Selective Mono- and Polymethylene Homologations of Copper Reagents Using (Iodomethyl)zinc Iodide

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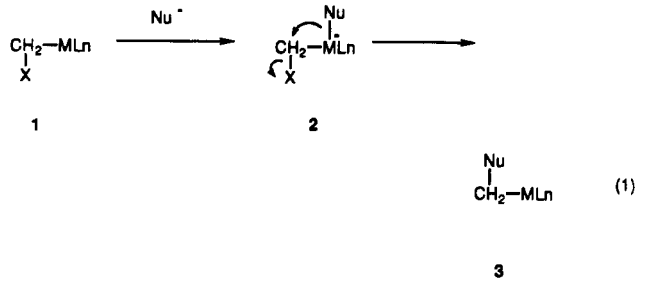
A wide range of unsaturated aryl-, alkenyl-, alkynylcopper compounds can be selectively homologated by a methylene unit using (iodomethyl)zinc iodide or bis(iodomethyl)zinc. These reactions allow the generation of mixed allylic zinc–copper compounds which can be efficiently trapped with carbonyl compounds. An application to a general preparation of functionalized α-methylene-γ-butyrolactones is described. The homologation of alkynylcoppers with (iodomethyl)zinc iodide allows a one-pot preparation of propargylic copper reagents which in the presence of a carbonyl compound provide various homopropargylic alcohols in excellent yields. In the absence of an electrophile, a clean quadruple methylene homologation of alkynylcoppers occurs to furnish dienic copper reagents. The homologation of other types of copper reagents is also possible, and carbanions at the α-position to amines as well as homoenolates of aldehydes or ketones can also be prepared by this method.

Introduction

Halogenomethyl organometallics of the type XCH_2ML_n (1) where M is Li or Mg are good nucleophiles and as such have found numerous applications in organic synthesis.[2] The corresponding Al,[3] Zn[4,5] Hg,[6,7] or Cu[8] carbenoids are far less nucleophilic. They have been used as carbene precursors, and cyclopropanation procedures using these reagents have been described.[9] The presence of a halide and a metal at the same carbon atom allows a unique reaction pathway. The reaction of the halogenomethyl organometallic 1 with a nucleophile Nu^- affords first an ate complex 2 which can undergo a 1,2 migration affording a new organometallic 3 (eq 1).



To be synthetically useful, the reactivity of the compound 3 has to be substantially lower than Nu^- in order to avoid further reaction with 1 (polymethylene insertions). Several examples of selective insertions of this type have been reported.[10] Herein we describe our results concerning the selective methylene homologation of *copper derivatives* with (iodomethyl)zinc iodide (ICH_2)ZnI (4)[4] or bis(iodomethyl)zinc $(ICH_2)_2Zn$ (5).[5] These reactions allow

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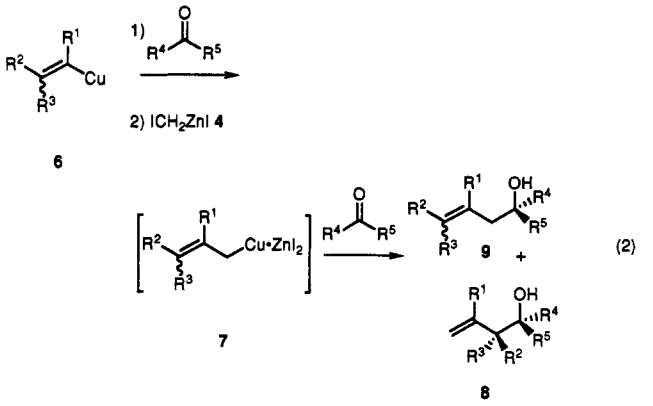
a unique conversion of alkenyl- or acetylenic copper species to allylic and propargylic zinc–copper reagents,[11-15] respectively. The scope and limitations of these and related reactions are described below.

Results and Discussion

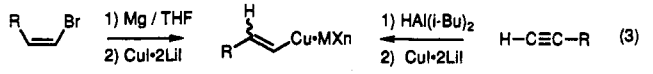
I. Methylene Homologation of Unsaturated Copper Reagents. A. Homologation of Alkenylcoppers Allylic organometallic compounds are highly reactive intermediates and react with a variety of electrophiles with the formation of a new carbon–carbon bond. Their preparation by the oxidative addition of the metal M into an allylic halide is often complicated by side reactions such as Wurtz coupling.[16] New experimental procedures have been developed to overcome these problems,[17] and alternative preparations using transmetalations,[18] the homologation of alkenylboronic esters,[19] and the hydrometalations of dienes[20] have been reported.

We found that the homologation reaction of alkenyl compounds **6** with (iodomethyl)zinc iodide represents a unique method for the direct conversion of alkenyl copper derivatives into allylic zinc–copper compounds **7**. The reaction has to be performed in the presence of an electrophile, since the allylic species **7** would undergo a further reaction with (iodomethyl)zinc iodide leading to a doubly homologated product. However, in the presence of an electrophile such as an aldehyde or ketone, the intermediate **7** is efficiently trapped and homoallylic alcohols of type **8** and **9** are obtained in good yields (Table I and eq 2).

The vinylic copper reagents **6** have been generated in two ways; either by treatment of a THF solution of the corresponding alkenylmagnesium bromide[21] with the



THF-soluble copper salt CuI·2LiI at −50 to −25 °C, resulting in an orange suspension of **6**[22] (eq 3), or by transmetalation of an alkenylalane, obtained by hydroalumination,[23] with CuI·2LiI[24] (eq 3).



The aldehyde or ketone (0.6–0.7 equiv) is then added to these copper reagents at −50 °C, and no addition to the carbonyl group is observed due to the low reactivity of vinylic copper reagents.[22] A THF solution of (iodomethyl)-zinc iodide (**4**) prepared from diiodomethane and cut zinc foil (THF, 25 °C, 2–3 h; ca. 80% yield) is then added at −50 °C, and the reaction mixture is warmed to −20 °C leading to the insertion of a methylene unit. The resulting allylic organometallic **7** (eq 2) is, in strong contrast to the vinylic precursor, very reactive and adds to the carbonyl compound present in solution affording homoallylic alcohols in good to excellent yields (64–95%). Various substituents can be attached at the 1 position of the alkenyl copper, including functional groups such as an acetal (entry 7), an allylic silane[25] (entry 8), or a dialkylamino group[26] (entries 9–11) leading to a variety of polyfunctional homoallylic alcohols.[27] The addition of the allylic organometallics **7** to imines or to an activated ester such as a formate is also possible, and the treatment of the vinylic copper reagent **6a** with the imine **10** produces in the presence of an excess of (iodomethyl)zinc iodide **4** the cyclopropylethylamine **11** (in 76% yield) via an intermediate homoallylic amine. The complexation of **4** to the amino functionality greatly facilitates the cyclopropanation. The reaction of **6a** with ethyl formate in the presence of (iodomethyl)zinc iodide **4** (1.0 equiv) leads to a double addition to the ester function. The resulting secondary alcohol is esterified by the remaining ethyl formate furnishing the product **12** in 94% yield (eq 4).

The presence of a substituent (R^2 or $R^3 \neq H$) in position 2 of **6** affords after the methylene homologation an unsymmetrical allylic organometallic **7**. Like allylic zinc

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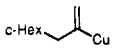
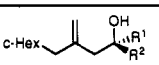
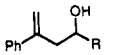
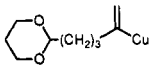
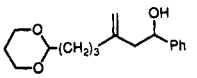
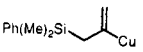
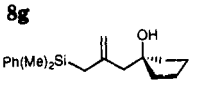
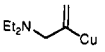
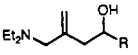
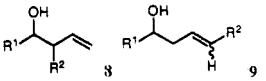
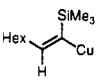
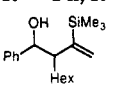
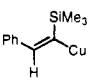
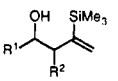
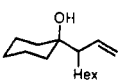
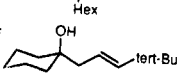
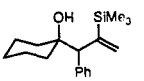
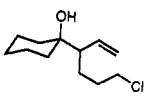
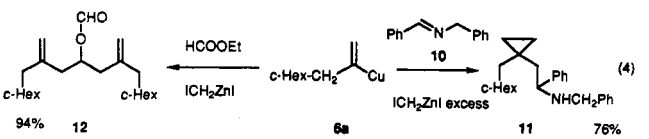
Table I. Methylene Homologation of Alkenylcoppers 6a–i to Allylic Copper Derivatives 7a–i and Their Trapping with an Aldehyde or Ketone Leading to Homoallylic Alcohols 8a–x and/or 9

entry	alkenylcopper 6	electrophile	product	yield[a] (%)
				
1	**6a**	PhCHO	**8a**: R^1 = Ph; R^2 = H	94
2	**6a**	PentCHO	**8b**: R^1 = Pent; R^2 = H	86
3	**6a**	cyclohexanone	**8c**: $R^1 = R^2 = -(CH_2)_5-$	91
4	**6a**	acetophenone	**8d**: R^1 = Ph; R^2 = CH_3	95
				
5	**6b**	PhCHO	**8e**: R = Ph	93
6	**6b**	Pent-CHO	**8f**: R = Pent	92
				
7	**6c**	PhCHO	**8g**	96
				
8	**6d**	cyclopentanone	**8h**	71
				
9	**6e**	PhCHO	**8i**: R = Ph	90
10	**6e**	PentCHO	**8j**: R = Pent	71
11	**6e**	$NC(CH_2)_2C(Et)_2CHO$	**8k**: $R = C(Et)_2(CH_2)_2CN$	75
			 8 9	
12	HexCH=CHCu **6f**	PhCHO	R^1 = Ph; R^2 = Hex: (**8l**:**9l** = 90:10)[b]	89
13	**6f**	PentCHO	R^1 = Pent; R^2 = Hex: (**8m**:**9m** = 94:6)[c]	79
14	PhCH=CHCu **6g**[e]	PHCHO	$R^1 = R^2$ = Ph (**8n**:**9n** > 98:2)[d]	73
15	t-BuCH=CHCu **6h**[e]	PHCHO	R^1 = Ph; R^2 = t-Bu: (**8o**:**9o** > 2:98)[f]	71
16	HexCH=CHCu **6f**[e]	c-HexCHO	R^1 = c-Hex; R^2 = Hex: (**8p**:**9p** = 93:7)[g]	76
17	$Cl(CH_2)_3CH$=CHCu **6g**	PhCHO	R^1 = Ph; R^2 = $(CH_2)_3Cl$: (**8q**:**9q** > 96:4)[h]	90
				
18	**6h**[e]	PhCHO	**8r** (dr > 98:2)	64
				
19	**6i**[e]	PhCHO	**8s**: R^1 = Ph; R^2 = Ph(dr > 98:2)	70
20	**6i**[e]	PentCHO	**8t**: R^1 = Pent; R^2 = Ph (dr = 79:21)	88
21	**6f**	cyclohexanone	**8u**: 	84
22	**6h**[e]	cyclohexanone	**8v**:[f] 	73
23	**6i**[e]	cyclohexanone	**8w**: 	82
24	**6g**	cyclohexanone	**8x**: 	90

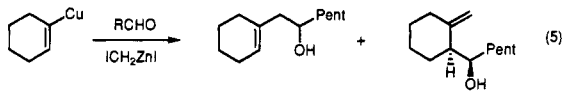
[a] All yields refer to the yields of isolated yields of products being over 98% pure by GC analysis and showing correct spectroscopic data (^1H, ^{13}C NMR, IR, and mass spectra). [b] **8p** was obtained as a 1:1 mixture of stereoisomers if **6f** is prepared from the corresponding Grignard reagent and as a 4:1 mixture of stereoisomers if **6f** is prepared from the aluminium derivative. [c] **8m** is obtained as a 1:1 mixture of diastereomers. [d] **8n** is obtained as a 2:1 mixture of diastereomers. [e] Prepared from the corresponding alkenylaluminium derivative. [f] 100% *E* isomer. [g] **8p** is obtained as a 86:14 mixture of diastereoisomers. [h] **8q** is obtained as a 60:40 mixture of diastereoisomers.



halides generated from zinc and an allylic bromide, the formation of the new carbon–carbon bond occurs preferentially on the more substituted end of the allylic system[16c–e] (entries 12–24) leading preferentially to products of type **8**; the ratio **8**:**9** typically being 9:1. However, if the substituent R^2 or R^3 is very bulky (R^2 = t-Bu), then the regioselectivity is inversed and the homoallylic alcohol **9** is the only product formed (entry 14). The alcohols **8** are usually formed as a mixture of diastereoisomers in variable ratios. The size of the aldehyde substituent R is certainly important, but the stereoselectivity also depends on the allylic organometallic geometry as shown in the following case: if the vinylic copper reagent **6f** (entry 12)

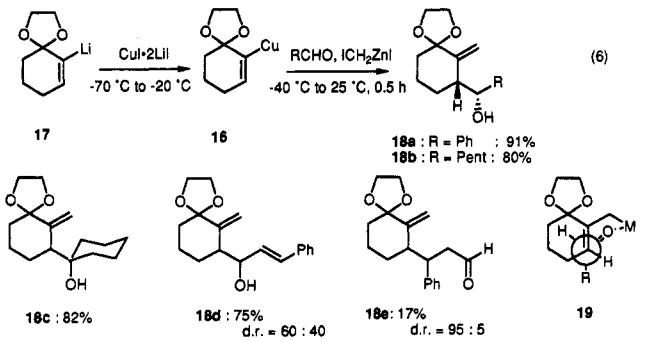
is prepared from the corresponding magnesium reagent (*E*:*Z* = ca. 15:85), a diastereoselectivity ratio (dr) of 1:1 is observed; however, if the copper reagent is prepared from the corresponding alkenyl alane (*E*:*Z* = ca. 98:2), then a 4:1 mixture of diastereoisomers is obtained.

The relatively rapid *E*/*Z* isomerization of the allylic zinc–copper reagents under our reaction conditions, leading to a thermodynamic isomer ratio, may be responsible for the variable and relatively low diastereoselectivity observed. In the case of 1-cyclohexenylcopper a mixture of the two possible regioisomers **14** and **15** is observed in a ratio which depends on the nature of the aldehyde (eq 5). Interest-



ingly, the regioisomer **15** is formed as only one diastereoisomer. The regioselectivity can be improved considerably by introducing a ketal functionality in position 6.

Thus, the functionalized alkenylcopper **16** prepared by transmetalation with CuI·2LiI of the readily available alkenyllithium **17**[28] reacted with an alipathic or aromatic aldehyde with complete regio- and diastereoselectivity affording the *lk* alcohol[29] **18a,b** in 80–91% yield (eq 6). An



X-ray structure of **18a** confirmed the relative stereochemistry of the alcohol **18**.[30] The trapping with a ketone such as cyclohexanone also proceeds well, providing the tertiary alcohol **18c** in 82% yield. Interestingly, with cinnamaldehyde the 1,2-adduct **18d** was the major product obtained (75%). It is accompanied by a small amount of the 1,4-adduct **18e** (17%). The high ratio between the 1,2- and 1,4-adducts (ca. 4:1) indicates the strong effect of the zinc cation on the reactivity of the allylic reagent. For example, no reaction was observed between the allylic organometallic **7a** and benzyl bromide or butyl iodide which is atypical for an allylic copper reagent.[18f-i] The reaction of **7a** with 3-methyl-2-cyclohexenone in the presence of Me_3SiCl provides only the 1,2-adduct. Also, addition of **7a** to benzonitrile could not be achieved, as would be expected for an allylic zinc reagent. In consequence, the allylic reagent generated under our reaction conditions should best be considered as being a mixed zinc–copper cluster displaying a reactivity which is different from both an allylic copper or zinc reagent. The relative stereochemistry of **18a,b** can be readily explained assuming a staggered transition state like **19** in which the sterically less demanding aldehyde hydrogen is below the cyclohexenyl ring. The methylene homologation can be applied to a one-pot preparation of highly functionalized α-methylene-γ-butyrolactones of type **20**.[14] Many members of this family display significant biological activity, and a number of different syntheses of this class of compounds have been reported.[31] The carbocupration[32] of acetylenic esters **21** with functionalized zinc–copper compounds FG-RCu(CN)ZnX[33,34] leads at low temperature to the syn-adducts **22** (THF, -50 °C, 3 h). After the addition of an aldehyde or a ketone (0.7 equiv), followed by a 2-fold excess of (iodomethyl)zinc iodide **4**, the expected homologation occurs leading to a highly functionalized allylic copper–zinc reagent **23**. This reactive intermediate adds regiospecifically and with good stereoselectivity to the carbonyl compound through a chair transition state **24** in which the largest group attached to the carbonyl group occupies an equatorial position. After workup, the cis-lactones **20** are obtained in 60–90% yield (cis:trans ratio = 1:1–100:0; Table II and Scheme I).

A variety of functionalized zinc–copper reagents FGR-Cu(CN)ZnX containing a triple bond, ester, nitrile, or chloride can be added to acetylenic esters[34] affording after homologation and addition to a carbonyl compound polyfunctional lactones **20**. The cis-selectivity depends on the nature of substituents and reaction conditions used for performing the carbocupration reaction leading to the intermediate alkenylcopper **22**. If the carbocupration occurs at low temperature (below -30 °C), the resulting syn-adduct **22** seems to be configurationally stable and furnishes after methylene homologation the cis-lactone

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(30) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

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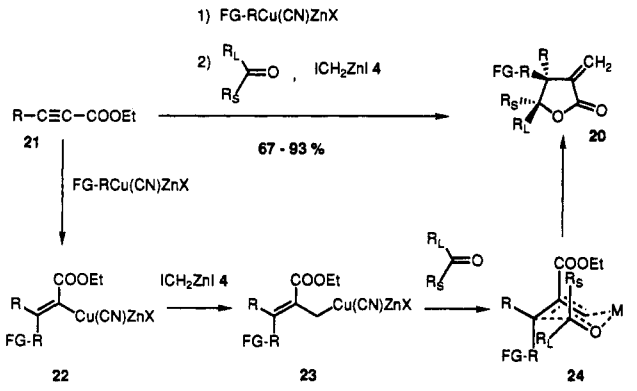
Table II. One-Pot Preparation of α-Methylene-γ-butyrolactones 20a–q from an Acetylenic Ester 21, FG-RCu(CN)ZnX, a Carbonyl Compound, and (Iodomethyl)zinc Iodide (4)

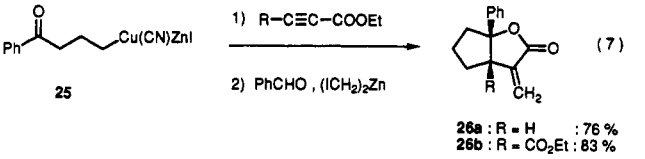
entry	R	FGR	R_L	R_S	lactone 20	cis:trans ratio[b]	yield[a] (%)
1	H	Bu	Ph	H	**20a**	85:15	79
2	H	Bu	c-Hex	H	**20b**	80:20	76
3	H	$PhCH_2$	Ph	H	**20c**	92:8	78
4	H	$NC(CH_2)_3$	Ph	H	**20d**	90:10	75
5	H	Bu-C≡$C(CH_2)_2$	Ph	H	**20e**	95:5	76
6	H	$EtO_2C(CH_2)_3$	Ph	H	**20f**	95:5[c]	85
7	H	$EtO_2C(CH_2)_3$	Pent	H	**20g**	50:50	70
8	H	$EtO_2C(CH_2)_3$	$-(CH_2)_5-$		**20h**		68
9	H	$EtO_2C(CH_2)_3$	Ph	CH_3	**20i**	90:10	69
10	H	$Cl(CH_2)_4$	Ph	CH_3	**20j**	100:0[d]	82
11	EtO_2C	$EtO_2C(CH_2)_3$	$Ph(CH_2)_2$	H	**20k**	85:15	96
12	EtO_2C	$EtO_2C(CH_2)_3$	Ph	H	**20l**	85:15	86
13	EtO_2C	$NC(CH_2)_3$	c-Hex	H	**20m**	95:5	93
14	Bu	Bu	Ph	H	**20n**		80
15	Bu	C-Hex	Ph	H	**20o**	75:25	60
16	c-Hex	Bu	Ph	H	**20o**	98:2[d]	67
17	Bu	Ph	Ph	H	**20p**	60:40	78
18	Ph	Bu	Ph	H	**20p**	98:2	85

[a] All yields refer to isolated yields of analytically pure products being over 98% pure by GC analysis. [b] GC ratio of the crude products. [c] Relative stereochemistry determined by ^1H NHR spectroscopy. [d] Relative stereochemistry determined by X-ray analysis.

Scheme I



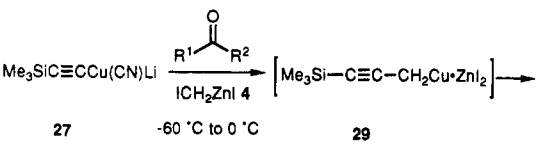
as the major diastereoisomer. This is usually the case if ethyl propiolate or diethyl acetylenedicarboxylate is used as the substrate for the carbocupration reaction. These reactive acetylenes undergo rapid addition of the copper–zinc reagent at low temperature (60 to −40 °C, ca. 2–4 h). However, even in these favorable cases, we observed that the addition of a 3-carbethoxypropyl group to ethyl propiolate leads, in the case of aliphatic aldehydes, to low cis/trans ratios of the lactone (entry 7 or Table II). If a relatively high temperature is required for the carbometalation step, then low stereoselectivities are observed. Thus, the addition of BuCu(CN)Li to ethyl 3-cyclohexylpropiolate gives stereospecifically the (*E*)-alkenyl copper **22o** (R = c-Hex, FGR = Bu) as confirmed by low-temperature iodolysis (−30 °C) leading only to (*E*)-ethyl 3-cyclohexyl-2-iodo-2-heptenoate. The methylene homologation of **22o** in the presence of benzaldehyde provides the allylic reagent **23o** and gives the lactone **20o** (cis:trans −98:2; entry 16 of Table II). However, if the alkenylcopper **22o** is warmed to −10 °C, a 75:25 mixture of (*E*)- and (*Z*)-alkenylcopper **22o** is obtained (as shown by iodolysis). After methylene homologation and reaction with benzaldehyde, the lactone **20o** is obtained as a cis/trans mixture of 75:25 (entry 15). Interestingly, the carbocupration of ethyl 2-heptynoate with c-HexCu(CN)ZnI·2LiCl, which is quite sluggish and occurs only above −10 °C, produces the alknenylcopper **22o** with the same *E*/*Z* ratio (75:25, (thermodynamic ratio)) and after addition of (iodomethyl)-zinc iodide and benzaldehyde, the butyrolactone **20o** is obtained as a 75:25 cis/trans mixture (entry 15). A similar behavior is observed in the case of the carbocupration of ethyl 2-heptynoate with PhCu(CN)Li which is particularly slow and requires higher reaction temperature. In this case, the lactone **20p** obtained after the addition of benzaldehyde and (iodomethyl)zinc iodide, is formed as a 60:40 mixture of the cis and trans isomers (entry 17). In the case of the fast carbocupration of the reactive ethyl 3-phenylpropiolate with BuCu(CN)Li, the cis-lactone **20p** is obtained almost exclusively (cis:trans ratio = 98:2). Improvement of the cis/trans selectivity by using *tert*-butyl propiolate instead of ethyl propiolate could not be achieved. The use of the copper reagent **25** bearing an electrophilic ketone functionality allows the construction of bicyclic α-methylene-γ-butyrolactones of type **26** in good yields (eq 7).

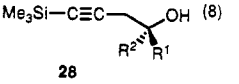


(7)

26a : R = H : 76 %
26b : R = CO_2Et : 83 %

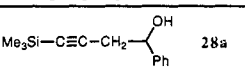
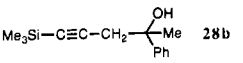
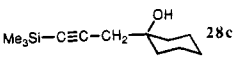
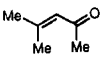
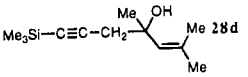
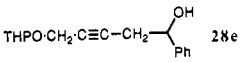
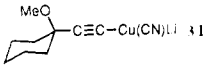
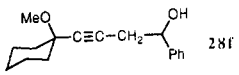
B. Homologation of Allenic and Acetylenic Copper Derivatives. Like alkenyl and allylic organometallics, acetylenic and propargylic reagents have very different reactivities, and this property can be exploited in performing a selective methylene homologation and selective trapping of the homologated organometallic. Thus, if [(trimethylsilyl)ethynyl]copper **27** is treated with an aldehyde or a ketone (0.6 equiv) and an excess of (iodomethyl)zinc iodide (**4**) (ca. 4 equiv) at −60 °C and the reaction mixture is warmed up to −40 °C, then an exothermic homologation reaction occurs and the homopropargylic alcohol **28** can be isolated in satisfactory to good yields (eq 8 and Table III).





