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5-Aminocyclopentadienes by intramolecular addition of enolether to aminoallene functionalities

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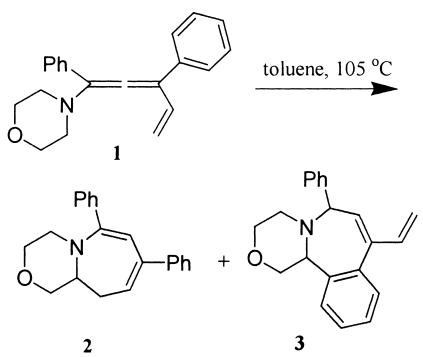
Abstract—3-(1-Alkoxyvinyl)-1-aminoallenes **6** were generated by conjugate addition of acyclic and cyclic (1-alkoxyvinyl)cuprates with the semicyclic propyne iminium salt **4**. They isomerized smoothly into spiroannellated cyclopentadienes **7** through a 1,5-cyclization that in some cases occurred already at ≤20°C. (1-Methoxyallenyl)cuprates reacted with salt **4** in a 2:1 ratio to give the 5,5-dimethoxy-4-methylenepentalene-1-spiro-2′-dihydroindole derivative **10**. The thermal isomerization of morpholinoallene **12** into cyclopentadiene **13** indicates that the novel 1,5-cyclization can be extended to other 3-(1-alkoxyvinyl)-1-aminoallenes as well.

1. Introduction

Vinylallenes are useful building blocks for the synthesis of polyenes and carbocycles of biological significance.[1] Many of these syntheses are based on the ability of vinylallenes to get involved in several pericyclic reactions, such as [1,5]-sigmatropic H shifts,[2] electrocyclic ring closure to form methylenecyclobutene derivatives,[3] and intra-[1] as well as intermolecular[4] [4+2] cycloaddition reactions.

Vinylallenes featuring a more electron-rich allene moiety, such as 1-morpholino-3-vinylallene **1**, rearrange thermally into [1,4]oxazino[4,3-*a*]azepine derivatives **2** (Scheme 1).[5] This isomerization is likely to proceed via a [1,4]-H shift in the C=C–NCH moiety and subsequent 1,7-electrocyclization of the resulting α,β,γ,δ-unsaturated azomethine ylide. As the concomitant formation of **3** as well as other examples[6] show, the 1,7-electrocyclization also takes place when the vinylic double bond is replaced by a (hetero)aromatic π bond.



Scheme 1.

We report now that the thermal isomerization pathway changes when the aminoallenes are decorated with a 1-alkoxyvinyl rather than a simple vinyl substituent at the allenic C-3 position.

2. Results and discussion

We have shown in previous work[5–7] that highly substituted aminoallenes can be prepared conveniently from propyne iminium salts and organocuprates. In an extension of these studies, we decided to use (1-alkoxyvinyl)cuprates because they would allow the introduction of additional functionality into the resulting aminoallenes and their thermal isomerization products (see Section 1).[8] In this paper, we focus on (alkoxyvinyl)allenes derived from the semicyclic propyne iminium salt **4**[9] because their thermal isomerization reactions cover a remarkably wide temperature range, depending on the enolether function. Salt **4** was allowed to react with (1-ethoxyvinyl)cuprate **5a** between −60 and −40°C (Scheme 2). To our surprise, the product that was obtained, after bringing the reaction mixture to room temperature followed by extraction into pentane, was not the expected vinylallene **6a** but rather, the spiroannellated cyclopentadiene **7a**. This product is likely to result from a 1,5-cyclization that includes nucleophilic attack of the enolether function's β-carbon at the amino-substituted allenic carbon atom, and subsequent 1,4-migration of a

Keywords: allenes; copper and compounds; cyclization; cyclopentadienes; iminium salts; spiro compounds.

