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NOVEL SYNTHESIS OF BUTATRIENE DERIVATIVES BY REACTIONS OF 3-BROMO-3-ALKEN-1-YNES WITH ORGANOCOPPER(I) SPECIES

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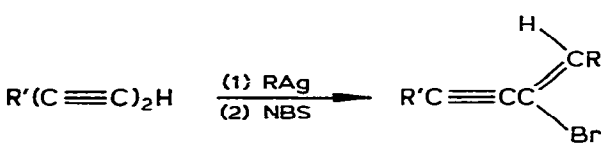
Summary

3-Bromo-3-alken-1-ynes (I) have been converted by isopropyl- and t-butylcopper into pure butatrienes (II) in an *anti*-S_N2'-process. n-Alkylcopper species produced highly impure butatrienes, presumably because of subsequent addition of unreacted n-alkylcopper to the initially formed butatrienes. Phenylcopper did not give the S_N2'-reaction with I and its homocuprate derivative also gave disappointing results.

Introduction

Several methods for the preparation of butatrienes are known [1,2], but only a few of them are suitable for preparation of geometrically pure butatrienes. *trans*-1,4-Disubstituted butatrienes have been obtained by reaction of 1-iodo-1-alkynes with alkylboranes [3], while the *cis* derivatives have been synthesized from (*Z*)-1-(methylthio)vinyl cuprates [4]. The cuprate method is also suited for the preparation of tetrasubstituted (*Z*)-butatrienes (see ref. 4).

The present paper concerns the reaction of 3-bromo-3-alken-1-ynes with organocopper compounds [5]. Such enynes are readily available by means of the regiospecific and stereoselective addition of alkylsilver to 1,3-alkadiynes and subsequent treatment of the produced adducts with *N*-bromosuccinimide [6]:



It will be shown that such 3-bromo-3-alken-1-ynes are suitable precursors for di- and tri-substituted butatrienes.

Results and discussion

Synthesis of butatrienes. Our first experiments were directed to the conversion of 3-bromo-3-alken-1-ynes (I) by Grignard reagents into butatrienes using a catalytic

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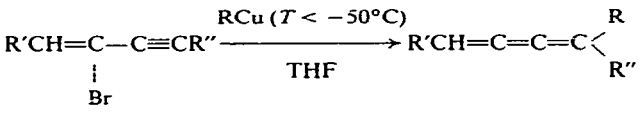
amount (5 mol%) of copper(I) bromide (solvent tetrahydrofuran (THF) or Et_2O). It soon became apparent that this approach was unsatisfactory because of the occurrence of substantial metal–halogen exchange and the formation of other unidentified products. The corresponding homocuprates, R_2CuMgX, also produced impure butatrienes because of halogen–metal exchange and, presumably, because of subsequent addition of the cuprate to the initially formed butatrienes.

From other work it was known that the use of organocopper(I) compounds, RCu, in substitution reactions may be more advantageous than that of the ate-derivatives when the homocuprate compounds induce substantial halogen–metal exchange [7]. It was therefore decided to subject compounds I to reaction with RCu. The purity of the produced butatrienes appeared to depend on the nature of the group R in the copper compound. Pure butatrienes were obtained when R was isopropyl or t-butyl, provided that the copper reagent was added carefully to a THF solution of I. Inverse addition gave rise to formation of contaminants which were presumably formed by addition of unreacted RCu to the produced butatrienes II (compare ref. 8). Unfortunately, n-alkylcopper compounds such as ethyl- and butyl-copper always gave butatrienes containing substantial amounts of higher boiling products. The structure of these contaminants has not been determined yet, but it is assumed that they again arise from subsequent attack of RCu on II. If this is true, it can be deduced that s- or t-alkylcopper compounds convert I into II much more readily than they add to II, while in the case of n-alkylcopper species both reactions must proceed with a comparable rate.

Hitherto no conditions have been found which allow a formation of butatrienes by means of phenylcopper-induced substitution in I. In fact, phenylcopper is almost inert towards I; its homocuprate derivative, $Ph_2CuMgBr$, mainly caused halogen–metal exchange in I. Phenyl substituted butatrienes must therefore be prepared from compounds I in which the phenyl group is already present (see compound IIh in Scheme 1 and Table 1). The data listed in Scheme 1 and Table 1 show that our method of preparing butatrienes is also appropriate for selectively deuterated butatrienes (compounds IIc, IId, and IIg).

