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Journal of Organometallic Chemistry 648 (2002) 109–118

Journal of Organometallic Chemistry

www.elsevier.com/locate/jorganchem

One pot stereoselective synthesis of chiral α,ω-diynes from bromoallenes and organobis(heterocuprates)

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Received 12 July 2001; accepted 7 November 2001

Dedicated to Professor L. Lardicci on the occasion of his 75th birthday and in recognition of his important contributions to organometallic chemistry and its applications to organic synthesis

Abstract

Organobis(heterocuprates), **7** and **8**, have been prepared reacting in situ 1,4-dilithiobutane and di-Grignard reagents, obtained from 1,4-dibromobutane and 1,4-dibromobenzene, respectively, with CuSPh and $LiCuBr_2$. The cross-coupling reaction of these di-cuprate reagents with 3-alkyl and 3,3-dialkyl 1-bromo-1,2-dienes (**1**) provides a general method for selective synthesis of 1,9-decadiynes (**5**) and 1,4-bis(2-propynyl)benzenes (**6**), characterized by two identical chiral centres in the α position to the triple bonds. The high 1,3-*anti* stereoselectivity of the coupling process allows us to obtain enantiomerically enriched α,ω-diynes **5** and **6** starting from optically active allenic substrates **1**. © 2002 Published by Elsevier Science B.V.

Keywords: Copper; 1,4-Butanedicuprates; 1,4-Benzenedicuprates; Coupling reactions; Bromoallenes; Chiral α,ω-diynes

1. Introduction

It is well known that the application of acetylene chemistry is one of the key tools of modern organic synthesis [1]. The acetylenic moiety provides a convenient unity which may be converted into a variety of functionalities, and optically active alkynyl compounds are employed as versatile building blocks for the design and construction of more complex chiral molecules [2].

In previous papers [3–6] we reported that the cross-coupling reaction of allenic bromides (**1**) with the complex bromocuprates (**2**), obtained from equimolar amounts of Grignard reagents and $LiCuBr_2$ in THF, provides one of the most convenient methods for the synthesis of chiral 1-alkynes (**3**) with a tertiary or a quaternary stereogenic centre in the α position to the triple bond (Scheme 1). The reaction proceeds, in general, in a high 1,3-*anti* stereoselective pattern even if the regioselectivity of the coupling process appears to be sensitive to steric interactions; an increase of the bulkiness of the substituent in the copper species favours the competitive formation of the allenic derivatives (**4**) (Scheme 1) [6]. However, an appropriate selection of the structure of both the allenic substrate and the copper reagent provides, with good yields, even quite hindered terminal alkynes **3** [6].

The possibility of extending this method to the preparation of chiral acetylenic compounds exhibiting an even higher synthetic versatility appeared particularly appealing. Recently [7] we emphasized the application of our procedure to the preparation of a large variety of functionalized acetylenic systems by employing zinc-based cuprates (Knochel reagents [8]) [FG–RCu(CN)ZnCl·2LiCl; FG = protected CHO, CO, OH groups, $CH{=}CH_2$, $Me_3SiC{\equiv}C$, COOEt]. In this paper we wish to describe the first examples of the selective synthesis of 1,9-decadiynes (**5**) and 1,4-bis(2-propynyl) benzenes (**6**) (Fig. 1), characterized by two identical chiral centres, which involves the reaction of bromoallenes **1** with organobis(heterocuprates) **7** and **8**, respectively, obtained from 1,4-dihalobutanes (Cl, Br) and 1,4-dibromobenzene, via the corresponding di-

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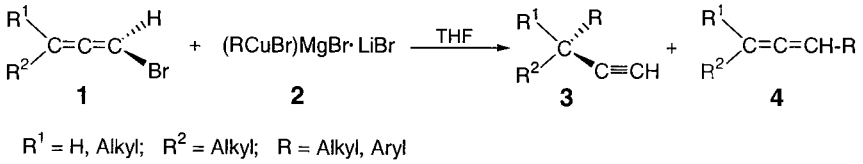
0022-328X/02/$ - see front matter © 2002 Published by Elsevier Science B.V.
PII: S0022-328X(01)01438-3



Scheme 1.

Grignard or dilithium reagents, **9**–**11**. These chiral α,ω-diacetylenic compounds might provide access to a variety of hitherto inaccessible, novel and theoretically interesting molecules by transition-metal-mediated transformations such as cyclizations [9–12], cyclodimerizations and cyclotrimerizations [13–16], cocyclization with monoalkynes [17], nitriles [18,19], isonitriles [20], carbon dioxide [21], carbonyl compounds [22], and so on.

2. Results and discussion

2.1. 1,9-Decadiynes (5)

Our first experiments were carried out with 1,4-butanedicuprates **7a**–**c**[1] and (*R*)(*S*)-1-bromo-3-methyl-1,2-pentadiene (**1a**) as model substrate. Reagents **7** were obtained from 1,4-bis(bromomagnesio)butane (**9**), and 1,4-dilithiobutane (**10**) (Scheme 2), according to well established procedures for the formation of the corresponding monocuprates from organomagnesium [23] and organolithium precursors [24,25]. In general, the organodimetallic reagent was added to a solution, or a suspension, of a copper(I) salt, in diethyl ether or THF, at the appropriate temperature (-78 °C ÷ -30 °C); the mixture was stirred for 20–30 min and used immediately. The bis-Grignard **9** was prepared from readily available 1,4-dibromobutane in THF solution (87% yield) [26] and the dilithiobutane **10** was obtained (82% yield) by reaction of 1,4-dichlorobutane with lithium (1% Na) in diethylether at 0 °C [25] (Scheme 2).