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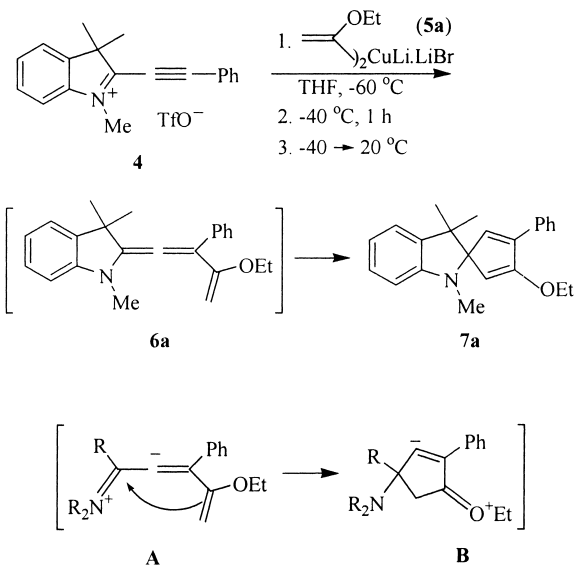
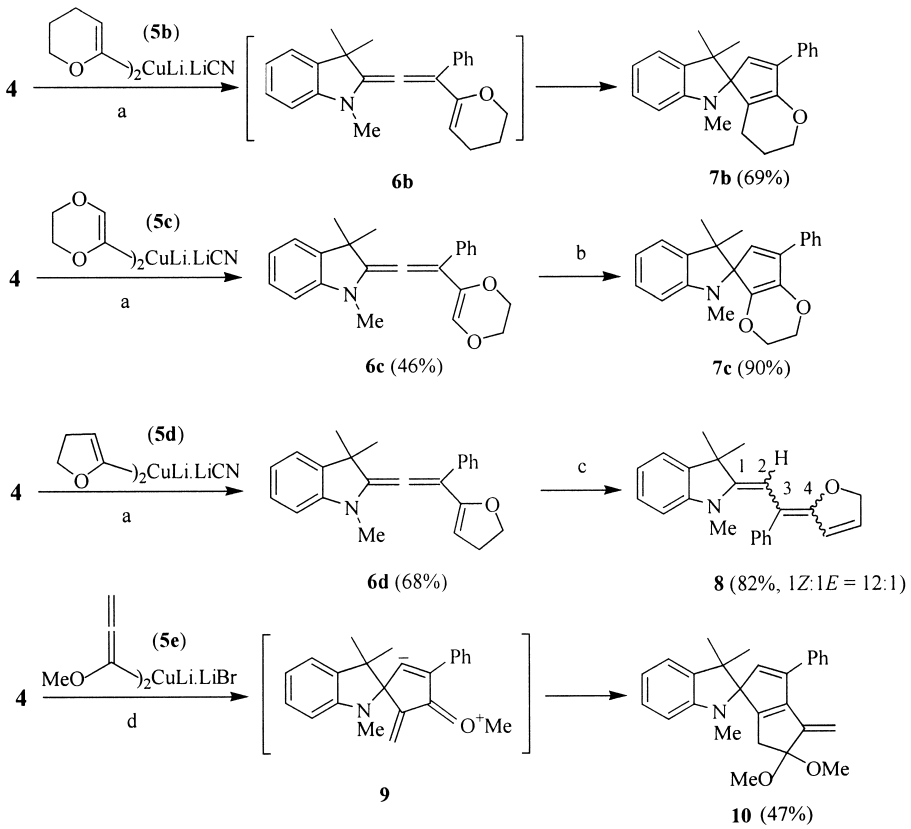


Scheme 2.

proton. The description of the cyclization step as **A→B** (Scheme 2), where **A** represents a resonance structure of the enamine function in **6a**, illustrates that it may also be called a 5-exo-trig iminium cyclization.

When iminium salt **4** was combined with Gilman–Lipshutz cuprates derived from cyclic enolethers,[10] the thermal stability and isomerization pathway was found to depend on the exact nature of the enolether function (Scheme 3). As in the case of **6a**, dihydropyran-2-yl-substituted aminoallene **6b** was not observed due to its rapid isomerization into cyclopenta[*b*]pyran derivative **7b**, the constitution of which was confirmed by XRD analysis. In contrast, allenes bearing 1,4-dioxen-2-yl (**6c**) and dihydrofuran-2-yl (**6d**) groups, respectively, could be isolated and fully characterized. When **6c** was heated in toluene (80°C, 12 h), it also underwent 1,5-cyclization yielding spiroannellated cyclopenta-1,4-dioxin derivative **7c**. Allene **6d** did not react analogously but rather rearranged into 1,3,5-triene **8** which was obtained as a 12:1 mixture of diastereomers. Based on the inspection of ^{1}H chemical shifts, we assume the presence of the *Z* and *E* isomers with respect to the enamine double bond. The phenyl ring at C-3 is expected to be in an almost perpendicular position with respect to the 1,3-diene system, and should therefore cause magnetic shielding of neighboring methyl groups at the dihydroindole ring. In agreement with this, we observed a shielding of the NMe protons in the major (*Z*) isomer by −0.49 ppm relative to the minor isomer and, conversely, a high-field shift of the CMe_2 protons in the *E* isomer ($\Delta\delta$=−0.34 ppm). The configuration at the C-3–C-4 double bond in **8** could not be assigned; nOe experiments were not applicable because of the very similar chemical shifts of 2-H and the allylic protons in the dihydrofuran ring which prevented selective irradiation at the 2-H resonance. The mechanism of the isomerization **6d→8** deserves some comment: what looks like a simple [1,5]-H shift, can hardly be a concerted sigmatropic reaction since the configuration of the endocyclic enolether double bond prevents the formation of an unstrained cyclic transition structure. We propose that this



Scheme 3. (a) THF, −60°C, then 1 h at −40°C, then −40°C→rt during 2 h. (b) Toluene, 80°C, 12 h. (c) Toluene, 100°C, 2.5 h. (d) Conditions as for (a), 1 or 2 equiv. of **5e**.

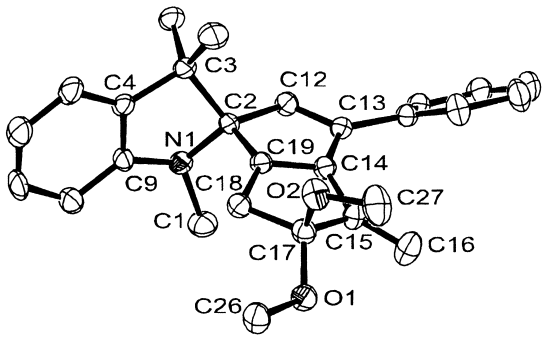
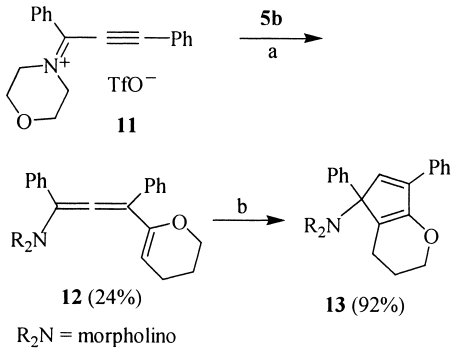


Figure 1. Molecular structure of **10** in the solid state (ORTEP plot). Only one of two molecules not related by space group symmetry is shown. Distances (Å): C12–C13 1.334(6), C14–C19 1.345(6), C15–C16 1.325(7), C17–C18 1.546(7).