SCHEME 1



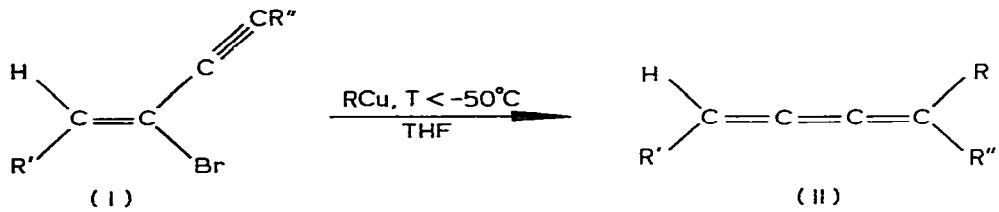
(I)

(IIa: R = t-Bu, R' = Bu, R'' = H;
IIb: R = R' = i-Pr, R'' = H;
IIc: R = R' = i-Pr, R'' = D;
IId: R = t-Bu, R' = i-Pr, R'' = D;
IIe: R = i-Pr, R' = t-Bu, R'' = H;
IIf: R = R' = t-Bu, R'' = H;
IIg: R = R' = t-Bu, R'' = D;
IIh: R = R' = t-Bu, R'' = Ph)

(Yields of II 85–95%)

Stereochemistry and mechanism Butatrienes can exhibit *Z/E*-isomerism, and all the compounds in Scheme 1 were obtained as mixtures of both isomers. Comparison of the third and sixth column of Table 1 indicates that the *Z/E*-ratio in the starting compound is almost the same as the *E/Z*-ratio in the product for compounds IIa–IIg or the *Z/E*-ratio for IIh. In our preliminary report on this subject it was

TABLE I

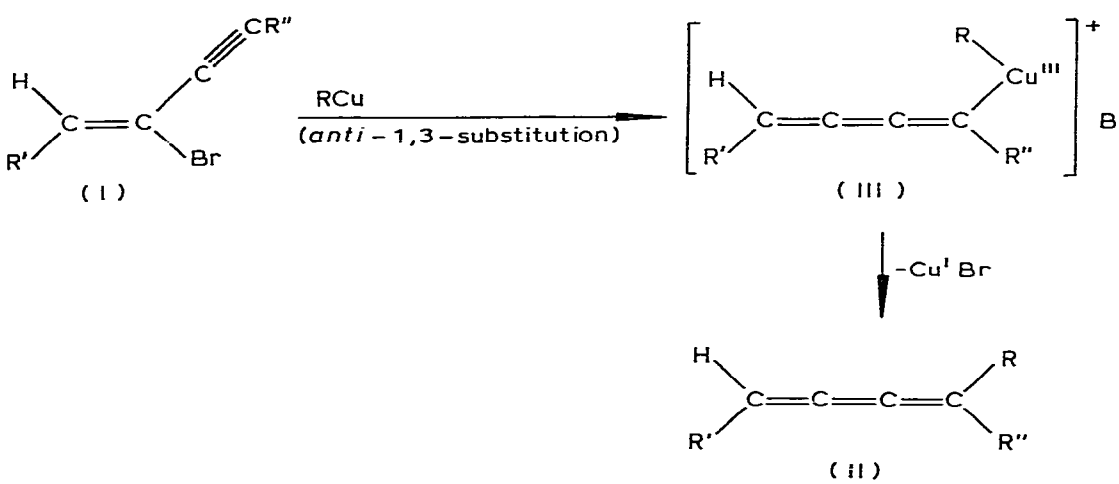


(I) (II)

Compound I			RCu	Product	Z/E-ratio [a] in II	Yield [b] of II (%)
R'	R"	Z/E				
Bu	H	82/18	t-BuCu	IIa	20/80	95
i-Pr	H	90/10	i-PrCu	IIb	15/85	90
i-Pr	D	90/10	i-PrCu	IIc	9/91	90
i-Pr	D	90/10	t-BuCu	IId	15/85	88
t-Bu	H	93/7	i-PrCu	IIe	10/90	85
t-Bu	H	93/7	t-BuCu	IIf	7/93	95
t-Bu	D	93/7	t-BuCu	IIg	7/93	95
t-Bu	Ph	91/9	t-BuCu	IIh	90/10	95