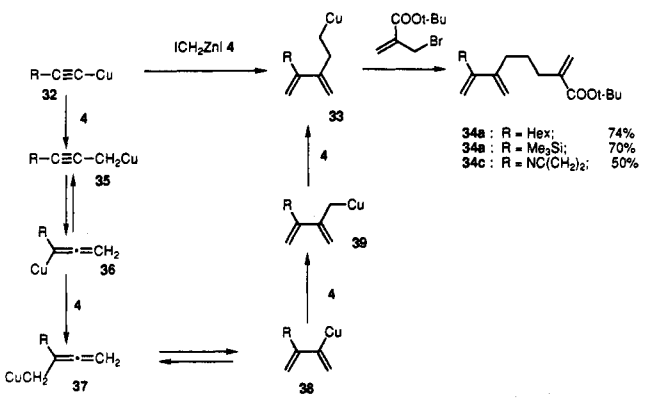
(8)

Table III. Homopropargylic Alcohols 28 obtained in a One-Pot Procedure from a Copper Acetylide (Iodomethyl)zinc Iodide and an Aldehyde or Ketone

entry	alkenylcopper	carbonyl compd	homopropargylic alcohol	yield[a] (%)
1	$Me_3Si-C\equiv C-Cu(CN)Li$ **27**	PhCHO	 **28a**	95
2	**27**	$PhCOCH_3$	 **28b**	89
3	**27**	cyclohexanone	 **28c**	90
4	**27**		 **28d**	95
5	$THPO{\cdot}CH_2{\cdot}C\equiv C-Cu(CN)Li$ **30**	PhCHO	 **28e**	80
6	 **31**	PhCHO	 **28f**	95

[a] All yields refer to isolated yields of compounds being over 98% pure by GC analysis and showing satisfactory spectral data.

Scheme II



The intermediate organometallic reacts only at the propargylic position,[35] and no allene formation was observed (entries 1–4 of Table III). A similar regioselectivity was observed with the functionalized copper acetylides **30** and **31** (entries 5 and 6). This behavior will not be general, since the addition of propargylic zinc organometallics to aldehydes usually gives, depending on the substituents, a mixture of homopropargylic and allenic alcohols.[36]

If an excess of (iodomethyl)zinc iodide is added to the copper acetylide **32** in the absence of an electrophile, then a multiple methylene insertion is observed and the dienic zinc–copper reagent **33** is obtained.[12] After the addition of an allylic bromide such as *tert*-butyl α-(bromomethyl)-acrylate,[37] the unsaturated esters **34** are obtained in 50–74% yield (Scheme II).

The formation of the quadruple homologation products **33** can be explained in the following way. The copper acetylide **32** is homologated by (iodomethyl)zinc iodide (**4**) to give the propargylic zinc–copper reagent **35**. This propargylic organometallic is in equilibrium with the allenic copper derivative **36** which can be further homologated by **4** to the allylic reagent **37**. This species is in equilibrium with the dienic zinc–copper compound **38** which after a third methylene homologation gives the allylic copper derivative **39**. This reagent undergoes a fourth methylene insertion providing the unsaturated alkylcopper–zinc derivative **33** which is unreactive toward further homologations and can be trapped in fair to good yields by an allylic bromide. Attempts to derivatize **33** with other electrophiles were not successful, due to the unreactivity of this copper reagent. One of the reasons for the unreactivity of **33** is the presence of an excess of zinc salts in the reaction medium. During the course of the reaction, 4 equiv of **4** are consummed and lead to the formation of 4 equiv of ZnI_2. We have already observed in different systems that the reactivity of a copper–zinc reagent RCu(CN)ZuI can be substantially lowered, if an excess of zinc salts is added. This can be explained by considering that mixed zinc–copper clusters are formed in which the proportion of copper atoms is now low. The organic group has a high probability to be attached to zinc and thus is not transferable to organic electrophiles.

The proposed reaction pathway of the quadruple methylene insertion has been confirmed by several experiments. Thus the propargylic copper **35a** (R = Hex) has been prepared from 1-bromo-2-nonyne[38] ((i) Zn (1.5 equiv), THF, 0 °C, 1 h, >85% yield;[39] (ii) CuCN·2LiCl (1 equiv), −60 to 0 °C, 1 h). It gives after reaction with (iodomethyl)zinc iodide (**4**) (3.5 equiv) and allylation with *tert*-butyl α-(bromomethyl)acrylate the ester **34a** in 70% yield. Also, we have demonstrated that an allylic organometallic reacts with **4** under our reaction conditions. Thus, the treatment of 2-butyl-2-propenylzinc bromide (**40**)[39] with an excess of **4** (ca. 4 equiv; 0–25 °C, 1 h) provides cleanly the homoallylic zinc reagent **41**. It is interesting to mention that the insertion of a methylene unit in an allylic zinc bromide does not require the addition of copper(I) salts. This is in contrast with most types of organometallic reagents which all underwent cleaner and faster, methylene insertions with **4** as copper derivatives, rather than as Mg, Li, or Zn derivatives. The resulting homoallylic species **41** is converted to the corresponding copper

(35) Zweifel, G.; Hahn, G. *J. Org. Chem.* **1984**, *49*, 4564.

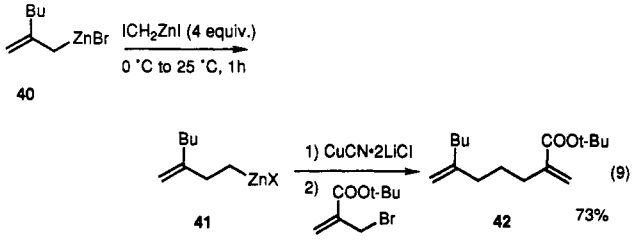
(36) For excellent reviews see: (a) Moreau, J.-L. In *The Chemistry of Ketenes, Allenes and Related Compounds*; Wiley: New York, 1980; Part I, p 363. (b) Yamamoto, H. In *Comprehensive Organic Chemistry*; Trost, B. M., Eds.; Pergamon Press: New York, 1991; Vol. 1, p 81. (c) Zeile, K.; Meyer, H. *Chem. Ber.* **1942**, *75*, 356. (d) Sondheimer, F.; Amiel, Y.; Gaoni, Y. *J. Am. Chem. Soc.* **1962**, *84*, 270. (e) Demole, E.; Winter, M. *Helv. Chim. Acta* **1962**, *45*, 1256. (f) Moreau, J.-L., Gaudemar, M. *Bull. Soc. Chim. Fr.* **1970**, 2175. (g) Gaudemar, M. *Bull. Soc. Chim. Fr.* **1962**, 974. (h) Yanagisawa, A.; Habaue, S.; Yamamoto, H. *J. Org. Chem.* **1989**, *54*, 5198. (i) Belyk, K.; Rozema, M. J.; Knochel, P. *J. Org. Chem.* **1992**, *57*, 4070.

(37) Villieras, J.; Rambaud, M. *Synthesis* **1982**, 924.

(38) Brandsma, L. *Preparative Acetylenic Chemistry*, 2nd ed.; Elsevier: Amsterdam, 1988; pp 81 and 247.

(39) Gaudemar, M. *Bull. Soc. Chim. Fr.* **1962**, 974.

reagent and is allylated with *tert*-butyl α-(bromomethyl)-acrylate leading to the ester **42** in 73% isolated yield (eq 9).



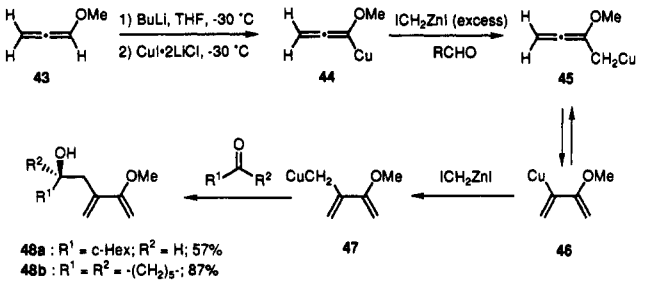
Allenic copper organometallics (intermediate of type **36** from Scheme II) have also been generated independently. Thus, the metalation of methoxyallene **43** with n-BuLi (THF, −30 °C),[40] followed by the transmetalation with CuI·2LiCl produces the allenylcopper derivative **44** (Scheme III).

Its reaction with **4** furnishes the allylic compound **45** which is in equilibrium with the dienic copper **46**. The copper reagent **46** is not reactive enough to add to the carbonyl compound present in the reaction mixture but rather undergoes a second methylene homologation providing a reactive allylic copper reagent **47**. This species is trapped by the carbonyl compound leading to the dienic alcohols **48a,b** in 57–87% yield. These two examples show that there is a competition between the addition of the organometallic to the carbonyl group and its further homologation by **4**. The result of this competition reaction depends on the reactivity of the carbonyl compound. Thus, the metalated propargylic ethers **30** and **31** afford after a monohomologation propargylic copper species which react only with reactive aldehydes such as benzaldehyde. If the homologation is performed in the presence of an unreactive carbonyl compound such as cyclopentanone the mono homologated propargylic organometallic formed is not reactive enough (deactivation by chelation) and a second and third homologation by **4** are observed providing a more reactive allylic organometallic reagent which adds to cyclopentanone giving products **49a,b** in 63%–70% yield. Similarly, the products **49c** and **49d** were obtained via this procedure using a functionalized aldehyde or a ketone (Scheme IV).

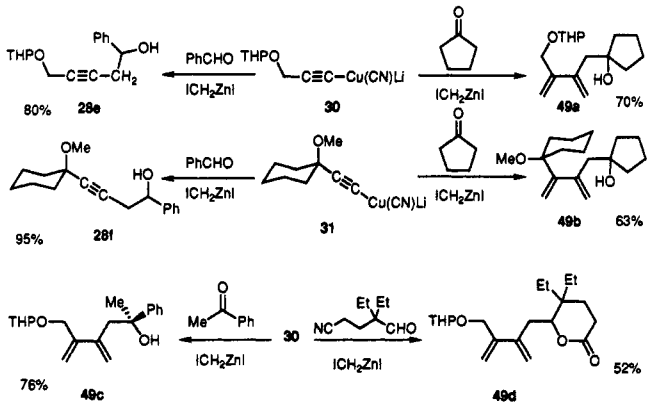
The homologation of copper acetylenides can be exploited to perform new types of cyclization reactions. Thus, the functionalized terminal alkynes **50** and **51** can be readily prepared starting from 5-iodopentyne **52** (Scheme V). The treatment of **52** with zinc dust in THF (25–30 °C, 2 h) provides after a transmetalation with CuCN·2LiCl the copper reagent **53** which reacts readily with 3-iodo-2-cyclohexen-1-one[41] (−30 °C, 1 h, then 0 °C, 1.5 h) and cyclohexanecarbonyl chloride (0 °C, 1 h) leading, respectively, to **50** (88% yield) and **51** (67% yield).[33d]

The deprotonation of **50** and **51** with 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU) and copper iodide[42] affords the corresponding copper acetylenides. They are efficiently homologated with bis(iodomethyl)zinc (**5**)[5] providing the intermediate allenic copper reagents **54** and **55** which undergo a ring closure leading, respectively, to the spiroketone **56** (65% yield) and to the allenic alcohol **57** (73% yield; Scheme VI).

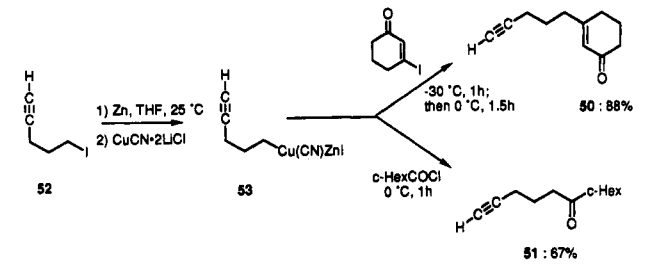
Scheme III



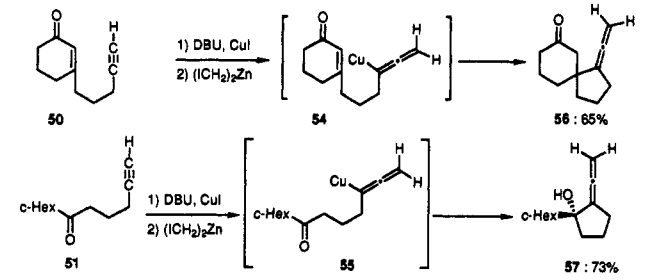
Scheme IV



Scheme V



Scheme VI

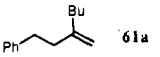
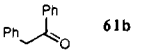
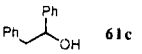
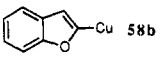
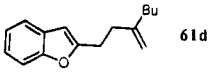
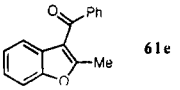
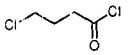
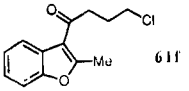
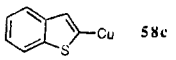
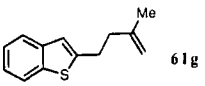
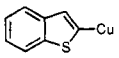
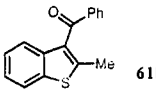
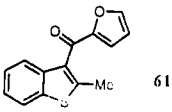
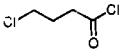
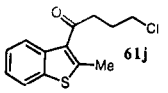
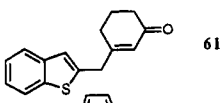
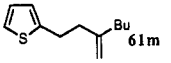


C. Homologation of Aromatic and Heteroaromatic Copper Compounds. Arylcopper and heteroarylcopper derivatives **58** can be homologated by (iodomethyl)zinc iodide (**4**) and furnish the benzylic organometallic **59** accompanied by ca. 15% of the double-homologated product **60** (eq 10). Since benzylic organometallics are usually more reactive than alkylcoppers (such as **60**), after addition of an electrophile (0.6 equiv), only the benzylated products of type **61** are obtained (Table IV).

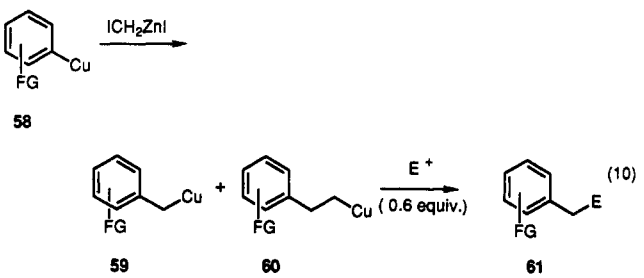
Due to the presence of several equivalents of zinc salts, the reactivity of the benzylic copper derivatives **59** are reduced and only the most reactive electrophiles (e.g., allylic halides, acid chlorides, benzaldehyde in the presence

(40) Hoff, S.; Brandsma, L.; Arens, J. F. *Rec. Trav. Chim. Pays-Bas* **1968**, *87*, 916.
(41) Piers, E.; Nagakura, I. *Synth. Commun.* **1975**, *5*, 193.
(42) Zhang, Y.; Wu, G.; Agnel, G.; Negishi, E. *J. Am. Chem. Soc.* **1990**, *112*, 8590.

Table IV. Products of Type 61 Obtained by the Reaction of an Aryl- or Heteroarylcopper 58 with (Iodomethyl)zinc Iodide (4) and an Electrophile

entry	aryl- or heteroarylcopper deriv	electrophile	product of type 61	yield[a] (%)
1	PhCu **58a**		 **61a**	80
2	**58a**	PhCOCl	 **61b**	69
3	**58a**	PhCHO[b]	 **61c**	92
4	 **58b**		 **61d**	73
5		PhCOCl	 **61e**	83
6	**58b**		 **61f**	92
7	 **58c**		 **61g**	93
8		PhCOCl	 **61h**	80
9	**58c**		 **61i**	74
10	**58c**		 **61j**	87
11	**58c**		 **61k**	60
12	 **58d**		 **61m**	96

[a] All yields refer to isolated yields of compounds being over 98% pure by GC analysis and showing satisfactory spectral data. [b] The reaction has been performed in the presence of BF_3·OEt_2 (3 equiv).

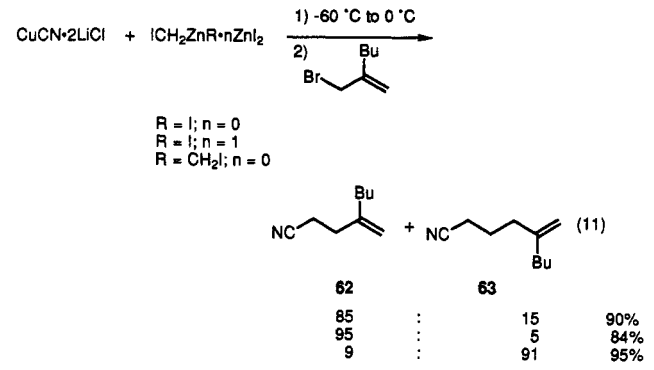


of BF_3·OEt_2[43]) react with these copper–zinc compounds in a satisfactory way. In the case of acid chlorides, the solvent THF has to be replaced by 1,2-dimethoxyethane, since considerable amounts of the THF ring opening product by the acid chloride are observed. With the heteroarylcoppers **58b–d**, the acylation occurs, like expected, on the aromatic ring affording 3-acyl-2-methyl-substituted heteroaromatic rings (entries 5–6, and 8–10 of Table IV).

II. Homologation of Other Copper Reagents. Several types of copper compounds RCu react with **4** leading to the methylene-homologated product RCH_2Cu. The reaction is in some cases complicated by further homologation reactions, especially if the reactivity of RCu and RCH_2Cu are very similar. The homologation of CuCN was studied in some detail. Thus, if CuCN is treated with **4** (0.5 equiv, –60 to 0 °C) and quenched with 2-(bromomethyl)hexene (0.3 equiv), then the ratio between the mono- and bis-methylene insertion products **62** and **63** is 85:15 (90% overall yield). We rationalized this result by assuming that **4** may contain some bis(iodomethyl)zinc (**5**) which is responsible for this double methylene insertion reaction. The addition of ZnI_2 to **4** should considerably reduce the amount of bis(iodomethyl)zinc (**5**) present in equilibrium with **4**. Indeed, by adding 1 equiv of ZnI_2 to **4**, we observed than CuCN (1.0 equiv) undergoes apparently a cleaner monohomologation, since after allylation with 2-(bromomethyl)hexene the ratio between **62** and **63** is now 95:5 (eq 11).

On another hand, the use of bis-(iodomethyl)zinc **5**[5] leads preferentially after allylation to the bis-methylene insertion product **63** (**62**:**63** = 9:91; 95% overall yield). The addition of ZnI_2 may have more complex effects than just

(43) Yeh, M. C. P.; Knochel, P.; Santa, L. E. *Tetrahedron Lett.* **1988**, *29*, 3887.



shifting the Schlenk equilibrium between **4** and **5**, since it also reduces the reactivity of the copper reagent and may therefore also affect the ratio of the products **62** and **63**, since the addition of ZnI_2 may modify the reactivity of the intermediate (cyanomethyl)copper and (2-cyanoethyl)copper differently. Preparatively useful selective monomethylene homologations could be achieved with several types of copper reagents **64** (Table V). The homologation of (cyanomethyl)copper **64a** and the α-substituted copper compound **64b** (entry 3 of Table V) provides a new access to (2-cyanoethyl)copper derivatives[44] which can be allylated or undergo Michael addition in satisfactory yields (entries 1–3). Lithium enolates can be converted to zinc homoenolates.[45] Both a ketone or an aldehyde enolate (generated from the corresponding trimethylsilylenol ether (MeLi, 25 °C, 0.5 h) are transformed to the corresponding homoenolate using bis(iodomethyl)zinc (**5**).[5] The resulting zinc homoenolates display a relatively low reactivity. They can, however, be allylated in fair yield after transmetalation with CuCN·2LiCl or undergo a coupling reaction with 3-iodo-2-cyclohexen-1-one[41] in the presence of catalytic amounts of $Pd(dba)_2$ (2 mol %) and PPh_3 (8 mol %);[46] (entry 5). Finally, various copper amides (**64e–g**) can be converted to carbanions at the α-position to amines. However, the low reactivity of these species allows only allylation reactions to be performed and provides homoallylic amines **65f–h** in 64–76% yields (entries 7–9).

Conclusion

In summary, we have shown that (iodomethyl)zinc iodide (**4**) and bis(iodomethyl)zinc (**5**) allow the selective methylene homologation of a wide variety of copper reagents. The methylene homologation of alkenyl- and alkynylcopper compounds is of considerable synthetic interest. It provides a unique way for directly converting alkenylcoppers to various functionalized allylic organometallics and generates in a one-pot procedure propargylic zinc–copper reagents from readily available alkynylcoppers. This method has been applied to a new stereoselective synthesis of α-methylene-γ-butyrolactones and to novel ring closure reactions. With appropriate reaction conditions, selective double, triple, or quadruple methylene homologations can also be performed.

Experimental Section

General. All reactions were carried out under argon. Solvents (ether, THF) were dried over sodium/benzophenone and freshly distilled. The zinc foil was purchased from Alfa (0.62 mm thick, purity m3N). LiCl and ZnI_2 were dried for 1–2 h under vacuum (0.1 mmHg) at 15 °C before use. The reactions were monitored by gas chromatography (GC) analysis. FT-IR spectra were recorded on sodium chloride plates. ^1H NMR spectra (300 MHz) and ^{13}C NMR spectra (75.5 MHz) were measured in $CDCl_3$ on a Bruker WM-300 spectrometer.

Preparation of Starting Materials. Preparation of 2-(4-Bromo-4-pentenyl)-1,3-dioxane. A solution of 2-(2-bromoethyl)-1,3-dioxane[47] (11.7 g, 60 mmol) in THF (20 mL) was added dropwise at 35–40 °C to magnesium turnings (2.5 g, 100 mmol) in THF (10 mL) which had been activated with 1,2-dibromoethane (0.94 g, 5 mmol). The Grignard reagent was formed within a period of 1 h at 35 °C and was added dropwise to a solution of copper cyanide (4.0 g, 45 mmol) and lithium chloride (3.8 g, 90 mmol) in THF (30 mL) at −30 °C. After the solution was warmed to 0 °C (in order to form the copper reagent) and cooled back to −20 °C, 2,3-dibromo-1-propene (8.0 g, 49 mmol) was added and the reaction mixture was stirred further for 30 min at 10 °C. After the usual workup, the distillation (110–115 °C/0.65 mmHg) of the residue gave 6.58 g of pure 2-(4-bromo-4-pentenyl)-1,3-dioxane (70% yield): ^1H NMR δ 5.59 (s, 1 H), 5.4 (s, 1 H), 4.55 (t, 1 H), 4.15–4.05 (m, 2 H), 3.85–3.70 (m, 2 H), 2.45 (t, 2 H), 2.15–2.0 (m, 1 H), 1.75–1.55 (m, 4 H), 1.4–1.3 (m, 1 H).

Preparation of Phenyldimethyl(2-bromo-2-propenyl)-silane. (Phenyldimethylsilyl)lithium[25] was formed in THF by the reaction of phenyldimethylchlorosilane (10.26 g, 60 mmol) in THF (100 mL) with an excess of lithium metal (1.68 g, 240 mmol) at −10 °C for 12 h. This reagent was added to a solution of copper cyanide (3.6 g, 40 mmol) and lithium chloride (3.6 g, 80 mmol) in THF (40 mL) at −50 °C. The dark red solution was stirred for 5 min, 2,3-dibromo-1-propene (8 g, 40 mmol) was added at −50 °C, and the reaction mixture was warmed to −20 °C and stirred for 30 min at this temperature. After the usual workup, the residue was purified by flash chromatography (solvent: hexane/ether (95/5)) yielding 7.39 g (72% of the desired product (purity 94%)): IR (neat) 3070 (s), 2957 (s), 1617 (s) cm^{-1}; ^1H NMR δ 7.55–7.5 (m, 2 H), 7.4–7.3 (m, 3 H), 5.25 (d, 1 H), 5.2 (d, 1 H), 2.35 (s, 2 H), 0.42 (s, 6 H); ^{13}C NMR δ 137.6, 133.5, 130.3, 129.2, 127.7, 114.7, 32.6, −2.9; MS (EI) 254 (8), 241 (10), 216 (18), 201 (25), 135 (100), 105 (13), 43 (10); exact mass calcd for $C_{11}H_{15}SiBr$ 254.0126, obsd 254.0123.

Preparation of 1-(2-Bromo-2-propenyl)cyclohexane.[33] c-HexCu(CN)ZnI was prepared by the addition of cyclohexylzinc iodide (obtained from iodocyclohexane (18.9 g, 90 mmol) in THF (35 mL) and zinc dust (13 g, 200 mmol)) to a solution of copper cyanide (4.0 g, 45 mmol) and lithium chloride (3.8 g, 90 mmol) in THF (50 mL) at 0 °C.[33] 2,3-Dibromo-1-propene (15 g, 75 mmol) was slowly added at −70 °C. The reaction mixture was warmed to 0 °C, stirred for 30 min at this temperature, and added to a solution of saturated NH_4Cl (100 mL). The aqueous layer was extracted with ether, and the combined organic layer was washed sequentially with H_2O (100 mL) and brine (100 mL) and dried ($MgSO_4$). After evaporation of the solvent, the residue was distilled (105–115 °C/20 mmHg) giving 12.2 g (80%) of bis(2-bromo-2-propenyl)cyclohexane which was used without further purification for the preparation of the corresponding organomagnesium reagent as described below.