Scheme 4. (a) THF/CH_2Cl_2, 3 h at −40°C, then −40°C→rt. (b) Toluene, 135°C, 4 h; or $CHCl_3$, rt, 2 h.

thermal rearrangement begins with the formation of an azomethine ylide by a [1,4]-H shift from the NMe group to the central allenic carbon. Instead of following the 1,7-electrocyclization pathway discussed in Section 1 (see also Scheme 1), this intermediate is flexible enough to allow an allylic hydrogen atom in the dihydrofuran ring to undergo a concerted [1,8]-migration.

Iminium salt **4** reacted with 1 equiv. of (1-methoxyallenyl)cuprate **5e** to form the 5,5-dimethoxy-4-methylene-pentalene-1-spiro-2′-dihydroindole derivative **10** in 47% isolated yield (Scheme 3). Its constitution was established beyond doubt by XRD analysis (Fig. 1). Evidently, two methoxyallene moieties are incorporated into **10**. This fact led us to repeat the reaction by applying 2 equiv. of the cuprate, since it is known that cuprates of the type R_2CuLi in general deliver only one organic residue.[11] However, no yield improvement was achieved. Furthermore, several variations of reaction parameters (Et_2O instead of THF as the solvent, reaction time; modification of the cuprate, e.g. RCu(CN)Li, RCuLi, R(2-thienyl)CuLi·LiCN (R=1-methoxyallenyl)) were probed, but in no case the yield could be improved.

Although further experimental investigations of this interesting transformation are required, the currently available results suggest that **4** reacts with alkoxyallenyl cuprates in two addition steps, the addition of the second allene moiety to a precursor of **10** being faster than the formation of the latter. In line with the formation of cyclopentadienes **7a–c**, it may be assumed that the initially formed bis(allene) undergoes a spontaneous 1,5-cyclization leading to the dipolar intermediate **9**. Due to the absence of a transferable proton, the latter cannot tautomerize to give a neutral cyclopentadiene, as in the cases of **7a–c**. Rapid addition of another organocopper species [a second molecule of excess R_2CuLi or, in the case of a 1:1 stoichiometry, (allenyl)copper(I)] followed by ring-closure and OMe migration would finally yield the tricylic compound **10**.

The widely differing reaction temperatures for the thermal isomerization of (alkoxyvinyl)allenes **6a–d** and **12** deserve some comments. Obviously, the indoline-derived allenes **6** are better suited for the cyclization reaction than the acyclic morpholinoallene **12** (**6b** isomerizes at ≤20°C, while **12** requires heating at 135°C), because the angle strain of the indoline ring in **7** is smaller than in **6** due to rehybridization of C-2(ring) from sp^2 to sp^3. On the other hand, the readiness of allenes **6** to undergo the cyclization depends on the nucleophilicity of the enolether moieties, and in this respect, the dihydrodioxin substituent in **6c** is clearly disfavored. In the case of **6d**, it can be argued that the distance between the β-C atom of the enolether function and the amino-substituted allenic carbon atom is larger than in all other cases due to the larger exocyclic bond angle at C-2 (dihydrofuran). This geometric factor may push the activation energy for 1,5-cyclization to a value that is higher than the barrier for the [1,4]-H shift generating an azomethine ylide intermediate.

The cases of **7a–c** and **10** illustrate that this novel synthesis of aminocyclopentadienes covers a range of useful enolether building blocks. The reaction shown in Scheme 4 indicates that there is also flexibility in the choice of the amino component, i.e. in the propyne iminium salt serving as starting material. Propynylidene-morpholinium salt **11** reacted with cuprate **5b** to give the expected morpholinoallene **12** which, in contrast to its relative **6b**, could be isolated. The low yield of **12** is caused by extensive homocoupling of the cuprate to give 2,2′-bis(5,6-dihydro-4*H*-pyran).[12] Efforts to suppress this side reaction, which was not a problem for the combination of **5b** with **4**, by variation of the reaction temperature were not successful so far. Allene **12** did not undergo the thermal isomerization shown for the vinylallene analogue **1** in Scheme 1, but could rather be rearranged into a cyclopentadiene, like the (alkoxyvinyl)allenes **6a–c**. Transformation of **12** into morpholino-substituted cyclopenta[*b*]pyran **13** required heating in toluene at 135°C (pressure vial), but was also achieved when **12** was kept in $CHCl_3$ solution at rt. In the latter case, the isomerization is obviously proton-catalyzed and proceeds via an iminium ion resulting from protonation of the enamine function.[13]

Unfortunately, our efforts to obtain further (alkoxyvinyl)-allenes from iminium salt **11** and other enolether cuprates **5** have not been successful so far since only product mixtures were obtained which could not be separated and identified. However, work with other acyclic propyne iminium salts reacting in the desired way is in progress.