When the organocopper reagents (**7**) were allowed to react with the bromoallene (**1a**) (molar ratio 1:2), the desired 3,8-diethyl-3,8-dimethyl-1,9-decadiyne (**5a**) was obtained, but, in general, together with substantial amounts of several by-products (Scheme 3, Table 1, entries 1–3). Such products, separated for identification by bulb-to-bulb distillation and/or column silica gel chromatography, derive from: (i) a reversal of regioselectivity of the coupling process (compound **12**), (ii) a single coupling reaction (compound **13**), (iii) a dimerization of the cuprate reagents followed by two regioselective coupling steps (compound **14**), (iv) two possible dimerization processes of the allenic substrate (compounds **15** and **16**); compounds **14**–**16** should probably be due to halogen–metal exchange reactions. The progress of the reactions was monitored by GLC analysis and all products were characterized by analytical and spectroscopic methods. The results obtained (Table 1, entries 1–3) showed, however, that the nature of the copper reagent plays a prominent role in determining both the reaction rate and the chemoselectivity of the reaction; in particular, it is noteworthy that with the thiophenoxydicuprate **7c** the substrate conversion was complete within 1 h at -70 to 20 °C and compound **5a** was obtained as the main product (75%), which was isolated chemically pure in good yield (Table 1, entry 3). In order to define the usefulness of **7c** for the synthesis of 1,9-decadiynes (**5**), we reacted this dicuprate reagent with 3-substituted 1-bromoallenes, such as (*R*)(*S*)-1-bromo-1,2-butadiene (**1b**), and (*R*)(*S*)-1-bromo-4,4-dimethyl-1,2-pentadiene (**1c**). The results, listed in Table 1 (entries 4 and 5), show that **7c** affords, quickly and in very mild experimental conditions, the diacetylenic compounds **5** with generally high yields,

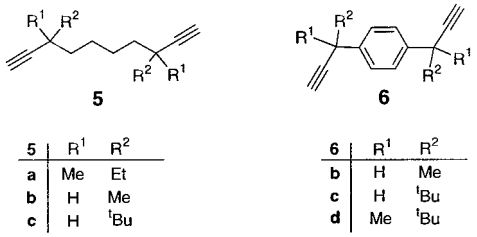
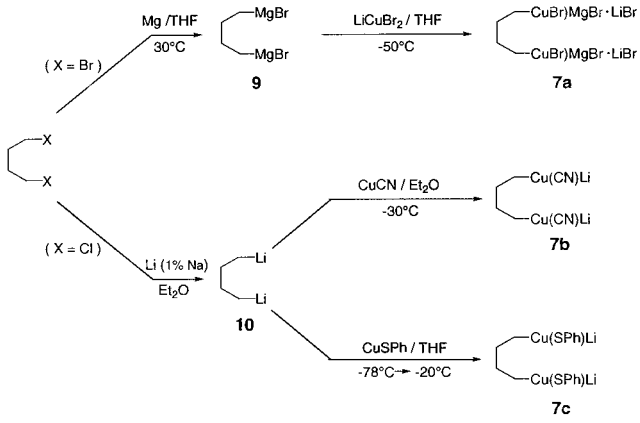


Fig. 1.



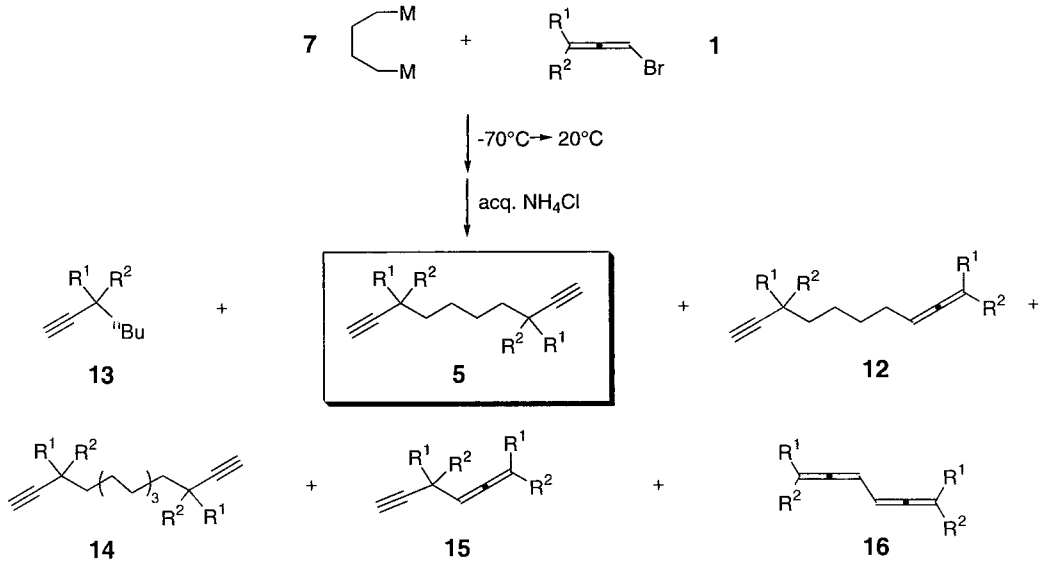
Scheme 2.

[1] The reagent structures given in this paper follow the convention established for the monocuprate analogous and do not necessarily reflect their structures in solution.

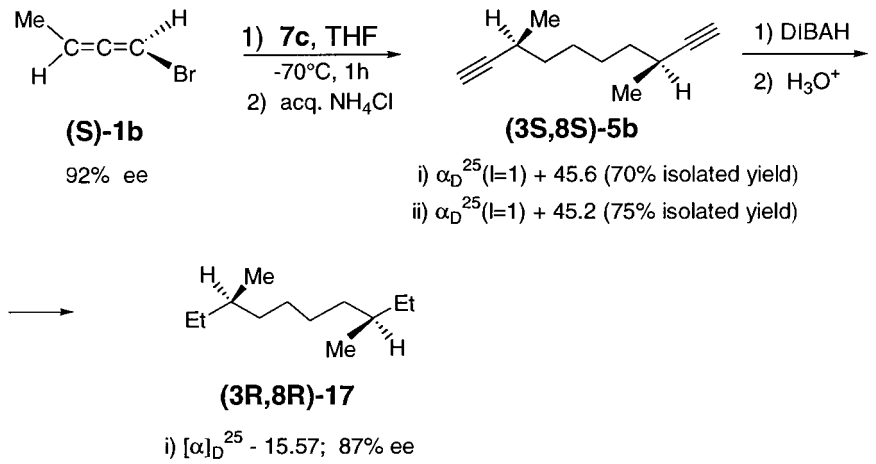
Table 1
Reactions of 1,4-butanedicuprates (**7a–c**) with 1-bromo-1,2-dienes $R^1R^2C{=}C{=}CHBr$ (**1a–c**) [a]

Entry	**1**	R^1	R^2	**7**	M	Reaction			Reaction mixture composition (%) [b]						
						Temperature (°C)	Time (h)	Conversion (%) [b]		**5**	**12**	**13**	**14**	**15**	**16**
1	**1a**	Me	Et	**7a**	Cu(Br)MgBr LiBr	−70 to 20	36	89	**a**	47	8	30	6	9	–
2 [c]	**1a**	Me	Et	**7b**	Cu(CN)Li	−70 to 20	2	97	**a**	9	5	1	34	–	46
3	**1a**	Me	Et	**7c**	Cu(SPh)Li	−70 to 20	1	96	**a**	74(57)	11	3	12	–	–
4	**1b**	H	Me	**7c**	Cu(SPh)Li	−70	0.5	100	**b**	98(87)	2	–	–	–	–
5	**1c**	H	^{t}Bu	**7c**	Cu(SPh)Li	−70	1	100	**c**	75(38)	25	–	–	–	–

[a] All reactions were performed by treating the organocopper reagent with the allenic substrate **1** at 1:2 molar ratio, in THF as solvent.
[b] Determined by GLC analyses of the reaction mixture after hydrolysis; isolated yields are shown in parentheses.
[c] In Et_2O as solvent.