[a] The configurational assignments are based on the assumption that the conversion of I into II is an *anti* process (see ref. 5). The ratios are derived from relative heights of the signals from R (and R') in the ^{1}H NMR spectra. [b] Yields refer to pure butatrienes.

shown that the conversion of I into IIf (R = R' = t-Bu, R" = H) proceeds *anti* [5]. It is not unreasonable to assume that this is also the stereochemical course for the other conversions given in Scheme 1, i.e. in all cases a highly stereoselective, if not stereospecific, *anti*-1,3-substitution is involved. *anti*-1,3-Substitution is the preferred pathway for organocopper(I) induced substitution of propargylic substrates in which the propargylic center bearing the leaving group is sp^3 hybridized [9,10]. Evidently, a change in hybridization of sp^3 into sp^2 does not alter the stereochemical course of the reaction.



(I) (III) (II)

The mechanistic course of organocopper induced substitutions is still a matter of speculation. Several authors have proposed that such reactions proceed through copper(III) intermediates [11]. If this is so, the initial formation of compounds III must be accepted for our reactions (see Scheme 2). Compounds III must then in their turn undergo reductive elimination. However, the available data do not allow exclusion of other possibilities, for example involving the formation of copper(II) instead of copper(III) intermediates [12] or the formation of adducts by *cis*-addition of RCu to the triple bond of I followed by *anti*-elimination of $Cu^{I}Br$ [5].

Conclusion

3-Bromo-3-alken-1-ynes satisfactorily give butatrienes when treated with RCu compounds containing branched alkyl groups. The high *anti*-stereoselectivity of the reaction may be utilized to prepare *Z*- or *E*-butatrienes starting from geometrically pure 3-bromo-3-alken-1-ynes.

Experimental

All reactions with organocopper(I) compounds were performed under dry nitrogen. The products were analysed by GLC (SE 33 column) and by NMR (Varian EM-390 and CFT-20 spectrometers) spectroscopy. The starting 3-bromo-3-alken-1-ynes I (R'' ≠ D) were obtained by the procedure given in ref. 6; the deuterated compounds I (R'' = D) were prepared by reaction of I (R'' = H) with an equimolar amount of methyllithium in Et_2O at −60°C during 30 min followed by deuterolysis with D_2O (yield ca. 95%).

General procedure for the reaction of I with RCu

A cold solution ($T < -50$°C) of RCu (0.020 mol) in THF (65 ml), prepared by stirring RMgCl (0.020 mol) with the THF soluble complex $LiCuBr_2$ (0.020 mol) for 30 min at −50°C, was carefully added in ca. 10 ml portions to a stirred solution of I (0.020 mol) in THF (20 ml). During the addition the temperature of the mixture was kept between −55– −50°C, and thereafter it was allowed to rise gradually to 0°C during 20 min. The mixture was then poured into an aqueous solution of ammonium chloride (200 ml) containing sodium cyanide (2 g). The products were isolated by extraction with pentane (3 × 50 ml). After washing of the combined extracts with water and drying with K_2CO_3, the solvent was stripped off in vacuo. The residue was distilled or was recrystallized from methanol; for yields and *Z*/*E*-ratios of the butatrienes see Table 1.

Compounds

$H^a > C^1{=}C^2{=}C^3{=}C^4 < \begin{matrix} R \\ R'' \end{matrix}$ (IIa–IIh)

R'

IIa (R = t-Bu, R' = Bu, R'' = H): b.p. 40–42°C/0.1 mmHg; n_D^{20} 1.4916. ^{1}H NMR (CCl_4, TMS): δ(ppm) 1.10 (t-Bu for *E*-IIa), 1.12 (t-Bu for *Z*-IIa), 2.00–2.35 (CH_2–C= for *Z*- + *E*-IIa), 5.30–5.60 (H^a + R'' for *Z*- + *E*-IIa). ^{13}C NMR ($CDCl_3$, TMS): δ(ppm) 162.6 + 158.0 (C(2) + C(3) for *E*-IIa), 162.6 + 158.1 (C(2) + C(3) for *Z*-IIa), 118.5 (C(4) for *E*-IIa), 118.4 (C(4) for *Z*-IIa), 107.1 (C(1) for *Z*- + *E*-IIa).