Preparation of 3-(*N*,*N*-Dimethylamino)-2-bromo-1-propene.[26] 2,3-Dibromo-1-propene (15 g, 75 mmol) was added dropwise to a solution of diethylamine (12 g, 165 mmol) in CH_2Cl_2 (10 mL) at 5 °C. After addition, the reaction mixture was heated to 50 °C and stirred for 30 min. After the usual workup,

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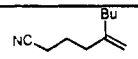
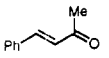
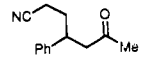
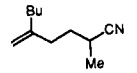
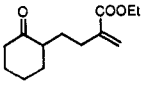
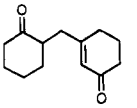
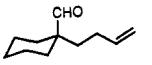
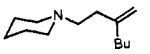
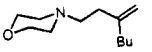
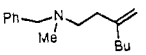
Table V. Products 65 Obtained after the Reaction of Nucleophiles 64 with (Iodomethyl)zinc Iodide (4) or Bis(iodomethyl)zinc (5) and an Electrophile

entry	nucleophile 64	electrophile	product 65 or 63	yield[a] (%)
1	$N{\equiv}CCH_2Cu$ **64a**		63 	91[b]
2	**64a**		65a 	76[c]
3	$N{\equiv}CCH(CH_3)Cu$ **64b**		65b 	69
4	 **64c**		65c 	85[d]
5	**64c**		65d 	76[e]
6	 **64d**		65e 	75
7	 **64e**		65f 	76
8	 **64f**		65g 	68
9	$PhCH_2N(Cu)Me$ **64g**		65h 	64

[a] All yields refer to isolated yields of compounds being over 98% pure by GC analysis. [b] Less than 5% of the double insertion product is obtained. [c] A 10:1 mixture of THF/DMPU was used as solvent. [d] After the methylene homologation, CuCN·2LiCl was added. [e] After the methylene homologation, $Pd(dba)_2$ (2 mol %) and PPh_3 (8 mol %) were added.

the residue was distilled (87–93 °C/10 mmHg) yielding 11.5 g (80%) of the desired compound: ^1H NMR δ 5.9 (s, 1 H), 5.55 (s, 1 H), 3.25 (s, 2 H), 2.6–2.5 (q, 4 H), 1.1–1.0 (t, 6 H). Compare with ref 26.

Preparation of (Iodomethyl)zinc iodide (4).[4] A three-necked flask equipped with a thermometer, septum cap, addition funnel, magnetic stirring bar, and argon outlet was charged with zinc foil (3.34 g, 51 mmol) and THF (4 mL). To the zinc suspension was added 1,2-dibromoethane (200 mg, 1 mmol), and the reaction mixture was heated to reflux for 1 min. After the mixture was cooled to 25 °C, chlorotrimethylsilane (0.1 mL, 0.8 mmol) was added, and the activated zinc was stirred for 5 min. A THF solution (15 mL) of diiodomethane (13.40 g, 50 mmol) was then added at 25 °C, via an addition funnel, within 15 min. After 4 h at this temperature the reagent was ready for use. A yield of 85% and a concentration of 1.4 M was assumed.

Preparation of Bis(iodomethyl)zinc (5).[5] A three-neck flask equipped with a thermometer, septum cap, magnetic stirring bar, and argon outlet was charged with diethylzinc (2.4 mL, 24 mmol) and THF (20 mL). This solution was cooled to −60 °C, and diiodomethane (13.40 g, 50 mmol) was added within 5 min via a syringe. After 0.5 h at −60 °C, the reaction was warmed to 0 °C and stirred for 0.5 h. The reagent was then ready for use, and a concentration of 1 M was assumed.

General Procedure for the Preparation of Vinylic Grignard Reagents in THF. All vinylic Grignard reagents[21] were prepared by the following procedure and were stored under Ar. Magnesium turnings (2.5 g, 100 mmol) covered with THF (5 mL) were activated by 1,2-dibromoethane (0.55 g, 3 mmol) in THF (3 mL). The alkenyl halide (40 mmol) in THF (15 mL) was slowly added at 35 °C and stirred for 1 h at 35 °C. The Grignard reagent precipitates out as white solid and was redissolved by the addition of THF (20 mL). The concentration of the solution was determined by titration[48] (usually 0.55 M).

The following starting materials were prepared according to the literature: 2-(bromomethyl)hexene from commercially available 2-butylacrolein,[49] *tert*-butyl α-(bromomethyl)acrylate,[37] 3-iodo-2-cyclohexene-1-one,[41] 1-(trimethylsiloxy)cyclohexene and [(trimethylsiloxy)methylidene]cyclohexene,[50] 1-ethynyl-1-(methyloxy)cyclohexane,[38] tetrahydro-2-(2-propynyloxy)-2*H*-pyran from propargyl alcohol and dihydropyran,[51] tetrahydro-2-[(1-pentyl-2-propynyl)oxy]-2*H*-pyran from 1-octyne-3-ol[38] and dihydropyran, and 4-cyano-2,2-diethylbutanal.[52]

General Procedure for the in Situ Generation of Allylic Zinc–Copper Reagents and Their Reactions with Aldehydes, Ketones, an Amine, and Methyl Formate. A solution of vinylic Grignard reagent (11.0 mL, 6 mmol) in THF was slowly added to a solution of copper iodide (1.15 g, 6 mmol) and lithium iodide (1.33 g, 10 mmol) in THF (25 mL) at −50 °C. The reaction mixture was warmed to −25 °C leading to an orange suspension and was cooled back to −50 °C. A solution of an aldehyde, ketone, imine, or ethyl formate (3.5–4 mmol) in THF (2 mL), was added and the reaction was warmed to −30 °C. A solution of (iodomethyl)zinc iodide (4) (10 mmol), freshly prepared from diiodomethane (2.72 g, 10 mmol) and zinc foil (0.72 g, 11 mmol) in THF (5 mL), was added at −50 °C. The reaction mixture was warmed to −20 °C and stirred for 15 min at this temperature. After this time, the reaction was complete as indicated by GC analysis, and the reaction mixture was added to a saturated solution of NH_4Cl (100 mL). The two layers were separated, and the aqueous layer was extracted with ether (2 × 100 mL). The organic layer was washed with H_2O (100 mL) and brine (100 mL)

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and dried ($MgSO_4$). The residue, obtained after removal of the solvent, was purified by flash chromatography leading to pure compounds (>98% pure capillary GC analysis) (Table I).

Analytical data of the compounds **8a–x** described in Table I.

3-(Cyclohexylmethyl)-1-phenyl-3-buten-1-ol (8a): flash chromatography (hexane/ether (19:1)); IR (neat) 3355 (s), 2984 (s), 1751 (s), 1733 (s), 1643 (s), 1625 (s) cm^{-1}; ^1H NMR δ 7.4–7.2 (m, 5 H), 4.9 (s, 1 H), 4.88 (s, 1 H), 4.75 (br s, 1 H), 2.4–2.3 (m, 3 H), 2.05–1.9 (m, 2 H), 1.75–1.6 (m, 5 H), 1.5–1.3 (br, s, 1 H), 1.3–1.1 (m, 3 H), 0.9–0.7 (m, 2 H); ^{13}C NMR δ 144.5, 144.0, 128.1, 127.1, 125.6, 113.7, 71.5, 46.1, 44.0, 35.5, 33.4, 32.9, 26.4 26.1; MS (CI, NH_3) 262 $(MNH_4)^+$ (100), 244 (75), 227 (30), 136 (50); exact mass calcd for $C_{17}H_{24}ONH_4$ 262.2170, obsd 262.2166 $(MNH_4)^+$.

2-(Cyclohexylmethyl)-1-nonen-4-ol (8b): flash chromatography (hexane/ether (19:1)); IR (neat) 3355 (s), 3071 (s), 2954 (s), 1642 (s), 1448 (s) cm^{-1}; ^1H NMR δ 5.45 (s, 2 H), 3.7 (br s, 1 H), 2.25 (dd, 1 H, J = 4 and 12 Hz), 2.2–1.9 (m, 4 H), 1.8 (s, 1 H), 1.75–1.6 (m, 4 H), 1.5–1.1 (m, 12 H), 0.9–0.8 (m, 4 H); ^{13}C NMR δ 145.1, 113.2, 68.7, 44.2, 44.1, 37.0, 35.5, 32.9, 31.8, 26.5, 26.3, 26.2, 25.3, 22.5, 13.9; MS (CI, CH_4 and NH_3) 256 $(MNH_4)^+$ (51), 239 (MH^+), (48), 221 (90), 139 (100); exact mass calcd for $C_{16}H_{30}OH$ 239.2374, obsd 239.2374 $(MH)^+$.

1-[2-(Cyclohexylmethyl)-2-propenyl]cyclohexanol (8c): flash chromatography (hexane/ether (19:1)); IR (neat) 3470 (s), 3066 (s), 2930 (s), 1635 (s), 1448 (s) cm^{-1}; ^1H NMR δ 4.88 (s, 1 H), 4.82 (s, 1 H), 2.15 (s, 2 H), 1.98 (d, 2 H, J = 9 Hz), 1.75–1.1 (m, 19 H), 0.9–0.8 (m, 2 H); ^{13}C NMR δ 144.7, 114.6, 70.8, 47.8, 46.2, 37.8, 36.0, 33.2, 26.5, 26.2, 25.7, 22.2; MS (CI, NH_3); 254 $(MNH_4)^+$ (75), 236 (55), 219 (100), 136 (50), 116 (35). Exact mass calcd for $C_{16}H_{28}ONH_4$: 254.2483. Observed: 254.2485 $(MNH_4)^+$.

4-(Cyclohexylmethyl)-2-phenyl-4-penten-2-ol (8d): flash chromatography (hexane/ether (19:1)); IR (neat) 3360 (s), 3066 (s), 3030 (s), 2922 (s), 1751 (s), 1732 (s), 1640 (s), 1620 (s) cm^{-1}; ^1H NMR δ 7.45 (m, 2 H), 7.35 (m, 2 H), 7.2 (m, 1 H), 4.88 (s, 1 H), 4.82 (s, 1 H), 2.65 (d, 1 H, J = 12 Hz), 2.45 (d, 2 H, J = 15 Hz), 1.7–1.5 (m, 7 H), 1.4 (dd, 2 H, J = 6 and 12 Hz), 1.3–1.0 (m, 4 H), 0.65 (m, 2 H); ^{13}C NMR δ 148.7, 144.7, 127.8, 126.2, 124.6, 115.6, 73.0, 49.5, 44.8, 35.5, 33.2, 32.7, 30.5, 26.4, 26.2, 26.1; MS (CI, CH_4) 259 $(MH)^+$ (10), 241 (100), 145 (25), 121 (98), 105 (20); exact mass calcd for $C_{18}H_{26}OH$ 259.2061, obsd 259.2080 $(MH)^+$.

1,3-Diphenyl-3-buten-1-ol (8e): flash chromatography (hexane/ether (19:1)); IR (neat) 3411 (s), 3060 (s), 2920 (s), 1732 (s), 1627 (s), 1600 (s) cm^{-1}; ^1H NMR δ 7.4–7.2 (m, 10 H), 5.4 (s, 1 H), 5.15 (s, 1 H), 4.7 (dd, 2 H, J = 4.5 and 9 Hz), 2.95 (dd, 1 H, J = 14.3 and 4.5 Hz), 2.85 (dd, 1 H, J = 14.3 and 9 Hz), 2.15 (br s, 1 H); ^{13}C NMR δ 144.8, 143.8, 140.3, 128.3, 128.2, 127.5, 127.3, 126.9, 126.1, 125.7, 115.4, 72.0, 45.7; MS (CI, NH_3) 242 $(MNH_4)^+$ (82), 224 (65), 207 (100), 136 (30), 119 (18); exact mass calcd for $C_{16}H_{16}ONH_4$ 242.1544, obsd 242.1533 $(MNH_4)^+$.

2-Phenyl-1-nonen-4-ol (8f): flash chromatography (hexane/ether (19:1)); IR (neat) 3410 (s), 3060 (s), 1732 (s), 1630 (s), 1608 (s), 1475 (m) cm^{-1}; ^1H NMR δ 7.4–7.25 (m, 5 H), 5.4 (s, 1 H), 5.15 (s, 1 H), 3.7–3.6 (m, 1 H), 2.8 (dd, 1 H, J = 14.2 and 3.8 Hz), 2.5 (dd, 1 H, J = 14.2 and 9 Hz), 1.65 (s, 1 H), 1.5–1.4 (m, 2 H), 1.3–1.2 (m, 5 H), 0.9–0.8 (m, 3 H); ^{13}C NMR δ 145.6, 140.7, 128.3, 127.5, 126.1, 114.9, 69.5, 43.8, 36.9, 31.8, 25.2, 22.5, 13.9; MS (EI) 218 (6), 118 (100), 83 (20); exact mass calcd for $C_{15}H_{22}O$ 218.1670, obsd 218.1674.

3-[3-(1,3-Dioxanyl)propyl]-1-phenyl-3-buten-1-ol (8g): flash chromatography (hexane/ether (16:4)); IR (neat) 3443 (s), 2954 (s), 1644 (s), 1430 (m) cm^{-1}; ^1H NMR δ 7.4–7.2 (m, 5 H), 4.9 (d, 2 H), 4.78 (dd, 1 H, J = 6 and 9 Hz), 4.5 (t, 1 H, J = 4.5 Hz), 4.08 (dd, 2 H, J = 6 and 9 Hz), 3.75 (dt, 2 H, J = 4 and 12 Hz), 2.5–2.35 (m, 2 H), 2.25 (s, 1 H), 2.1–2.0 (m, 3 H), 1.6–1.5 (m, 4 H), 1.35–1.3 (m, 1 H), ^{13}C NMR δ 145.6, 144.1, 128.0, 127.9, 127.0, 125.6, 125.5, 112.5, 101.8, 71.5, 66.5, 46.2, 35.3, 34.4, 25.5, 21.6; MS (CI, CH_4) 275 (s), $(MH)^+$, 259 (45), 183 (100), 173 (18); exact mass calcd for $C_{17}H_{23}O_3$ 275.1647, obsd 275.1656 $(MH)^+$.

2-[(Dimethylphenylsilyl)methyl]-2-propenyl-1-cyclopentanol (8h): flash chromatography (hexane/ether (19:1)); IR (neat) 3449 (s), 1627 (s) cm^{-1}; ^1H NMR δ 7.55–7.5 (m, 2 H), 7.38–7.3 (m, 3 H), 4.7 (s, 2 H), 2.15 (s, 2 H), 1.9 (s, 2 H), 1.8–1.7 (m, 2 H), 1.65–1.45 (m, 6 H), 0.3 (s, 6 H); ^{13}C NMR δ 144.2, 138.4, 128.8, 127.7, 127.6, 111.7, 80.7, 48.6, 39.8, 27.6, 23.3, –3.083; MS (CI, CH_4) 273 $(MH)^+$ (18), 257 (85), 245 (25), 135 (100); exact mass calcd for $C_{17}H_{25}SiO$ 273.1674, obsd 273.1679 $(MH)^+$.

4-(*N,N*-Diethylamino)-3-methylene-1-phenyl-1-butanol (8i): flash chromatography (hexane/ethyl acetate (16:4)); IR (neat) 3371 (br s), 3071 (s), 1642 (s), 1451 (s) cm^{-1}; ^1H NMR δ 7.4–7.15 (m, 5 H), 4.95 (d, 2 H), 4.65 (d, 1 H), 3.1–2.9 (q, 2 H), 2.8–2.6 (m, 3 H), 2.55–2.3 (m, 3 H), 1.1 (t, 6 H); ^{13}C NMR δ 145.4, 143.8, 127.6, 126.2, 125.3, 118.0, 73.4, 59.8, 48.4, 45.3, 10.3; MS (EI) 233 (10), 218 (8), 159 (5), 127 (12), 112 (15), 105 (28), 86 (100); exact mass calcd for $C_{15}H_{23}NO$ 233.1779, obsd 233.1782.

4-(*N,N*-Diethylamino)-2-methylene-4-nonanol (8j): flash chromatography (hexane/ethyl acetate (16:4)); IR (neat) 3424 (s), 2922 (s), 1641 (s) cm^{-1}; ^1H NMR δ 5.0 (s, 1 H), 4.9 (s, 1 H), 3.55–3.45 (br s, 1 H), 2.98 (dd, 2 H, J = 13.5 and 30.5 Hz), 2.7–2.6 (m, 2 H), 2.55–2.4 (m, 3 H), 2.1–2.0 (m, 1 H), 1.5–1.3 (m, 9 H), 1.05 (t, 6 H), 0.9 (t, 3 H); ^{13}C NMR δ 144.9, 117.8, 70.0, 60.2, 46.0, 45.7, 37.6, 32.0, 25.8, 22.5, 14.1, 10.5; MS (EI) 227 (4), 212 (15), 156 (10), 127 (8), 112 (12), 86 (100); exact mass calcd for $C_{14}H_{29}NO$ 227.2249, obsd 227.2235.

4,4-Diethyl-5-hydroxy-7-methylene-8-(*N,N*-diethylamino)-octanenitrile (8k): flash chromatography (hexane/ethyl acetate (16:4)); IR (neat) 3430 (s), 3115 (s), 1641 (s), 1437 (s) cm^{-1}; ^1H NMR δ 4.95 (s, 1 H), 4.92 (s, 1 H), 3.3 (d, 1 H, J = 9 Hz), 3.05 (d, 1 H, J = 12 Hz), 2.85 (d, 1 H, J = 12 Hz), 2.78–2.62 (m, 3 H), 2.58–2.3 (m, 4 H), 1.95–1.85 (m, 1 H), 1.8–1.6 (m, 2 H), 1.58–1.2 (m, 4 H), 1.05 (t, 6 H), 0.85 (t, 6 H); ^{13}C NMR δ 145.4, 120.9, 117.2, 76.0, 59.9, 45.6, 40.7, 40.2, 30.1, 26.3, 24.5, 12.5, 10.5, 7.8, 7.4; MS (CI, CH_4) 281 $(MH)^+$ (100), 265 (20), 251 (21), 226 (10), 208 (25); exact mass calcd for $C_{17}H_{32}N_2OH$ 281.2592, obsd 281.2587 $(MH)^+$.

2-Hexyl-1-phenyl-3-buten-1-ol (8l) (1:1 mixture of two diastereomers): flash chromatography (hexane/ether (19:1)); IR (neat) 3432 (s), 3116 (s), 1650 (s), 1454 (s) cm^{-1}; ^1H NMR δ 7.35–7.2 (m, 5 H), 5.7–5.4 (m, 1 H), 5.3–5.15 (m, 1 H), 5.1–4.95 (m, 1 H), 4.6 (d, 1 H, J = 6 Hz), 4.38 (d, 1 H, J = 7 Hz), 2.5–2.0 (m, 2 H), 1.6–1.5 (m, 1 H), 1.4–1.1 (m, 10 H), 0.9–0.8 (m, 3 H); ^{13}C NMR δ 142.6, 139.2, 138.6, 128.0, 127.7, 127.3, 127.1, 126.8, 126.6, 118.2, 116.8, 76.5, 52.4, 51.3, 31.7, 31.6, 30.3, 29.5, 29.2, 27.1, 27.0, 22.5, 22.4, 13.9, 13.9; MS (CI, CH_4, and NH_3) 250 $(MNH_4)^+$ (5), 233 $(MH)^+$ (16), 215 (85), 113 (12), 107 (100); exact mass calcd for $C_{16}H_{24}OH$ 233.1905, obsd 233.1910 $(MH)^+$.

3-Hexyl-1-nonen-4-ol (8m) (1:1 mixture of 2 diastereoisomers): flash chromatography (hexane/ether (19:1)); IR (neat) 3430 (s), 1625 (s), 1450 (s) cm^{-1}; ^1H NMR δ 5.7–5.5 (m, 1 H), 5.2–5.05 (m, 2 H), 3.48 (br s, 1 H), 2.15–1.95 (m, 1 H), 1.55–1.15 (m, 19 H), 1.0–0.8 (m, 6 H); ^{13}C NMR δ 139.5, 139.1, 117.5, 116.8, 74.4, 73.7, 50.8, 50.3, 34.7, 33.9, 31.9, 31.9, 31.8, 30.8, 29.9, 29.9, 29.8, 27.3, 25.7, 25.4, 22.6, 14.0; MS (CI, CH_4 and NH_3) 244 $(MNH_4)^+$ (60), 227 $(MH)^+$ (30), 209 (100), 139 (40); exact mass calcd for $C_{15}H_{30}OH$ 227.2374, obsd 227.2358 $(MH)^+$.

8-Pentadecen-6-ol (9m) (E/Z ratio ~ 85:15): flash chromatography (hexane/ether (19:1)); IR (neat) 3410 (s), 3045 (s), 1640 (s) cm^{-1}; ^1H NMR δ 5.6–5.5 (m, 1 H), 5.45–5.35 (m, 1 H), 5.25–5.22 (m, 1 H), 5.15–5.1 (m, 1 H), 3.6 (br s, 1 H), 2.25–2.2 (t, 2 H, J = 6 Hz), 2.1–2.0 (m, 3 H), 1.6–1.2 (m, 25 H), 0.95–0.85 (m, 10 H); ^{13}C NMR δ 134.6, 133.5, 125.8, 125.1, 71.5, 70.9, 40.6, 36.7, 36.6, 35.3, 32.5, 31.9, 31.8, 31.7, 31.6, 31.6, 31.5, 30.2, 29.5, 29.3, 28.9, 28.7, 27.3, 25.3, 25.2, 25.1, 24.1, 23.6, 23.2, 22.5, 14.0, 13.9, 13.9; MS (CI, NH_3) 244 $(MNH_4)^+$ (60), 226 (5), 218 (100); exact mass calcd for $C_{15}H_{30}ONH_4$ 244.2640; obsd 244.2634 $(MNH_4)^+$.

1,2-Diphenyl-3-buten-1-ol (8n) (2:1 mixture of two diastereoisomers): flash chromatography (hexane/ethyl acetate (8:2)); IR (neat) 3429 (br), 3083 (s), 1637 (s), 1601 (s), 1494 (s) cm^{-1}; ^1H NMR δ 7.36–7.0 (m, 10 H), 6.3–6.16 (m, 1 H), 5.95–5.82 (m, second diast), 5.29–5.16 (m, 2 H), 5.0–4.96 (m, second diast), 4.93–4.87 (m, second diast), 4.85–4.79 (m, 1 H), 3.65 (t, second diast), 3.55 (t, 1 H, J = 8.4 Hz), 2.38 (d, 1 H, J = 2.6 Hz), 2.02 (d, second diast), ^{13}C NMR δ 141.8, 141.8, 140.5, 140.1, 137.6, 137.5, 128.5, 128.3, 128.1, 128.0, 127.7, 127.5, 127.3, 127.0, 126.8, 126.6, 126.4, 126.2, 125.6, 117.8, 116.8, 77.1, 76.9, 58.6, 58.1; MS (CI, NH_3) 242 $(MNH_4)^+$ (52), 224 (88), 207 (60), 91 (100); exact mass calcd for $C_{16}H_{16}ONH_4$ 242.1544, obsd 242.1549.

(*E*)-5,5-Dimethyl-1-phenyl-3-hexen-1-ol (8o): flash chromatography (hexane/ether (9.5:0.5); IR (neat) 3372 (br), 3030 (s), 2902 (br s), 1454 (m) cm^{-1}; ^1H NMR δ 7.39–7.22 (m, 5 H), 5.58 (d, 1 H, J = 16 Hz), 5.37–5.26 (m, 1 H), 4.7–4.63 (m, 1 H), 2.5–2.35 (m, 2 H), 2.11 (d, 1 H, J = 3.0 Hz), 1.01 (s, 9 H); ^{13}C NMR δ 145.4, 144.1, 128.0, 127.0, 125.7, 120.1, 73.7, 42.5, 32.8, 29.6; MS (CI,

NH_3) 222 $(MNH_4)^+$ (4), 204 (84), 187 (100), 136 (9), 117 (25); exact mass calcd for $C_{14}H_{20}ONH_4$ 222.1857, obsd 222.1847.