Scheme 3.



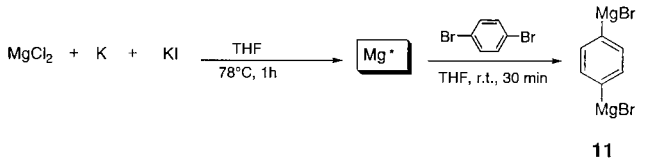
Scheme 4.

although the steric hindrance at C-3 of the bromoallenic substrate can determine the regioselectivity of the coupling processes. Pure samples of 3,8-dimethyl-1,9-decadiyne (**5b**) (fractional distillation) and 3,8-bis(1,1-dimethylethyl)-1,9-decadiyne (**5c**) (silica gel chromatography, hexane as eluant) were so obtained with excellent to satisfactory yields and characterized with analytical and spectroscopic data.

To establish the synthetic value of this method for the preparation of enantiomerically enriched diynes **5**, we checked further the *anti* stereochemical outcome of the involved coupling reactions. Thus, samples of (*S*)-1-bromo-1,2-butadiene ((*S*)-**1b**), prepared in 92% ee according to the procedure described by Vermeer and co-workers [27], were converted, with highly reproducible chemical and optical yields, into pure dextrorotatory **5b** by treatment with the dicuprate **7c** (Scheme 4). The enantiomeric purity and the (*S*) absolute configuration of the stereogenic centres of (+)-**5b** were evaluated by conversion, via hydroalumination with diisobutylaluminium hydride (DIBAH), of the diyne compound into the levorotatory 3,8-dimethyldecane ((−)-**17**) of known (3*R*,8*R*) stereochemistry [28] (Scheme 4). This result and the very high enantiomeric purity of recovered (3*R*,8*R*)-**17** (87% ee; 97.4% of *anti* stereoselectivity for the coupling reaction) confirm that our reaction between bromoallenes **1** and aliphatic heterocuprates to give acetylenic products proceeds in an almost complete *anti* stereochemical fashion [3–7].

2.2. 1,4-Bis(2-propynyl)benzenes (6)

As previously emphasized, the synthesis of 3-aryl-1-alkynes (**3**) via the coupling reaction between 1-bromo-1,2-dienes and arylcopper reagents proceeds with satisfactory results only when arylbromocuprates [(Ar-



Scheme 5.

CuBr)MgBr·LiBr], prepared reacting in THF a Grignard reagent, ArMgBr, with $LiCuBr_2$, are employed (Scheme 1) [3,4,7]. Heterocuprates of different nature, such as lithium cyanocuprates [RCu(CN)Li] and zinc cyanocuprates [RCu(CN)ZnCl·2LiCl], which appear somewhat attractive for preparation of aliphatic acetylenic compounds, mainly afford allenes **4** when R is a phenyl or an aryl group [3,4,7] (Scheme 1). Thus, for the preparation of compounds **6**, we attempted to synthesize, as key intermediate, the 1,4-benzenedibromocuprate (**8**) starting from 1,4-bis(bromomagnesio) benzene (**11**).[2]

According to reported procedures [31,32], the bis-Grignard reagent was obtained in a quantitative way by oxidative metalation, in THF at room temperature, of 1,4-dibromobenzene with activated magnesium slurries, prepared by reduction, in boiling THF, of $MgCl_2$ with potassium in the presence of KI [31] (Scheme 5).

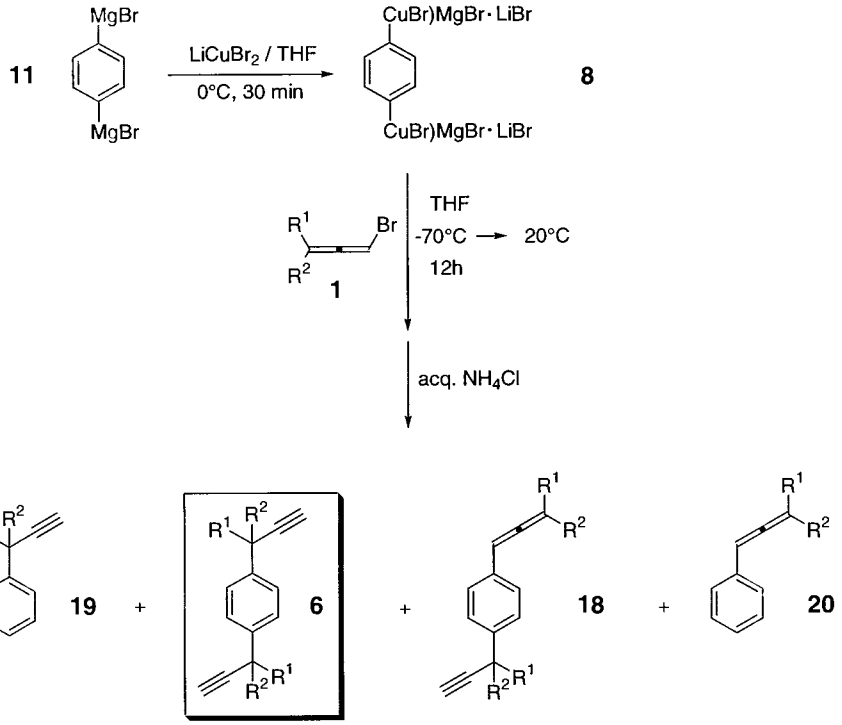
The di-Grignard **11** was reacted, at 0 °C, with two equivalents of a well-stirred THF solution of $LiCuBr_2$ and the so obtained bis-cuprate reagent **8** was successively treated, at −70 °C, with 1-bromo-1,2-dienes **1b–d** (Scheme 6). The mixture was allowed to warm to room temperature and the progress of the reaction monitored by GLC. In any case, after 12 h, the bromoallenic substrate was completely converted leading to the corresponding 1,4-bis(2-propynyl)benzenes (**6b–d**), as main products, together with minor amounts of the isomeric allenynes (**18**) and compounds derived from a single coupling reaction, as the 3-phenyl-1-alky-

