then recrystallized (aqueous methanol, etc.). Ten millimoles of the amide was then dissolved in methanol; 11 mmol of methyl iodide was then added, and the solution was allowed to reflux for 3 h. The resulting precipitate was then collected by filtration and dried. The pyridinium salt was reduced as previously described.

The 3-quinolinecarboxamide and 4-isoquinolinecarboxamide were prepared according to literature procedures,[14] quaternized with methyl iodide, and reduced as previously described.

Kinetic Analysis. The rate of ferricyanide-mediated oxidation of various dihydropyridines was determined using a modification of published methods. In this procedure, the rate of decrease of the band III absorbance (~360 nm) was determined in buffered 20% aqueous acetonitrile solutions [0.1 mM $K_4Fe(CN)_6$, 60 mM KCl, and 1.0 mM K_2CO_3] containing various concentrations of $K_3Fe(CN)_6$ (1-50 mM). The dihydropyridine in acetonitrile was added to the test solutions using a Hamilton syringe. The solutions were maintained at 37 °C in a thermostated cell holder and contained in anerobic screw-top cuvettes (Spectrocell, Inc.) fitted with Teflon septa. For a given ferricyanide concentration, the pseudo-first-order rate constant was determined, and then these values were plotted as a function of ferricyanide ion concentration, generating a slope from which the second-order rate constant (k_0 s^{-1} M^{-1}) was obtained.

In all of the kinetic studies, solutions were prepared with water that had been boiled for 1 h and cooled with a stream of helium passing through it. Throughout the studies, the oxidation of 1-benzyl-1,4-dihydronicotinamide (**17**) was used to confirm the integrity of ferricyanide solutions since oxygen is known to affect the rates of reaction. Acceptable second-order rates for this reaction were 2.25 ± 0.25 s^{-1} M^{-1}. If the rate fell outside of this range, new solutions were prepared. In all cases slopes were linear ($r > 0.995$).

In two cases the extremely slow rate of oxidation (compounds **19** and **20**) prompted the use of HPLC rather than UV analysis. In these circumstances, four different concentrations of ferricyanide (4, 6, 8, and 10 mM) in buffer were prepared as before. At time $t = 0$, the dihydropyridines were added to these solutions and then sampled every 3 h for 100 h. Both compounds could be analyzed with the same mobile phase (70:30 acetonitrile-H_2O) flowing at 1 mL/min. Separation was achieved on a Spherisorb C-18 Alltech Associates/Applied Science 4.6 mm i.d. × 25 cm reversed-phase column operating at ambient (26 °C) temperatures. The retention times for **19** and **20** in this study were 7.0 and 7.8 min, respectively. Samples were provided in duplicate, and each sample was analyzed twice. As in the previous section, slopes were linear ($r > 0.999$).

Supplementary Material Available: Compound characterization data (2 pages). Ordering information is given on any current masthead page.

Highly Stereoselective Synthesis of Chiral Alkylallenes by Organocopper(I)-Induced Anti 1,3-Substitution of Chiral Propynyl Esters[1,2]

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The synthesis of chiral 1,3-dialkylallenes $R^1CH{=}C{=}CHR^2$ of high enantiomeric purity, by applying homogeneous reactions between organocopper(I) reagents of the type [{R^2CuX}$MgX{\cdot}LiX$] and chiral propynyl methanesulfonates or sulfinates at low temperatures in THF, is reported. The reactions are generally fast; typically complete conversion is obtained within a few minutes at -60 °C. Overall, high anti stereoselectivity is observed. A plausible mechanism is put forward, and comparison is made with the stereochemistry of reactions of comparable substrates with d^{10} complexes, e.g. of Pd(0).

Introduction

During the last decade a revival in the synthesis of optically active allenes can be noted.[3] This renewed interest can also be deduced from the recent successful efforts to implement chiral NMR probes for the assessment of enantiomeric purity of (in this respect thusfar elusive) 1,3-dialkylallenes and trialkylallenes.[4]

In 1978 Tadema et al. reported on the efficient synthesis of chiral phenylallenes from 1-phenylprop-2-yn-1-yl esters by applying organocopper(I) reagents.[5] The stereochemistry of the 1,3-substitution involved (see Scheme I) was disputed at first, but it could be unambiguously shown by X-ray crystallography that methylcopper(I) induces stereospecific anti 1,3-substitution in steroidal substrates,[6] in accord with an early proposal by Crabbé c.s.[7] Meanwhile, several more or less successful approaches to chiral allenes have appeared in the literature.[3,8-11] Most of these rely on the same reaction principle but, despite their well-known tendency to racemize chiral allenes,[8] di-

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(9) Neef, G.; Eder, U.; Seeger, A. *Tetrahedron Lett.* **1980**, *21*, 903.