1-(1-Hexyl-2-propenyl)-1-cyclohexan-1-ol (8p) (86:14 mixture of diastereoisomers): purified by flash chromatography (hexane/ether (99:1)); IR (neat) 3320 (br), 3071 (m), 2903 (s), 1638 (m), 1430 (s) cm^{-1}; ^1H NMR δ 5.65 (m, 1 H), 5.58 (m, minor diast), 5.10 (m, 2 H), 3.15 (m, 1 H), 2.18 (m, 1 H), 1.85–1.60 (m, 4 H), 1.4–1.0 (m, 18 H), 0.85 (t, J = 7 Hz, 3 H); ^{13}C NMR δ 140.3 (minor (m)), 138.9 (major (M)), 116.8 (M), 115.3 (m), 78.6 (m), 77.6 (M), 47.3 (m), 46.6 (M), 40.6 (M), 40.4 (m), 31.7, 31.2, 29.6, 29.2, 27.8, 27.2, 26.5, 26.3, 26.0, 22.5, 13.9; MS (EI, 70 eV) 238 (0.2), 126 (55), 113 (22), 95 (100); exact mass calcd for $C_{16}H_{30}$ 238.2297, obsd 238.2281.

1-(3-Chloropropyl)-1-phenyl-3-buten-1-ol (8q) (60:40 mixture of diastereoisomers): flash chromatography (hexane/ethyl acetate (9:1)); IR (neat) 3417 (br), 3029 (s), 2877 (br, s), 1639 (s), 1306 (m) cm^{-1}; ^1H NMR δ 7.4–7.16 (m, 5 H), 5.72–5.58 (m, 1 H), 5.56–5.45 (m, other diast), 5.3–5.15 (m, 2 H), 5.1–4.95 (m, other diast), 4.65–4.58 (m, other diast), 4.41 (d, 1 H, J = 7.5 Hz), 3.56–3.45 (m, other diast), 3.44–3.3 (m, 2 H), 2.46–2.25 (m, 1 H), 2.2 (d, 1 H, J = 1.9 Hz), 2.07 (d, other diast), 1.88–1.6 (m, 2 H), 1.68–1.52 (m, other diast), 1.4–1.2 (m, 2 H); ^{13}C NMR δ 142.4, 142.2, 138.2, 138.0, 127.9, 127.7, 127.3, 127.1, 126.6, 126.5, 126.4, 118.4, 117.1, 76.6, 76.4, 51.5, 50.6, 44.8, 44.5, 30.3, 30.2, 27.6, 26.7; MS (CI, NH_3) 242 (MNH_4) (18), 224 $(MNH_4 - H_2O)^+$ (100), 207 (22), 148 (9), 136 (40); exact mass calcd for $C_{13}H_{17}{}^{35}ClONH_4$ 242.1311, obsd 242.1318.

2-Hexyl-1-phenyl-3-(trimethylsilyl)-3-buten-1-ol (8r) (obtained as a major diastereoisomer (>98:2): flash chromatography (hexane/ether (9.5:0.5)); IR (neat) 3417 (br), 3031 (s), 2925 (br s), 1634 (s), 1493 (m) cm^{-1}; ^1H NMR δ 7.36–7.21 (m, 5 H), 5.78 (d, 1 H, J = 2.2 Hz), 5.64 (d, 1 H, J = 2.4 Hz), 4.68–4.61 (m, 1 H), 2.7–2.6 (m, 1 H), 2.04 (d, 1 H, J = 2.6 Hz), 1.68–1.4 (m, 2 H), 1.3–1.1 (m, 7 H), 1.05–0.94 (m, 1 H), 0.85 (t, 3 H, J = 6.4 Hz), 0.05 (s, 9 H); ^{13}C NMR δ 153.3, 143.2, 127.8, 126.8, 126.3, 125.9, 75.3, 50.8, 31.6, 29.4, 27.4, 22.5, 14.0, –1.2; MS (CI, NH_3) 322 $(MNH_4)^+$ (5), 304 $(MNH_4 - H_2O)^+$ (48), 287 (41), 213 (13), 200 (8), 124 (6), 106 (6), 90 (100); exact mass calcd for $C_{19}H_{32}SiONH_4$ 322.2566, obsd 322.2560.

1,2-Diphenyl-3-(trimethylsilyl)-3-buten-1-ol (8s) (obtained as major diastereoisomer >98:2): flash chromatography (hexane/ether (9:1)); IR (neat) 3453 (br), 3029 (s), 2955 (s), 1598 (s), 1417 (m), 1037 (m) cm^{-1}; ^1H NMR δ 7.72–7.6 (m, 10 H), 6.4 (d, 1 H, J = 1.8 Hz), 5.59 (d, 1 H, J = 1.9 Hz), 5.56 (dd, 1 H, J = 2.8, 7.9 Hz), 4.24 (d, 1 H, J = 8 Hz), 2.3 (d, 1 H, J = 3 Hz); ^{13}C NMR δ 152.7, 141.8, 139.2, 129.0, 128.5, 128.1, 128.0, 127.6, 127.5, 127.0, 126.7, 126.2, 125.5, 124.2, 76.1, 58.8, –1.5; MS (CI, NH_3) δ 314 $(MNH_4)^+$ (4), 296 $(MNH_4 - H_2O)$ (10), 279 (38), 190 (7), 136 (23), 90 (100); exact mass calcd for $C_{19}H_{24}OSiNH_4$ 314.1940, obsd 314.1927.

3-Phenyl-2-(trimethylsilyl)-1-nonen-4-ol (8t): 79:21 mixture of two diastereoisomers; flash chromatography (hexane/ether (9:1)); IR (neat) 3456 (br), 3027 (s), 2924 (brs) 1596 (s) cm^{-1}; ^1H NMR δ 7.47–7.25 (m, 5 H), 6.02 (d, 1 H, J = 1 Hz), 5.75 (d, 1 H, J = 2 Hz), 4.27–4.1 (m, 1 H), 3.57 (d, 1 H, J = 7.4 Hz), 1.88–1.33 (m, 8 H), 1.02 (t, 3 H, J = 6.4 Hz), 0.09 (s, 9 H); ^{13}C NMR δ 152.9, 140.2, 129.4, 128.1, 126.5, 125.0, 72.9, 56.0, 35.1, 31.7, 25.6, 13.9, –1.4; MS (CI, NH_3) 308 $(MNH_4)^+$ (100), 273 (8), 136 (74); exact mass calcd for $C_{18}H_{30}OSiNH_4$ 308.2409, obsd 308.2412.

1-(1-Hexyl-2-propenyl)-1-cyclohexan-1-ol (8u): flash chromatography (hexane/ethyl acetate (8:2)); IR (neat) 3465 (br), 3073 (s), 2913 (br s), 1637 (s), 1448 (m) cm^{-1}; ^1H NMR δ 5.68–5.53 (m, 1 H), 5.18–5.0 (m, 2 H), 1.98–1.85 (m, 1 H), 1.7–1.4 (m, 10 H), 1.38–1.1 (m, 10 H), 0.89 (t, 3 H, J = 6.9 Hz); ^{13}C NMR δ 139.0, 117.3, 72.2, 55.5, 34.7, 34.6, 31.7, 29.2, 27.8, 27.7, 25.8, 22.4, 22.0, 13.9; MS (CI, NH_3) 242 $(MNH_4)^+$ (10), 224 $(MNH_4 - H_2O)$ (22), 207 (100), 99 (8), 81 (18); exact mass calcd for $C_{15}H_{28}ONH_4$ 242.2483, obsd 242.2482.

(*E*)-1-(4,4-Dimethyl-2-pentenyl)-1-cyclohexan-1-ol (8v): flash chromatography (hexane/ether (9.5:0.5)); IR (neat) 3376 (br), 3030 (s), 2909 (br s), 1642 (s) cm^{-1}; ^1H NMR δ 5.48 (d, 1 H, J = 15.6 Hz), 5.38–5.27 (m, 1 H), 2.06 (d, 2 H, J = 7.3 Hz), 1.6–1.15 (m, 10 H), 0.97 (s, 9 H); ^{13}C NMR δ 146.1, 119.0, 70.8, 45.4, 37.4, 33.0, 29.6, 25.7, 22.1; MS (CI, NH_3) 214 $(MNH_4)^+$ (3), 196 $(MNH_4 - H_2O)^+$ (17), 179 (100); exact mass calcd for $C_{13}H_{24}ONH_4$ 214.2170, obsd 214.2175.

1-[1-Phenyl-2-(trimethylsilyl)-2-propenyl]-1-cyclohexan-1-ol (8w): flash chromatography (hexane/ether (9:1)); IR (neat) 3493 (br), 3024 (s), 2899 (br s), 1596 (s) cm^{-1}; ^1H NMR δ 7.65–7.4 (m, 5 H), 6.75 (d, 1 H, J = 2.7 Hz), 5.95 (d, 1 H, J = 2.7 Hz), 3.74 (s, 1 H), 2.3–2.17 (br d, 1 H), 1.9–1.31 (m, 10 H), 0.19 (s, 9 H); ^{13}C NMR δ 151.6, 140.3, 130.3, 127.7, 127.0, 126.2, 73.9, 58.0, 37.8, 36.2, 25.7, 22.0, 21.9, –1.4; MS (CI, NH_3) 306 $(MNH_4)^+$ (5), 288 $(MNH_4 - H_2O)^+$ (2), 271 (100), 210 (12), 190 (15), 90 (83); exact mass calcd for $C_{18}H_{28}OSiNH_4$ 306.2253, obsd 306.2258.

1-[1-(4-Chlorobutyl)-2-propenyl]-1-cyclohexanol (8x): flash chromatography (hexane/ethyl acetate (9:1)); IR (neat) 3459 (br), 3073 (s9, 2935 (br s), 1636 (s), 1287 (m) cm^{-1}; ^1H NMR δ 5.7–5.55 (m, 1 H), 5.21–5.03 (m, 2 H), 3.6–3.5 (m, 2 H), 1.98–1.75 (m, 3 H), 1.69–1.1 (m, 12 H); ^{13}C NMR δ 138.2, 117.7, 72.1, 54.6, 44.8, 34.9, 34.4, 30.8, 25.6, 24.8, 21.5; MS (CI, NH_3) 234 $(MNH_4)^+$ (100), 216 $(MNH_4 - H_2O)$ (98), 199 (68), 136 (25); exact mass calcd for $C_{21}H_{21}{}^{35}ClONH$ 234.1624, obsd 234.1612.

1-(Cyclohexylmethyl)-1-(2,4-diphenyl-3-azabutyl)cyclopropane (11): flash chromatography (hexane/ether (19:1)); IR (neat) 3320 (s), 3060 (s), 1732 (s), 1640 (s) cm^{-1}; ^1H NMR δ 7.4–7.2 (m, 10 H), 3.7 (dd, 1 H, J = 6, 9 Hz), 3.6 (dd, 2 H, J = 13, 6 Hz), 1.95 (s, 1 H), 1.8 (dd, 2 H, J = 6, 13 Hz), 1.7–1.5 (m, 4 H), 1.49–1.0 (m, 6 H), 0.9–0.8 (m, 3 H), 0.35 (m, 1 H), 0.22–0.09 (m, 2 H), 0.01 to –0.08 (m, 1 H); ^{13}C NMR δ 145.0, 140.8, 128.2, 128.0, 127.2, 126.7, 126.6, 60.3, 51.5, 44.8, 43.4, 35.8, 34.1, 33.5, 26.6, 26.4, 26.3, 14.9, 12.1, 11.7; MS (CI, CH_4) 348 $(MH)^+$ (100), 270 (15), 196 (30); exact mass calcd for $C_{25}H_{33}NH$ 348.2691, obsd 348.2682 $(MH)^+$.

1,7-Dicyclohexyl-2,6-dimethylene-4-heptyl formate (12): flash chromatography (hexane/ether (19:1)); IR (neat) 3070 (s), 2936 (s), 2700 (s), 1724 (s), 1644 (s), 1448 (s) cm^{-1}; ^1H NMR δ 8.0 (s, 1 H), 5.3–5.2 (m, 1 H), 4.8 (d, 4 H, J = 4.5 Hz), 2.25 (d, 4 H, J = 6.5 Hz), 2.0–1.85 (m, 4 H), 1.7–1.6 (m, 10 H), 1.5–1.35 (m, 2 H), 1.3–1.1 (m, 6 H), 0.9–0.8 (m, 4 H); ^{13}C NMR δ 160.3, 143.4, 113.5, 70.6, 44.0, 40.7, 35.5, 33.3, 33.1, 26.5, 26.3, 26.2; MS (CI, NH_3) 350 $(MNH_4)^+$ (84), 333 $(MH)^+$ (10), 287 (70), 204 (40), 190 (100), 149 (63); exact mass calcd for $C_{22}H_{36}O_2H$ 333.2793, obsd 333.2809 $(MH)^+$.

1-(1-Cyclohexenyl)-2-heptanol (14) (minor regioisomer, purity ca. 94%): purified by flash chromatography (hexane/ether (95:5)); ^1H NMR δ 5.52 (s, 1 H), 3.65 (m, 1 H), 2.15 (m, 1 H), 2.05 (m, 4 H), 1.85 (m, 1 H), 1.75 (s, 1 H), 1.60 (m, 4 H), 1.5–1.25 (m, 8 H), 0.84 (t, J = 6 Hz, 3 H); ^{13}C NMR δ 135.0, 124.8, 68.8, 46.6, 37.2, 32.0, 28.5, 25.4, 25.1, 22.9, 22.6, 22.4, 14.0.

(*R,*S**)-1-(2-Methylene-1-cyclohexyl)-1-hexanol (15)** (major regioisomer, isolated as only one stereoisomer): purified by flash chromatography (hexane/ether (95:5)); IR (neat) 3450 (bs), 2930 (s), 1634 (s), 1450 (s) cm^{-1}; ^1H NMR 4.82 (s, 1 H), 4.72 (s, 1 H), 3.75 (t, J = 6 Hz, 1 H), 2.15 (m, 3 H), 1.75–1.20 (m, 15 H), 0.85 (t, J = 6 Hz, 3 H); ^{13}C NMR δ 149.9, 109.9, 69.2, 50.1, 33.9, 33.1, 32.0, 29.0, 28.1, 25.1, 22.6, 22.4, 14.0; MS (CI, NH_3) 214 $(MNH_4)^+$ (12), 197 $(MH)^+$ (6), 179 (21), 123 (13), 118 (19); exact mass calcd for $C_{13}H_{24}OH$ 197.1905, obsd 197.1901.

(*R,*R**)-7-(1-Hydroxybenzyl)-6-methylene-1,4-dioxaspiro[5.4]decane (18a)**: mp 108–110 °C; relative stereochemistry of this compound determined by X-ray analysis; flash column chromatography (hexane/ethyl acetate (8:2)); IR (KBr) 3472 (br), 3060 (s), 2855 (br s), 1640 (s), 1194 (m) cm^{-1}; ^1H NMR δ 7.4–7.26 (m, 5 H), 5.42 (d, 1 H, J = 1.9 Hz), 5.1 (d, 1 H, J = 2.7 Hz), 4.89 (dd, 1 H, J = 2.6, 9.6 Hz), 4.08–3.97 (m, 4 H), 2.75–2.63 (m, 1 H), 2.32 (d, 1 H, J = 2.6 Hz), 1.95–1.56 (m, 4 H), 1.4–1.2 (m, 2 H); ^{13}C NMR δ 146.5, 143.1, 128.1, 127.4, 126.8, 111.3, 108.2, 74.2, 64.5, 64.2, 51.0, 37.2, 28.9, 21.0; MS (CI, NH_3) 278 $(MNH_4)^+$ (1), 261 $(MH)^+$ (4), 243 (100), 199 (6), 153 (15); exact mass calcd for $C_{16}H_{20}O_3H$ 261.1490, obsd 261.1487.

(*R,*S**)-7-(1-Hydroxyhexyl)-6-methylene-1,4-dioxaspiro[5.4]decane (18b)**: flash chromatography (hexane/ethyl acetate (8:2)); IR (neat) 3463 (br), 2826 (br s), 1638 (s), 1456 (s) cm^{-1}; ^1H NMR δ 5.36 (s, 1 H), 4.95 (s, 1 H), 4.05–3.9 (m, 4 H), 3.86–3.75 (m, 1 H), 2.48–2.38 (m, 1 H), 2.22 (d, 1 H, J = 1.8 Hz), 1.96–1.5 (m, 8 H), 1.4–1.22 (m, 6 H), 0.9 (t, 3 H, J = 5.5 Hz); ^{13}C NMR δ 146.5, 110.9, 108.1, 71.3, 64.5, 64.1, 49.3, 37.1, 34.8, 31.9, 28.7, 25.4, 22.5, 21.1, 13.9; MS (CI, NH_3) 272 $(MNH_4)^+$ (22), 255 $(MH)^+$ (100), 224 (22), 155 (16), 136 (49); exact mass calcd for $C_{15}H_{26}O_3H$ 255.1960, obsd 255.1972.

7-(1-Hydroxycyclohexyl)-6-methylene-1,4-dioxaspiro[5.4]-decane (18c): flash chromatography (hexane/ethyl acetate (8:2)); IR (neat) 3476 (br), 3060 (s), 2857 (br s), 1625 (s), 1446 (s), 1184 (m), 921 (s) cm^{-1}; ^1H NMR δ 5.36 (d, 1 H, J = 2.3 Hz), 4.92 (d, 1 H, J = 2.3 Hz), 4.08–3.89 (m, 5 H), 2.48–2.4 (m, 1 H), 2.26–2.08 (m, 2 H), 2.0–1.86 (m, 2 H), 1.72–1.38 (m, 8 H), 1.36–1.12 (m, 4 H); ^{13}C NMR δ 145.1, 108.3, 71.7, 64.9, 63.6, 52.4, 37.9, 37.5, 36.2, 25.8, 25.7, 22.1, 21.8, 21.6; MS (CI, NH_3) 253 $(MH)^+$ (3), 235 (100), 154 (14), 136 (7), 111 (4); exact mass calcd for $C_{15}H_{24}O_3H$ 253.1803, obsd 253.1783.

7-(1-Hydroxy-3-phenyl-2-propenyl)-6-methylene-1,4-dioxaspiro[5.4]decane (18d) (mixture of two diastereoisomers in the ratio (4:6): flash chromatography (hexane/ethyl acetate (4:1)); IR (neat) 3460 (bs), 3082 (s), 3058 (s), 1599 (s) cm^{-1}; ^1H NMR δ 7.49–7.20 (m, 5 H), 6.63 (d, 1 H, J = 15.8 Hz), 6.25 (d × d, J = 15.8, 6 Hz, 1 H, minor diast (m)), 6.18 (d × d, J = 15.8, 6.4 Hz, 1 H, major diast (M)), 5.38 (s, 1 H, (M)), 5.27 (s, 1 H (m)), 5.08 (s, 1 H, (M)), 4.98 (s, 1 H, (m)), 4.66 (t, J = 5.5 Hz, 1 H, (m)), 4.51 (t, J = 8.4 Hz, 1 H, (M)), 4.03–3.8 (m, 5 H), 2.55 (m, 1 H), 2.2 (m, 1 H), 2.0–1.5 (m, 8 H); ^{13}C NMR δ 146.6, 145.8, 136.6, 136.4, 132.0, 131.0, 130.9, 129.8, 128.0, 127.0, 126.8, 126.0, 125.8, 110.3, 109.6, 107.9, 107.8, 72.6, 71.3, 63.9, 48.4, 37.2, 36.9, 28.6, 26.4, 21.0, 20.8; MS (CI, NH_3) 301 $(MH)^+$ (15), 283 (100), 221 (97), 197 (6), 154 (4); exact mass calcd for $C_{19}H_{24}O_3H$ 301.1803, obsd 301.1801.

3-(6-Methylene-1,4-dioxaspiro[5.4]dec-7-yl)-3-phenylpropionaldehyde (18e) (mixture of diastereoisomers ca. 95:5; determination by ^{13}C NMR): IR (neat) 2939 (s), 2884 (s), 1724 (s), 1452 (m) cm^{-1}; ^1H NMR δ 9.64 (s, 1 H), 7.3–7.1 (m, 5 H), 5.08 (s, 1 H), 4.62 (s, 1 H), 3.85 (m, 2 H), 3.65 (m, 3 H), 2.90–2.6 (m, 3 H), 1.9–1.6 (m, 5 H), 1.45 (m, 1 H); ^{13}C NMR δ 201.8, 147.1, 128.2, 128.0, 126.2, 109.9, 108.2, 64.4, 63.9, 47.6, 46.6, 40.3, 37.7, 29.4, 21.4; MS (EI, 70 eV) 207 (9), 154 (15), 153 (100), 125 (12); exact mass calcd for $C_{18}H_{22}O_3$ 286.1569, obsd 286.1561.

Typical Procedure for the One-Pot Preparation of an α-Methylene-γ-butyrolactone: Preparation of 4-(3-Cyanopropyl)-4,5-dihydro-3-methylene-5-phenyl-2-(3*H*)-furanone (20d). A THF solution of 4-iodobutyronitrile (1.38 g, 7.1 mmol) in THF (4 mL) was added at 25 °C to zinc dust (1.3 g, 20 mmol pretreated with 1,2-dibromethane (0.3 g, 1.5 mmol)) and Me_3SiCl (0.1 mL)).[33] An exothermic reaction occurred, and the reaction mixture was stirred 1.5 h at 40 °C. The excess of zinc was allowed to settle, and the supernatant solution was added to a solution of CuCN (0.635 g, 7.1 mmol) and LiCl (0.6 g, 14 mmol) in THF (10 mL) at −10 °C. After 5 min, the reaction mixture was cooled to −60 °C and ethyl propiolate (0.588 g, 6 mmol) was added and stirred for 4 h between −60 and −40 °C. A solution of PhCHO (0.53 g, 5 mmol) in THF (2 mL) was added, followed by the dropwise addition of a THF solution of (iodomethyl)zinc iodide (ca. 16 mmol) prepared from CH_2I_2 (5.4 g, 20 mmol) and zinc foil (1.35 g, 20 mmol) in THF (10 mL) at 25–26 °C (3 h). The reaction mixture was allowed to warm to 0 °C and was stirred 0.5 h at this temperature. After the usual workup, the residual oil was purified by flash chromatography affording **20d** as a cis–trans mixture (90:10; 0.9 g; 75% yield). All experiments described in Table II were performed on the same scale and with similar reaction conditions.

Analytical data of the α-methylene-γ-butyrolactones **20a–q** described in Table II.

4-Butyl-5-phenyl-4,5-dihydro-3-methylene-2(3*H*)-furanone (20a) (0.815 g; 79% yield; cis/trans (85:15)). Prepared from the reaction of BuCu(CN)Li (8 mmol), ICH_2ZnI (16 mmol), benzaldehyde (477 mg, 4.5 mmol), and ethyl propiolate (686 mg, 7 mmol): flash chromatography (hexane/ethyl acetate (9:1)); IR (neat) 3035 (s), 2958 (s), 2931 (s), 2872 (br s), 1768 (s), 1680 (s), 1456 (s), 1265 (m), 1130 (m), 1000 (m), 700 (s) cm^{-1}; ^1H NMR δ 7.4–7.18 (m, 5 H), 6.35 (d, 1 H, J = 2.5 Hz), 5.62 (d, 1 H, J = 2.5 Hz (trans isomer)), 5.6–5.5 (m, 2 H), 5.14 (m, 2 H, trans isomer), 3.3–3.2 (m, 1 H), 3.03–2.95 (m, trans isomer), 1.74–1.7 (m, 6 H, trans isomer), 1.4–0.95 (t, 3 H, J = 5.5 Hz); ^{13}C NMR δ 169.9, 169.6, 139.3, 139.0, 138.6, 135.7, 128.3, 128.1, 127.9, 127.9, 125.8, 125.4, 121.5, 121.1, 83.5, 81.6, 47.0, 43.9, 32.8, 28.1, 27.9, 22.0, 21.8, 13.3, 13.2; MS (EI) 230 (7), 173 (3) 124 (65), 96 (54), 82 (79), 54 (100); exact mass calcd for $C_{15}H_{18}O_2$ 230.1306, obsd 230.1318.

4-Butyl-5-cyclohexyl-4,5-dihydro-3-methylene-2(3*H*)-furanone (20b) (0.896 g; 76%; cis/trans (80:20)). Prepared from the reaction of BuCu(CN)Li (87.1 mmol), ICH_2ZnI (16 mmol), cyclohexanecarboxaldehyde (0.56 g, 5.0 mmol), and ethyl propiolate (0.59 g, 6.0 mmol): flash chromatography (hexane/ethyl acetate (9:1)); IR (neat) 2928 (br s), 1766 (s), 1664 (s), 1406 (s), 1190 (m), 1056 (m) cm^{-1}; ^1H NMR δ 6.25 (d, 1 H, J = 2.4 Hz), 5.59 (d, 1 H, J = 2.0 Hz), 4.0 (dd, 1 H, J = 3.2, 5.7 Hz), 2.84–2.74 (m, 1 H), 1.85–1.71 (m, 3 H), 1.70–1.6 (m, 2 H), 1.59–1.4 (m, 3 H), 1.39–1.28 (m, 4 H), 1.27–0.98 (m, 5 H), 0.96–0.84 (m, 3 H); ^{13}C NMR δ 170.0, 139.6, 121.2, 86.8, 42.7, 41.4, 34.9, 28.4, 28.0, 27.2, 26.0, 25.7, 25.5, 22.3, 13.5; MS (EI) 236 (14), 207 (22), 181 (6), 170 (8), 153 (71), 124 (100); exact mass calcd for $C_{15}H_{24}O_2$ 236.1776, obsd 236.1757.