Table 2
Reactions of 1,4-benzenedicuprate (**8**) with 1-bromo-1,2-dienes $R^1R^2C{=}C{=}CHBr$ (**1b–d**) [a]

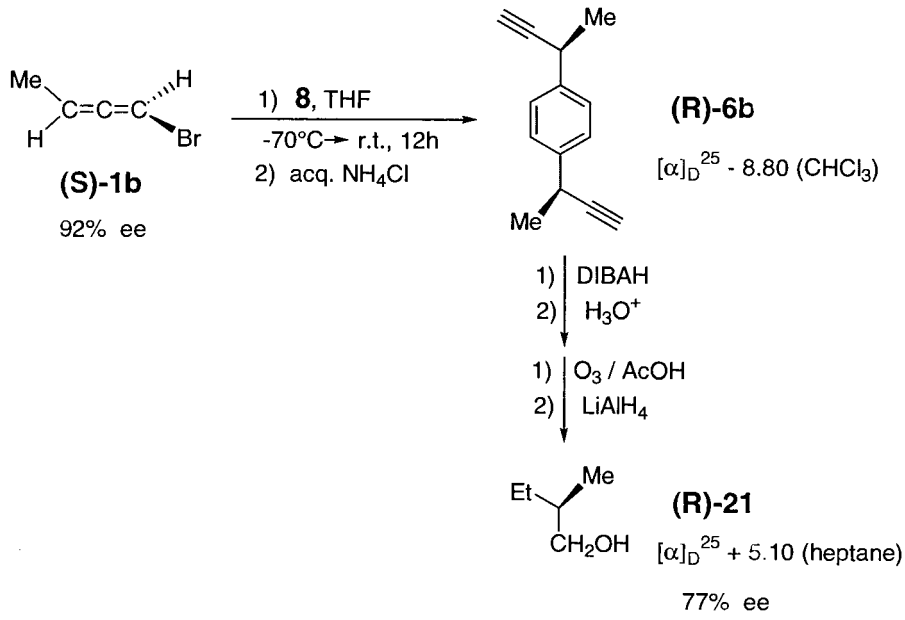
Entry	1	R^1	R^2		Reaction mixture composition (%) [b]			
					6	**18**	**19**	**20**
1	**1b**	H	Me	**b**	63(38)	23	14	–
2	**1c**	H	^{t}Bu	**c**	67(37)	17	12	4
3	**1d**	Me	^{t}Bu	**d**	77(49)	4	17	–

[a] All reactions were performed by treating the organocopper reagent with the allenic substrate **1** (molar ratio 1:2) in THF at −70 °C and allowing the mixture to warm to room temperature (12 h).
[b] Determined by GLC analyses of the reaction mixture after hydrolysis; isolated yields by silica gel chromatography (hexane) are shown in parentheses.

[2] Several attempts to selectively obtain 1-alkynes by using in the coupling reaction with bromoallenes **1** aryl lithium thiophenoxy cuprates and, in particular, the 1,4-benzene bisthiophenoxycuprate, obtained from *p*-phenylen dilithium [29,30], were really unsuccessful according to the reactivity previously reported for other lithium heterocuprates [3,4,7].



Scheme 6.



Scheme 7.

nes (**19**) and the substituted allenes (**20**) (Scheme 6, Table 2). While compounds **19** and **20** were identified by comparison of their GLC retention times with those of authentic samples [3], column silica gel chromatography (*n*-hexane) afforded samples of diynes **6** and allenynes **18** which were characterized by spectroscopic data. The desired 1,4-bis(2-propynyl)benzenes were recovered chemically pure with satisfactory yields (40–50%), taking into account the not optimized purification procedure (Table 2).

These data suggest that the method can be really useful for the preparation of the aromatic α,ω-diynes **6** having also bulky alkyl substituents in the α position to the triple bonds; interestingly the **6**/**18** molar ratio increases when the bulkiness of the above substituents increases [3]. The 1,3-*anti* stereoselectivity, widely proved for the coupling process between heterocuprates and 1-bromo-1,2-dienes (**1**) [3–7] (see also Scheme 4), makes easily accessible the synthesis of compounds **6** enantiomerically enriched too. Thus, chemically pure levorotatory 1,4-bis[(*R*)-1-methyl-2-propynyl]benzene ((*R*)-**6b**), was obtained in 42% yield starting from a sample of (*S*)-1-bromo-1,2-butadiene ((*S*)-**1b**) (92% ee) (Scheme 7). To evaluate the stereoselectivity extent of the double coupling reaction carried out with the aryl bis-cuprate, the diyne (*R*)-**6b** was converted via hydroalumination with DIBAH into the corresponding 1,4-bis[(*R*)-1-methylpropyl]benzene which was related, by reductive ozonolysis [33], to (*R*)-2-methyl-1-butanol ((*R*)-**21**), of 77% enantiomeric purity (Scheme 7). This result confirms that once again the coupling process occurs with high 1,3-*anti* stereoselectivity (> 92%) even if it shows significant racemization phenomena. This racemization, which is consistent with our previous data for the formation of (*S*)-3-phenyl-1-butyne from the phenyl monocuprate (PhCuBr)MgBr·LiBr [3], can be related to the mobility, in the reaction conditions, of the hydrogen atoms (benzylic and also propargylic) bound to the stereogenic centres. In fact, when we reacted optically active 3,3-disubstituted allenic bromides **1** with arylbromocuprates for the synthesis of chiral 3-aryl-1-alkynes characterized by quaternary stereogenic centres we observed a complete (100%) stereoselectivity [34].