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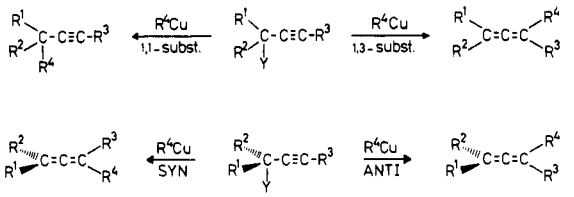
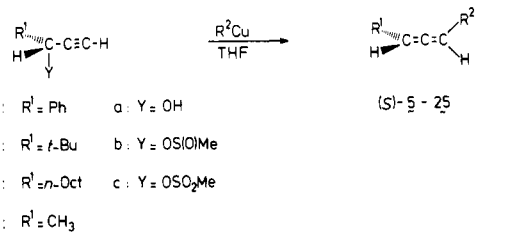
0022-3263/89/1954-3726$01.50/0

Scheme I



Scheme II



organocuprates $[\{R_2Cu\}M]_n$ (M = Li, MgX) have been applied instead of organocopper(I) species $[\{RCuX\}\cdot M]_n$ in many cases. Interestingly, there seem to be no or less problems regarding racemization when diethyl ether is used as the solvent,[3e] whereas with THF as solvent fast racemization of allenes by excess $[R_2CuLi]$ or $[R_2CuLi\cdot MgX_2]$ was reported.[12]

Although methods for the preparation of highly diastereomerically pure steroidal allenes are known, e.g. ref 3b,i, 6, 9, as yet only few straightforward methods have been published pertaining to the synthesis of simple, noncyclic chiral alkylallenes of high enantiomeric purity.[3c,h,j,5] Here we report on our successful efforts in this field, applying organocopper(I)-mediated 1,3-substitutions of methanesulfonate or sulfinate esters of several optically pure (or enriched) prop-2-yn-1-ols.[13]

Results and Discussion

A. Synthesis. Organocopper(I) reagents prepared in situ in THF from $LiCuBr_2$ and 1 equiv of the appropriate Grignard reagent were used as the nucleophiles. Organocopper(I) reagents of the type $[\{RCuX\}M]$ were used rather than diorganocuprates $[\{R_2Cu\}M]$ because of the ability of the latter to racemize chiral allenes (vide supra).[8,12] The choice of the solvent stems from the fact that $LiCuBr_2$ is very soluble in THF at −70 °C, so the complex organocopper reagent $[\{RCuBr\}MgBr\cdot LiBr]$ can be conveniently prepared at low temperatures in a homogeneous environment. Most alkylcopper(I) reagents of this type are quite soluble in THF at low temperatures, only for R = Me and Ph suspensions are obtained. In THF the substitution of excellent nucleofugal groups such as methanesulfonate and -sulfinate occurs at a high rate at low temperatures. Generally, reaction times of 3–5 min at −65 °C were adequate for complete conversion of the propynyl methanesulfonates or -sulfinates into the corresponding allenes. Propynyl trifluoromethanesulfonates appeared to be unstable to thermal decomposition, even when prepared in situ at low temperature. Reactions with heterogeneous copper(I) reagents required prolonged reaction times and higher temperature. It was checked that substrates and products retained their stereochemical integrity under the conditions of the reaction.[14]

Starting from the homochiral series of enantiomerically pure or enriched secondary propynyl esters (*S*)-**1b**, (*R*)-**2c–4c**,[2] *dextrorotatory* 1,3-dialkylallenes **5–25** were obtained in high chemical and optical yields, see Table I. Dextrorotatory (noncyclic) 1,3-dialkylallenes and 1-alkyl-3-phenylallenes have a definite *S* configuration, as has been elaborated by means of (vacuum) circular dichroism studies for representative examples, e.g. **5**, **14**, **21**, and related 1,3-dialkylallenes.[15] The *S* configuration of the allenes formed from (*S*)-**1** or (*R*)-**2–4** can further be deduced by using the now well-established synthetic criterion that similar S_N2' type allene formations from propynyl esters occur with *anti* stereoselectivity.[2,3e,6,16]

The values for the optical rotations of the chiral allenes **5–25** are quite high. The following considerations seem to corroborate our estimate that the molar rotations in Table I refer to (almost) enantiomerically pure allenes:

(i) The allenes **5** and **19** have slightly higher optical rotations (in EtOH, cf. Table I) than the extrapolated values calculated by Mannschreck et al.[4a] for these compounds: $[\alpha]^{20}_D$ 237° (acetone) and 80° (CH_2Cl_2), respectively.[17] These authors presented a method based on binary chiral NMR shift reagents to determine ee's of allenes from integrals in the proton NMR.

(ii) Similar 1,3-substitutions leading to steroidal allenes occur with >98% anti stereoselectivity.[3b,3e,6]

(iii) (*S*)-(+)-1,3-Diphenylallene (**15**) prepared in the described way from (*S*)-**1** and $[\{PhCuBr\}MgBr\cdot LiBr]$ had $[\alpha]^{20}_D$ +1130° (EtOH), which is in magnitude equal to the value of −1137° ($CHCl_3$) reported by Rossi and Diversi for pure (*R*)-**15** obtained after repeated crystallizations.[18]

(iv) An indication of the fact that the reactions with different organocopper(I) reagents R^2Cu and/or with different substrates proceed with equal (high) selectivity is provided by the observation that allenes **5** and **14** are obtained with almost identical optical purities, irrespective of the mode of introduction of the substituents; i.e. whether one is introduced via the propynyl ester and the other via the organocopper(I) reagent, or vice versa (compare entries 1 and 23, 10 and 18 in Table I).

