Tetrahedron Letters,Vol.25,No.45,pp 5193-5196,1984
Printed in Great Britain

0040-4039/84 $3.00 + .00

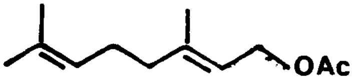
SYNTHESIS OF 2-SUBSTITUTED I,3-BUTADIENYL COMPOUNDS BY PALLADIUM-CATALYZED REGIOSELECTIVE I,2-ELIMINATION REACTION OF METHYLVINYLCARBINOL ACETATES

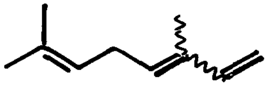
Adriano Carpita, Fabrizio Bonaccorsi, and Renzo Rossi

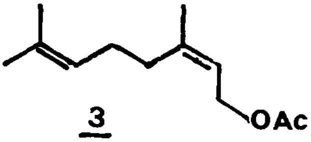
Istituto di Chimica Organica - Facoltà di Scienze MFN - Università
Via Risorgimento 35 - 56I00 Pisa - ITALY

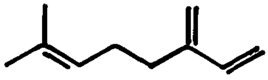
Summary: Alkylation of the dianion of 3-methyl-3-buten-2-ol, followed by acetylation and palladium-catalyzed I,2-elimination reaction of the so obtained methylvinylcarbinol acetates allows to synthesize regioselectively 2-substituted I,3-butadienyl compounds having high isomeric purity.

Recently it was reported that primary allylic acetates undergo to regioselective I,4--elimination when reacted with propargylzinc bromide, in the presence of $(PPh_3)_4Pd$[I]. The regioselectivity of the reaction was shown to depend either from the presence of propargylzinc bromide, or from the configuration of the used primary allylic acetate[I,2]. In fact, geranyl acetate (I) afforded a stereoisomeric mixture of ocimene (2), whereas neryl acetate (3) gave myrcene (4a) which was contamined by less than I% of 2[I].