3. Concluding remarks

The reported results confirm that the procedures usually employed for the preparation of mono-heterocuprates from organomagnesium and organolithium precursors can be successfully extended to obtain organodicuprate reagents, at least as far as aliphatic and aromatic di-bromocuprates (**7a** and **8**), and di-tiophenoxycuprates (**7c**) are concerned. The cross-coupling reaction of these copper reagents with 3-substituted 1-bromo-1,2-dienes **1** represents a suitable and general synthetic procedure for chiral 1,9-decadiynes (**5**), and 1,4-bis(2-propynyl)benzenes (**6**), which occurs with high regio- and stereoselectivity. As concerns the *meso*/*dl* diastereoselectivity possibly related to the double cross-coupling reactions, we observed that, in all cases we employed racemic bromoallenic substrates, we obtained products **5** and **6** which showed only one gas-chromatographic signal and ^{1}H- and ^{13}C-NMR spectra characterized by single resonances (apart from

the obvious multiplicity) for non equivalent hydrogens and carbons (see Section 4). These findings seem to make the formation of diastereomeric mixtures improbable, suggesting a high diastereoselectivity for the double coupling process. However, a more careful structural investigation with more sophisticated instruments must be necessary to clarify this point.

As previously emphasized, the given dicuprate structures do not necessarily reflect the real structure in solution, however, on the bases of the shown reactivity with bromoallenes,[2] reagents **7a**,**c** and **8** would be structurally very similar to the analogous monocuprates [6].

The anomalous results obtained for the reaction between **1a** and reagent **7b** (Table 1, entry 2) can be attributed to the incomplete transformation of 1,4-dilithiobutane **10** to the corresponding di-cyanocuprate. In fact, the dilithium reagent **10**, in analogous experimental conditions, reacts with **1a** affording, after hydrolysis, products mainly from halogen–metal exchange reactions (bromobutane, 1,4-dibromobutane, and, in particular, 3-methyl-1,2-pentadiene). Several attempts to optimize the preparation of bis-cyanocuprate **7b** modifying experimental conditions, such as reaction temperature, reaction time, or nature of the reaction solvent (THF in place of diethyl ether) were unsuccessful.

4. Experimental

4.1. General

IR spectra were recorded on a Perkin–Elmer FTIR 1710 spectrophotometer as neat films. ^{1}H- and ^{13}C-NMR spectra were recorded on a Varian Gemini 200 instrument in $CDCl_3$ solution at 200 and 50.29 MHz, respectively. Chemical shifts were determined relative to internal $Si(CH_3)_4$ ($\delta = 0$ ppm); coupling constants J are in Hz. GLC-MS spectra were recorded on a Perkin–Elmer Q-Mass 910 spectrometer connected with a Perkin–Elmer 8500 gas chromatograph. GLC analyses were performed on a Perkin–Elmer 8600 gas chromatograph, equipped with a flame ionization detector (FID), using a SiO_2 'Wide Bore' column (DB1, 30 m × 0.53 mm, 5 μm) and helium as carrier gas. Optical rotations were measured with a Perkin–Elmer 142 automatic polarimeter, using standard cuvettes ($l = 0.1$ and 1 dm). Analytical thin-layer chromatography (TLC) was performed on aluminium sheets precoated with silica gel (Merck, Kieselgel 60 F_{254}) and preparative column chromatography on Fluka Silica gel 60 (230–400 mesh). Microanalyses were carried out by the Laboratorio di Microanalisi, Facoltà di Farmacia, Università di Pisa, Italy.

All operations were performed under dry Argon. Solvents were reagent-grade materials, purified by standard methods, redistilled and stored under argon. 1,4-Dichlorobutane and 1,4-dibromobutane, purchased from Fluka A.G. Co., Buchs, were distilled before use. The racemic 1-bromo-1,2-dienes (**1a**–**d**), were prepared and purified as previously described (70–85% yield) [27,35], starting from the appropriate propargylic alcohols. (*S*)-1-Bromo-1,2-butadiene ((*S*)-**1b**) (92% ee), was obtained from optically active (*R*)-1-butyn-3-ol [36], by reacting the corresponding methanesulfonate ester with $LiCuBr_2$, according to the procedure described by Vermeer and co-workers [27]. Commercial (Fluka) 1,4-dibromobenzene, lithium bromide, magnesium chloride, cuprous bromide, cuprous iodide and cuprous cyanide were used without purification. Cuprous thiophenoxide was obtained in situ reacting equimolar quantities of lithium thiophenoxide and cuprous iodide, at 25 °C in THF–hexane solution [37]. The dilithiobutane **10** was prepared in Et_2O (0.84 M, 82% yield) by reaction of 1,4-dichlorobutane with lithium (ca. 1% sodium content) [25]. 1,4-Bis(bromomagnesio)butane (**9**), was prepared (0.34 M, 87% yield) from the corresponding dibromide by using an excess of magnesium turnings in anhydrous THF, according to a previously reported procedure [26].

4.2. 1,4-Butanedicuprates (*7a–c*)

Typically, the organobis(cuprate) (**7a**) was prepared by adding, at −50 °C over a 15-min period, 1,4-bis-(bromomagnesio)butane (15 ml of a 0.34 M THF solution, 5.1 mmol) to a well-stirred solution of $LiCuBr_2$ (10.2 mmol) obtained in THF (25 ml) from stoichiometric amounts of cuprous bromide and lithium bromide [23]. Stirring was continued at −50 °C for 30 min, and the mixture then used immediately.

Cyanocuprate (**7b**) was prepared by treating a suspension of cuprous cyanide (7.7 mmol) in anhydrous Et_2O (40 ml) at −30 °C with 1,4-dilithiobutane (4.6 ml of a 0.84 M Et_2O solution, 3.9 mmol); the mixture was stirred at −30 °C for 30 min and the solution then used [24].

Lithiumtiophenoxy dicuprate (**7c**) was obtained by adding, at −78 °C over a 30-min period, 1,4-dilithiobutane (16.1 ml, 13.5 mmol) to a solution of cuprous thiophenoxide (27 mmol) in THF (90 ml) [25]. The mixture was allowed to warm to −20 °C over a 20-min period, during which the colour changed from yellow to red, and then used immediately.

4.3. Reaction of 1-bromo-1,2-dienes (*1a–c*) with 1,4-butanedicuprates (*7a–c*). General procedure

All reactions were carried out at least in duplicate. In a typical experiment, a solution of 1-bromo-1,2-diene (**1**) (10–30 mmol), in THF or Et_2O (5–20 ml) was

added, at −70 °C during 5–10 min, to the cuprate reagent (5–15 mmol) prepared by the procedures described above. The progress of the reactions was monitored by GLC analysis until they were complete; if necessary, after stirring was continued at −70 °C for 30 min, the mixture was allowed to warm to 20 °C (Table 1). The reaction mixture was quenched with saturated ammonium chloride solution (50 ml), and the organic materials were extracted with ether (3 × 50 ml). The combined extracts were washed with additional ammonium chloride (2 × 50 ml) and water (50 ml), then dried (Na_2SO_4) and analyzed by GLC and GLC–MS. Fractional bulb-to-bulb distillation and/or column silica gel chromatography afforded pure samples of diynes **5** and compounds **12**–**16** (Scheme 3, Table 1) which were identified and characterized by spectroscopic and analytical data.