B. Mechanistic Aspects. In all cases reported thusfar, organocopper(I)-mediated S_N2' reactions with propynyl esters proceed with anti stereochemistry, as depicted in Scheme II. A rationalization of the stereochemical outcome of this type of reactions is given in Scheme III. It is likely that first a π-complex between the organocopper(I) fragment and the acetylenic moiety of e.g. **1b** occurs; examples of isolated copper(I)–acetylene complexes are

(12) Westmijze, H.; Nap, I. A.; Meijer, J.; Kleijn, H.; Vermeer, P. *Recl. Trav. Chim. Pays-Bas* **1983**, *102*, 154.

(13) Taken in part from Elsevier, C. J. Ph.D. Thesis, Utrecht, 1984.

(14) (a) Instead of isolable sulfinate **1b** also the thermally unstable methanesulfonate **1c** can be employed. It is then important that within 2 min after the addition of methanesulfonyl chloride to the alcoholate of **1**, the prepared organocopper(I) reagent is added (−65 °C) in order to avoid competitive direct substitution by chloride (which occurs with inversion). The resulting prop-2-ynyl chloride will also react with RCu, but now to give the allene with opposite configuration. (b) Hydrolysis of excess (*S*)-**1b** or (*R*)-**2c** recovered after reaction with 0.5 equiv of EtCu gave the corresponding alcohols of the same ee as the starting propynyl alcohol. (c) Treatment of optically active allenes (*S*)-**5**, **6**, **21**, or **25** with 2 or 3 molar equiv of the organocopper(I) species from which they were generated, during 60 min at the temperature at which the allenes are prepared, resulted in no detectable loss of optical activity. A mixture of $[\{EtCuBr\}MgBr\cdot LiBr]$ and $[\{Et_2Cu\}MgBr\cdot LiBr]$ caused a loss of ca 40% of the optical activity of (*S*)-**6** within 30 min at −60 °C.

(15) (a) Crabbé, P.; Velarde, E.; Anderson, H. W.; Clark, S. D.; Moore, W. R.; Drake, A. F.; Mason, S. F. *Chem. Commun.* **1971**, 1261. (b) Elsevier, C. J.; Vermeer, P.; Gedanken, A.; Runge, W. *J. Am. Chem. Soc.* **1985**, *107*, 2537. (c) Runge, W.; Baumann, H. F.; Hezemans, A. M. F.; van de Coolwijk, P. J. F. M.; Elsevier, C. J.; Vermeer, P. *Chem. Phys.* **1986**, *105*, 227.

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(17) Solvent effects may slightly affect the optical rotations, see: Runge, W.; Ruch, E.; Kresze, G. *J. Am. Chem. Soc.* **1977**, *99*, 5597.

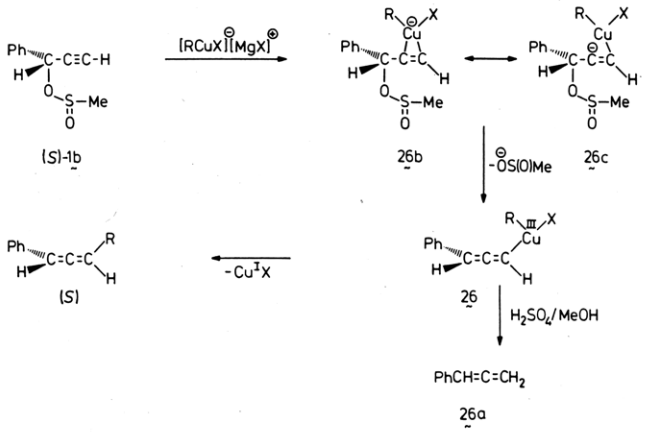
(18) (a) Rossi, R.; Diversi, P. *Synthesis* **1973**, 25. (b) Walbrick, J. M.; Wilson, J. W.; Jones, W. M. *J. Am. Chem. Soc.* **1968**, *90*, 2895.

Table I

entry no.	propynyl ester config[a]	R^1	reagent R^2[b]	allene config	yield,[c] %	$[\alpha]_D^{20}$,[d] deg	$[\Phi]_D^{20}$,[e] deg
1	(*S*)-**1b**	Ph	Me[f]	(*S*)-**5**	78	+256	+333
2	(*S*)-**1b**	Ph	Et	(*S*)-**6**	81	+314	+452
3	(*S*)-**1b**	Ph	*n*-Pr	(*S*)-**7**	77	+317	+501
4	(*S*)-**1b**	Ph	*n*-Bu	(*S*)-**8**	75	+317	+545
5	(*S*)-**1b**	Ph	*n*-Pe	(*S*)-**9**	70	+318	+591
6	(*S*)-**1b**	Ph	*n*-Hex	(*S*)-**10**	72	+308	+616
7	(*S*)-**1b**	Ph	*n*-Oct	(*S*)-**11**	78	+298	+680
8	(*S*)-**1b**	Ph	i-Pr	(*S*)-**12**	71	+345	+545
9	(*S*)-**1b**	Ph	*s*-Bu	(*S*)-**13**	84	+344	+592
10	(*S*)-**1c**	Ph	*t*-Bu	(*S*)-**14**	82	+370	+637
11	(*S*)-**1b**	Ph	Ph[f]	(*S*)-**15**	75	+1130	+2189
12	(*R*)-**2c**	*t*-Bu	Et	(*S*)-**16**	76	+94	+116
13	(*R*)-**2c**	*t*-Bu	*n*-Pr	(*S*)-**17**	82	+96	+133
14	(*R*)-**2c**	*t*-Bu	*n*-Bu	(*S*)-**18**	84	+97	+147
15	(*R*)-**2c**	*t*-Bu	*n*-Pe	(*S*)-**19**	83	+96	+159
16	(*R*)-**2c**	*t*-Bu	i-Pr	(*S*)-**20**	92	+110	+152
17	(*R*)-**2c**	*t*-Bu	*t*-Bu	(*S*)-**21**	96	+124	+188
18	(*R*)-**2c**	*t*-Bu	Ph[f]	(*S*)-**14**	95	+368	+634
19	(*R*)-**3c**	*n*-Oct	Et	(*S*)-**22**	87	+74	+126
20	(*R*)-**3c**	*n*-Oct	*n*-Pr	(*S*)-**23**	86	+72	+140
21	(*R*)-**3c**	*n*-Oct	*n*-Bu	(*S*)-**24**	92	+76	+160
22	(*R*)-**3c**	*n*-Oct	*t*-Bu	(*S*)-**25**	95	+92	+192
23	(*R*)-**4c**	Me	Ph[g]	(*S*)-**5**	90	+245	+320