4-Benzyl-4,5-dihydro-3-methylene-5-phenyl-2(3*H*)-furanone (20c) (1.03 g; 78% yield; cis/trans (92:8)). Prepared from the reaction of $PhCH_2Cu(CN)ZnBr{\cdot}2LiCl$ (7.1 mmol), ICH_2ZnI (16 mmol), benzaldehyde (0.53 g, 5.0 mmol), and ethyl propiolate (0.59 g, 6.0 mmol): flash chromatography (hexane/ethyl acetate (8:2)); IR (neat) 3063 (s), 1760 (s), 1662 (s), 1450 (s) cm^{-1}; ^1H NMR δ 7.4–7.3 (m, 3 H), 7.29–7.1 (m, 5 H), 6.98–6.88 (m, 2 H), 6.3 (d, trans isomer), 6.24 (d, 1 H, J = 2.3 Hz), 5.66 (d, 1 H, J = 7.2 Hz), 5.4 (d, trans), 5.24 (d, trans isomer), 5.02 (d, 1 H, J = 2.1 Hz), 3.68–3.55 (m, 1 H), 2.36 (dd, 2 H, J = 10, 7 Hz); ^{13}C NMR δ 170.0, 137.7, 137.4, 137.1, 135.8, 129.0, 128.9, 128.5, 128.4, 128.3, 128.1, 126.8, 126.3, 126.1, 125.2, 122.8, 82.9, 81.4, 48.8, 45.2, 40.2, 35.5; MS (EI) 264 (14), 219 (9), 172 (17), 158 (68), 129 (44), 91 (100); exact mass calcd for $C_{18}H_{16}O_2$ 264.1150, obsd 264.1151.

4-(3-Cyanopropyl)-4,5-dihydro-3-methylene-5-phenyl-2-(3*H*)-furanone (20d) (0.90 g; 75% yield; cis/trans (90:10)). Prepared from the reaction of $NC(CH_2)_3Cu(CN)ZnI{\cdot}2LiCl$ (7.1 mmol), $IZnCH_2I$ (16 mmol), benzaldehyde (0.53 g, 5.0 mmol), and ethyl propiolate (0.59 g, 6.0 mmol): flash chromatography (hexane/ethyl acetate (7:3)); IR (neat) 3065 (s), 3035 (s), 2941 (br s), 2246 (s), 1750 (s), 1662 (s) cm^{-1}; ^1H NMR δ 7.43–7.1 (m, 5 H), 6.38 (d, 1 H, J = 2.3 Hz), 5.67 (d, 1 H, J = 2.1 Hz), 5.58 (d, 1 H, J = 7.2 Hz), 3.35–3.2 (m, 1 H), 2.41–2.3 (m, 1 H), 2.15 (t, 2 H, J = 6.8 Hz), 1.75–1.5 (m, 1 H), 1.5–1.2 (m, 2 H), 1.2–1.05 (m, 1 H); ^{13}C NMR δ 169.3, 138.1, 137.1, 135.1, 128.5, 128.4, 128.3, 128.1, 127.9, 127.8, 127.6, 125.6, 125.5, 125.2, 125.0, 124.9, 122.1, 118.5, 83.2, 81.0, 77.6, 46.2, 43.1, 33.3, 31.5, 28.2, 27.8, 23.4, 21.8, 21.7, 16.4, 16.2, 16.0; MS (EI) 241 (15), 135 (53), 120 (26), 106 (100); exact mass calcd for $C_{15}H_{15}O_2N$ 241.1102, obsd 241.1085.

4,5-Dihydro-3-methylene-4-(3-octynyl)-5-phenyl-2(3*H*)-furanone (20e) (1.07 g; 76% yield; cis/trans (95:5)). Prepared from the reaction of $BuC{\equiv}C(CH_2)_2Cu(CN)ZnI{\cdot}2LiCl$ (7.1 mmol), $IZnCH_2I$ (16 mmol), benzaldehyde (0.53 g, 5.0 mmol), and ethyl propiolate (0.59 g, 6.0 mmol): flash chromatography (hexane/ethyl acetate (8:2)); IR (neat) 3034 8s), 2956 (s), 2930 (s), 2871 (br s), 1769 (s), 1662 (s) cm^{-1}; ^1H NMR δ 7.42–7.2 (m, 5 H), 6.37 (d, 1 H, J = 2.2 Hz), 5.71 (d, 1 H, J = 2.0 Hz), 5.65 (d, 1 H, J = 7.2 Hz), 3.6–3.5 (m, 1 H), 2.2–2.1 (m, 2 H), 2.1–2.0 (m, 2 H), 1.5–1.1 (m, 6 H), 0.9 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 169.7, 138.7, 135.8, 128.3, 128.2, 125.9, 121.8, 81.7, 81.5, 77.8, 42.8, 30.9, 27.9, 21.7, 18.1, 15.4, 13.3; MS (EI) 282 (5), 253 (6), 240 (20), 225 (14), 191 (27), 176 (47), 147 (85), 133 (54), 117 (48), 105 (100); exact mass calcd for $C_{19}H_{22}O_2$ 282.1619, obsd 282.1622.

4-(3-Carbethoxypropyl)-4,5-dihydro-3-methylene-5-phenyl-2(3*H*)-furanone (20f) (1.22 g; 85% yield, cis/trans (95:5)). Prepared from the reaction of $Et_2OC(CH_2)_3Cu(CN)ZnI{\cdot}2LiCl$ (7.1 mmol), ICH_2ZnI (16 mmol), benzaldehyde (0.53 g, 5 mmol), and ethyl propiolate (0.59 g, 6 mmol): flash chromatography (hexane/ethyl acetate (8:2)); IR (neat) 2980 (s), 2939 (s), 1770 (s), 1729 (s), 1662 (s) cm^{-1}; ^1H NMR δ 7.45–7.2 (m, 5 H), 6.38 (d, 1 H, J = 2.4 Hz), 5.68 (8d, 1 H, J = 2.2 Hz), 5.6 (d, 1 H, J = 7.3 Hz), 4.09 (q, 2 H, J = 7.0 Hz), 3.3–3.2 (m, 1 H), 2.15 (t, 2 H, J = 7.3 Hz), 1.68–1.55 (m, 1 H), 1.53–1.36 (m, 1 H), 1.32–1.22 (m, 1 H), 1.2 (t, 3 H, J = 7.2 Hz), 1.1–0.96 (m, 1 H); irradiation at 3.25 ppm (HC(4)) leads to an NOE enhancement for the signal at 5.6 ppm (HC(5)) of 20%; ^{13}C NMR δ 172.3, 169.7, 138.7, 135.6, 128.2, 128.1, 125.9, 121.5, 81.4, 59.8, 43.9, 33.4, 28.1, 21.5, 13.8; MS (CI, NH_3) 306 $(MNH_4)^+$ (100), 289 $(MH)^+$ (10), 171 (78), 136 (36); exact mass calcd for $C_{17}H_{20}O_4H$ 289.1439, obsd 289.1435.

4-(3-Carbethoxypropyl)-4,5-dihydro-3-methylene-5-pentyl-2(3*H*)-furanone (20g) (0.88 g, 70% yield; cis/trans (1:1)). Prepared from the reaction of $EtO_2C(CH_2)_3Cu(CN)ZnI{\cdot}2LiCl$ (7.5 mmol), ICH_2ZnI (16 mmol), hexanal (500 mg, 5 mmol), and ethyl propiolate (0.75 g, 7.5 mmol): flash chromatography

(hexane/ether (9:1)); IR (neat) 2950 (s), 2870 (s), 1765 (s), 1663 (m); ^{1}H NMR δ 6.38 (d, J = 3 Hz, 1 H), 5.62 (d, J = 3 Hz, 1 H), 4.25–4.1 (m, 3 H), 2.65 (m, 1 H), 2.35 (t, J = 7 Hz, 3 H), 1.8–1.55 (m, 6 H), 1.4–1.2 (m, 9 H), 0.89 (t, J = 7 Hz, 3 H); ^{13}C NMR δ 172.5, 139.3, 139.1, 121.6, 120.4, 82.8, 80.6, 60.0, 44.1, 42.8, 36.2, 35.8, 33.7, 33.6, 33.4, 33.2, 33.1, 31.3, 31.2, 31.0, 29.9, 26.7, 26.3, 25.0, 24.5, 23.9, 23.2, 22.2, 21.9, 21.5, 13.9, 13.6; MS (EI, 70 eV) 282 (M^+, 2), 225 (11), 182 (13), 179 (13), 166 (17), 165 (100); exact mass calcd for $C_{16}H_{26}O_4$ 282.1831, obsd 282.1830.

4-(3-Carbethoxypropyl)-3-methylene-1-oxaspiro[4.5]-2-decanone (20h) (0.952 g; 68% yield). Prepared from the reaction of $EtO_2C(CH_2)_3Cu(CN)ZnI\cdot 2LiCl$ (7.1 mmol), $IZnCH_2I$ (16 mmol), cyclohexanone (0.49 g, 5 mmol), and ethyl propiolate (0.59 g, 6 mmol): flash chromatography (hexane/ethyl acetate (8:2)); IR (neat) 2977 (s), 2937 (s), 2863 (br s), 1760 (s), 1662 (s), 1449 (s), 1373 (s), 1270 (m), 1109 (s), 945 (s) cm^{-1}; ^{1}H NMR δ 6.25 (d, 1 H, J = 2.7 Hz), 5.58 (d, 1 H, J = 2.4 Hz), 4.14 (q, 2 H, J = 7.2 Hz), 2.64–2.54 (m, 1 H), 2.37 (t, 2 H, J = 7.1 Hz), 1.89–1.4 (m, 14 H), 1.29 (t, 3 H, J = 7.2 Hz); ^{13}C NMR δ 172.3, 168.9, 140.1, 120.4, 85.2, 59.8, 48.9, 36.9, 33.6, 31.0, 27.3, 24.6, 22.3, 22.0, 21.3, 13.7; MS (EI) 280 (6), 262 (7), 189 (8), 182 (44), 154 (100); exact mass calcd for $C_{16}H_{24}O_4$ 280.1674, obsd 280.1663.

(4*R,5*R**)-4-(3-Carbethoxypropyl)-4,5-dihydro-5-methyl-3-methylene-5-phenyl-2(3*H*)-furanone (20i)** (0.82 g, 68% yield, cis/trans (90:10)). Prepared from the reaction of $EtO_2C(CH_2)_3Cu(CN)ZnI\cdot 2LiCl$ (7.5 mmol), ICH_2ZnI (16 mmol), acetophenone (0.6 g, 4 mmol), and ethyl propiolate (0.8 g, 8 mmol): flash chromatography (hexane/ethyl acetate (8:2)); IR (neat) 2979 (s), 2937 (s), 2871 (br s), 1765 (s), 1731 (s), 1662 (s) cm^{-1}; ^{1}H NMR δ 7.42–7.28 (m, 5 H), 6.35 (d, 1 H, J = 2.0 Hz), 5.65 (d, 1 H, J = 1.7 Hz), 4.6 (q, 2 H, J = 7.2 Hz), 2.98–2.9 (m, 1 H), 2.01 (t, 2 H, J = 7.4 Hz), 1.75 (s, 3 H), 1.65–1.4 (m, 2 H), 1.2 (t, 3 H, J = 7.2 Hz), 1.1–0.8 (m, 2 H); ^{13}C NMR δ 172.4, 169.1, 140.0, 139.6, 128.2, 128.0, 127.3, 124.8, 123.8, 122.1, 86.7, 59.8, 50.4, 33.5, 29.6, 28.8, 21.5, 13.8; MS (EI) 302 (6), 284 (26), 199 (28), 182 (83), 154 (100); exact mass calcd for $C_{18}H_{22}O_4$ 302.1518, obsd 302.1522.

4-(4-Chlorobutyl)-4,5-dihydro-5-methyl-3-methylene-5-phenyl-2(3*H*)-furanone (20j) (1.14 g; 82% yield; cis/trans (100:0)). Prepared from the reaction of $Cl(CH_2)_4Cu(CN)ZnI\cdot 2LiCl$ (7.1 mmol), $IZnCH_2I$ (16 mmol), acetophenone (0.6 g; 5 mmol), and ethyl propiolate (0.59 g, 6 mmol): flash chromatography (hexane/ethyl acetate (8:2)); IR (neat) 3061 (s), 3029 (s), 1087 (m) cm^{-1}; ^{1}H NMR δ 7.43–7.25 (m, 5 H), 6.35 (d, 1 H, J = 2.0 Hz), 5.65 (d, 1 H, J = 1.8 Hz), 3.39 (t, 2 H, J = 6.5 Hz), 2.99–2.89 (m, 1 H), 1.76 (s, 3 H), 1.65–1.5 (m, 2 H), 1.48–1.22 (m, 2 H), 1.08–0.9 (m, 2 H); ^{13}C NMR δ 169.1, 140.0, 139.7, 128.0, 127.3, 124.8, 122.4, 86.7, 50.4, 44.1, 31.9, 29.3, 28.9, 23.2; MS (EI) 278 (3), 263 (6), 187 (6), 158 (65), 123 (22), 105 (37), 54 (100); exact mass calcd for $C_{16}H_{19}{}^{35}ClO_2$ 278.1073, obsd 278.1073.

4-Carbethoxy-4-(3-carbethoxypropyl)-4,5-dihydro-3-methylene-5-(2-phenethyl)-2(3*H*)-furanone (20k) (1.66 g; 86% yield; cis/trans (85:15)). Prepared from the reaction of $Et_2OC(CH_2)_3Cu(CN)ZnI\cdot 2LiCl$ (7.1 mmol), $IZnCH_2I$ (16 mmol), 3-phenylpropionaldehyde (0.67 g, 5 mmol), and diethyl acetylenedicarboxylate (1.02 g, 60 mmol): flash chromatography (hexane/ethyl acetate (8:2)); IR (neat) 3062 (s), 3027 (s), 2980 (s), 1771 (s), 1736 (s), 1728 (s), 1661 (s) cm^{-1}; ^{1}H NMR δ 7.35–7.16 (m, 5 H), 6.5 (s, 1 H), 6.48 (s, trans isomer), 5.96 (s, trans isomer), 5.85 (s, 1 H), 4.3 (q, trans isomer), 4.2 (q, 2 H, J = 7.1 Hz), 4.1 (q, 2 H, J = 7.1 Hz), 3.3–2.9 (m, 1 H), 2.8–2.65 (m, 1 H), 2.34–2.24 (m, 2 H), 2.06–1.7 (m, 4 H), 1.66–1.4 (m, 2 H), 1.35–1.2 (m, 7 H); ^{13}C NMR δ 172.2, 172.1, 170.2, 169.9, 168.5, 168.1, 140.3, 140.1, 137.2, 136.8, 128.3, 128.3, 128.1, 125.9, 124.8, 124.5, 82.0, 81.0, 61.5, 61.3, 60.0, 56.0, 55.4, 34.7, 33.7, 33.6, 33.2, 32.0, 31.6, 31.4, 31.3, 19.4, 19.1, 13.8, 13.7, 13.7; MS (EI) 388 (8), 370 (5), 375 (4), 342 (13), 225 (13), 181 (16), 117 (100); exact mass calcd for $C_{22}H_{28}O_6$ 388.1885, obsd 388.1871.

(4*R,5*S**)-4-(3-Carbethoxypropyl)-4-carbethoxy-4,5-dihydro-3-methylene-5-phenyl-2(3*H*)-furanone (20l)** (1.21 g, 96% yield; diastereomeric ratio 85:15). Prepared from $EtO_2C(CH_2)_3Cu(CN)ZnI\cdot 2LiCl$ (7.5 mmol), ICH_2ZnI (16 mmol), benzaldehyde (371 mg, 3.5 mmol), and diethyl acetylenedicarboxylate (0.85 g, 5 mmol): flash chromatography (hexane/ethyl acetate (7:3)); IR (neat) 3064 (s), 3032 (s), 1774 (s), 1764 (s), 1722 (s), 1660 (s), cm^{-1}; ^{1}H NMR δ 7.4–7.18 (m, 5 H), 6.63 (s, 1 H), 6.54 (s, trans isomer), 6.0 (s, trans isomer), 5.95 (s, trans isomer), 5.92 (s, 1 H), 5.37 (s, 1 H), 4.3 (q, trans isomer), 4.18 (q, 2 H, J = 7.2 Hz), 4.0 (q, trans isomer), 3.68 (dq, 2 H, J = 2.1, 7.2 Hz), 2.39 (t, 2 H, J = 7.1 Hz), 2.3–2.18 (m, trans isomer), 2.08–1.9 (m, 2 H), 1.82–1.66 (m, 1 H), 1.62–1.48 (m, 1 H), 1.35 (t, trans isomer), 1.27 (t, 3 H, J = 7.1 Hz), 1.19 (t, trans isomer), 0.89 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 172.1, 171.8, 170.3, 169.0, 168.6, 167.8, 132.2, 135.6, 135.6, 134.4, 128.4, 128.3, 127.9, 127.8, 126.3, 125.9, 125.5, 125.0, 84.0, 82.3, 61.7, 60.8, 59.9, 59.6, 58.1, 56.8, 35.2, 33.5, 33.1, 32.9, 19.0, 18.7, 13.7, 13.7, 13.6, 12.9; MS (CI, NH_3) 378 $(MNH_4)^+$ (100), 361 $(MH)^+$ (2.3), 255 (2), 136 (48); exact mass calcd for $C_{20}H_{24}O_6H$ 361.1651; obsd 361.1642.

(4*R,5*S**)-4-Carbethoxy-4-(3-cyanopropyl)-5-cyclohexyl-4,5-dihydro-3-methylene-2(3*H*)-furanone (20m)** (1.48 g; 93% yield; cis/trans (95:5)). Prepared from the reaction of $NC(CH_2)_3Cu(CN)ZnI\cdot 2LiCl$ (7.1 mmol), $IZnCH_2I$ (16 mmol), cyclohexanecarboxaldehyde (0.56 g, 5 mmol), and diethyl acetylenedicarboxylate (1.02 g, 6 mmol): flash chromatography (hexane/ethyl acetate (7:3)); IR (neat) 2932 (br s), 2857 (s), 1767 (s), 1724 (s), 1660 (s), 1451 (s) cm^{-1}; ^{1}H NMR δ 6.48 (s, 1 H), 5.96 (s, 1 H), 4.29 (q, 2 H, J = 7.1 Hz), 6.16 (d, 1 H, J = 4.5 Hz), 2.42–2.32 (m, 2 H), 2.3–2.18 (m, 1 H), 1.97–1.84 (m, 1 H), 1.8–1.58 (m, 7 H), 1.57–1.42 (m, 1 H), 1.37–1.05 (m, 7 H), 0.9–0.82 (m, 1 H); ^{13}C NMR δ 169.5, 167.9, 136.3, 123.4, 118.3, 86.5, 61.0, 54.7, 39.8, 35.3, 29.1, 26.6, 25.3, 25.2, 24.8, 19.4, 16.2, 13.3; MS (EI) 319 (10), 301 (15), 273 (41), 207 (90), 179 (100), 164 (52); exact mass calcd for $C_{18}H_{24}O_4N$ 319.1783; obsd 319.1786.

4,4-Dibutyl-4,5-dihydro-3-methylene-5-phenyl-2(3*H*)-furanone (20n) (1.15 g, 80% yield). Prepared from the reaction of $BuCu(CN)Li$ (8 mmol), ICH_2ZnI (16 mmol), benzaldehyde (535 mg, 5 mmol), and ethyl heptynoate (1.08 g, 7 mmol): flash chromatography (hexane/ethyl acetate (9:1)); IR (neat) 3034 (s), 2957 (s), 1768 (s), 1664 (s), 1457 (s) cm^{-1}; ^{1}H NMR δ 7.4–7.2 (m, 5 H), 6.4 (s, 1 H), 5.45 (s, 1 H), 5.3 (s, 1 H), 1.84–1.7 (m, 1 H), 1.65–1.55 (m, 1 H), 1.4–1.2 (m, 6 H), 1.1–0.8 (m, 7 H), 0.66 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 169.9, 142.0, 136.1, 128.0, 127.9, 126.3, 120.9, 85.9, 49.7, 35.3, 33.5, 25.5, 24.7, 22.8, 22.5, 13.5, 13.2; MS (EI) 286 (11), 180 (90), 152 (63), 138 (46), 68 (100); exact mass calcd for $C_{19}H_{26}O_2$ 286.1932, obsd 286.1936.

4-Butyl-4-cyclohexyl-4,5-dihydro-3-methylene-5-phenyl-2(3*H*)-furanone (20o) (entry 15 of Table II) (0.936 g, 60% yield; cis/trans (75:25)). Prepared from the reaction of c-HexCu(CN)ZnI·2LiCl (7.1 mmol), $IZnCH_2I$ (16 mmol), benzaldehyde (0.53 g, 5 mmol), and ethyl 2-heptynoate (0.924 g, 6 mmol): flash chromatography (hexane/ethyl acetate (9:1)); IR (neat) 2956 (s), 2929 (s), 2871 (br s), 1772 (s), 1711 (s) cm^{-1}; ^{1}H NMR δ 7.4–7.3 (m, 3 H), 7.22–7.15 (m, 2 H), 6.47 (s, 1 H, trans isomer), 6.46 (s, 1 H, cis isomer), 5.55 (s, 1 H, trans isomer), 5.49 (s, 1 H, cis isomer), 5.4 (s, 1 H, trans isomer), 5.36 (s, 1 H, cis isomer), 1.9–1.78 (m, 3 H), 1.54–1.32 (m, 3 H), 1.3–1.09 (m, 3 H), 1.08–0.82 (m, 4 H), 0.8–0.67 (m, 1 H), 0.6 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 170.9, 168.5, 141.2, 140.0, 137.5, 128.3, 128.1, 128.0, 127.6, 127.3, 125.7, 122.3, 121.6, 86.4, 83.5, 53.2, 52.1, 44.9, 42.3, 32.9, 32.2, 28.2, 27.6, 26.9, 26.8, 26.4, 26.2, 26.1, 26.0, 25.9, 25.0, 23.4, 22.7, 13.8, 13.3; MS (EI) 312 (15), 230 (30), 206 (100), 185 (65); exact mass calcd for $C_{21}H_{28}O_2$ 312.2089, obsd 312.2084.

4-Butyl-4-cyclohexyl-4,5-dihydro-3-methylene-5-phenyl-2(3*H*)-furanone (20o) (entry 16 of Table II) (1.04 g; 67% yield; cis/trans (98:2)). Prepared from the reaction of $BuCu(CN)Li$ (7.1 mmol), $IZnCH_2I$ (16 mmol), benzaldehyde (0.53 g, 5 mmol), and ethyl 3-cyclohexyl propiolate (1.08 g, 6 mmol): flash chromatography (hexane/ethyl acetate (9:1)); ^{1}H NMR δ 7.4–7.3 (m, 3 H), 7.22–7.16 (m, 2 H), 6.46 (s, 1 H), 5.49 (s, 1 H), 1.9–1.78 (m, 3 H), 1.75–1.6 (m, 3 H), 1.56–1.45 (m, 1 H), 1.35–0.84 (m, 9 H), 0.8–0.67 (m, 1 H), 0.6 (t, 3 H, J = 7.0 Hz); ^{13}C NMR δ 171.1, 140.9, 137.3, 128.3, 127.9, 127.3, 122.6, 86.6, 51.9, 44.5, 32.0, 27.4, 26.7, 26.2, 26.1, 26.0, 24.8, 22.6, 13.2.

4-Butyl-4,5-dihydro-4,5-diphenyl-3-methylene-2(3*H*)-furanone (20p) (entry 17 of Table II) (1.15 g; 78% yield; cis/trans (60:40)). Prepared from the reaction of $PhCu(CN)Li$ (7.1 mmol), $IZnCH_2I$ (16 mmol), benzaldehyde (0.53 g, 5 mmol), and ethyl 2-heptynoate (0.924 g, 6 mmol). Flash chromatography (hexane/ethyl acetate (9:1)): IR (neat) 3091 (s), 3062 (s), 3033 (s), 2956 (br s), 1762 (s), 1657 (s), 1602 (s), 1498 (s) cm^{-1}; ^{1}H NMR δ 7.46–7.24 (m, 10 H), 7.1–6.9 (m, 6 H), 6.89–6.8 (m, 2 H), 6.79–6.7 (m, 2 H), 6.69 (s, 1 H), 6.6 (s, 1 H), 5.61 (s, 1 H), 5.51 (s, 1 H), 5.45 (s, 1 H), 5.39 (s, 1 H), 2.4–2.29 (, 1 H), 2.2–2.16 (m, 1 H), 1.5–1.2

(m, 6 H), 1.19–1.02 (m, 3 H), 0.95–0.8 (m, 4 H), 0.78 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 170.1, 169.1, 142.9, 140.8, 139.5, 138.5, 136.4, 133.8, 128.3, 128.0, 127.9, 127.8, 127.6, 127.5, 127.3, 127.2, 127.1, 126.9, 126.1, 125.7, 124.4, 123.4, 88.9, 88.0, 56.2, 55.2, 37.5, 31.1, 30.9, 25.6, 24.8, 22.6, 22.4, 13.6, 13.4; MS (CI, NH_3) 324 $(MNH_4)^+$ (56), 307 $(MH)^+$ (95), 289 (8), 229 (10), 200 (100), 91 (11); exact mass calcd for $C_{21}H_{22}O_2H$ 307.1698, obsd 307.1707.