In conclusion, a previously unknown thermal isomerization of 1-amino-3-(1-alkoxyvinyl)allenes has allowed us to develop a novel synthesis of 5-amino-cyclopentadienes of

various structural types. This methodology is complementary, in terms of substituents and substitution patterns, to the recently reported cyclopentadiene synthesis by a formal [3+2] cycloaddition of β-(dialkylamino)alkenylidene chromium complexes with terminal alkynes.[14]

3. Experimental

3.1. General

NMR spectra: Bruker AC 200 (^{1}H: 200.13 MHz, ^{13}C: 50.32 MHz) and Bruker AM 400 (^{1}H. 400.13 MHz, ^{13}C: 100.61 MHz). Unless stated otherwise, the spectra were recorded with the latter instrument. TMS was applied as the internal standard. IR spectra: Perkin–Elmer IR-Spectrophotometers 1310 and 883, wavenumbers (cm^{-1}) are given. Elemental analyses: Perkin–Elmer EA 2240. Mass spectra: Varian MAT 711. Flash column chromatography was performed on silica gel Si60 (Macherey-Nagel, 0.063–0.2 mm).

All reactions were carried out in rigorously dried glassware under an argon atmosphere. Solvents were dried according to standard methods and stored under an argon atmosphere. Compounds **4**[9] and **11**[15] were prepared by published procedures.

3.2. Preparation of cuprates 5a–e

All cuprates were prepared by variation of procedures reported in the literature.

3.2.1. (1-Ethoxyvinyl)$_2$CuLi·LiBr (5a). A solution of freshly distilled ethyl vinyl ether (0.57 mL, 6.0 mmol) in THF (5 mL) was cooled at −30°C, and a 1.7 M solution of *tert*-butyl lithium in hexane (3.53 mL, 6.0 mmol) was added. The yellow solution was brought to 0°C and stirred for 15 min whereupon the color faded, then slowly added to a suspension of CuBr·Me$_2$S (0.62 g, 3.0 mmol) in THF (15 mL) that was kept at −60°C. The suspension was warmed at −30°C to form a clear red solution which was cooled again at −60°C for further use.

3.2.2. (5,6-Dihydro-4*H*-pyran-2-yl)$_2$CuLi·LiCN (5b). A solution of freshly distilled 5,6-dihydro-4*H*-pyran (0.56 mL, 6.0 mmol) in THF (5 mL) was cooled at 0°C and a 1.7 M solution of *tert*-butyl lithium in hexane (3.53 mL, 6.0 mmol) was added dropwise. The yellow solution was stirred until the color had disappeared (ca. 1 h), then it was gradually added to a suspension of copper(I) cyanide (0.269 g, 3.0 mmol) in THF (15 mL) kept at −60°C. The suspension was warmed to −20°C in order to form a homogeneous solution. This solution was cooled to −60°C for further use.

3.2.3. (5,6-Dihydro-1,4-dioxin-2-yl)$_2$CuLi·LiCN (5c). A solution of freshly distilled 5,6-dihydro-1,4-dioxin (0.48 mL, 6.0 mmol) in THF (5 mL) was cooled at −40°C and a 1.7 M solution of *tert*-butyl lithium in hexane (3.53 mL, 6.0 mmol) was added dropwise. The yellow solution was brought to 0°C and stirred for 10 min whereupon the color faded. It was then added gradually to a suspension of copper(I) cyanide (0.269 g, 3.0 mmol) in THF (15 mL) cooled at −60°C. After the addition was completed, the mixture was brought to 0°C within 5 min and after a homogeneous yellowish solution had formed (ca. 15 min), it was cooled to −60°C for further use.

3.2.4. (4,5-Dihydrofuran-2-yl)$_2$CuLi·LiCN (5d). A solution of freshly distilled 4,5-dihydrofuran (0.47 mL, 6.0 mmol) in THF (5 mL) was cooled at 0°C and a 1.6 M solution of *n*-butyl lithium in hexane (3.75 mL, 6.0 mmol) was added dropwise. After 30 min, this solution was added to a suspension of copper(I) cyanide (0.269 g, 3.0 mmol) in THF (15 mL) cooled at −60°C. After the addition was completed, the mixture was brought to −10°C and kept at this temperature for 15 min to form a homogeneous solution. It was then cooled to −60°C for further use.

3.2.5. (1-Methoxy-1,2-propadienyl)$_2$CuLi·LiBr (5e). THF (5 mL) was cooled at −30°C and a 1.6 M solution of *n*-butyl lithium in hexane (3.75 mL, 6.0 mmol) in hexane was added. After dropwise addition of methoxypropa-1,2-diene (0.51 mL, 6 mmol) and stirring for another 15 min at −30°C, the solution was added dropwise to a suspension of copper(I) bromide dimethyl sulfide complex (CuBr·SMe$_2$) (0.62 g, 3.0 mmol) in THF (15 mL) kept at −60°C. The mixture was brought to −40°C and after formation of a clear orange-colored solution cooled again at −60°C for further use.