[a] Homochiral dextrorotatory substrates. [b] 1.0 molar equiv of R^2Cu in THF at −70 to −60 °C during 3–5 min, unless otherwise stated. [c] After chromatography. [d] Measured in EtOH (*c* 0.6–1.2). For entries 12–23 the values are obtained by extrapolation; ee of propynyl alcohols 32–64%. [e] Molar rotation $[\Phi]_D = M\cdot[\alpha]_D/100$. [f] 60 min stirring at 0 °C. [g] 60 min stirring at 0 °C, then 30 min at 20 °C.

Scheme III



known.[19] Subsequent elimination of the leaving group will take place only when the copper and leaving group moieties are in a mutual antiperiplanar disposition (**26b**). In this geometry not only interaction of relevant copper(I) p and d orbitals with the acetylenic π and π^* systems, respectively, is conceivable but an additional donation from the copper $3d_{xz}$ orbital into the C–O antibonding σ^* orbital may occur (see Figure 1). It is this latter interaction that electronically initiates the decoupling of the leaving group. The directional specificity of this process guarantees that the 1,3-substitution occurs with a very high level of anti stereoselectivity. As a result the unstable σ-allenylcopper(III) species (*S*)-**26** is generated, which readily collapses by means of reductive elimination of CuX to give the (*S*)-allenes **5**–**15**. This latter step is assumed to proceed with complete retention of configuration as is usually observed for such alkyl shifts on transition metal centers.[20] An analogous mechanism will pertain in case of the other alkyl-substituted propynyl substrates **2**–**4**.

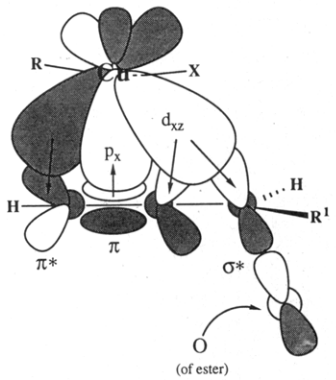


Figure 1. Relevant orbital interactions between copper(I) and the propynyl ester accounting for specific anti substitution.

As to the proposed Cu(III) intermediate, we think that it provides a working scheme and that its occurrence in transient species is quite possible. Occurrence of this type of Cu(III) intermediates has in the past been corroborated: Crabbé c.s.[21a] trapped these chiral species by using e.g. iodine, which experiment provided chiral iodoallenes. Pasto et al. suggested the occurrence of allenylcopper(III) intermediates on the basis of hydrolysis experiments carried out on achiral [(allenyl)Cu(R)Li] species.[21b] The existence of transient dialkylcopper(III) intermediates has earlier been corroborated by Johnson and Dutra,[22a] and allenylcopper(III) species were proposed by Vermeer.[22b] In this work we obtained upon quenching with H_2SO_4 in MeOH after short (ca. 30 s) incubation of the reactants [{RCuBr}MgBr·LiBr] and **1b** at −90 °C, apart from the 1-alkyl-3-phenylallene and **1b**, small amounts (5–10%) of phenylallene (**26a**) as the only other compound. This observation points to the intermediacy of **26**.

(19) Pasquali, M.; Floriani, C.; Venturi, G.; Geantani-Manfredotti, A. *Inorg. Chem.* **1982**, *21*, 4324.

(20) Kochi, J. K. *Organometallic Mechanisms and Catalysis*; Academic: London, 1978; Chapters 7 and 14.

(21) (a) Dollat, J. M.; Luche, J.-L.; Crabbé, P. *J. Chem. Soc., Chem. Commun.* **1977**, 761. (b) Pasto, D. J.; Shine-King, C.; Fritzen, E.; Shults, R. H.; Waterhouse, A.; Hennion, G. F. *J. Org. Chem.* **1978** *43*, 1389.

(22) (a) Johson, C. R.; Dutra, G. A. *J. Am. Chem. Soc.* **1973**, *95*, 7783. (b) Vermeer, P.; Meijer, J.; Brandsma, L. *Recl. Trav. Chim. Pays-Bas* **1975**, *94*, 112.