IIb (R = R' = i-Pr, R'' = H): b.p. 70–72°C/20 mmHg; n_D^{20} 1.4965. ^{1}H NMR

(CCl_4, TMS): δ(ppm) 1.07 ($2 \times (CH_3)_2CH$ for *E*-IIb), 1.09 ($2 \times (CH_3)_2CH$ for *Z*-IIb), 2.15–2.65 ($2 \times CH(CH_3)_2$ for *Z*- + *E*-IIb), 5.30–5.58 (H^a + R″ for *Z*- + *E*-IIb). ^{13}C NMR ($CDCl_3$, TMS): δ(ppm) 160.4 (C(2) + C(3) for *E*-IIb), 114.2 (C(1) + C(4) for *E*-IIb).

IIc (R = R′ = i-Pr, R″ = D): b.p. 70–72°C/20 mmHg; n_D^{20} 1.4963. ^1H NMR (CCl_4, TMS): δ(ppm) 1.07 ($2 \times (CH_3)_2CH$ for *E*-IIc), 1.09 ($2 \times (CH_3)_2CH$ for *Z*-IIc, 2.15–2.65 ($2 \times CH(CH_3)_2$ for *Z*- + *E*-IIc), 5.43 (H^a for *E*-IIc).

IId (R = t-Bu, R′ = i-Pr, R″ = D): b.p. 72°C/20 mmHg; n_D^{20} 1.4950. ^1H NMR (CCl_4, TMS): δ(ppm) 1.09 (t-Bu for *E*-IId), 1.07 ($2 \times (CH_3)_2CH$ for *E*-IId), 1.09 ($2 \times (CH_3)_2CH$ for *Z*-IId), 2.43 ($CH(CH_3)_2$ for *E*-IId), 5.50 (H^a for *E*-IId). ^{13}C NMR ($CDCl_3$, TMS): δ(ppm) 161.1 + 159.1 (C(2) + C(3) for *E*-IId), 118.0 (C(4) for *E*-IId), 113.9 (C(1) for *E*-IId). Raman: 2060 cm^1 (C=C=C=C).

IIe (R = i-Pr, R′ = t-Bu, R″ = H): b.p. 70–72°C/20 mmHg; n_D^{20} 1.4930. ^1H NMR (CCl_4, TMS): δ(ppm) 1.09 (t-Bu for *E*-IIe), 1.07 ($2 \times (CH_3)_2CH$ for *E*-IIe), 1.09 ($2 \times (CH_3)_2CH$ for *Z*-IIe), 2.40 ($CH(CH_3)_2$ for *E*-IIe), 5.30–5.58 (H^a + R″ for *Z*- + *E*-IIe). ^{13}C NMR ($CDCl_3$, TMS): δ(ppm) 161.1 + 159.2 (C(2) + C(3) for *E*-IIe), 113.9 (C(4) for *E*-IIe), 118.3 (C(1) for *E*-IIe).

IIf (R = R′ = t-Bu, R″ = H): m.p. 68–70°C. ^1H NMR (CCl_4, TMS): 1.09 (2 × t-Bu for *E*-IIf), 1.11 (2 × t-Bu for *Z*-IIf), 5.44 (H^a + R″ for *Z*-IIf), 5.48 (H^a + R″ for *E*-IIf). ^{13}C NMR ($CDCl_3$, TMS): δ(ppm) 159.8 (C(2) + C(3) for *E*-IIf), 118.4 (C(1) + C(4) for *E*-IIf).

IIg (R = R′ = t-Bu, R″ = D): m.p. 68–70°C. ^1H NMR (CCl_4, TMS): δ(ppm) 1.09 (2 × t-Bu for *E*-IIg), 1.11 (2 × t-Bu for *Z*-IIg), 5.44 (H^a for *Z*-IIg), 5.48 (H^a for *E*-IIg). Raman: 2060 cm^{-1} (C=C=C=C).

IIh (R = R′ = t-Bu, R″ = Ph): b.p. 85–90°C/0.001 mmHg; n_D^{20} 1.5600. ^1H NMR (CCl_4, TMS): δ(ppm) 1.01 + 1.28 (2 × t-Bu for *Z*-IIh), 5.48 (H^a for *Z*-IIh), 7.05–7.45 (R″ for *Z*-IIh). ^{13}C NMR ($CDCl_3$, TMS): δ(ppm) 160.5 + 157.7 (C(2) + C(3) for *Z*-IIh), 129.1 (C(4) for *Z*-IIh), 118.4 (C(1) for *Z*-IIh).

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