3.3. Aminoallenes 6 and their isomerization products

3.3.1. 2,3-Dihydro-2-[2-(5,6-dihydro-1,4-dioxin-2-yl)-2-phenylvinylidene]-1,3,3-trimethyl-1*H*-indole (6c). To a solution of cuprate **5c** (3 mmol) in THF, kept at −60°C, was added dropwise a suspension of iminium salt **4** (1.23 g, 3.0 mmol) in THF (15 mL). The reaction mixture was then stirred for 1 h at −40°C and was finally allowed to assume rt within 2 h. The solvent was evaporated (0.01 mbar), and the dark residue was extracted with pentane (3×70 mL). Concentration of the combined pentane extracts gave a yellow oil which could be crystallized when dissolved in pentane and cooled at −30°C. Yield: 0.48 g (46%); light-brown powder, mp 68°C. IR (KBr): ν 1920 (s, br, C═C═C), 1625 (s), 1590 (vs) cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.34/1.43 (2s, CMe_2), 2.96 (s, NMe), 4.10 (m, 4H, OCH_2CH_2O), 6.16 (s, 1H, OCH═), 6.49 (d, J=7.7 Hz, 1H), 6.72 (t, J=7.4 Hz, 1H), 7.05–7.47 (m, 7H$_{arom}$). ^{13}C NMR ($CDCl_3$): δ 29.0/29.1 (CMe_2), 30.3 (NMe), 44.7 (CMe_2), 64.1/64.2 (OCH_2CH_2O), 105.0 (CH), 117.5 (NC═C═*C*), 117.7 (CH), 121.6 (CH), 127.2 (CH), 127.5 (CH), 127.6 (OCH═), 127.9 (2CH), 128.4 (2CH), 134.8, 137.0, 137.5, 146.5 (N*C*═C═C), 191.3 (NC═*C*═C). Anal. calcd for $C_{23}H_{23}NO_2$: C 79.97, H 6.71, N 4.06; found C 80.0, H 6.9, N 4.1.

3.3.2. 2,3-Dihydro-2-[2-(4,5-dihydrofuran-2-yl)-2-phenylvinylidene]-1,3,3-trimethyl-1*H*-indole (6d). Prepared from cuprate **5d** (3 mmol) and iminium salt **4** (1.23 g, 3.0 mmol) as described for **6c**. Yield: 0.67 g (68%), colorless powder, mp 62°C. IR (KBr): ν 1920 (m, br, C═C═C), 1700 (m), 1595 (vs) cm^{-1}. ^{1}H NMR (400 MHz): δ 1.34/1.44 (2s, CMe_2), 2.68 (dt, J=9.3, 9.4 Hz, 2H, OCH_2CH_2), 2.91 (s, NMe), 4.35 (m_c, 2H, OCH_2), 4.95 (m_c, 1H, OCH═), 6.43 (d, J=7.7 Hz, 1H),

6.67 (t, J=7.4 Hz, 1H), 6.99–7.09 (m, 2H), 7.18 (m_c, $1H_{Ph}$), 7.24–7.28 (m, $2H_{Ph}$), 7.49 (m_c, $2H_{Ph}$). ^{13}C NMR: δ 29.0 (CMe_2), 30.3 (CH_2), 30.7 (NMe), 44.6 (*C*Me$_2$), 69.9 (CH_2), 100.0 (CH), 105.0 (CH), 115.0 (NC=C=*C*), 117.7 (CH), 121.5 (CH), 127.1 (CH), 127.5 (CH), 127.8 (2CH), 128.0 (2CH), 135.0, 137.4, 137.7, 146.4 (N*C*=C), 194.3 (NC=*C*=C).

3.3.3. (2-Ethoxy-3-phenylcyclopenta-1,4-diene)-5-spiro-2′-(2′,3′-dihydro-1,3,3-trimethyl-1*H*-indole) (7a). A suspension of iminium salt **4** (1.23 g, 3.0 mmol) in THF (15 mL) was gradually added at −60°C to the solution of cuprate **5a** (3 mmol). Then, the mixture was warmed at −40°C, stirred for 1 h, and allowed to assume rt during 2 h The solvent was removed (0.01 mbar), and the residue was extracted with pentane (3×70 mL). The combined extracts were concentrated, the remaining oil was purified by flash chromatography (silica gel), and the product was crystallized from CH_2Cl_2–pentane at −30°C to give **7a** as orange crystals (0.74 g, 74%), mp 58°C. IR (KBr): ν 1620 (w), 1590 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.24/1.27 (2s, CMe_2), 1.39 (t, CH_2*Me*), 2.58 (s, NMe), 3.96 (q, OCH_2), 4.93 (d, ^5J=2.4 Hz, =CH), 6.34 (d, ^5J=2.4 Hz, =CH), 6.48 (d, J=7.7 Hz, 1H), 6.73 (dt, J=6.7, 0.8 Hz, 1H), 6.99 (dd, J=7.1, 0.8 Hz, 1H), 7.12 (dt, J=7.7, 1.3 Hz, 1H), 7.25–7.33 (m, 3H), 7.64–7.67 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 14.4 (OCH_2*Me*), 23.8/26.0 (C*Me*$_2$), 30.0 (NMe), 46.4 (*C*Me$_2$), 65.4 (OCH_2), 85.5 (spiro-C), 99.2 (=$CH_{cyclopent}$), 107.4, 117.7, 121.1, 127.3 (2C), 127.6, 128.1 (2C), 131.6, 133.5, 135.3 (=$CH_{cyclopent}$), 139.5, 141.5, 151.1, 159.7. Anal. calcd for $C_{23}H_{25}NO$ (331.5): C 83.34, H 7.60, N 4.23; found C 82.3, H 7.4, N 4.2.