As an alternative a mechanism involving two successive one-electron transfers from a copper(I) cluster to the substrate, yielding an adduct containing two Cu(II) centers rather than a Cu(III) center, was put forward.[23] Although such a sequence cannot be ruled out, most of the experimental facts seem to indicate a mechanism involving Cu(III). Furthermore, a reaction sequence via Cu(III) as outlined in Scheme III has an analogy in the known mechanism of Pd-catalyzed alkylation (phenylation) of propynyl halides and esters.[3c,d] In that type of catalytic reaction, also high levels of anti 1,3-substitution have been observed and the intermediacy of chiral σ-allenylpalladium(II) compounds could be established.[3c,24] In both cases an oxidative addition (with substitution of the leaving group) with formal changes $d^{10} \rightarrow d^8$ or $d^9s^1 \rightarrow d^8$ occurs on the transition metal. It should be kept in mind, however, that these palladium nucleophiles occur as monomeric species in solution, whereas the organocopper(I) reagents are probably not monomers.

Conclusion

The synthesis of chiral allenes of high enantiomeric purity can advantageously be conducted by reaction of propynyl sulfonates (or sulfinates) with organocopper(I) reagents of the type [{RCuX}MgX·LiX] in THF at low temperatures. Access to enantiomerically pure chiral propynyl alcohols with various substituents is well documented.[25] Methods relying on (isolated) intermediates such as halogenoallenes[3d,j] or allenyl sulfones[9] seem unnecessarily tedious as they involve at least one extra step. However, these methods may prove to be advantageous in particular cases, e.g. when enantiomerically pure alkynes $R^1R^2CHC{\equiv}CH$ are the desired products.[3k]

The stereoselectivity of our method appears to be appreciably higher than a reported Ti-mediated S_E2' type reaction[10] and slightly better than the Pd-catalyzed phenylation of propynyl esters.[3c] The mechanistic background of this and related S_N2' type reactions[3,21,26] merits further study.

Experimental Section

General. All reactions were carried out in an atmosphere of dry nitrogen. Solvents were purified and dried according to standard procedures. Standard syringe techniques were applied for transfer of solvents and organometallic compounds. ^1H and ^{13}C NMR spectra were recorded on Varian EM-390 and Bruker WP-200 and AC-100 spectrometers, by using CCl_4 or $CDCl_3$ as solvents. Mass spectra (GC/MS) were determined on a HP 5710A gas chromatograph with a capillary column (Chrompack CPSil5-CB) combined with a HP 5980A mass spectrometer (EI, 70 eV). Infrared spectra were recorded on a Perkin-Elmer 457 IR spectrophotometer. Optical rotations were measured in a Perkin-Elmer 241 Polarimeter, using capillary or standard cuvettes (c = 0.6–1.4 g/100 mL; l = 1 dm) at 20 °C.

Materials. Copper(I) bromide was prepared according to Keller and Wycoff.[27] Lithium bromide was purchased from BDH Chemicals Ltd., Poole, UK, dried in high vacuum at 200 °C, and used as a 3.0 M solution in THF. Optically active propynyl alcohols (*S*)-**1a** and (*R*)-**2a**–**4a** were obtained as described previously.[2] Generally, enantiomerically pure (*S*)-**1a** was used, whereas (*R*)-**2a**–**4a** were used in varying enantiomeric purities, usually 22–60% ee. The methane sulfinate (*S*)-**1b** and sulfonates (*R*)-**2c**–**4c** were prepared as in the case of racemic esters[6b,28] but were stored at −30 °C.

The methane sulfonate **1b** is thermally unstable and should be prepared at −70 °C by successively adding to 5.0 mmol of (*S*)-**1a** in THF (50 mL) 5.0 mmol of *n*-BuLi in hexane (3 min of vigorous stirring) and 5.0 mmol of methanesulfonyl chloride. The temperature must be kept below −60 °C during 2 min, after which period the organocopper reagent (5.0 mmol) should be added *immediately*, see ref 14.

Organocopper(I) reagents were prepared by cautiously adding, at −70 °C, 1.0 molar equiv of RMgBr to a well-stirred THF solution of equimolar amounts of CuBr and LiBr (ca. 25 mL for 0.010 mol). After 10–15 min of stirring at −65 °C (R = Me or Ph: 30 min at 0 °C) the organocopper(I) reagents were used as such, generally in batches of 0.005 or 0.010 mol.

Procedure. To a well-stirred solution of the alkylcopper(I) compound in dry THF was added, at −70 °C, a solution of 1.0 molar equiv of the esters (*S*)-**1b**/**1c** or (*R*)-**2c**–**4c** in 2 mL of dry THF in one portion. Generally (for exceptions see Table I) after stirring during 3–5 min at −65 °C, the mixture was poured into 100 mL of aqueous 2–3% NH_4Cl containing NaCN (ca. 1 g for 0.005 mol Cu(I)) and extracted with pentane (2 × 50 mL). After washing the extracts with 2–3% aqueous NH_4Cl (5 × 250 mL) and drying over anhydrous K_2CO_3, the pentane was removed at reduced pressure. Then the optical rotation and a ^1H NMR spectrum of the crude chiral allene were determined. Subsequently, the allene was either distilled or chromatographed on alumina (neutral, 5% H_2O, eluent pentane or hexane), the specific rotation then being equal or, in most cases, slightly higher. Yields and specific rotations after purification are given in Table I. Other physical constants are given below. IR refers to ν_{as}(C=C=C).