4-Butyl-4,5-dihydro-4,5-diphenyl-3-methylene-2(3*H*)-furanone (20p) (entry 18 of Table II) (1.30 g; 85% yield, cis/trans (98:2)). Prepared from the reaction of BuCu(CN)Li (7.1 mmol), $IZnCH_2I$ (10 mmol), benzaldehyde (0.53 g, 5 mmol), and ethyl 3-phenyl propiolate (1.04 g, 6 mmol): flash chromatography (hexane/ethyl acetate (9:1)); ^{1}H NMR δ 7.46–7.25 (m, 8 H), 7.0–6.92 (m, 2 H), 6.6 (s, 1 H), 5.52 (s, 1 H), 5.45 (s, 1 H), 1.5–1.24 (m, 2 H), 1.2–1.0 (m, 3 H), 0.96–0.84 (m, 1 H), 0.75 (t, 3 H, J = 7.0 Hz); ^{13}C NMR δ 169.4, 143.1, 139.8, 133.9, 128.4, 128.0, 127.9, 127.7, 127.1, 125.9, 123.6, 89.1, 55.4, 31.1, 25.0, 22.5, 13.4.

4-Methylene-2-oxa-1-phenylbicyclo[3.3.0]-3-octanone (26a) (0.81 g, 76% yield). Prepared from the reaction of $PhC(O)(CH_2)_3$-$Cu(CN)ZnI{\cdot}2LiCl$ (7 mmol), $Zn(CH_2I)_2$ (16 mmol), and ethyl propiolate (0.49 g, 5 mmol): flash chromatography (hexane/ethyl acetate (9:1)); IR (neat): 3061 (s), 3028 (s), 2961 (br s), 2871 (s), 1762 (s), 1661 (s), 1438 (s), 1403 (s) cm^{-1}; ^{1}H NMR δ 7.4–7.24 (m, 5 H), 6.28 (d, 1 H, J = 2.3 Hz), 5.65 (d, 1 H, J = 2.0 Hz), 3.46 (dd, 1 H, J = 1.4 Hz, 8.8 Hz), 2.45–2.22 (m, 2 H), 2.12–1.98 (m, 1 H), 1.97–1.7 (m, 3 H); ^{13}C NMR δ 169.9, 142.9, 140.6, 128.2, 127.3, 124.2, 122.5, 94.1, 51.5, 41.9, 36.8, 24.6; MS (EI) 214 (20), 185 (3), 144 (7), 120 (17), 109 (68), 105 (100); exact mass calcd for $C_{14}H_{14}O_2$ 214.0993, obsd 214.0977.

5-Carbethoxy-4-methylene-2-oxa-1-phenylbicyclo[3.3.0]-3-octanone (26b) (1.18 g, 83% yield). Prepared from the reaction of $PhC(O)(CH_2)_3Cu(CN)ZnI{\cdot}2LiCl$ (7 mmol), $Zn(CH_2I)_2$ (16 mmol), and diethyl acetylenedicarbonylate (0.85 g, 5 mmol): flash chromatography (hexane/ethyl acetate (9:1)); IR (neat) 3031 (s), 2977 (s), 2903 (br s), 1771 (s), 1657 (s) cm^{-1}; ^{1}H NMR δ 7.36–7.22 (m, 5 H), 6.45 (s, 1 H), 5.7 (s, 1 H), 3.65–3.54 (m, 1 H), 3.44–3.32 (m, 1 H), 2.9–2.78 (m, 1 H), 2.45–2.35 (m, 2 H), 2.1–1.95 (m, 2 H), 1.8–1.64 (m, 1 H), 0.69 (t, 3 H, J = 7.2 Hz); ^{13}C NMR δ 170.1, 168.4, 140.3, 139.8, 127.6, 127.5, 124.8, 123.7, 95.7, 65.0, 60.8, 41.0, 39.8, 22.7, 12.8; MS (EI) 286 (68), 258 (10), 212 (12), 166 (90), 138 (55), 119 (20), 105 (100); exact mass calcd for $C_{17}H_{18}O_4$ 286.1205, obsd 286.1214.

Iodolysis Experiments. (*E*)-Ethyl 3-Cyclohexyl-2-iodo-2-heptenoate (0.91 g; 89% yield; cis/trans (100:0)). Prepared from the reaction of BuCu(CN)Li (4.5 mmol), ethyl 3-cyclohexylpropiolate (0.54 g, 3 mmol), and iodine (0.762 g, 6 mmol): flash chromatography (hexane/ether (49:1)); IR (neat) 2857 (br s), 1715 (s), 1600 (s), 1466 (m), 1248 (m), 1137 (s), 1095 (s), 1032 (s) cm^{-1}; ^{1}H NMR δ 4.25 (q, 2 H, J = 7.0 Hz), 2.74–2.6 (m, 1 H), 2.28–2.18 (m, 2 H), 1.8–1.7 (m, 2 H), 1.69–1.58 (m, 3 H), 1.52–1.1 (m, 12 H), 0.96 (t, 3 H, J = 7.0 Hz); ^{13}C NMR δ 166.3, 158.0, 84.4, 61.4, 45.1, 36.5, 31.2, 29.9, 26.2, 25.7, 23.0, 13.8, 13.6; MS (EI) 364 (10), 307 (17), 261 (11), 237 (26), 191 (70); exact mass calcd for $C_{15}H_{25}IO_2$ 364.0899, obsd 364.0908.

Ethyl 3-Cyclohexyl-2-iodo-2-heptenoate (1.82 g; 83% yield; cis/trans (75:25)). Prepared from the reaction of c-HexCu(CN)-$ZnI{\cdot}2LiCl$ (7.5 mmol), ethyl 2-heptynoate (0.92 g, 6 mmol), and iodine (1.52 g, 12 mmol): flash chromatography (hexane/ether (49:1)); ^{1}H NMR δ 4.25 (q, 2 H, J = 7.2 Hz, merged with trans isomer ester CH_2), 2.69–2.58 (m, 1 H), 2.38–2.28 (m, 2 H), 2.26–2.18 (m, trans isomer), 1.88–1.76 (m, 3 H), 1.75–1.6 (m, 3 H), 1.49–1.15 (m, 12 H), 0.9 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 166.5, 166.1, 158.6, 158.1, 84.8, 84.5, 61.5, 51.2, 45.1, 36.5, 32.0, 31.2, 31.0, 30.0, 29.9, 26.2, 26.1, 25.8, 25.7, 23.0, 22.9, 13.8, 13.7, 13.6.

General Procedure for the One-Pot Conversion of Copper Acetylides to Homopropargylic Alcohols Using (Iodomethyl)zinc Iodide (Table III).[12] A three-neck flask, equipped with a thermometer, septum cap, magnetic stirring bar, and argon outlet was charged with the alkyne (5 mmol) and THF (5 mL). A solution of butyllithium (3.1 mL, 5 mmol, 1.6 M in hexane) was added, via syringe, at –60 °C; the reaction was warmed to 0 °C and then cooled back to –60 °C. To the resulting lithium acetylide was added a THF solution (5 mL) of CuCN (450 mg, 5 mmol) and LiCl (420 mg, 10 mmol) at –60 °C, via syringe. The reaction was then warmed to 0 °C and then cooled back to –60 °C. To the resulting copper acetylide was added successively the aldehyde or ketone (3 mmol) and (iodomethyl)zinc iodide (4) (14.3 mL, 20 mmol, 1.4 M in THF) at –60 °C, via syringe. The reaction was then allowed to warm to 0 °C carefully (a very exothermic reaction occurs at about –10 °C, and a dry ice/acetone bath was necessary to keep the temperature below 0 °C) and stirred at this temperature for 0.5 h. The reaction was then worked up as described above, and purification by flash chromatography afforded the pure product. All the reaction described in Table III were performed on the same scale.

Analytical data of products **28a–f** described in Table III.

1-Phenyl-4-(trimethylsilyl)-3-butyn-1-ol[12,53] **(28a).** A clear oil (620 mg, 95%) was obtained from (trimethylsilyl)acetylene (490 mg, 5 mmol) and benzaldehyde (320 mg, 3 mmol): chromatography solvent, 10% ethyl acetate in hexane; IR (neat) 3374 (br), 2959 (m), 2900 (m), 2178 (s), 1454 (m) cm^{-1}; ^{1}H NMR δ 7.40–7.26 (m, 5 H), 4.86–4.82 (m, 1 H), 2.66 (d, J = 6.2 Hz), 2.59–2.57 (bs, 1 H), 0.17 (s, 9 H); ^{13}C NMR δ 142.5, 128.1, 127.6, 125.7, 103.1, 87.5, 72.2, 30.8, –0.10; MS (EI, 70 eV) 218 (M^+, 1), 179 (55), 112 (16), 107 (100), 79 (43); exact mass calcd for $C_{13}H_{18}SiO$ 218.1127, found 218.1125.

1-Methyl-1-phenyl-4-(trimethylsilyl)-3-butyn-1-ol[12,54] **(28b).** A clear oil (620 mg, 89%) was obtained from (trimethylsilyl)-acetylene (490 mg, 5 mmol) and acetophenone (360 mg, 3 mmol): chromatography solvent, 10% ethyl acetate in hexane; IR (neat) 3434 (br), 2960 (s), 2900 (s), 2176 (s), 1447 (m) cm^{-1}; ^{1}H NMR δ 7.49–7.26 (m, 5 H), 2.73 (s, 1 H), 2.72 (s, 1 H), 2.47 (s, 1 H), 1.65 (s, 3 H), 0.13 (s, 9 H); ^{13}C NMR δ 146.5, 128.1, 126.9, 124.8, 103.0, 88.6, 73.1, 36.3, 28.9, –0.08; MS (EI, 70 eV) 232 (M^+, 12), 214 (10), 193 (8), 121 (100); exact mass calcd for $C_{14}H_{20}SiO$ 232.1283, found 232.1288.

1-Hydroxy-1-[3-(trimethylsilyl)-2-propynyl]cyclohexane[12,55] **(28c):** white crystals (mp 42–43 °C, 570 mg, 90%); obtained from (trimethylsilyl)acetylene (490 mg, 5 mmol) and cyclohexanone (290 mg, 3 mmol); chromatography solvent, 10% ethyl acetate in hexane; IR (neat) 3332 (br), 2941 (s), 2855 (s), 2175 (s), 1447 (s) cm^{-1}; ^{1}H NMR δ 2.39 (s, 2 H), 1.80 (s, 1 H), 1.65–1.52 (m, 4 H), 1.50–1.43 (m, 4 H), 1.31–1.24 (m, 2 H), 0.16 (s, 9 H); ^{13}C NMR δ 103.1, 88.1, 70.2, 36.8, 34.4, 25.6, 22.1, 0.01; MS (CI, NH_3) 228 (MNH_4^+, 100), 211 (10), 193 (34), 171 (12); exact mass calcd for $C_{12}H_{22}SiOH$ 211.1518, found 211.1529.

4,6-Dimethyl-1-(trimethylsilyl)hept-5-en-1-yn-4-ol (28d). A three-neck flask, equipped with a thermometer, addition funnel, septum cap, magnetic stirring bar, and argon outlet was charged with (trimethylsilyl)acetylene (490 mg, 5 mmol) and THF (5 mL). A solution of butyllithium (3.1 mL, 5 mmol, 1.6 M in hexane) was added, via syringe, at –60 °C; the reaction was warmed to 0 °C and then cooled back to –60 °C. To the resulting lithium acetylide was added a THF solution (5 mL) of CuCN (450 mg, 5 mmol) and LiCl (420 mg, 10 mmol) at –60 °C, via syringe. The reaction was then warmed to 0 °C and then cooled back to –60 °C. To the resulting copper acetylide were added successively mesityl oxide (290 mg, 3 mmol) and (iodomethyl)zinc iodide (5.7 mL, 8 mmol, 1.4 M in THF), mixed with a THF solution (10 mL) of ZnI_2 (2.55 g, 8 mmol, previously dried at 150 °C under vacuum ca. 0.1 mmHg, 2 h), via an addition funnel, at such a rate that the temperature remained below –10 °C. The reaction was then allowed to warm to 0 °C and stirred for 0.5 h. The reaction mixture was worked up as described above, and purification by flash chromatography (1% ethyl acetate in hexane) gave the product **20d** (650 mg, 95%) as a white crystalline solid (mp 44–45 °C): IR (neat) 3322 (br), 2988 (s), 2170 (s), 1669 (m), 1030 (m) cm^{-1}; ^{1}H NMR δ 5.28 (t, J = 1.3 Hz, 1 H), 2.52 (d, J = 16.6 Hz, 1 H), 2.42 (d, J = 16.6 Hz, 1 H), 2.01 (s, 1 H), 1.85 (d, J = 1.3 Hz, 3 H), 1.69 (d, J = 1.3 Hz, 3 H), 1.39 (s, 3 H), 0.15 (s, 9 H); ^{13}C NMR δ 135.3, 129.5, 103.6, 87.7, 71.8, 35.9, 28.1, 27.1, 18.8, 0.02; MS (CI, NH_3) 228 (MNH_4^+, 9), 210 (32), 193 (100); exact mass calcd for $C_{12}H_{22}SiONH_4$ 228.1784, found 228.1787.

1-Phenyl-5-(2-tetrahydro-2*H*-pyranyloxy)-3-pentyn-1-ol (28e). A clear oil (620 mg, 80%) was obtained from tetrahydro-2-(2-propynyloxy)-2*H*-pyran (700 mg, 5 mmol) and benzaldehyde

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(320 mg, 3 mmol): chromatography solvent 10% ethyl acetate in hexane; IR (neat) 3428 (br), 2942 (s), 2869 (s), 1453 (m), 1441 (m), 1077 (m), 1022 (s) cm^{-1}; ^1H NMR δ 7.40–7.28 (m, 5 H), 4.87–4.83 (m, 1 H), 4.74 (t, J = 3.3 Hz, 1 H), 4.31–4.18 (m, 2 H), 3.82–3.78 (m, 1 H), 3.52–3.48 (m, 1 H), 2.69–2.65 (m, 3 H), 1.82–1.50 (m, 6 H); ^{13}C NMR δ 142.9, 128.3, 127.7, 125.8, 96.7, 82.8, 78.6, 72.3, 61.9, 54.5, 30.2, 29.7, 25.2, 18.9; MS (CI, NH_3) 278 (MNH_4^+, 9), 261 (MH^+, 2), 194 (17), 136 (27), 102 (54), 85 (100); exact mass calcd for $C_{16}H_{20}O_3H$ 261.1491, found 261.1498.

1-Phenyl-3-pentyne-1,5-diol. To confirm the structure of **28e** (mixture of diastereoisomers) the tetrahydropyranyl group was removed and the diol analyzed. The THF ether **28e** was dissolved in methanol (10 mL), a catalytic amount of *p*-toluenesulfonic acid (ca. 50 mg) was added, and the mixture was stirred for 1 h. The methanol was removed in vacuo, and the resulting oil was dissolved in ether (100 mL) and washed with $NaHCO_3$ (50 mL) and brine (50 mL). The organic layer was dried ($MgSO_4$) and concentrated in vacuo. Purification by flash chromatography afforded a clear oil in a quantitative yield: IR (neat) 3280 (br), 2930 (s), 2115 (w), 1455 (s) cm^{-1}; ^1H NMR δ 7.36–7.27 (m, 5 H), 4.87–4.83 (m, 1 H), 4.23 (s, 2 H), 3.03 (s, 1 H), 2.67–2.64 (m, 3 H); ^{13}C NMR δ 142.8, 128.6, 128.0, 125.8, 82.6, 81.1, 72.6, 51.2, 29.8; MS (CI, NH_3) 191 (MNH_4^+, 100), 159 (42), 141 (19), 136 (10).

1-(4-Hydroxy-4-phenyl-1-butynyl)-1-methoxycyclohexane[12] (28f). A clear oil (760 mg, 95% yield) was obtained from 1-ethynyl-1-methoxycyclohexane (690 mg, 5 mmol) and benzaldehyde (320 mg, 3 mmol): chromatography solvent, 10% ethyl acetate in hexane; IR (neat) 3416 (br), 2939 (s), 2824 (m), 1452 (s) cm^{-1}; ^1H NMR δ 7.42–7.27 (m, 5 H), 4.88–4.83 (m, 1 H), 3.27 (s, 3 H), 2.72 (d, J = 6.4 Hz, 2 H), 2.38 (bs, 1 H), 1.84–1.79 (m, 2 H), 1.63–1.23 (m, 8 H); ^{13}C NMR δ 142.9, 128.2, 127.7, 125.9, 83.9, 82.3, 73.9, 72.6, 50.3, 36.8, 36.7, 29.5, 22.6; MS (EI, 70 eV) 258 (M^+, 6), 152 (11), 137 (19), 124 (12), 121 (19), 120 (100); exact mass calcd for $C_{17}H_{22}O_2$ 258.1620, found 258.1621.

Quadruple Homologations of Copper Acetylides Using (Iodomethyl)zinc Iodide (4). Preparation of 34a–c. Typical Procedure. A three-neck flask, equipped with a thermometer, addition funnel, septum cap, magnetic stirring bar, and argon outlet was charged with the alkyne (5 mmol) and THF (5 mL). A solution of butyllithium (3.1 mL, 5 mmol, 1.6 M in hexane) was added at –60 °C; the reaction was warmed to 0 °C and cooled back to –60 °C. To the resulting lithium acetylide was added a THF solution (5 mL) of CuCN (450 mg, 5 mmol) and LiCl (420 mg, 10 mmol) at –60 °C, via an addition funnel. The reaction was warmed to 0 °C and then cooled back to –60 °C. To the resulting copper acetylide, was added (iodomethyl)zinc iodide (4) (14.3 mL, 20 mmol, 1.4 M in THF), mixed with a THF solution (10 mL) of ZnI_2 (2.55 g, 8 mmol), via an addition funnel, at –60 °C. The reaction was then allowed to warm to 0 °C carefully (a very exothermic reaction occurs at about –40 °C, and a dry ice/acetone bath was necessary to keep the temperature below 0 °C) and stirred at this temperature for 0.5 h. The reaction was then cooled to –60 °C, *tert*-butyl α-(bromomethyl)acrylate[37] (660 mg, 3 mmol) was added, via syringe, and the reaction warmed to 0 °C. After 2 h at this temperature the reaction was worked up as described above. Purification by flash chromatography afforded the pure product. All of the reactions leading to **34a–c** were performed on the same scale.

***tert*-Butyl 2,6,7-Trimethylenetridecanoate[12] (34a).** A clear oil (680 mg, 74%) was obtained from octyne (550 mg, 5 mmol): chromatography solvent, 0.5% ethyl acetate in hexane; IR (neat) 2977 (s), 2931 (s), 2859 (s), 1715 (s), 1630 (m), 1594 (m) cm^{-1}; ^1H NMR δ 6.04 (d, J = 1.7 Hz, 1 H), 5.44–5.43 (m, 1 H), 5.07 (d, J = 1.5 Hz, 1 H), 5.04 (d, J = 1.5 Hz, 1 H), 4.93 (s, 1 H), 4.91 (s, 1 H), 2.29–2.19 (m, 6 H), 1.64–1.40 (m, 10 H), 1.28 (s, 9 H), 0.90–0.86 (br t, 3 H); ^{13}C NMR δ 166.6, 148.0, 147.6, 142.4, 123.4, 111.7, 111.4, 80.3, 34.4, 33.9, 31.8, 31.7, 29.2, 28.6, 28.1, 27.6, 22.6, 14.0; MS (CI, NH_3) 324 (MNH_4^+, 44), 307 (MH^+, 1), 296 (15), 268 (44), 240 (15), 136 (68), 90 (100); exact mass calcd for $C_{20}H_{34}O_2H$ 307.2637, found 307.2631.

***tert*-Butyl 2,6-Dimethylene-7-(trimethylsilyl)-7-octenoate[12] (34b).** A clear oil (620 mg, 70% yield) was obtained from (trimethylsilyl)acetylene (490 mg, 5 mmol): chromatography solvent, 0.5% ethyl acetate in hexane; IR (neat) 2936 (s), 2901 (s), 1715 (s), 1630 (m), 1457 (m) cm^{-1}; ^1H NMR δ 6.02 (d, J = 1.7 Hz, 1 H), 5.67 (d, J = 2.9 Hz, 1 H), 5.43–5.41 (m, 1 H), 5.39 (d, J = 2.9 Hz, 1 H), 4.83 (s, 1 H), 4.79 (d, J = 1.8 Hz, 1 H), 2.27–2.16 (m, 4 H), 1.69–1.40 (m, 2 H), 1.48 (s, 9 H), 0.13 (s, 9 H); ^{13}C NMR δ 166.7, 153.3, 151.6, 142.4, 125.2, 123.5, 111.3, 80.4, 35.3, 31.7, 28.1, 27.0, –0.7; MS (CI, NH_3) 312 (MNH_4^+, 61), 295 (MH^+, 5), 256 (95), 239 (50), 228 (42), 136 (10), 90 (100); exact mass calcd for $C_{17}H_{30}SiO_2H$ 295.2093, found 295.2091.

***tert*-Butyl 9-Cyano-2,6,7-trimethylenenonanoate[12] (34c).** A clear oil (410 mg, 50%) was obtained from pent-4-ynenitrile (395 mg, 5 mmol): flash chromatography solvent, 10% ethyl acetate in hexane; IR (neat) 2977 (s), 2244 (w), 1710 (s), 1630 (m), 1597 (m) cm^{-1}; ^1H NMR δ 6.04 (d, J = 1.5 Hz, 1 H), 5.45 (s, 1 H), 5.44 (d, J = 1.4 Hz, 1 H), 5.21 (s, 1 H), 5.08 (s, 1 H), 5.04 (s, 1 H), 5.02 (s, 1 H), 2.62–2.58 (m, 2 H), 2.51–2.46 (m, 2 H), 2.29–2.23 (m, 4 H), 1.67–1.56 (m, 2 H), 1.48 (s, 9 H); ^{13}C NMR δ 166.4, 145.9, 143.8, 142.1, 123.5, 119.1, 114.1, 112.5, 80.3, 33.5, 31.6, 30.0, 28.0, 27.4, 16.7; MS (CI, NH_3) 293 (MNH_4^+, 12), 276 (MH^+, 17), 237 (100), 220 (62), 202 (63), 174 (31), 160 (31), 145 (15); exact mass calcd for $C_{17}H_{25}NO_2H$ 276.1964, found 276.1962.

Preparation of *tert*-Butyl 2,6,7-Trimethylenetridecanoate (34a) by the Methylene Homologation of 3-Nonynylzinc Bromide with (Iodomethyl)zinc Iodide (4). A three-neck flask, equipped with a thermometer, addition funnel, septum cap, magnetic stirring bar, and argon outlet was charged with zinc dust (490 mg, 7.5 mmol) and THF (0.5 mL). To the zinc suspension was added 1,2-dibromomethane (200 mg, 1 mmol), and the reaction was heated to reflux for 1 min. After the solution was cooled to 25 °C, chlorotrimethylsilane (0.1 mL, 0.8 mmol) was added and the activated zinc was stirred for 5 min. A THF solution (2 mL) of 1-bromo-3-nonyne (1.02 g, 5 mmol) was then added, via an addition funnel, at 0 °C, over 15 min and was stirred at this temperature for 0.5 h. The stirring was stopped, and the excess zinc dust was allowed to settle out. To the resulting propargylic zinc reagent was then added a THF solution (5 mL) of CuCN (450 mg, 5 mmol) and LiCl (420 mg, 10 mmol) at –40 °C, via syringe. The resulting copper compound was warmed to 0 °C and then cooled to –60 °C. To the resulting copper compound was then added (iodomethyl)zinc iodide (4) (14.3 mL, 20 mmol, 1.4 M in THF), previously mixed with a THF solution (10 mL) of ZnI_2 (2.55 g, 8 mmol), via an addition funnel, at –60 °C. The reaction was allowed to warm to 0 °C carefully (a very exothermic reaction occurs about –40 °C, and a dry ice/acetone bath was necessary to keep the temperature below 0 °C) and stirred at this temperature for 0.5 h. The reaction was then cooled to –60 °C, *tert*-butyl α-(bromomethyl)acrylate (660 mg, 3 mmol) was added, via syringe, and the reaction mixture was warmed to 0 °C and was worked up after 2 h at this temperature. Purification by flash chromatography (0.5% ethyl acetate in hexane) afforded **34a** (640 mg, 70%) as a colorless oil with ^1H NMR and ^{13}C NMR spectra matching those obtained previously.