3.3.4. (3,4-Dihydro-2*H*,5*H*-7-phenylcyclopenta[*b*]-pyran)-5-spiro-2′-(2′,3′-dihydro-1′,3′,3′-trimethyl-1*H*-indole) (7b). Prepared as described for **7a** from iminium salt **4** and cuprate **5b**; yield: 0.71 g (69%); colorless crystals, mp 111°C. IR (KBr): ν 1650 (m, OC=C), 1595 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.21/1.30 (2s, CMe_2), 1.61–1.77 (m, 4H, 4-/5-H_{pyran}), 2.49 (s, NMe), 4.00/4.16 ($2m_c$, 2H, 6-H_{pyran}), 6.35 (s, 1H, 5-$H_{cyclopent}$), 6.44 (d, J=7.7 Hz, 1H), 6.68 (dt, J=7.4, 0.9 Hz, 1H), 6.96 (dd, J=7.1, 0.9 Hz, 1H), 7.08 (t, J=7.6, 1.3 Hz, 1H), 7.25 (d, J=7.5, 1.3 Hz, 1H), 7.31 (m_c, 2H), 7.70 (m_c, 2H). ^{13}C NMR ($CDCl_3$): δ 21.6/21.9 (OCH_2*C*H_2), 22.2/27.2 (C*Me*$_2$), 30.1 (NMe), 46.4 (*C*Me$_2$), 67.4 (OCH_2), 85.6 (spiro-C), 106.6 (CH), 113.6, 117.3 (CH), 120.8 (CH), 127.1 (2CH), 127.4 (CH), 127.7 (CH), 128.2 (2CH), 130.9 (CH), 133.4, 139.5, 142.2, 151.4, 153.3. Anal. calcd for $C_{24}H_{25}NO$ (343.5): C 83.93, H 7.34, N 4.08; found C 84.0, H 7.2, N 4.0.

3.3.5. (2,3-Dihydro-7-phenyl-5*H*-cyclopenta-1,4-dioxin)-5-spiro-2′-(2′,3′-dihydro-1′,3′,3′-trimethyl-1*H*-indole) (7c). A solution of allene **6c** (0.69 g, 2.0 mmol) in toluene (3 mL) was heated at 80°C for 12 h (color change to dark-green). The solvent was evaporated (0.01 mbar), the residue was dissolved in dichloromethane, and pentane was added. At −30°C, orange-colored crystals of **7c** were obtained. Yield: 0.62 g, 90%; mp 134°C. IR (KBr): ν 1660 (s, OC=C), 1590 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.32/1.33 (2s, CMe_2), 2.60 (s, NMe), 4.06/4.17 ($2m_c$, 4H, OCH_2CH_2O), 5.92 (s, 1H, $CH_{cyclopent}$), 6.50 (d, J=7.7 Hz, 1H), 6.72 (dt, J=7.4, 0.9 Hz, 1H), 6.98 (dd, J=7.2, 1.1 Hz, 1H), 7.10 (dt, J=7.6, 1.2 Hz, 1H), 7.29 (m_c, 1H), 7.33–7.37 (m, 2H), 7.69–7.72 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 23.0/27.1 (C*Me*$_2$), 30.5 (NMe), 46.4 (*C*Me$_2$), 64.9/65.7 (OCH_2CH_2O), 82.5 (spiro-C), 107.1 (CH), 117.8 (CH), 120.3 (CH), 120.8 (CH), 126.7 (2CH), 127.5 (CH), 128.1 (CH), 128.4 (2CH), 133.3, 134.5, 137.7, 139.3, 140.7, 151.3. Anal. calcd for $C_{23}H_{23}NO_2$: C 79.97, H 6.71, N 4.06; found C 80.0, H 6.8, N 3.8.

3.3.6. 2,3-Dihydro-2-[2-(2,5-dihydrofuran-2-ylidene)-2-phenylethen-1-ylidene]-1,3,3-trimethyl-1*H*-indole (8). A solution of allene **6d** (0.66 g, 2.0 mmol) in toluene (3 mL) was heated at 100°C for 2.5 h. The solvent was evaporated (0.01 mbar), a few drops of ether were added to the residue, and pentane was then added until crystallization started. Yield: 0.54 g (82%); off-white powder, mp 97°C. According to NMR, the product is a 12:1 mixture of *E*/*Z* diastereomers with respect to the NC=C bond. ^{1}H NMR ($CDCl_3$): δ (major/minor isomer) 1.44/1.10 (s, CMe_2), 2.64/3.12 (NMe), 5.11/5.05 (m_c, 2H, OCH_2), 5.15/5.36 (s, br, 1H, NC=CH), 6.24 (dt, J=6.0, 2.3 Hz, 1H, 4-H_{furan}), 6.38 (d, J=8.2 Hz, 1H), 6.56 (dt, J=6.0, 2.3 Hz, 1H, 3-H_{furan}), 6.78 (t, J=7.4 Hz, 1H), 7.07–7.11 (m, 2H), 7.15–7.19 (m, 1H), 7.23–7.31 (m, 4H). ^{13}C NMR ($CDCl_3$): δ (major isomer) 30.3 (C*Me*$_2$), 33.6 (NMe), 45.8 (*C*Me$_2$), 77.2 (OCH_2), 89.6 (NC=*C*H), 106.1 (CH), 109.1 (OC=*C*Ph), 118.8 (CH), 121.5 (CH), 124.9 (CH), 125.8 (CH), 127.4 (CH), 128.0 (2CH), 129.1 (2CH), 131.2 (CH), 138.1, 141.3, 148.0, 155.9 (N*C*=CH), 157.3 (OC=CPh). Anal. calcd for $C_{23}H_{23}NO$ (329.4): C 83.85, H 7.04, N 4.25; found C 82.8, H 7.1, N 4.1.