1-Phenylbuta-1,2-diene (5): bp 79 °C (15 mmHg); n^{20}_D 1.5760; IR 1950 cm^{-1}; mass, m/e 130, $M^{\bullet+}$; ^1H NMR (CCl_4) δ 7.19 (br m, 5 H), 5.99 (dq, H_A), 5.43 (dq, H_B), 1.75 (dd, 3 H_X), simulated ABX_3 system (90 MHz) $^3J_{BX}$ = 6.97, $^4J_{AB}$ = −6.40, $^5J_{AX}$ = 3.16 Hz; ^{13}C NMR ($CDCl_3$) δ 205.9 C(2), 134.9, 128.4, 126.5 (arom C ipso, m, p + o), 93.9 C(1), 89.6 C(3), 13.9 C(4).

1-Phenylpenta-1,2-diene (6): bp 93 °C (15 mmHg); n^{20}_D 1.5645; IR 1949 cm^{-1}; mass, m/e 144, $M^{\bullet+}$; ^1H NMR (CCl_4) δ 7.18 (br m, 5 H), 6.04 (dt, H_A), 5.52 (dt, H_B), 2.12 (ddq, 2 H_X), 1.06 (br t, 3 H, ^3J = 7.5 Hz), simulated ABX_2 system (90 MHz) $^3J_{BX}$ = 6.12, $^4J_{AB}$ = −6.39, $^5J_{AX}$ = 3.26 Hz; ^{13}C NMR ($CDCl_3$) δ 204.9 C(2), 135.0, 128.4, 126.5, 126.4 (arom C ipso, m, p, o), 96.6 C(1), 95.1 C(3), 21.8 C(4), 13.3 C(5).

1-Phenylhexa-1,2-diene (7): bp 107 °C (15 mmHg); n^{20}_D 1.5550; IR 1951 cm^{-1}; mass, m/e 158, $M^{\bullet+}$; ^1H NMR (CCl_4) δ 7.18 (br m, 5 H), 6.02 (dt, H_A), 5.47 (dt, H_B), 2.08 (ddt, 2 H_X), 1.50 (tq, 2 H), 0.94 (br t, 3 H), simulated ABX_2 system (90 MHz) $^3J_{BX}$ = 6.56, $^4J_{AB}$ = −6.42, $^5J_{AX}$ = 2.92 Hz; ^{13}C NMR ($CDCl_3$) δ 205.1 C(2), 135.0, 128.4, 126.4 (arom C ipso, m, p + o), 94.7, 94.4 C(1) + C(3), 30.7, 22.4, 13.6 C(4)–C(6).

1-Phenylhepta-1,2-diene (8): bp 118 °C (15 mmHg); n^{20}_D 1.5470; IR 1951 cm^{-1}; mass, m/e 172, $M^{\bullet+}$; ^1H NMR (CCl_4) δ 7.18 (br m, 5 H), 6.01 (dt, H_A), 5.46 (dt, H_B), 2.09 (ddt, 2 H_X), 1.15–1.60 (m, 4 H), 0.90 (unresolved t, 3 H), simulated ABX_2 system (90 MHz) $^3J_{BX}$ = 6.69, $^4J_{AB}$ = −6.27, $^5J_{AX}$ = 3.05 Hz; ^{13}C NMR ($CDCl_3$) δ 205.0 C(2), 135.1, 128.4, 126.4 (arom C ipso, m, p + o), 94.9, 94.4 C(1) + C(3), 31.2, 28.3, 22.1, 13.7 C(4)–C(7).

1-Phenylocta-1,2-diene (9): bp 128 °C (15 mmHg); n^{20}_D 1.5380; IR 1951 cm^{-1}; mass, m/e 186, $M^{\bullet+}$; ^1H NMR (CCl_4) δ 7.19 (br m, 5 H), 6.02 (dt, H_A), 5.48 (dt, H_B), 2.10 (m, 2 H), 1.15–1.60 (m, 6 H), 0.87 (unresolved t, 3 H); ^{13}C NMR ($CDCl_3$) δ 205.0 C(2), 135.1, 128.4, 126.4 (arom C ipso, m, p + o), 94.9, 94.5 C(1) + C(3), 31.3, 28.7, 28.6, 22.3, 13.9 C(4)–C(8).

1-Phenylnona-1,2-diene (10): bp 140 °C (15 mmHg), 98 °C (0.5 mmHg); n^{20}_D 1.5340; IR 1951 cm^{-1}; mass, m/e 200, $M^{\bullet+}$; ^1H NMR (CCl_4) see **9**, with δ 1.15–1.60 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 205.1 C(2), 135.1, 128.4, 126.4 (arom C ipso, m, p + o), 94.9, 94.5

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C(1) + C(3), 31.5, 29.0, 28.7 (2×), 22.5, 13.9 C(4)–C(9).

1-Phenylundeca-1,2-diene (11): bp 120 °C (0.4 mmHg); n^{20}_D 1.5320; IR 1951 cm^{-1}; mass, *m/e* 228, M$^{\bullet+}$; ^{1}H NMR (CCl_4) see **9**, with δ 1.15–1.60 (m, 12 H); ^{13}C NMR –.

