

Spectral data: Table 3

2-Morpholino-4,4-diphenyl-1,3-butadiene (12b):
To a magnetically stirred solution of **6e**, prepared as described above from PhLi (1.6 M solution in hexane, 6.05 mL, 9.7 mmol) and CuCN (0.45 g, 5.0 mmol) in THF (25 mL), is added gradually at – 70 °C a suspension of salt **1b**[1] (1.76 g, 4.8 mmol) in THF (25 mL). The mixture is brought to 0 °C (45 min), stirred for 1 h, brought to r.t. and stirred for 30 min. The solvent is evaporated at 0.003 mbar, and the residue is extracted with petroleum ether/Et_2O (2.5:1 v/v, 3 × 65 mL). The combined extracts are concentrated at 22 °C/0.003 mbar to a volume of ca 10 mL. After 12 h at – 78 °C, the deposited yellow powder is quickly filtered off in a cooled funnel; yield: 0.75 g (53 %); mp 70 °C.

$C_{20}H_{21}NO$	calc.	C 82.44	H 7.26	N 4.81
(291.4)	found	82.2	7.3	5.0

Spectral data: Table 3

4-(*tert*-Butyldiphenylsilyl)-2-morpholino-4-phenyl-1,3-butadiene (12c):
To a magnetically stirred solution of **6g**, prepared[3] from *t*$BuPh_2SiCl$ (5.68 g, 20.6 mmol), Li (0.83 g, 120.0 mmol), and CuCN (0.93 g, 10.3 mmol), in THF (25 mL), is added gradually at – 70 °C a suspension of salt **1b**[1] (3.00 g, 8.3 mmol) in THF (25 mL). The mixture is warmed to – 10 °C within 30 min, stirred for 1 h, brought to r.t., and stirred for 30 min. The solvent is evaporated at 22 °C/0.003 mbar, and the residue is extracted with petroleum ether (3 × 65 mL). The solid residue left after evaporating the solvent (2.01 g) consists mostly of (3*Z*)-**12c** (= **12cA**) and probably of the allene **11c** (^{1}H-NMR: δ(Me) = 1.96). After stirring a solution of the mixture in $CHCl_3$ (15 mL) for 48 h at 20 °C, or by bulb-to-bulb distillation at 225 °C/0.005 mbar, pure (3*E*)-**12c** (= **12cB**) is obtained as a viscous yellow oil; yield: 1.88 g (59 %).

$C_{30}H_{35}NOSi$	calc.	C 78.93	H 7.73	N 3.07
(456.5)	found	78.2	7.5	2.1

Spectral data: Table 3

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