1

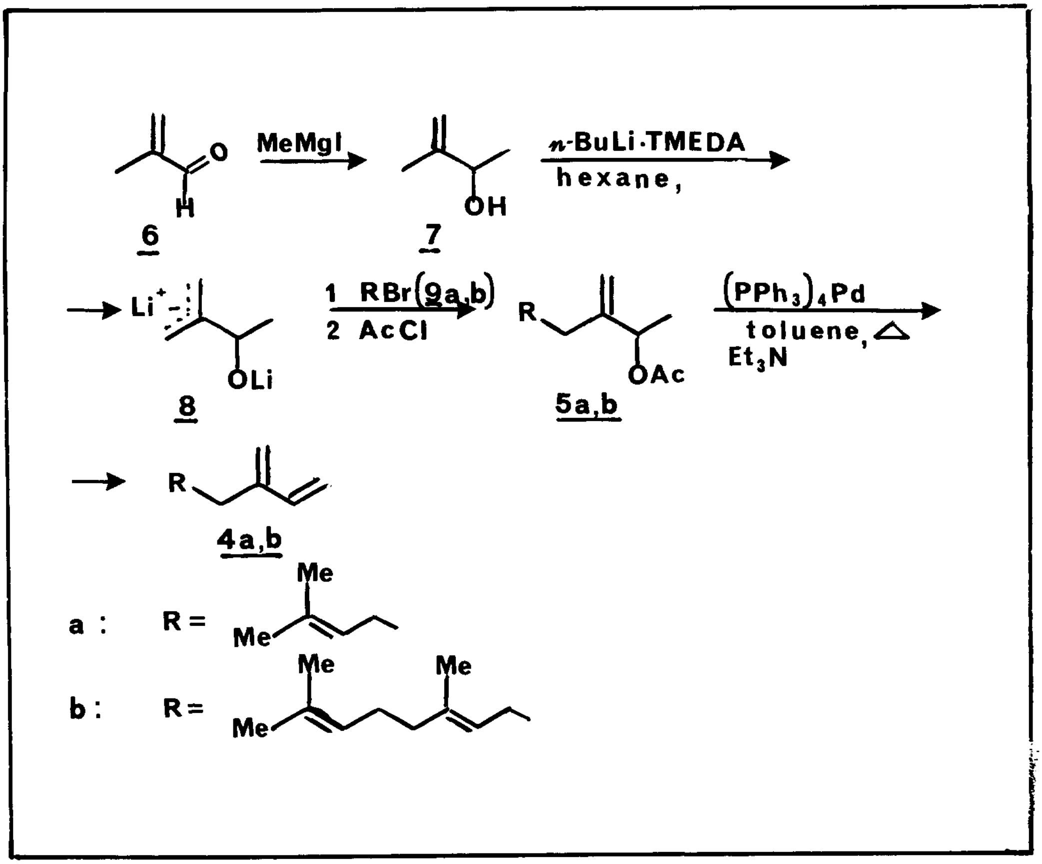

2


3


4a

In the course of our continuing studies on the stereoselective synthesis of terpenoid allomone and pheromone components[3,4], we have found that 2-substituted I,3-butadienyl compounds (4) may be conveniently synthesized by palladium-catalyzed I,2-elimination reaction of methylvinylcarbinol acetates (5). Such elimination occurs regioselectively in toluene solution at ca. 65°C in the presence of triethylamine and does not require the use either of propargylzinc bromide or of well configurationally defined allylic acetates. The here reported syntheses of myrcene (4a)[5] and (E)-β-farnesene (4b)[6] from the easily available allylic acetates 5a and 5b, respectively, illustrate the procedure (Scheme).

SCHEME



Compound 5a was so prepared. Reaction of methacrolein (6) with methylmagnesium iodide afforded 3-methyl-3-buten-2-ol (7) (84% yield) which was transformed into the corresponding dianion (8) by treatment with n-butyllithium - TMEDA complex in hexane at -78°C[7]. Compound 8 was then reacted with I-bromo-3-methyl-2-butene (9a) to give a crude alkylated derivative, which was acetylated to afford 2-acetoxy-3-methylene-7-methyl-6-octene (5a) in 40% overall yield based on 7. Analogously, reaction of geranyl bromide (9b) with 8, followed by acetylation gave (E)-2-acetoxy-7,II-dimethyl-3-methylene-6,IO-dodecadiene (5b)[8] in 42% overall yield.

Some experiments were carried out in order to establish the best conditions to convert 5a into 4a (Table)[9]. The best results were obtained using toluene as solvent and operating at 65°C for 20 h. The yields were in any case not higher than 66% owing to the thermal instability of myrcene.

Taking into account the results reported in Table, compound 5b was converted into (E)-β-farnesene (4b) according to the following procedure. A mixture of $(PPh_3)_4Pd$ (0.87 g, 0.76

mmol), toluene (I5 ml), triethylamine (I,68 g) I6.6 mmol) and 5b (4.0 g, I5.I mmol) was stirred at 65°C for I8 h under nitrogen atmosphere. The reaction mixture was then diluted with pentane, filtered, washed sequetially with diluted HCl, water, aqueous $NaHCO_3$, water, dried over Na_2SO_4, and concentrated in vacuo. The residue[IO] (3.05 g) was purified by liquid chromatography on a silica gel column (Merck H-60) using hexane as eluant to afford 4b (2.44 g) in 79% yield. IR (neat): ν_{max} 3095, 2970, 2930, 2860, 2730, I820, I790, I670, I635, I595, I440, I378, I372, II05, 990, 900, 890, 835, 825, 755, and 740 cm^{-I}. ^{I}H NMR (CCl_4): δ I.57 (s, 6H), I.67 (s, 3H), I.96 (br, 4H), 2.I7 (m, 4H), 4.8-5.4 (m, 6H), and 6.32 ppm (dd, IH). MS: m/e 204 (M^+, 3.9), I6I (9.2), I33 (20.I), I20 (I3.6), I07 (7.I), 93 (37.2), 9I(I2.8), 79 (I5.7), 69 (67.7), 4I (I00). GLC analysis on a FFAP glass-capillary column showed that 4b was chemically pure and had isomeric purity higher than 98%.