The products **5** and **12**–**16** of the reactions summarized in Table 1 were as follows.

*4.3.1. 3,8-Diethyl-3,8-dimethyl-1,9-decadiyne (**5a**)*

IR: ν (cm^{-1}) 3309, 2109, 628. ^{1}H-NMR: δ 0.89 (6H, t, $J = 7.2$ Hz, CH_3), 1.06 (6H, s, CH_3), 1.36 (12H, m, CH_2), 2.00 (2H, s, ≡CH). ^{13}C-NMR: δ 8.8, 25.1, 25.7, 33.9, 35.0, 40.9, 68.6, 91.0. MS: m/z 217 ($M^+ - 1$), 203, 189(10%), 161(13), 147(16), 105(45) 81(100). Anal. Found: C, 88.07; H, 11.93. Calc. for $C_{16}H_{26}$: C, 87.99; H, 12.01%.

*4.3.2. 2,8-Dimethyl-1,9-decadiyne (**5b**)*

IR: ν (cm^{-1}) 3306, 2112, 631. ^{1}H-NMR: δ 1.18 (6H, d, $J = 7.0$ Hz, CH_3), 1.44 (8H, m, CH_2), 2.03 (2H, d, $J = 2.4$ Hz, ≡CH), 2.42 (2H, m, CHC≡). ^{13}C-NMR: δ 20.7, 25.4, 26.8, 36.4, 68.1, 89.1. MS: m/z 147 ($M^+ - 15$), 133(1%), 119(7), 105(21), 91(22), 41(100). Anal. Found: C, 88.95; H, 11.05. Calc. for $C_{12}H_{18}$: C, 88.81; H, 11.19%.

*4.3.3. 3,8-Bis(1,1-dimethylethyl)-1,9-decadiyne (**5c**)*

IR: ν (cm^{-1}) 3310, 2109, 630. ^{1}H-NMR: δ 0.98 (18H, s, CH_3), 1.21–1.78 (8H, m, CH_2), 2.04 (2H, d, $J = 2.1$ Hz, ≡CH), 2.05 (2H, m, CHC≡). ^{13}C-NMR: δ 27.4, 28.4, 29.4, 33.1, 43.6, 70.4, 86.6. MS: m/z 231 ($M^+ - 15$), 189(1%), 175(2), 161(2), 147(2), 57(100). Anal. Found: C, 87.85; H, 12.14. Calc. for $C_{18}H_{30}$: C, 87.72; H, 12.28%.

*4.3.4. 3-Ethyl-3,10-dimethyl-8,9-dodecadien-1-yne (**12a**)*

^{1}H-NMR: δ 0.97 (6H, m, CH_3), 1.13 (3H, s, CH_3), 1.20–1.50 (8H, m, CH_2), 1.67 (3H, d, $J = 3$ Hz, =C–CH_3), 1.90 (4H, m, =C–CH_2), 2.05 (1H, s, ≡CH), 5.06 (1H, m, =C=CH). MS: m/z 189 ($M^+ - 29$, 10%), 161(7), 147(10), 133(14), 119(16), 105(17), 96(96), 81(100).

*4.3.5. 3-Methyl-8,9-undecadien-1-yne (**12b**)*

^{1}H-NMR: δ 1.18 (3H, d, $J = 7.0$ Hz, CH_3), 1.44 (6H, m, CH_2), 1.65 (3H, dd, $J = 4.9$ and 5.2 Hz, =C–CH_3), 1.99 (2H, m, =C–CH_2), 2.03 (1H, d, $J = 2.4$ Hz, ≡CH), 2.42 (1H, m, ≡C–CH), 5.05 (2H, m, CH=C=CH). ^{13}C-NMR: δ 14.6, 20.9, 25.7, 26.6, 28.7, 28.9, 36.6, 68.0, 85.5, 89.2, 90.1, 204.7. MS: m/z 161 ($M^+ - 1$), 147(3%), 133(2), 119(7), 105(15), 41(100).

*4.3.6. 3-(1,1-dimethylethyl)-11,11-dimethyl-8,9-dodecadien-1-yne (**12c**)*

^{1}H-NMR: δ 0.98 (9H, s, CH_3), 1.03 (9H, s, CH_3), 1.20–1.40 (6H, m, CH_2), 1.96 (2H, m, =C–CH_2), 2.03 (1H, m, ≡C–CH), 2.05 (1H, d, $J = 2.1$ Hz, ≡CH), 5.15 (2H, m, CH=C=CH). MS: m/z 161 ($M^+ - 1$), 147(3%), 133(2), 119(7), 105(15), 41(100).

*4.3.7. 3-Ethyl-3-methyl-1-heptyne (**13a**)*

^{1}H-NMR: δ 0.92 (3H, t, $J = 7.1$ Hz, CH_3), 0.97 (3H, t, $J = 6.8$ Hz, CH_3), 1.13 (3H, s, CH_3), 1.39 (8H, m, CH_2), 2.05 (1H, s, ≡CH). MS: m/z 137 ($M^+ - 1$), 123(5%), 109(56), 96(16), 95(11) 81(100), 67(69).

*4.3.8. 3,12-Diethyl-3,12-dimethyl-1,13-tetradecadiyne (**14a**)*

^{1}H-NMR: δ 0.97 (6H, t, $J = 7.4$ Hz, CH_3), 1.14 (6H, s, CH_3), 1.2–1.6 (20H, m, CH_2), 2.08 (2H, s, ≡CH). ^{13}C-NMR: δ 8.8, 24.6, 25.7, 29.5, 30.0, 33.9, 35.0, 41.0, 68.5, 91.1. MS: m/z 259 ($M^+ - 15$, 1%), 245(4), 189(2), 175(5), 161(6), 147(10), 135(12), 121(20), 95(48), 81(100), 67(48).