***tert*-Butyl 2,6-Dimethylenedecanoate[12] (42).** A three-neck flask, equipped with a thermometer, addition funnel, septum cap, magnetic stirring bar, and argon outlet, was charged with zinc dust (1 g, ca. 15 mmol) and THF (0.5 mL). To the zinc suspension was added 1,2-dibromoethane (200 mg, 1 mmol), and the reaction was heated to reflux for 1 min. After being cooled to 25 °C, chlorotrimethylsilane (0.1 mL, 0.8 mmol) was added, and the activated zinc was stirred for 5 min. A THF solution (2 mL) of 2-(bromomethyl)hexene was added, via an addition funnel, at 0 °C, over 15 min and was stirred at this temperature for 1 h. The stirring was stopped, and the excess zinc dust was allowed to settle out. The resulting allylic zinc reagent was then transferred to another flask, equipped as above, and (iodomethyl)-zinc iodide (4) (5.7 mL, 8 mmol, 1.4 M in THF) was added at 0 °C via an addition funnel. The reaction was warmed to 0 °C and stirred 1 h. To the resulting homoallylic zinc compound was added a THF solution (5 mL) of CuCN (450 mg, 5 mmol) and LiCl (420 mg, 10 mmol) at –40 °C, via syringe. The resulting copper compound was warmed to 0 °C and then cooled to –60 °C. *tert*-Butyl α-(bromomethyl)acrylate[37] (660 mg, 3 mmol) was then added, via syringe, and the reaction was warmed to room temperature. After 2 h at this temperature the reaction was worked as described above, and purification by flash chromatography (0.5% ethyl acetate in hexane) afforded the product (590 mg, 73%) as a clear oil.

1-Cyclohexyl-4-methoxy-3-methylene-4-buten-1-ol (48a). A solution of 1-methoxyallene (490 mg, 7 mmol) in THF (2 mL)

was added within 10 min at −30 °C to a solution of n-BuLi[40] (7 mmol, 1.45 M in hexane) in THF (15 mL). After 15 min at this temperature the light yellow solution was cooled to −60 °C and a THF solution (10 mL) of CuI (1.15 g, 6 mmol) and LiCl (0.52 g, 12 mmol) was added. The reaction mixture was warmed to −20 °C and was stirred for 15 min at this temperature (turned dark). The reaction mixture was cooled to −60 °C, and cyclohexanone (343 mg, 3.5 mmol) in THF (3 mL) followed by (iodomethyl)zinc iodide (12 mL of a 1.67 M THF solution; ca. 20 mmol) were added. The reaction mixture was warmed to 25 °C and was stirred for 1 h at this temperature. After the usual workup and evaporation of the solvents, a crude oil was obtained which was purified by flash chromatography (hexane/ether (95:5)) affording 400 mg (57%) of the desired product **48a**: IR (neat) 3427 (br), 2998 (br s), 1645 (s), 1584 (s) cm^{-1}; ^1H NMR δ 5.6 (d, 1 H, J = 2.1 Hz), 5.09 (s, 1 H), 4.32 (d, 1 H, J = 2.7 Hz), 4.15 (d, 1 H, J = 1.9 Hz), 3.62 (s, 3 H), 3.55–3.45 (m, 1 H), 2.6 (dd, 1 H, J = 1.1 Hz, 10.5 Hz), 2.16 (dd, 1 H, J = 4.2 Hz, 9.8 Hz), 1.95–1.6 (m, 6 H), 1.45–1.0 (m, 6 H); ^{13}C NMR δ 160.3, 140.7, 115.0, 83.0, 73.7, 54.7, 43.3, 38.6, 29.0, 27.9, 26.5, 26.2, 26.1; MS (EI) 210 (0.5), 192 (1), 135 (5), 99 (100); exact mass calcd for $C_{13}H_{22}O_2$ 210.1619, obsd 210.1618.

1-(3-Methoxy-2-methylene-1-but-3-enyl)-1-cyclohexan-1-ol (48b). Same procedure and same scale as above; 602 mg (87% yield) of the alcohol **48b** was obtained. Purification by flash chromatography (hexane/ethyl acetate (9:1)): IR (neat) 3473 (br), 2931 (br s), 1677 (s), 1448 (s), 1260 (m), 1066 (m) cm^{-1}; ^1H NMR δ 5.6 (d, 1 H, J = 2.1 Hz), 5.0 (d, 1 H, J = 1.3 Hz), 4.42 (d, 1 H, 2.6 Hz), 4.1 (d, 1 H, J = 1.5 Hz), 3.61 (s, 3 H), 2.45 (s, 2 H), 1.88 (s, 1 H), 1.7–1.2 (m, 10 H); ^{13}C NMR δ 162.2, 139.9, 116.9, 83.1, 70.6, 54.7, 45.3, 37.5, 25.6, 22.0; MS (EI) 196 (1), 181 (1), 164 (2), 139 (3), 121 (6); exact mass calcd for $C_{12}H_{20}O_2$ 196.1463, obsd 196.1453.

General Procedure for the Preparation of the Dienes 49. A three-neck flask, equipped with a thermometer, septum cap, magnetic stirring bar, and argon outlet, was charged with the alkyne (5 mmol) and THF (5 mL). A solution of butyllithium (3.1 mL, 5 mmol, 1.6 M in hexane) was added via syringe, at −60 °C, the reaction was warmed to 0 °C and then cooled back to −60 °C. To the resulting lithium acetylide was added a THF solution (5 mL) of CuCN (450 mg, 5 mmol) and LiCl (420 mg, 10 mmol) at −60 °C, via syringe. The reaction was then warmed to 0 °C and then cooled back to −60 °C. To the resulting copper acetylide **30** or **31** was added the aldehyde or ketone (3 mmol), followed (iodomethyl)zinc iodide (**4**) (14.3 mL, 20 mmol, 1.4 M in THF) at −60 °C, via syringe. The reaction was allowed to warm to 0 °C carefully (a very exothermic reaction occurs about −40 °C, and a dry ice/acetone bath was necessary to keep the temperature below 0 °C) and stirred at this temperature for 0.5 h. The reaction was then worked up as described above, and purification by flash chromatography afforded the pure product. All of the reactions were performed on this scale.

Tetrahydro-2-[(2,3-dimethylene-4-(1-hydroxycyclopentyl)butyl)oxy]-2*H*-pyran (49a). A clear oil (540 mg, 70% yield) was obtained from tetrahydro-2-(2-propynyloxy)-2*H*-pyran (700 mg, 5 mmol) and cyclopentanone (250 mg, 3 mmol); chromatography, 10% ethyl acetate in hexane; IR (neat) 3453 (br), 2944 (s), 2871 (s), 1595 (m), 1456 (m) cm^{-1}; ^1H NMR δ 5.30 (s, 1 H), 5.28 (s, 1 H), 5.24 (d, J = 1.9 Hz, 1 H), 5.04 (s, 1 H), 4.65 (t, J = 3.3 Hz, 1 H), 4.43 (d, J = 12.5 Hz, 1 H), 4.13 (d, J = 12.5 Hz, 1 H), 3.88–3.80 (m, 1 H), 3.55–3.47 (m, 1 H), 2.59 (s, 2 H), 2.02 (s, 1 H), 1.86–1.48 (m, 14 H); ^{13}C NMR δ 145.6, 143.7, 115.7, 114.5, 97.9, 81.6, 68.7, 61.9, 45.0, 39.5, 30.4, 25.3, 23.3, 19.1; MS (CI, NH_3) 284 (MNH_4^+, 89), 267 (MH^+, 21), 249 (83), 231 (11), 200 (100); exact mass calcd for $C_{16}H_{26}O_2H$ 267.1960, found 267.1966.

4-(1-Hydroxycyclopentyl)-2-(1-methoxycyclohexyl)-3-methylene-1-butene (49b). A clear oil (500 mg, 63% yield) was obtained from 1-ethynyl-1-methoxycyclohexane (770 mg, 5 mmol) and cyclopentanone (250 mg, 3 mmol): chromatography, 10% ethyl acetate in hexane; IR (neat) 3460 (br), 2937 (s), 2858 (s), 1616 (m) cm^{-1}; ^1H NMR δ 5.19 (d, J = 1.6 Hz, 1 H), 5.12 (d, J = 2.6 Hz, 1 H), 5.11 (d, J = 1.6 Hz, 1 H), 5.01 (d, J = 2.6 Hz, 1 H), 3.09 (s, 3 H), 2.58 (s, 2 H), 2.10 (s, 1 H), 1.89–1.20 (m, 18 H); ^{13}C NMR δ 154.6, 147.6, 118.1, 115.0, 82.0, 77.7, 48.9, 46.8, 40.1, 34.1, 25.6, 23.7, 22.1; MS (CI, NH_3) 265 (MH^+, 9), 233 (100), 215 (39), 149 (83); exact mass calcd for $C_{17}H_{28}O_2H$ 265.2168, found 265.2171.

Tetrahydro-2-[(5-hydroxy-5-methyl-2,3-dimethylene-5-phenylpentyl)oxy]-2*H*-pyran (49c). A clear oil (690 mg, 76% yield) was obtained from tetrahydro-2-(2-propynyloxy)-2*H*-pyran (700 mg, 5 mmol) and acetophenone (360 mg, 3 mmol): chromatography, 10% ethyl acetate in hexane; IR (neat) 3457 (br), 2943 (s), 2871 (m), 1594 (m), 1465 (m), cm^{-1}; ^1H NMR δ 7.47–7.19 (m, 5 H), 5.25–5.22 (m, 3 H), 4.88 (d, J = 3.1 Hz, 1 H), 4.65–4.61 (m, 1 H), 4.41–4.35 (m, 1 H), 4.11–4.03 (m, 1 H), 3.90–3.81 (m, 1 H), 3.56–2.69 (m, 1 H), 1.89–1.47 (m, 9 H); ^{13}C NMR δ 148.2, 145.6, 142.6, 127.9, 126.3, 124.8, 117.1, 115.0, 98.0, 74.1, 68.7, 68.6, 62.0, 61.9, 48.1, 48.0, 30.4, 29.8, 29.7, 25.3, 19.2; MS (CI, NH_3): 320 (MNH_4^+, 5), 285 (100), 267 (37), 218 (37), 201 (41), 183 (21), 165 (12), 155 (13), 138 (13), 118 (11), 102 (61), 85 (93); exact mass calcd for $C_{19}H_{26}O_3NH_4$ 320.2226, found 320.2240.

4,4-Diethyl-5-[2,3-dimethylene-4-(tetrahydro-2*H*-pyranyloxy)butyl]valerolactone (49d). A clear oil (520 mg, 52% yield) was obtained from tetrahydro-2-(2-propynyloxy)-2*H*-pyran (700 mg, 5 mmol) and 4-cyano-2,2-diethylbutanal (460 mg, 3 mmol): chromatography, 10% ethyl acetate in hexane; IR (neat) 2942 (s), 2880 (s), 1736 (s), 1465 (m) cm^{-1}; ^1H NMR δ 5.33 (d, J = 3.7 Hz, 1 H), 5.25 (d, J = 2.5 Hz, 1 H), 5.19 (s, 1 H), 5.12 (s, 1 H), 4.66–4.23 (m, 1 H), 4.43 (t, J = 14.0 Hz, 1 H), 4.34–4.21 (m, 1 H), 4.13 (t, J = 31.1 Hz, 1 H), 3.90–3.82 (m, 1 H), 3.54–3.47 (m, 1 H), 2.69–2.36 (m, 4 H), 1.88–1.24 (m, 14 H), 0.90 (t, J = 7.4 Hz, 3 H), 0.86 (t, J = 7.4 Hz, 3 H); ^{13}C NMR δ 171.8, 143.9, 141.6, 115.6, 115.5, 113.4, 113.2, 98.0, 97.9, 83.1, 68.1, 68.0, 62.2, 37.3, 34.7, 30.6, 27.4, 27.3, 25.4, 25.1, 19.4, 7.7, 7.6; MS (CI, NH_3) 354 (MNH_4^+, 93), 270 (100), 253 (5), 136 (34); exact mass calcd for $C_{20}H_{32}O_4NH_4$ 354.2644, found 354.2636.

4,4-Diethyl-5-(4-hydroxy-3,2-dimethylenebutyl)valerolactone. To confirm the structure of **49c**, which is a mixture of diastereoisomers, the tetrahydropyranyl group was removed. The lactone **49d** and a catalytic amount of *p*-TsOH (ca. 5 mg) were stirred in methanol (10 mL) for 1 h. The methanol was removed in vacuo, and the resulting oil was dissolved in ether (100 mL) and was washed with $NaHCO_3$ (50 mL) and brine (50 mL). The organic layer was then dried ($MgSO_4$) and concentrated in vacuo. Purification by flash chromatography afforded the product, as a clear oil, in a quantitative yield: IR (neat) 3436 (br), 2967 (s), 2941 (s), 2882 (s), 1734 (s) cm^{-1}; ^1H NMR δ 5.30 (s, 1 H), 5.22 (s, 1 H), 5.14 (s, 1 H), 5.13 (s, 1 H), 4.32 (s, 2 H), 2.66–2.04 (m, 4 H), 1.79–1.71 (br s, 1 H), 1.69–1.20 (m, 6 H), 0.90 (t, J = 7.5 Hz, 3 H), 0.86 (t, J = 7.5 Hz, 3 H); ^{13}C NMR δ 171.9, 146.8, 141.6, 115.2, 111.9, 83.6, 64.0, 37.1, 34.8, 27.1, 26.1, 24.9, 7.6, 7.5; MS (CI, NH_3) 270 (MH^+, 6), 253 (MNH_4^+, 6), 242 (10), 164 (30), 136 (100); exact mass calcd for $C_{15}H_{24}O_3H$ 253.1804, found 253.1805.

Typical Procedure for the Preparation of 3-Pentynylzinc Iodide, Its Transmetalation to the Corresponding Copper Reagent, and Its Reaction with an Electrophile: Preparation of 3-(4-Pentynyl)cyclohexen-1-one (50). A dry, three-necked 100-mL flask was charged with zinc dust (3.27 g, 50 mmol) and flushed with argon. After zinc activation with 1,2-dibromoethane and Me_3SiCl as described previously, a THF solution of 4-pentynyl iodide (**52**) (4.46 g, 23 mmol) in THF (8 mL) was slowly added. The temperature was maintained below 40 °C during the addition. After 0.5–1 h of stirring at 25 °C, the reaction was complete as indicated by GC analysis. After the addition of dry THF (10 mL), the excess of zinc was allowed to settle for 1 h. One-half of this solution (ca. 10 mmol) was transferred via syringe to a solution of CuCN (0.90 g, 10 mmol) and LiCl (0.84 g, 20 mmol) in THF (10 mL) at −20 °C. A dark red solution of **53** was formed. The reaction mixture was cooled to −60 °C after 5 min of stirring, and 3-iodo-2-cyclohexen-1-one (1.55 g, 7 mmol (0.7 equiv)) was added. The reaction mixture was stirred for 1 h at −30 °C and then was slowly warmed to 0 °C (1–2 h) and worked up as usual. The resulting crude oil was purified by flash chromatography (CH_2Cl_2/ether/hexane (1:1–5:90)) affording 1.0 g (88% yield) of pure product **50**.

3-(4-Pentynyl)-2-cyclohexen-1-one (50). Purified by flash chromatography (hexane/CH_2Cl_2/ether (80:10:0–5)): IR (neat) 3275 (s), 2924 (s), 2115 (m), 1672 (s), 1623 (m) cm^{-1}; ^1H NMR δ 5.87 (s, 1 H), 2.35–2.17 (m, 8 H), 2.01–1.89 (m, 3 H), 1.76–2.66 (m, 2 H); ^{13}C NMR δ 198.0, 164.6, 125.7, 83.1, 68.9, 37.1, 36.4,

29.4, 25.5, 22.5, 17.7; HRMS (EI) exact mass calcd for $C_{11}H_{14}O$ 162.1045, obsd 162.1031.

1-Cyclohexylhex-5-yn-1-one (51). Reaction conditions: 0 °C, 1 h; purified by flash chromatography (hexane/ethyl acetate (19:1)); IR (neat) 3304 (s), 2931 (s), 2854 (s), 2116 (m), 1708 (s) cm^{-1}; ^1H NMR δ 2.56 (t, 2 H, J = 7.1 Hz), 2.35–2.15 (m, 1 H), 2.18 (dt, 2 H, J = 6.8 Hz, 2.6 Hz), 1.93 (t, 1 H, J = 2.6 Hz), 1.84–1.65 (m, 7 H), 1.38–1.19 (m, 5 H); ^{13}C NMR δ 213.3, 83.7, 68.9, 50.9, 38.9, 28.5, 25.9, 25.7, 22.2, 17.8; HRMS (EI) exact mass calcd for $C_{12}H_{18}O$ 178.1358, obsd 178.1373.

Typical Cyclization Procedure Mediated by Bis(iodomethyl)zinc (5). A three-neck flask, equipped with a thermometer, septum cap, magnetic stirring bar, and argon outlet, was charged with the alkyne (5 mmol), CuI (1.43 g, 7.5 mmol), THF (5 mL), DBU (1.14 g, 7.5 mmol). The reaction was stirred at 30 °C for 48 h. To the resulting copper acetylide 41 was added bis(iodomethyl)zinc (5)[5] (10 mL, 10 mmol, 1 M in THF) at −10 °C, via syringe. The reaction mixture was warmed to 25 °C, and after 1 h more bis(iodomethyl)zinc (5) (10 mL, 10 mmol, 1 M in THF) was added. After 1 h of stirring, the reaction was worked up as described above and the product was purified by flash chromatography.

1-Vinylidenespiro[5.4]decan-7-one (56).[56] A clear oil (570 mg, 65%) was obtained from 3-(4-pentynyl)-2-cyclohexen-1-one in the presence of Me_3SiCl (1.3 mL, ca. 10 mmol): chromatography solvent, 5% ethyl acetate in hexane; IR (neat) 2953 (s), 2872 (s), 1956 (m), 1713 (s), 1446 (m) cm^{-1}; ^1H NMR δ 4.80 (t, J = 4.5 Hz, 2 H), 2.51–2.43 (m, 2 H), 2.40–2.22 (m, 4 H), 2.07–1.97 (M, 1 H), 1.84–1.65 (m, 5 H), 1.62–1.47 (m, 2 H); ^{13}C NMR δ 210.2, 202.2, 110.6, 78.3, 52.0, 48.9, 40.7, 37.5, 35.6, 30.1, 23.4, 22.6, 21.5; MS (EI, 70 eV) 176 (M^+, 29), 134 (58), 119 (43), 105 (56), 91 (100), 84 (57), 79 (59), 50 (60), 41 (57), 39 (63); exact mass calcd for $C_{12}H_{16}O$ 176.1201, found 176.1207.

1-Cyclohexyl-2-vinylidenecyclopentanol (57). A clear oil (700 mg, 73% yield) was obtained from 1-cyclohexylhex-5-yn-1-one (890 mg, 5 mmol): chromatography solvent, 5% ethyl acetate in hexane; IR (neat) 3445 (br), 2924 (s), 2852 (s), 1958 (m), 1451 (m) cm^{-1}; ^1H NMR δ 4.9–4.78 (m, 2 H), 2.64–2.55 (m, 1 H), 2.36–2.26 (m, 1 H), 2.06–2.02 (m, 1 H), 1.87–1.65 (m, 7 H), 1.59–1.50 (m, 1 H), 1.31–0.88 (m, 5 H); ^{13}C NMR δ 210.6, 109.7, 84.3, 77.9, 46.1, 35.2, 30.6, 28.4, 27.2, 26.4, 26.3, 23.3; MS (EI, 70 eV) 192 (M^+, 1), 123 (10), 109 (100); exact mass calcd for $C_{13}H_{20}O$ 192.1514, found 192.1514.

In Situ Generation of Benzylcopper from Phenylcopper and Its Reaction with an Electrophile (Entries 1–3 of Table IV). A three-neck flask, equipped with a thermometer, addition funnel, septum cap, magnetic stirring bar, and argon outlet, was charged with CuI (970 mg, 5 mmol), LiI (1.34 g, 10 mmol, previously dried at 150 °C under vacuum ca. 0.1 mmHg, 2 h), and THF (5 mL). A solution of phenyllithium (2.8 mL, 5 mmol, 1.8 M in cyclohexane/ether (70:30)) was then added, via an addition funnel, at −40 °C over 2 min. The resulting suspension was warmed to −20 °C within 10 min and cooled back to −60 °C. To the resulting solution of phenylcopper was added, via an addition funnel, (iodomethyl)zinc iodide (4) (5.7 mL, 8 mmol, 1.4 M in THF), previously mixed with a THF solution (10 mL) of ZnI_2 (2.55 g, 8 mmol), at such a rate that the temperature remained below −40 °C. The reaction was then warmed to −20 °C, and the resulting benzylcopper was cooled to −60 °C. The electrophile was added via syringe, and the completion of the reaction was followed by performing the GC analysis of hydrolyzed reaction aliquots. The reaction mixture was hydrolyzed as described before, and the crude residue was purified by flash chromatography.

1-(3-Butyl-3-butenyl)benzene[57] **(61a).** A clear oil (450 mg, 80% yield) was obtained from 2-(bromomethyl)hexene (530 mg, 3 mmol, 0 °C, 14 h): chromatography solvent, hexane; IR (neat) 3028 (s), 2928 (s), 2859 (s), 1645 (s), 1454 (s) cm^{-1}; ^1H NMR δ 7.28–7.16 (m, 5 H), 4.76 (s, 2 H), 2.75 (t, J = 6.5 Hz, 2 H), 2.33 (t, J = 6.7 Hz, 2 H), 2.08 (t, J = 6.7 Hz, 2 H), 1.49–1.26 (m, 4 H), 0.93 (t, J = 6.7 Hz, 3 H); ^{13}C NMR δ 149.4, 142.3, 128.3, 128.2, 125.7 109.0, 37.8, 36.0, 34.4, 30.0, 22.4, 13.9; MS (EI, 70 eV) 188 (M^+, 12), 146 (13), 131 (20), 104 (27), 91 (100); exact mass calcd for $C_{14}H_{20}$ 188.1565, found 188.1556.

Benzyl Phenyl Ketone (61b).[58] A clear oil (400 mg, 69% yield) was obtained from benzoyl chloride (420 mg, 3 mmol, DME was substituted for THF, 0 °C, 14 h): chromatography, 5% ether in hexane; IR (neat) 3072 (w), 1697 (m), 1685 (m), 1273 (s) cm^{-1}; ^1H NMR δ 8.03–8.01 (m, 2 H), 7.59–7.53 (m, 1 H), 7.49–7.43 (m, 2 H), 7.37–7.22 (m, 5 H), 4.29 (s, 2 H); ^{13}C NMR δ 197.3, 136.5, 134.4, 132.9, 129.3, 128.4, 126.7, 45.3; MS (EI, 70 eV) 196 (M^+, 3), 105 (100); exact mass calcd for $C_{14}H_{12}O$ 196.0888, found 196.0884.

1,2-Diphenylethanol (61c).[58] A clear oil (540 mg, 84% yield) was obtained from benzaldehyde (320 mg, 3 mmol, −20 °C, 14 h, in the presence of $BF_3{\cdot}OEt_2$ (2 mL, 16 mmol): chromatography solvent, 20% ether in hexane; IR (neat) 3456 (br), 3065 (m), 3031 (s), 1496 (s), 1454 (s); ^1H NMR δ 7.45–7.15 (m, 10 H), 4.95–4.85 (m, 1 H), 3.20–2.95 (m, 2 H), 2.05 (s, 1 H); ^{13}C NMR δ 143.8, 138.0, 129.4, 128.1, 127.3, 126.3, 125.9, 75.1, 45.8; (EI, 70 eV) 198 (M^+, 1), 107 (78), 92 (100); exact mass calcd for $C_{14}H_{14}O$ 198.1045, found 198.1029.

Typical Procedure for the Homologation of Aromatic and Heteroaromatic Copper Reagents with (Iodomethyl)zinc Iodide (4), Followed by Its Reaction with an Allylic Halide or an Acid Chloride. Preparation of 2-(3-Methyl-3-butenyl)benzo[*b*]thiophene (61g). A three-neck flask, equipped with a thermometer, addition funnel, septum cap, magnetic stirring bar, and argon outlet, was charged with benzo[b]thiophene (685 mg, 5.1 mmol) and THF (5 mL). A solution of butyllithium (3.4 mL, 5.1 mmol, 1.5 M in hexane) was then added, via an addition funnel, at −78 °C over 2 min, and the mixture was allowed to warm to 0 °C within 5 min.[59] The reaction mixture was cooled to −60 °C, CuI (970 mg, 5 mmol) was added, via a powder funnel, and the reaction mixture was warmed to 0 °C. The resulting 2-benzo[b]thienylcopper was cooled to −60 °C, and (iodomethyl)-zinc iodide (4) (5.7 mL, 8 mmol, 1.4 M in THF), mixed with a THF solution (10 mL) of ZnI_2 (2.55 g, 8 mmol), was added at such a rate that the temperature remained below −40 °C. The reaction was warmed to −20 °C, and the resulting [(2-benzo[b]thienyl)-methyl]copper was cooled to −60 °C. A THF solution (2 mL) of 3-bromo-2-methylpropene (410 mg, 3 mmol) was added, and the reaction mixture was warmed to 0 °C and was stirred 14 h at this temperature. The reaction mixture was worked up, and the residue obtained after evaporation of the solvents was purified by flash chromatography (hexane) affording **61g** (560 mg, 93% yield) as a clear oil. In the case of the reaction with acid chlorides, THF was replaced by 1,2-dimethoxyethane (DME). Typical reaction time: 14 h at 0 °C.