4-Methyl-1-phenylpenta-1,2-diene (12): bp 102 °C (15 mmHg); n^{20}_D 1.5395; IR 1945 cm^{-1}; mass, *m/e* 158, M$^{\bullet+}$; ^{1}H NMR (CCl_4) δ 7.18 (br m, 5 H), 6.09 (dd, H_A), 5.51 (dd, H_B), 2.42 (ddsept, H_X), 1.08 (br d, 6 H, $J \simeq 7$ Hz), simulated ABX system (90 MHz) $^3J_{BX}$ = 5.75, $^4J_{AB}$ = –6.35, $^5J_{AX}$ = 3.07 Hz; ^{13}C NMR ($CDCl_3$) δ 203.5 C(2), 135.1, 128.4, 126.5, 126.3 (arom C ipso, m, p, o), 102.3 C(3), 95.6 C(1), 28.3 C(4), 22.4 C(5).

4-Methyl-1-phenylhexa-1,2-diene (13): bp 112 °C (15 mmHg), 72 °C (0.5 mmHg); n^{20}_D 1.5465; IR 1949 cm^{-1}; mass, *m/e* 172, M$^{\bullet+}$; 200-MHz ^{1}H NMR ($CDCl_3$), 2 diastereomer pairs (I) δ 7.07–7.31 (br m, 5 H), 6.15 (dd, H_A), 5.53 (dd, H_B), 2.19 (appar septet, H_M), 1.30–1.55 (m, H_X), 1.07 (d, H_Y), 0.95 (t, H_Z), $^4J_{AB}$ = –6.38, $^3J_{BM}$ = 6.39, $^5J_{AM}$ = 2.75, $^3J_{MY}$ = 6.75, $^3J_{XZ}$ = 7.30 Hz; (II) δ 7.07–7.31 (br m, 5 H), 6.14 (dd, H_A), 5.52 (dd, H_B), 2.18 (appar septet, H_M), 1.30–1.55 (m, H_X), 1.06 (d, H_Y), 0.94 (t, H_Z), $^4J_{AB}$ = 6.40, $^3J_{BM}$ = 6.55, $^5J_{AM}$ = 2.49, $^3J_{MY}$ = 6.75, $^3J_{XZ}$ = 7.30 Hz; ^{13}C NMR ($CDCl_3$) δ 204.0 C(2), 135.1, 128.4, 126.4 (arom C ipso, m, p + o), 100.7 C(3), 95.2 C(1), 35.3/35.2, 29.9/29.7, 19.9/19.8, 11.6/11.6 diaster C(4)–C(7).

4,4-Dimethyl-1-phenylpenta-1,2-diene (14): bp 102 °C (15 mmHg); n^{20}_D 1.5395; IR 1950 cm^{-1}; mass, *m/e* 172, M$^{\bullet+}$; ^{1}H NMR (CCl_4) δ 7.18 (br m, 5 H), 6.09 (d, H_A), 5.48 (d, H_B), 1.10 (s, 9 H), $^4J_{AB}$ = –6.45 Hz; ^{13}C NMR ($CDCl_3$) δ 202.4 C(2), 135.2, 128.5, 126.5, 126.3 (arom C ipso, m, p, o), 106.7 C(3), 96.2 C(1), 32.6 C(4), 30.2 C(5).

2,2-Dimethylhepta-3,4-diene (16): bp 32 °C (15 mmHg); n^{20}_D 1.4370; IR 1954 cm^{-1}; mass, *m/e* 124 M$^{\bullet+}$; ^{1}H NMR (CCl_4) δ 4.95–5.25 (m, 2 H), 1.95 (m, 2 H), 1.01 (s, 9 H), 0.97 (br t, 3 H); ^{13}C NMR ($CDCl_3$) δ 200.6 C(4), 103.6 C(3), 94.3 C(5), 31.5 C(2), 30.1 C(1), 22.0 C(6), 13.2 C(7).

2,2-Dimethylocta-3,4-diene (17): bp 48 °C (15 mmHg); n^{20}_D 1.4390; IR 1958 cm^{-1}; mass, *m/e* 138, M$^{\bullet+}$; ^{1}H NMR (CCl_4) δ 4.95–5.25 (m, 2 H), 1.95 (m, 2 H), 1.42 (m, 2 H), 1.01 (s, 9 H), 0.95 (br t, 3 H); ^{13}C NMR ($CDCl_3$) δ 201.1 C(4), 102.8 C(3), 92.5 C(5), 31.6 C(2), 30.2 C(1), 31.3, 22.4, 13.7 C(6)–C(8).

2,2-Dimethylnona-3,4-diene (18): bp 62 °C (15 mmHg); n^{20}_D 1.4402; IR 1958 cm^{-1}; mass, *m/e* 152, M$^{\bullet+}$; ^{1}H NMR (CCl_4) δ 4.90–5.20 (m, 2 H), 1.93 (m, 2 H), 1.10–1.50 (m, 4 H), 1.01 (s, 9 H), 0.88 (unresolved t, 3 H); ^{13}C NMR ($CDCl_3$) δ 201.0 C(4), 102.9 C(3), 92.6 C(5), 31.5 C(2), 30.1 C(1), 31.4, 28.8, 22.2, 13.8 C(6)–C(9).

2,2-Dimethyldeca-3,4-diene (19): bp 76 °C (15 mmHg); n^{20}_D 1.4417; IR 1958 cm^{-1}; mass, *m/e* 166, M$^{\bullet+}$; ^{1}H NMR (CCl_4) δ 4.90–5.20 (m, 2 H), 1.93 (m, 2 H), 1.10–1.50 (m, 6 H), 1.01 (s, 9 H), 0.87 (unresolved t, 3 H); ^{13}C NMR ($CDCl_3$) δ 201.0 C(4), 102.9 C(3), 92.7 C(5), 31.5 C(2), 30.1 C(1), 31.4, 29.1, 28.9, 22.4, 13.9 C(6)–C(10).