*4.3.9. 3-Ethyl-3,6-dimethyl-4,5-ottadien-1-yne (**15a**)*

^{1}H-NMR: δ 1.02 (6H, t, $J = 7.0$ Hz, CH_3), 1.27 (3H, s, CH_3), 1.57 (2H, m, CH_2), 1.73 (3H, d, $J = 3$ Hz, =C–CH_3), 1.90 (2H, m, =C–CH_2), 2.12 (1H, s, ≡CH), 5.13 (1H, m, =C=CH). MS: m/z 162 (M^+, 19%), 147(77), 133(67), 119(64), 105(98), 91(79), 81(74), 67(41), 41(100).

*4.3.10. 3,8-Dimethyl-3,4,6,7-decatetraene (**16a**)*

^{1}H-NMR: δ 0.93 (6H, t, $J = 7.3$ Hz, CH_3), 1.64 (6H, m, CH_3), 1.88 (4H, m, CH_2), 5.47 (2H, m, =C=CH). ^{13}C-NMR: δ 12.0, 18.8, 27.0, 90.8, 103.0, 203.2. MS: m/z 162 (M^+, 98%), 147(47), 133(19), 119(40), 105(84), 91(74), 81(100).

*4.4. (3S,8S)-3,8-Dimethyl-1,9-decadiyne ((3S,8S)-**5b**)*

According to the general procedure, a solution of 4.0g (30 mmol) of (+)(*S*)-1-bromo-1,2-butadiene ((*S*)-**1b**), (92% ee) in THF (20 ml) was added during 15 min at −70 °C to a stirred suspension of lithium tiophenoxy dicuprate **7c** (15 mmol). After stirring was continued at −70 °C for 30 min, the reaction mixture was quenched with saturated NH_4Cl solution. Usual work

up gave a crude product which was purified by column chromatography (*n*-hexane) affording chemically pure (GLC) (3*S*,8*S*)-**5b** (1.7 g, 70% yield), having $\alpha_D^{25}(l=1)$ + 45.6° and characteristic spectroscopic data fully consistent with those reported for the racemic compound.

A second analogous experiment gave chemically pure (3*S*,8*S*)-**5b** (1.83 g, 75% yield) having $\alpha_D^{25}(l=1)$ + 45.2°.

4.5. (3R,8R)-3,8-Dimethyldecane ((3R,8R)-17)

(3*S*,8*S*)-**5b** (0.94g, 5.8 mmol), $\alpha_D^{25}(l=1)$ + 45.6°, was added at 0 °C to diisobutylaluminium hydride (DIBAH) (8.5 g, 60 mmol). The mixture was stirred at room temperature (r.t.) for 24 h and then heated at 80 °C for 12 h. After hydrolysis at 0 °C with water and dilute sulphoric acid (5%), the organic materials were extracted with ether and the combined extracts washed with water and dried (Na_2SO_4). Fractional distillation gave chemically pure (3*R*,8*R*)-**17** (0.81 g, 82% yield): b.p. 83 °C at 17 mmHg, $[\alpha]_D^{25}$ − 15.57. ^{1}H-NMR: δ 0.78 (12H, m, CH_3), 0.96–1.36 (14H, m, CH_2 and CH). ^{13}C-NMR: δ 11.4, 19.2, 27.5, 29.6, 34.5, 36.8. MS: *m*/*z* 141 ($M^+ - 29$, 1%), 113(4), 111(1), 99(2), 85(6), 71(6), 57(63), 56(20), 43(65), 41(100). (Lit. [28], $[\alpha]_D^{25}$ + 17.9 for optically pure (3*S*,8*S*)-**17**.)

4.6. 1,4-Bis(bromomagnesio)benzene (11)

In a typical run, freshly cut potassium (1.55 g, 40 mmol), $MgCl_2$ (2.02 g, 21 mmol), KI (1.4 g, 8.4 mmol) and THF (50 ml) were stirred and heated to reflux for 1 h [29]. To the dark grey mixture, cooled at r.t., was added 1,4-dibromobenzene (1.25 g, 5.3 mmol) in THF (5 ml). The resulting mixture was stirred at r.t. for 30 min and then used immediately. GLC analysis of a NH_4Cl solution hydrolysed sample showed a 100% yield of bis(bromomagnesio)benzene **11**, detected as benzene. MS-GLC analyses of the reaction mixture after deuterolitic work-up confirmed the presence of the bis-organometallic reagent.

4.7. 1,4-Benzenedicuprate (8)

Typically, the organobis(cuprate) **8** was prepared by adding, at 0 °C over a 15-min period, a THF solution of 1,4-bis(bromomagnesio)benzene (5 mmol, 50 ml) to a well-stirred solution of $LiCuBr_2$ (10 mmol) obtained in THF (40 ml) from stoichiometric amounts of CuBr (1.45 g) and LiBr (0.87 g) [23]. Stirring was continued at 0 °C for 30 min, and the mixture then used immediately.

4.8. Reaction of 1-bromo-1,2-dienes (1b–d) with 1,4-benzenedicuprate (8). General procedure.

All reactions were carried out at least in duplicate. In a typical experiment, a solution of 1-bromo-1,2-diene (**1**) (10 mmol) in THF (10 ml) was added, at − 70 °C during 5 min, to the bis-cuprate reagent (5 mmol) prepared by the above described procedure. After stirring was continued at − 70 °C for 5 min, the mixture was allowed to warm to 20 °C and stirred for 12 h. The progress of the reactions was monitored by GLC analysis (Table 2). The reaction mixture was quenched with saturated ammonium chloride solution (50 ml), and worked-up as previously described for experiments with 1,4-butane-dicuprates. Column silica gel chromatography (*n*-hexane) afforded pure samples of diynes **6** and allenynes **18** which were identified and characterized by spectroscopic and analytical data. 3-Phenyl-1-alkynes **19** and phenylallenes **20** (Scheme 6, Table 2) were identified by comparison of their GLC retention times with those of authentic samples [3].

The products **6** and **18** of the reactions summarized in Table 2 were as follows.

4.8.1. 1,4-Bis(1-methyl-2-propynyl)benzene (6b)

^{1}H-NMR: δ 1.49 (6H, d, $J = 6.2$ Hz, CH_3), 2.24 (2H, d, $J = 2.5$ Hz, ≡CH), 3.75 (2H, dq, $J = 2.5$ and 6.2 Hz, CHPh), 7.35 (4H, s, PhH). ^{13}C-NMR: δ 24.1, 31.2, 70.0, 87.1, 127.0, 141.1. MS: *m*/*z* 182 (M^+, 37%), 173(3), 167(61), 165(40), 152(46), 129(100). Anal. Found: C, 92.43; H, 7.57. Calc. for $C_{14}H_{14}$: C, 92.25; H, 7.75%.