Analytical data of the products **61d–l** described in Table IV.

2-(3-Methyleneheptyl)[2,3]benzofuran (61d). A clear oil (500 mg, 73% yield) was obtained from 2-(bromomethyl)hexene (530 mg, 3 mmol, 0 °C, 14 h): chromatography solvent, hexane; IR (neat): 2871 (s), 2858 (s), 1603 (m), 1589 (m), 1184 (m) cm^{-1}; ^1H NMR δ 7.48–7.38 (m, 2 H), 7.22–7.13 (m, 2 H), 6.38 (s, 1 H), 4.78 (s, 1 H), 2.91 (t, J = 7.2 Hz, 2 H), 2.46 (t, J = 7.2 Hz, 2 H), 2.07 (t, J = 7.2 Hz, 2 H), 1.50–1.33 (m, 2 H), 1.32–1.25 (m, 2 H), 0.93–0.87 (br t, 3 H); ^{13}C NMR δ 159.1, 154.7, 148.4, 129.0, 123.3, 123.1, 122.4, 120.3, 120.2, 110.7, 109.5, 101.9, 35.9, 33.9, 30.0, 27.1, 22.5, 13.9; MS (EI, 70 eV) 228 (M^+, 9), 132 (11), 131 (100); exact mass calcd for $C_{16}H_{20}O$ 228.1514, found 228.1501.

2-Methyl-3-benzoyl[2,3]benzofuran (61e). A clear oil (590 mg, 83% yield) was obtained from benzoyl chloride (420 mg, 3 mmol): chromatography solvent, 5% ether in hexane; IR (neat) 3064 (m), 2924 (m), 1736 (m), 1650 (s), 1578 (s), 1454 (s) cm^{-1}; ^1H NMR δ 7.83–7.79 (m, 2 H), 7.62–7.56 (m, 1 H), 7.50–7.39 (m 4 H), 7.30–7.16 (m, 2 H), 2.54 (s, 1 H); ^{13}C NMR δ 191.4, 161.6, 153.4, 139.2, 132.2, 128.8, 128.2, 128.7, 126.7, 124.1, 123.3, 121.1, 116.7, 110.6, 14.4; MS (EI, 70 eV) 236 (M^+, 48), 235 (56), 159 (36); exact mass calcd for $C_{16}H_{12}O_2H$ 237.0916, found 237.0900.

2-Methyl-3-(4-chlorobutynyl)[2,3]benzofuran (61f). A clear oil (650 mg, 92% yield) was obtained from 4-chlorobutyryl chloride (429 mg, 3 mmol): chromatography solvent, 5% ether in hexane; IR (neat) 3056 (m), 2926 (m), 1672 (s), 1569 (s) cm^{-1};

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^{1}H NMR δ 7.95–7.92 (m, 1 H), 7.47–7.45 (m, 1 H), 7.36–7.26 (m, 2 H), 3.73 (t, J = 6.2 Hz, 2 H), 3.16 (t, J = 6.9 Hz, 2 H), 2.80 (s, 3 H), 2.28 (quint, J = 6.4 Hz, 2 H); ^{13}C NMR δ 195.0, 162.7, 153.4, 125.6, 124.3, 123.9, 121.3, 117.0, 110.9, 44.6, 39.6, 26.3, 15.4; MS (EI, 70 eV) 236 (M^+, 12), 174 (19), 159 (100), 103 (13), 77 (21), 43 (11), 41 (10); exact mass calcd for $C_{13}H_{13}ClO_2$ 236.0604, found 236.0594.

2-(3-Methyl-3-butenyl)benzo[*b*]thiophene (61g). A clear oil (560 mg, 93% yield) was obtained from 3-bromo-2-methylpropene (410 mg, 3 mmol): chromatography solvent, hexane; IR (neat) 3070 (m), 2952 (s), 1940 (w), 1642 (m) cm^{-1}; ^{1}H NMR δ 7.72 (d, J = 7.6 Hz, 1 H), 7.65 (d, J = 7.6 Hz, 1 H), 7.18–7.32 (m, 2 H), 7.01 (s, 1 H), 4.75 (br s, 2 H), 3.08 (t, J = 7.8 Hz, 2 H), 2.48 (t, J = 7.8 Hz, 2 H), 1.78 (s, 3 H); ^{13}C NMR δ 145.9, 144.3, 140.1, 139.3, 124.0, 123.4, 122.7, 122.0, 120.5, 110.8, 39.0, 29.1, 22.5; MS (EI, 70 eV) 202 (M^+, 16), 160 (7), 147 (100); exact mass calcd for $C_{13}H_{14}S$ 202.0816, found 202.0811.

2-Methyl-3-benzoylbenzo[*b*]thiophene (61h). A white crystalline solid (mp 70–72 °C, 600 mg, 80% yield) was obtained from benzoyl chloride (420 mg, 3 mmol): chromatography solvent, 5% ether in hexane; IR (neat) 3063 (m), 3050 (m), 3026 (m), 1888 (w), 1654 (s) cm^{-1}; ^{1}H NMR δ 7.85–7.75 (m, 3 H), 7.62–7.43 (m, 4 H), 7.32–7.23 (m, 2 H), 2.49 (s, 3 H); ^{13}C NMR δ 193.1, 145.5, 139.0, 138.6, 137.9, 133.1, 132.3, 129.5, 128.5, 124.6, 124.2, 123.2, 121.6, 15.6; MS (EI, 70 eV) 252 (M^+, 100), 235 (12), 175 (29), 147 (13); exact mass calcd for $C_{16}H_{12}SOH$ 253.0687, found 253.0676.

2-Methyl-3-furanoylbenzo[*b*]thiophene (61i). A clear oil mg, 74% yield) was obtained from 2-furoyl chloride (300 mg, 3 mmol): chromatography solvent, 5% ether in hexane; IR (neat) 3128 (m), 3055 (m), 2854 (m), 1644 (s), 1564 (s), 1461 (s) cm^{-1}; ^{1}H NMR δ 7.76–7.71 (m, 1 H), 7.65–7.61 (m, 2 H), 7.32–7.20 (m, 2 H), 7.11–7.04 (m, 1 H), 6.55–6.53 (m, 1 H), 1.26 (s, 3 H); ^{13}C NMR δ 179.6, 153.1, 147.1, 145.2, 138.5, 137.8, 131.5, 124.5, 124.2, 122.7, 121.5, 120.2, 112.3, 15.2; MS (EI, 70 eV) 242 (M^+, 100), 213 (51), 188 (10), 186 (15), 185 (38), 184 (15), 175 (14), 147 (22), 95 (26), 39 (18); exact mass calcd for $C_{14}H_{10}SO_2$ 242.0402, found 242.0398.

2-Methyl-3-(4-chlorobutynyl)benzo[*b*]thiophene (61j). A clear oil (660 mg, 87% yield) was obtained from 4-chlorobutyryl chloride (420 mg, 3 mmol): chromatography solvent, 5% ether in hexane; IR (CH_2Cl_2) 3054 (m), 2986 (w), 2927 (w), 1666 (m), 1451 (m) cm^{-1}; ^{1}H NMR δ 8.13 (d, J = 8.2 Hz, 1 H), 7.74 (d, J = 8.2 Hz, 1 H), 7.34 (t, J = 8.2 Hz, 1 H), 7.30 (t, J = 8.2 Hz, 1 H), 3.69 (t, J = 6.2 Hz, 1 H), 3.13 (t, J = 6.9 Hz, 2 H), 2.77 (s, 3 H), 2.27 (quint, J = 6.6 Hz, 2 H); ^{13}C NMR δ 196.9, 148.0, 138.1, 137.1, 132.5, 125.0, 124.2, 123.4, 121.4, 44.4, 40.3, 26.8, 16.7; MS (EI, 70 eV) 252 (M^+, 9), 176 (12), 175 (100), 147 (19); exact mass calcd for $C_{13}H_{13}ClSO$ 252.0376, found 252.0361.

3-(Benzo[*b*]thienylmethyl)-2-cyclohexen-1-one (61k). A clear oil (670 mg, 60% yield) was obtained from 3-iodo-2-cyclohexen-1-one (670 mg, 3 mmol, −20 °C, (14 h): chromatography solvent, 10% ether in hexane; IR (CCl_4) 2943 (m), 2931 (m), 1676 (s), 1631 (m), 1436 (m) cm^{-1}; ^{1}H NMR δ 7.76–7.66 (m, 2 H), 7.34–7.24 (m, 2 H), 7.06 (s, 1 H), 5.99 (s, 1 H), 3.75 (s, 1 H), 2.34–2.31 (m, 4 H), 1.99–1.93 (m, 2 H); ^{13}C NMR δ 199.3, 162.4, 140.0, 139.7, 139.6, 126.9, 124.1, 123.9, 123.4, 122.7, 38.8, 37.1, 28.8, 22.5; MS (EI, 70 eV) 242 (M^+, 100), 213 (13), 199 (11), 187 (16); exact mass calcd for $C_{15}H_{14}OS$ 242.0765, found 242.0748.

2-(3-Butyl-3-butenyl)thiophene (61l). A clear oil (534 mg, 96% yield) was obtained from (2-bromomethyl)hexene (531 mg, 3 mmol, 20 °C, 14 h): chromatography solvent, hexane; IR (neat) 3075, 2956, 2929, 2871, 2858, 1645 cm^{-1}; ^{1}H NMR δ 7.26 (dd, 1 H, J = 5.2, 1.3 Hz), 6.96 (dd, 1 H, J = 5.2, 3.6 Hz), 16.80 (dd, 1 H, J = 1.3, 3.6 Hz), 4.80 (s, 2 H), 3.0 (t, 2 H, J = 7.2 Hz), 2.45 (t, 2 H, J = 7.2 Hz), 2.10 (t, 2 H, J = 7.2 Hz), 1.40 (m, 4 H), 0.92 (t, 3 H, J = 7.2 Hz); ^{13}C NMR δ 148.8, 145.1, 126.6, 124.0, 122.8, 109.4, 38.0, 35.9, 30.0, 28.4, 22.4, 13.9; MS (EI, 70 eV) 194 (M^+, 4), 110 (12), 97 (100); HRMS calcd for $C_{12}H_{18}S$ 194.1129, found 194.1127.

Analytical Data of Compounds 62, 63, and 65a–i (Table V) Obtained by the Homologation of Various Copper Organometallics (See Typical Procedure). A detailed procedure will also be given for the preparation of zinc homoenolates from lithium enolates.

4-Butyl-4-pentenenitrile (62). A three-neck flask, equipped with a thermometer, addition funnel, septum cap, magnetic stirring bar, and argon outlet, was charged with CuCN (450 mg, 5 mmol), LiCl (420 mg), and THF (5 mL). To this solution was added, via an addition funnel, (iodomethyl)zinc iodide (**4**)[4] (5.7 mL, 8 mmol, 1.4 M in THF), mixed with a THF solution (10 mL) of ZnI_2 (2.55 g, 8 mmol) at such a rate that the temperature remained below −40 °C. The resulting cyanomethyl copper was cooled to −60 °C, and a THF solution (3 mL) of 2-(bromomethyl)-hexene (530 mg, 3 mmol) was added via a syringe. The reaction was allowed to warm to 0 °C and stirred at this temperature for 1 h. The reaction was poured into ether (100 mL) and a saturated aqueous NH_4Cl solution (100 mL). The aqueous layer was separated and extracted twice more with ether (100 mL); the organic layers were combined, washed with brine, and dried ($MgSO_4$). Evaporation of the solvent in vacuo, and purification by flash chromatography (eluting with hexane), afforded the pure product (345 mg, 84% yield) as a clear oil: IR (neat) 3081 (m), 2958 (s), 2931 (s), 2873 (s), 2247 (s), 1648 (s), 1426 (br) cm^{-1}; ^{1}H NMR δ 4.88 (s, 1 H), 4.82 (s, 1 H), 2.48 (t, J = 6.8 Hz, 2 H), 2.36 (t, J = 7.5 Hz, 2 H), 2.05 (t, J = 7.5 Hz, 2 H), 1.47–1.26 (m, 4 H), 0.91 (t, J = 7.5 Hz, 2 H); ^{13}C NMR δ 145.7, 119.3, 110.9, 35.3, 31.4, 29.7, 22.2, 15.9, 13.8; MS (EI, 70 eV) 137 (M^+, 10), 122 (10), 108 (12), 96 (97), 80 (30), 67 (33), 55 (100), 43 (78); exact mass calcd for $C_9H_{15}N$ 137.1204, found 137.1202.

5-Butyl-5-hexenenitrile (63). A three-neck flask, equipped with a thermometer, addition funnel, septum cap, magnetic stirring bar, and argon outlet, was charged with CuCN (450 mg, 5 mmol), LiCl (420 mg, 10 mmol, previously dried at 150 °C under vacuum ca. 0.1 mmHg, 2 h), and THF (5 mL). To this solution was added, bis(iodomethyl)zinc (**5**)[5] (5 mL, 5 mmol, 1 M in THF) at such a rate that the temperature remained below −40 °C. The resulting (2-cyanoethyl)copper was cooled to −60 °C, and THF solution (3 mL) of 2-(bromomethyl)hexene (530 mg, 2 mmol) was added. The reaction mixture was allowed to warm to 0 °C and stirred at this temperature for 1 h and then worked up as described above. Purification by flash chromatography (hexane) afforded the pure product (390 mg, 86% yield) as a clear oil: IR (neat) 3086 (m), 2957 (s), 2931 (s), 2871 (m), 2251 (w), 1645 (m), 1457 (m) cm^{-1}; ^{1}H NMR δ 4.78 (s, 1 H), 4.72 (s, 1 H), 2.32 (t, J = 7.5 Hz, 2 H), 2.17 (t, J = 7.5 Hz, 2 H), 2.08 (t, J = 7.5 Hz, 2 H), 1.82 (q, J = 7.5 Hz, 2 H), 1.25–1.45 (m, 4 H), 0.88 (t, J = 7.5 Hz, 3 H); ^{13}C NMR δ 147.2, 119.4, 110.3, 35.4, 34.6,, 29.9, 23.4, 22.3, 16.4, 13.8; MS (EI, 70 eV) 152 (M + 1, 2), 136 (5), 122 (10), 109 (33); exact mass calcd for $C_{10}H_{18}NH$ 152.1439, found 152.1446.

6-Oxo-4-phenylheptanenitrile (65a): IR (neat) 3929 (m), 2932 (m), 1716 (s), 1494 (s) cm^{-1}; ^{1}H NMR δ 7.1–7.4 (m, 5 H), 3.2 (m, 1 H), 2.7 (m, 2 H), 2.0–2.2 (m, 6 H), 1.8 (m, 1 H); ^{13}C NMR 206.0, 141.0, 128.9, 127.5, 127.2, 119.1, 50.0, 40.2, 31.7, 30.3, 15.2. Compare with ref 60.

5-Butyl-2-methyl-5-hexenenitrile (65b): IR (neat) 3076 (w), 2979 (s), 2957 (s), 2931 (s), 2873 (s), 2239 (w), 1645 (m) cm^{-1}; ^{1}H NMR δ 4.78 (s, 1 H), 4.72 (s, 1 H), 2.61 (m, 1 H), 2.20 (m, 2 H), 2.00 (t, 2 H), 1.72 (m, 2 H), 1.28–1.47 (m, 6 H), 0.92 (t, 3 H); ^{13}C NMR 147.7, 122.6, 109.9, 35.5, 33.1, 32.2, 29.8, 24.9, 22.3, 17.8, 13.8; MS (CI, CH_4) 166 (M, 100), 110 (3); exact mass calcd for $C_{11}H_{20}N$ 166.1596, found 166.1596.

2-(3-Carbethoxy-3-butenyl)cyclohexan-1-one (65c). A three-neck flask, equipped with a thermometer, septum cap, magnetic stirring bar, and argon outlet, was charged with methyllithium (3.4 mL, 5 mmol, 1.4 M in ether). (Trimethylsiloxy)cyclohexene (850 mg, 5 mmol) was added at 25 °C, via syringe, and after 0.5 h at this temperature the lithium enolate was generated. The ether was then removed under vacuum (ca. 0.1 mmHg, 30 min), and THF (2 mL) was added. Bis(iodomethyl)zinc (**5**) (5 mL, 5 mmol) was added at −40 °C, and the reaction mixture was warmed to 25 °C. After 0.5 h the resulting zinc homoenolate was added to a THF solution (5 mL) of CuCN (450 mg, 5 mmol) and LiCl (420 mg, 10 mmol) at −40 °C, via syringe. The resulting copper homoenolate was warmed to 0 °C and cooled to −60 °C. Ethyl α-(bromomethyl)acrylate (580 mg, 3 mmol) was added, and the reaction was warmed to 25 °C. After 1 h, the reaction mixture was worked up as described above, and purification by flash chromatography (5% ethyl acetate in hexane) afforded the pure product (570 mg, 85% yield) as a clear oil: IR (neat) 2979 (s), 2935 (s), 2862 (s), 1715 (s), 1630 (s) cm^{-1}; ^{1}H NMR δ 6.14 (s, 1 H), 5.54 (s, 1 H), 4.19 (q, J = 7.1

Hz, 2 H), 2.42–2.24 (m, 5 H), 2.16–1.73 (m, 4 H), 1.71–1.60 (m, 2 H), 1.46–1.32 (m, 2 H), 1.29 (t, J = 7.1 Hz, 3 H); ^{13}C NMR δ 211.7, 166.4, 140.4, 123.8, 59.9, 49.5, 41.4, 33.5, 28.9, 27.8, 27.5, 24.4, 13.6; MS (CI, NH_3) 242 (MNH_4^+, 100), 225 (MH^+, 29), 136 (36); exact mass calcd for $C_{13}H_{20}O_3H$ 225.1491, found 225.1487.

3-[(2-Oxocyclohexyl)methyl]-2-cyclohexen-1-one (65d). A three-neck flask, equipped with a thermometer, septum cap, magnetic stirring bar, and argon outlet was charged with methyllithium (3.4 mL, 5 mmol, 1.5 M in diethyl ether). (Trimethylsiloxy)cyclohexene (850 mg, 5 mmol) was added at 25 °C, via syringe, and after 0.5 h at this temperature the lithium enolate was generated. The ether was then removed under vacuum (ca. 0.1 mmHg, 30 min), and THF (2 mL) was added. Bis(iodomethyl)zinc (**5**)[5] (5 mL, 5 mmol) was added at −40 °C, and the reaction mixture was warmed to 25 °C. After 0.5 h, the zinc homoenolate was added to a THF solution (4 mL) of Pd(dba)$_2$ (57 mg, 0.10 mmol), triphenylphosphine (105 mg, 0.40 mmol), and 3-iodo-2-cyclohexen-1-one (670 mg, 3 mmol). An exothermic reaction occurred, and it was necessary to control the temperature with an ice bath. After 1 h, the reaction was worked up as described above. Purification by flash chromatography (20% ethyl acetate in hexane) afforded the pure product (470 mg, 76% yield) as a clear oil: IR (neat) 2938 (s), 2865 (s), 1712 (s), 1668 (s), 1625 (m), 1449 (m) cm^{-1}; ^{1}H NMR δ 5.81 (s, 1 H), 2.80–2.73 (m, 1 H), 2.62–2.51 (m, 1 H), 2.46–2.17 (m, 5 H), 2.11–1.73 (m, 5 H), 1.71–1.53 (m, 3 H), 1.41–1.25 (m, 2 H); ^{13}C NMR δ 211.1, 199.4, 164.3, 126.6, 48.3, 41.9, 37.5, 37.2, 33.8, 29.9, 27.7, 24.9, 22.5; MS (EI, 70 eV) 206 (M^+, 21), 178 (15), 149 (32), 135 (14), 110 (100); exact mass calcd for $C_{13}H_{18}O_2$ 206.1306, found 206.1305.

1-(3-Butenyl)cyclohexanecarboxaldehyde (65e).[61] A three-neck flask, equipped with a thermometer, septum cap, magnetic stirring bar, and argon outlet, was charged with methyllithium (3.4 mL, 5 mmol, 1.5 M in ether). [(Trimethylsiloxy)methylidene]-cyclohexane (920 mg, 5 mmol) was added at 25 °C, and after 0.5 h the lithium enolate was generated. The ether was then removed under vacuum (ca. 0.1 mmHg, 30 min), and THF (2 mL) was added. Bis(iodomethyl)zinc (**5**) (5.0 mL, 5 mmol) was added at −40 °C, and the reaction mixture was warmed to 25 °C. After 0.5 h, the resulting zinc homoenolate was added to a THF solution (5 mL) of CuCN (450 mg, 5 mmol) and LiCl (420 mg, 10 mmol) at −40 °C. The resulting copper homoenolate was warmed to 0 °C and then cooled to −60 °C. Allyl bromide (3 mL, 35 mmol) was added, via syringe, and the reaction was warmed to 25 °C. After 1 h, the reaction mixture was worked up as described above. Purification by flash chromatography (1% ethyl acetate in hexane) afforded the pure product (620 mg, 75% yield) as a clear oil: IR (neat) 2933 (s), 2690 (m), 2853 (s), 1726 (s), 1641 (m), 1453 (m) cm^{-1}; ^{1}H NMR δ 9.43 (s, 1 H), 5.81–5.68 (m, 1 H), 5.03–4.92 (m, 2 H), 1.97–1.87 (m 4 H), 1.59–1.49 (m, 5 H), 1.39–1.24 (m, 5 H); ^{13}C NMR δ 206.6, 138.2, 114.7, 49.4, 35.6, 31.0, 27.7, 25.7, 22.5; MS (EI, 70 eV) 166 (M^+, 2), 136 (26), 128 (26); exact mass calcd for $C_{11}H_{18}O$ 166.1358, found 166.1355.

***N*-(3-Methyleneheptyl)piperidine (65f):** IR (neat) 3105 (w), 2931 (s), 2871 (s), 1644 (s) cm^{-1}; ^{1}H NMR δ 4.65 (br s, 2 H), 2.32 (m, 6 H), 2.18 (t, 2 H), 1.97 (t, 2 H), 1.57 (m, 4 H), 1.20–1.42 (m, 6 H), 0.84 (t, 3 H); ^{13}C NMR 148.4, 109.3, 58.4, 54.6, 36.1, 33.3, 30.0, 26.0, 22.4, 13.9; MS (CI, NH_3) 196 (20), 98 (100); exact mass calcd for $C_{13}H_{26}N$ (MH^+) 196.2065, found 196.2063.

***N*-(3-Methyleneheptyl)morpholine (65g):** IR (neat) 3070, 2957, 2929, 2875, 2856, 1640 cm^{-1}; ^{1}H NMR δ 4.78 (s, 1 H), 4.70 (s, 1 H), 3.80 (m, 4 H), 2.50 (m, 4 H), 2.20 (t, 2 H, J = 7.0 Hz), 2.00 (t, 2 H, J = 7.0 Hz), 1.30 (m, 4 H), 0.96 (t, 3 H, J = 7.0 Hz); ^{13}C NMR δ 109.6, 66.9, 57.9, 53.7, 36.0, 33.0, 29.9, 22.3, 13.9; MS (CI, CH_4) 198 (MH^+, 24), 176 (2), 163 (6), 119 (2), 100 (100); exact mass calcd for $C_{12}H_{24}NO$ (MH^+) 198.1858, found 198.1854.

***N*-Benzyl-*N*-methyl-3-butyl-3-butenylamine (65h):** IR (neat) 3065 (m), 3027 (m), 2955 (s), 1644 (m) cm^{-1}; ^{1}H NMR δ 7.20–7.30 (m, 5 H), 4.72 (s, 2 H), 3.51 (s, 2 H), 2.52 (t, 2 H), 2.50 (d, 2 H), 2.20 (s, 3 H), 2.00 (t, 2 H), 1.20–1.45 (m, 4 H), 0.9 (t, 3 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 148.2, 139.2, 128.9, 128.0, 126.8, 109.5, 62.2, 56.2, 42.1, 35.9, 33.8, 30.0, 22.4, 13.9; MS (CI, CH_4) 232 (36), 134 (100); exact mass calcd for $C_{16}H_{26}N$ (MH^+) 232.2065, found 232.2056.

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Supplementary Material Available: ^{1}H and ^{13}C spectra of new products (190 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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