2,2,6-Trimethylhepta-3,4-diene (20): bp 39 °C (15 mmHg); n^{20}_D 1.4356; IR 1957 cm^{-1}; mass, *m/e* 138, M$^{\bullet+}$; ^{1}H NMR ($CDCl_3$) simulated $ABMX_3X'_3$ (200 MHz) δ 5.17 (dd, H_A), 5.12 (dd, H_B), 2.26 (ddsept, H_M), 1.02 (s, 9 H), 0.99 (d, 3 H_X), 0.98 (d, 3 $H_{X'}$) diaster Me, $^3J_{XM}$ = $^3J_{X'M}$ = 6.76, $^3J_{BM}$ = 5.31, $^4J_{AB}$ = –6.22, $^5J_{AM}$ = 3.36 Hz; ^{13}C NMR ($CDCl_3$) δ 199.4 C(4), 104.1 C(3), 100.1 C(5), 31.5 C(2), 30.1 C(1), 27.9 C(6), 22.5, 22.3 diaster C(7).

2,2,6,6-Tetramethylhepta-3,4-diene (21): bp 52 °C (15 mmHg); n^{20}_D 1.4375; IR 1958 cm^{-1}; mass, *m/e* 152, M$^{\bullet+}$; ^{1}H NMR (CCl_4) δ 5.09 (s, 2 H), 1.00 (s, 18 H); ^{13}C NMR ($CDCl_3$) δ 198.1 C(4), 104.6 C(3) + C(5), 31.5 C(2) + C(6), 30.1 C(1) + C(7).

Trideca-3,4-diene (22): bp 98 °C (18 mmHg); n^{20}_D 1.4545; IR 1959 cm^{-1}; mass, *m/e* 180, M$^{\bullet+}$; ^{1}H NMR (CCl_4) δ 4.85–4.20 (m, 2 H), 1.75–2.20 (m, 4 H), 1.10–1.70 (m, 12 H), 0.98 (br t, 3 H), 0.87 (unresolved t, 3 H); ^{13}C NMR ($CDCl_3$) δ 203.4 C(4), 92.5, 91.5 C(3) + C(5), 31.8, 29.3, 29.2 (2×), 29.0 (2×), 22.6, 14.0 C(6)–C(13), 22.0 C(2), 13.4 C(1).

Tetradeca-4,5-diene (23): bp 110 °C (18 mmHg); n^{20}_D 1.4558; IR 1960 cm^{-1}; mass, *m/e* 194, M$^{\bullet+}$; ^{1}H NMR (CCl_4) δ 4.85–5.15 (m, 2 H), 1.75–2.15 (m, 4 H), 1.10–1.65 (m, 14 H), 0.90 (br t, 3 H), 0.87 (unresolved t, 3 H); ^{13}C NMR ($CDCl_3$) δ 203.9 C(5), 90.8, 90.6 C(4) + C(6), 31.8, 31.1, 29.3, 29.2 (2×), 29.0, 28.9, 22.6, 22.4, 14.0, 13.5 C(1)–C(3) + C(7)–C(14).

Pentadeca-5,6-diene (24): bp 125 °C (18 mmHg); n^{20}_D 1.4563; IR 1960 cm^{-1}; mass, *m/e* 208, M$^{\bullet+}$; ^{1}H NMR (CCl_4) as **23**, but δ 1.10–1.65 (m, 16 H), 0.88, 0.87 (2 unresolved t, 6 H); ^{13}C NMR ($CDCl_3$) δ 203.8 C(6), 90.8 C(5) + C(7), 31.8, 31.3, 29.4, 29.2 (2×), 29.0 (2×), 28.6, 22.6, 22.1, 14.0, 13.8 C(1)–C(4) + C(8)–C(15).

2,2-Dimethyltrideca-3,4-diene (25): bp 120 °C (18 mmHg); n^{20}_D 1.4512; IR 1958 cm^{-1}; mass, *m/e* 208, M$^{\bullet+}$; ^{1}H NMR (CCl_4) δ 4.93–5.20 (m, 2 H), 1.70–2.15 (m, 2 H), 1.10–1.60 (m, 10 H), 1.01 (s, 9 H), 0.87 (unresolved t, 3 H); ^{13}C NMR ($CDCl_3$) δ 201.0 C(4), 102.9 C(3), 92.7 C(5), 31.5 C(2), 30.1 C(1), 31.8, 29.4, 29.2 (3×), 28.8, 22.6, 14.0 C(6)–C(13).

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Notes

Ortho Substitution of *m*-Anisaldehyde via α-Amino Alkoxide Directed Lithiation

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The addition of aromatic aldehydes to certain lithium dialkylamides gives α-amino alkoxides that can be ring-lithiated with alkyllithiums. Alkylation and hydrolysis on workup provides ortho-substituted aryl aldehydes via a one-pot reaction.[2] This methodology works well for the one-pot substitution of heterocyclic aromatic aldehydes[3] as well as for benzaldehyde derivatives.[2] Several research groups have used this methodology with success;[4] however, two laboratories[5] have informed us that the substitution

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