4.8.2. 1,4-Bis(1-ethynyl-2,2-dimethylpropyl)benzene (6c)

^{1}H-NMR: δ 0.96 (18H, s, CH_3), 2.23 (2H, d, $J = 2.5$ Hz, ≡CH), 3.39 (2H, d, $J = 2.5$ Hz, CHC≡), 7.22 (4H, s, PhH). ^{13}C-NMR: δ 27.5, 34.9, 49.2, 71.3, 85.5, 128.8, 137.3. MS: *m*/*z* 266 (M^+, 3%), 251, 210(11), 209(5), 195(3), 179(1), 167(1), 154(8), 115(1), 57(100). Anal. Found: C, 90.30; H, 9.70. Calc. for $C_{20}H_{26}$: C, 90.16; H, 9.84%.

4.8.3. 1,4-Bis(1-ethynyl-1,2,2-trimethylpropyl)benzene (6d)

IR: ν (cm^{-1}) 3300, 2960, 2880, 900, 780. ^{1}H-NMR: δ 0.96 (18H, s, CH_3), 1.65 (6H, s, CH_3), 2.23 (2H, s, ≡CH), 7.43 (4H, s, PhH). ^{13}C-NMR: δ 23.3, 26.3, 36.9, 47.0, 71.0, 90.2, 127.2, 140.4. MS: *m*/*z* 237 ($M^+ - 57$, 21%), 207(4), 181(53), 165(16), 152(3), 115(4), 77(3), 57(100). Anal. Found: C, 89.79; H, 10.20. Calc. for $C_{22}H_{30}$: C, 89.72; H, 10.28%.

4.8.4. 1-(1-Methyl-2-propynyl)-4-(1,2-butadienyl)-benzene (18b)

^{1}H-NMR: δ 1.45 (3H, d, $J = 7.0$ Hz, CH_3), 1.73 (3H, dd, $J = 3.2$ and 7.0 Hz, =C–CH_3), 2.12 (1H, d, $J = 2.8$ Hz, ≡CH), 3.73 (1H, dq, $J = 2.8$ and 7.0 Hz, ≡C–CH), 5.45 (1H, m, =C=CH), 6.03 (1H, m, =C=CH), 7.10–7.30 (4H, m, PhH). MS: *m*/*z* 182 (M^+, 56%), 167(100), 129(2), 115(3), 41(70).

*4.8.5. 1-(1-Ethynyl-2,2-dimethylpropyl)-4-(4,4-dimethyl-1,2-pentadienyl)benzene (**18c**)*

^{1}H-NMR: δ 0.97 (9H, s, CH_3), 1.12 (9H, s, CH_3), 2.22 (1H, d, $J = 2.5$ Hz, ≡CH), 3.38 (1H, d, $J = 2.5$ Hz, ≡C–CH), 5.56 (1H, d, $J = 6.3$ Hz, =C=CH), 6.16 (1H, d, $J = 6.3$ Hz, =C=CH), 7.10–7.35 (4H, m, PhH). ^{13}C-NMR: δ 27.5, 30.3, 32.8, 34.9, 49.5, 71.3, 85.4, 95.7, 106.8, 125.6, 129.6, 133.8, 138.6, 202.4. MS: m/z 266 (M^+,16%), 251(1), 210(20), 209(15), 195(4), 179(3), 165(2), 153(9), 115(3), 57(100).

*4.8.6. 1-(1-Ethynyl-1,2,2-trimethylpropyl)-4-(3,4,4-trimethyl-1,2-pentadienyl)benzene (**18d**)*

^{1}H-NMR: δ 0.99 (9H, s, CH_3), 1.13 (9H, s, CH_3), 1.63 (3H, s, CH_3), 1.79 (3H, d, $J = 2.7$ Hz, =C–CH_3), 2.30 (1H, s, ≡CH), 6.04 (1H, q, $J = 2.7$ Hz, =C=CH), 7.18 (2H, d, $J = 8.3$ Hz, PhH), 7.45 (2H, d, $J = 8.3$ Hz, PhH). ^{13}C-NMR: δ 14.7, 23.4, 26.3, 29.2, 34.2, 37.1, 47.2, 71.1, 90.1, 93.7, 112.5, 125.0, 128.9, 134.2, 140.6, 201.9. MS: m/z 237 ($M^+ - 57$, 56%), 181(100), 165(29), 152(22), 128(25), 78(10), 57(81).

*4.9. 1,4-Bis[(R)-1-methyl-2-propynyl]benzene ((R)-**6b**)*

According to the general procedure, a solution of 4.17 g (31.4 mmol) of (+)(*S*)-1-bromo-1,2-butadiene ((*S*)-**1a**), (92% ee) in THF (15 ml) was added during 15 min at −70 °C to 1,4-benzenedicuprate **8** (15.7 mmol). After stirring was continued at −70 °C for 5 min, the reaction mixture was heated at r.t. for 12 h and then quenched with saturated NH_4Cl solution. Usual work-up gave a crude product which was purified by column chromatography (*n*-hexane) affording chemically pure (GLC) (*R*)-**6b** (1.2 g, 42% yield), having $[\alpha]_D^{25}$ −8.80 ($c = 5.98$, $CHCl_3$) and spectroscopic data fully consistent with those reported for the racemic compound.

A sample of (*R*)-**6b** (1.0 g, 5.5 mmol) was added, at 0 °C, to diisobutylaluminium hydride (DIBAH, 60 mmol) and the resulting mixture was heated at 50–80 °C for 24 h. After hydrolysis, the crude product recovered was ozonized in acid acetic solution (20 ml) according to a previously reported procedure [33]. Most of the acetic acid was removed under vacuum at 40 °C, and the crude ozonide was decomposed in ethereal solution (100 ml) with lithium aluminium hydride (5 g). After hydrolysis, usual work-up gave a sample of (*R*)-2-methyl-1-butanol ((*R*)-**21**), having $[\alpha]_D^{25}$ +5.10 ($c =$ 3.61, heptane).

(Lit. [33], $[\alpha]_D^{25}$ +6.60 for optically pure (*R*)-**21**).

Acknowledgements

This work was in part financially supported by the Ministero dell'Università e della Ricerca Scientifica e Tecnologica (MURST), Roma (National Project no. 9903558918).

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