3.3.7. (1,4,5,6-Tetrahydro-5,5-dimethoxy-4-methylene-pentalene)-1-spiro-2′-(2′,3′-dihydro-1′,3′,3′-trimethyl-1*H*-indole) (10). Prepared from iminium salt **4** (1.23 g, 3.0 mmol) and cuprate **5e** (3 mmol) as described for **7a**. Yield: 0.56 g (47%), yellow crystals, mp 96°C. IR (KBr): ν 1630 (m), 1580 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.20/1.31 (2s, CMe_2), 2.26/2.33 (AB system, J=17.6 Hz, 2H), 2.51 (s, NMe), 3.22/3.24 (2s, 6H, OMe), 5.12 (s, 2H, =CH_2), 6.26 (s, 1H, =$CH_{cyclopent.}$), 6.49 (d, J=7.7 Hz, 1H), 6.73 (dt, J=7.4, 0.9 Hz, 1H), 6.99 (dd, J=7.3, 0.7 Hz, 1H), 7.10 (dt, J=7.6, 1.2 Hz, 1H), 7.31–7.40 (m, 3H), 7.51 (m_c, 2H). ^{13}C NMR ($CDCl_3$): δ 22.8/26.8 (C*Me*$_2$), 30.8 (NMe), 40.9 (CH_2), 46.8 (*C*Me$_2$), 49.4 (OMe), 49.5 (OMe), 86.8 (spiro-C), 107.5 (CH), 107.5 (=CH_2), 111.1 (*C*(OMe)$_2$), 118.0 (CH), 121.1 (CH), 127.5 (2CH), 127.6 (CH), 127.8 (CH), 128.1 (2CH), 135.1, 135.4 (CH), 139.1, 142.5, 144.6, 144.7, 150.8, 156.6.

3.3.8. 4-[1,3-Diphenyl-3-(5,6-dihydro-4*H*-pyran-2-yl)propadienyl]morpholine (12). To a solution of cuprate **5b** (3 mmol, see above) in THF, cooled at −40°C, was added the solution of iminium salt **11** (1.27 g, 3.0 mmol) in dichloromethane (15 mL). After the mixture had kept with stirring at this temperature for 3 h, it was brought to rt and the solvent was evaporated (0.01 mbar). The brown residue was extracted with petroleum ether 40–70°C (2×70 mL) and ether (1×5 mL). The combined organic extracts were concentrated (0.02 mbar) to leave a yellow oil which was redissolved in a small volume of petroleum ether. Low-temperature crystallization gave **12** as a yellow powder which still contained a small amount of 2,2′-bis(5,6-dihydro-4*H*-pyran). Yield: 0.25 g (ca. 24%). ^{1}H NMR

(200.13 MHz, CD_3CN): δ 1.76–1.96 (m, 2H, 5-H_{pyran}), 2.06–2.16 (m, 2H, 4-H_{pyran}), 2.80 (m_c, 4H, NCH_2), 3.79 (pseudo-t, 4H, OCH_2-morph.), 4.05 (pseudo-t, 2H, OCH_2-pyran), 4.84 (t, J=3.8 Hz, 1H, 3-H_{pyran}), 7.20–7.53 (m, 10H_{arom}). ^{13}C NMR (50.32 MHz, CD_3CN): δ 20.9 (5-C_{pyran}), 22.4 (4-C_{pyran}), 51.3 (NCH_2), 66.4 (6-C_{pyran}), 67.0 (OCH_2-morph.), 96.7 (3-C_{pyran}), 114.9 (NC═C═*C*), 116.7, 127.1, 127.3, 127.7, 128.1, 128.2, 128.3, 129.3, 134.7, 136.5, 148.0. 150.0, 200.7 (NC═*C*═C).

3.3.9. 3,4-Dihydro-2*H*,5*H*-5,7-diphenyl-5-morpholino-cyclopenta[*b*]pyran (13). A solution of **12** (0.27 g, 0.75 mmol) in chloroform (5 mL) was stirred for 2 h. The solvent was evaporated, and the residue was purified by flash chromatography (silica gel) to give the product as a yellow powder. Yield: 0.25 g (92%). ^1H NMR (200.13 MHz, $CDCl_3$): δ 1.8–2.0 and 2.05–2.20 (2 m, 4H, $OCH_2CH_2CH_2$), 2.65 (m_c, 4H, NCH_2), 3.70 (pseudo-t, 4H, OCH_2-morph), 3.95–4.10 (m, 2H, 2-H_2), 6.75 (s, 1H, 6-H), 7.20–7.80 (m, 10H_{arom}). ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 19.3 (CH_2), 22.3 (CH_2), 48.4 (NCH_2), 67.4 (OCH_2-pyran), 67.8 (C-5), 67.9 (OCH_2-morph.), 117.0 (C-4a), 127.2, 127.5, 127.8, 128.1, 128.3, 128.5, 129.2, 129.4, 132.7, 133.4, 141.4, 142.1, 151.7. MS (FD, 8 keV): *m*/*z* 359 (100%) [M^+].

3.4. X-Ray diffraction analysis of compounds 7b and 10

Data collection on single crystals of **7b** and **10** was performed with a diffractometer CAD4 (Enraf-Nonius), operating in the omega-2theta scan mode, with monochromatized Mo Kα radiation (λ=0.71073 Å). The structures were solved with direct methods and refined with full-matrix least-squares procedures using F^2 values. Relevant crystal data and details of the structure determination are given below. Crystallographic data have been deposited as CCDC-186967 (for **7b**) and 186968 (for **10**). These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge crystallographic data centre, 12, Union road, Cambridge CB2 1EZ, UK; fax: +44-1223-336-033).