TABLE

PALLADIUM-CATALYZED 1,2-ELIMINATION OF 2-ACETOXY-3-METHYLENE-7-METHYL-6-OCTENE[a]

Catalyst system	Solvent	T/h	Myrcene	
			GC yield %	Isomeric purity %
$Pd(OAc)_2+PPh_3$[b]	dioxane	100°/8	66	86
$(PPh_3)_4Pd$	Et_3N+THF	70°/8	61	93
$(PPh_3)_4Pd$	toluene+ +Et_3N	100°/1.5	61	96
$(PPh_3)_4Pd$	toluene+ Et_3N	65°/20	66	98

a) Unless otherwise mentioned the reactions were carried out in the presence of 5 mol % of $Pd(PPh_3)_4$.

b) The reaction was carried out in the presence of I mol % of $Pd(OAc)_2$ and I0 mol% of PPh_3.

In conclusion, alkylation of the dianion of 3-methyl-3-buten-2-ol (7), followed by acetylation and palladium-catalyzed I,2-elimination reaction of the so obtained methylvinylcarbinol acetates (5) represents a synthetically useful method to prepare 2-substituted I,3-butadienyl compounds having high isomeric purity[II].

Acknowledgment. The investigation was supported by the Special "ad hoc" Project "Increment of Productivity of the Agricultural Resources" (IPRA) of C.N.R. (Rome).

References and Notes

I. H. Matsushita and E. Negishi, J. Org. Chem., 47, 4I6I (I982)

2. For the conversion of allylic acetates into conjugated dienes under the influence of Pd complexes see also : i) J. Tsuji, T. Yamakawa, M. Kaito, and T. Mandai, Tetrahedron Lett., 2075 (I978); ii) B.M. Trost, T.R. Verhoeven, and J.M. Fortunak, Tetrahedron Lett., 230I (I979)

3. R. Rossi, A. Carpita, and F. Bonaccorsi, Chim. Ind. (Milan), 65, 694 (I983).

4. A. Carpita, F. Bonaccorsi, and R. Rossi, Gazz. Chim. Ital., in press

5. For previous syntheses of myrcene see Ref. I and references cited therein; S. Tanaka, A. Yasuda, H. Yamamoto, and H. Nozaki, J. Am. Chem. Soc.,97, 3252 (I975)

6. For previous syntheses of (E)-β-farnesene see Ref. 4 and: T. Mandai, M. Kawada, and J. Otera, J. Org. Chem., 48, 5I83 (I983)

7. The procedure was similar to that described for the selective metallation of 3-methyl-3-buten-I-ol: G. Cardillo, M. Contenti, and S. Sandri, Tetrahedron Lett., 22I5 (I974)

8. All new compounds gave the expected microanalytical results and all were fully characterized by IR, ^{I}H NMR, and mass spectra

9. The reactions were monitored by GLC on a FFAP glass-capillary column (25 m x 0.25 mm i.d.)

I0. GLC/MS analysis of the residue showed the presence of ca. 94.5% of 4b and of ca. 5.5% of a mixture constituted of three isomeric acetates in a ca. 6:I:3 molar ratio. The principal component of this mixture was 5b and the other two components were presumably the stereoisomers of I-acetoxy-6,I0-dimethyl-2-ethylidene-(5E)-5,9-undecadiene which derived from the π-allilic complex formed by oxidative addition of 5b to zerovalent palladium

II. For some recent advances in the isoprenylation reactions see: i) H. Sakurai, A. Osomi, M. Saito, K. Sasaki, H. Iguchi, J. Sasaki, and Y. Araki, Tetrahedron, 39, 883 (I983) and references cited therein; ii) G. Cainelli and G. Cardillo, Acc. Chem. Res., I4, 89 (I98I)

(Received in UK 23 July 1984)