3.4.1. Compound 7b. $C_{24}H_{25}NO$, M_r=343.5; triclinic, space group $P\bar{1}$ (no. 2), a=9.926(2), b=12.028(3), c=8.660(3) Å, α=106.31(2), β=104.99(2), γ=74.77(2)° V=938.2(8) Å^3, Z=2; D_{calc}=1.216 mg m^{-3}, μ=0.07 mm^{-1}. Data collection: Crystal size 0.30×0.30×0.75 mm, T=293(2) K; theta range for data collection 2.00–24.00°; $-9\le h\le 9$, $-10\le k\le 11$, $0\le l\le 13$; 3088 collected reflections, 2774 independent reflections (R(int)=0.053), 1977 observed reflections [$I>2\sigma(I)$]. Final R indices of the structure refinement (1977 data with $I>2\sigma(I)$, 310 parameters): $R1$=0.0576, $wR2$=0.0515, residual electron density between 0.17 and −0.09 e. Å^{-3}.

3.4.2. Compound 10. $C_{27}H_{29}NO_2$, M_r=399.5; triclinic, space group $P\bar{1}$ (no. 2), a=8.7098(6), b=16.354(8), c=18.392(12) Å, α=64.69(6), β=89.48(4), γ=74.91(5)° V=2270(2) Å^3, Z=4; D_{calc}=1.169 mg m^{-3}, μ=0.073 mm^{-1}. Data collection: Crystal size 0.65×0.50×0.30 mm, T=293(2) K; theta range for data collection 2.24–22.91°; $0\le h\le 9$, $-16\le k\le 17$, $-19\le \mathbf{l}\le 20$; 6472 collected reflections, 6240 independent reflections (R(int)=0.037), 3345 observed reflections [$I>2\sigma(I)$]. Structure refinement with 6235 data and 551 parameters gave the following final R indices: $R1$=0.0731, $wR2$=0.1281 ($I>2\sigma(I)$); $R1$=0.1518, $wR2$=0.1784 (all data); residual electron between 0.20 and −0.21 e. Å^{-3}.

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References

1. (a) Okamura, W. H.; Curtin, M. L. *Synlett* **1990**, 1–9. (b) Okamura, W. H. *Acc. Chem. Res.* **1983**, *16*, 81–89.
2. (a) Wu, K-M.; Midland, M. M.; Okamura, W. H. *J. Org. Chem.* **1990**, *55*, 4381–4392. (b) Shen, G.-Y.; Tapia, R.; Okamura, W. H. *J. Am. Chem. Soc.* **1987**, *109*, 7499–7506.
3. (a) Lopez, S.; Rodriguez, J.; Rey, J. G.; de Lera, A. R. *J. Am. Chem. Soc.* **1996**, *118*, 1881–1891. (b) Murakami, M.; Amii, H.; Itami, K.; Ito, Y. *Angew. Chem.* **1995**, *107*, 1649–1650.
4. Koop, U.; Handke, G.; Krause, N. *Liebigs Ann. Chem.* **1996**, 1487–1500.
5. Mayer, T.; Maas, G. *Tetrahedron Lett.* **1992**, *33*, 205–208.
6. Reinhard, R.; Glaser, M.; Neumann, R.; Maas, G. *J. Org. Chem.* **1997**, *62*, 7744–7751.
7. Schlegel, J.; Maas, G. *J. Prakt. Chem.* **2000**, *342*, 235–239.
8. In contrast to other organocuprates, (1-alkoxyvinyl)cuprates have been applied surprisingly little for C–C bond forming reactions; see, e.g. Friesen, R. W. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1969–2001, review.
9. Reinhard, R.; Maas, G.; Bohrisch, J.; Liebscher, J. *Liebigs Ann. Chem.* **1994**, 429–432.
10. We found that in the case of cyclic enolethers, cuprates $R_2CuLi{\cdot}LiCN$ (Gilman–Lipshutz type) gave cleaner reactions and better yields than cuprates R_2CuLi (Gilman type), while the opposite was true for cuprates derived from ethyl vinyl ether and methoxyallene, respectively.
11. Recent reviews on cuprate chemistry (a) Krause, N. *Angew. Chem.* **1997**, *109*, 194–213. (b) Krause, N. *Angew. Chem. Int., Ed. Engl.* **1997**, *36*, 186–204. (c) Lipshutz, B. H. In *Organometallics in Synthesis*. Schlosser, M., Ed.; Wiley: Chichester, 1994; pp 283–382. (d) In *Modern Organocopper Chemistry*. Krause, N., Ed.; Wiley/VCH: Weinheim, 2002.
12. (5,6-Dihydro-4*H*-pyran-2-yl) lithium undergoes homocoupling in high yield under the action of copper(II) chloride: Ley, S. V.; Leslie, R.; Tiffin, P. D.; Woods, M. *Tetrahedron Lett.* **1992**, *33*, 4767–4770.
13. See Ref. 4 for a transformation that appears to include a Lewis acid mediated vinylallene-to-cyclopentadiene isomerization.
14. (a) Flynn, B. L.; Schirmer, H.; Duetsch, M.; de Meijere, A. *J. Org. Chem.* **2001**, *66*, 1747–1754. (b) Schirmer, H.; Funke, F. J.; Müller, S.; Noltemeyer, M.; Flynn, B. L.; de Meijere, A. *Eur. J. Org. Chem.* **1999**, 2025–2031. (c) Flynn, B. L.; de Meijere, A. *J. Org. Chem.* **1999**, *64*, 400–404.
15. Maas, G.; Rahm, R. *Synthesis* **1994**, 295–299.