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Metal-Assisted Terpenoid Synthesis. IV.[1] Nickel-Catalyzed Reactions of 1,3-Dienes with Ketones. A New Synthesis of Long Chain Tertiary Alcohols

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Catalytic reactions of 1,3-butadiene with ketones were carried out with a nickel-ligand system to give stereoselectively tertiary alcohols having a (2*Z*, 5*E*)-2,5,7-octatrienyl- or a (2*Z*, 6*E*, 9*E*)-2,6,9,11-dodecatetraenyl chain. Similar reactions of isoprene gave a mixture of terpenic and apoterpenic alcohols. A possible reaction scheme was discussed in terms of an insertion of the carbonyl group to a σ-allyl end of octadienyl or dodecatrienyl nickel complexes.

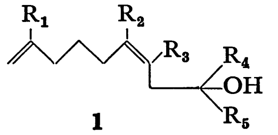
Despite extensive studies on telomerization of conjugated dienes with various protic substances[2] including carbonyl-activated methylene compounds, no report has been given on the catalytic formation of tertiary alcohols from ketones and oligodienes. A closely related reaction may be the secondary alcohol formation in the palladium-catalyzed reactions of 1,3-butadiene with aldehydes.[3a-d] A nickel catalyst system has been found to be effective for the synthesis of tertiary alcohols of types **1** and **2**. The reaction provides a convenient synthetic route for long chain alcohols, some of which are useful for terpenoid synthesis.

The reactions of conjugated dienes with ketones were carried out at 70 °C for 10 h in the presence of a nickel catalyst (5 mol % of dienes) either prepared *in situ* by reducing an equimolar mixture of acetylacetonatonickel(II) and a ligand with triethyl aluminum or treating bis(cyclooctadienyl)nickel(0) with an equimolar amount of the ligand. The products were identified by means of VPC and IR, UV, mass and NMR spectroscopy. The physical properties of **1a**—**e** and **2** are summarized in Table 1. The reaction of 1,3-butadiene

TABLE 1. SPECTRAL DATA OF THE PRODUCTS

Product	NMR[a] (δ)	IR[b] (cm^{-1})	UV[c] (nm)	Bp (°C/Torr)
1a	1.18 (6H, s), 2.15 (2H, d, J=7.0 Hz), 2.82 (2H, t, J=8.0 Hz), 3.12 (1H, s), 4.90—5.32 (3H, ABX), 5.51 (2H, q, J=7.0 Hz), 5.63—7.01 (2H, m, J=16.0 Hz)	3365, 1800, 1640, 1598, 1150, 973, 952, 900	238 (ε 18000)	72/15
1b	1.17 (6H, d), 1.18 (3H, s), 2.15 (2H, d, J=7.0 Hz), 2.82 (2H, t, J=8.0 Hz), 3.05 (1H, s), 4.90—5.32 (3H, ABX), 5.51 (2H, q, J=7.0 Hz), 5.63—7.01 (2H, m, J=16.0 Hz)	3365, 1800, 1640, 1598, 1150, 995, 973, 952, 900	231 (ε 21000)	85/3
1c	1.18 (3H, s), 2.15 (2H, d, J=7.0 Hz), 2.82 (2H, t, J=8.0 Hz), 3.45 (1H, s), 4.90—5.32 (3H, ABX), 5.51 (2H, q, J=7.0 Hz), 5.63—7.01 (2H, m, J=16.0 Hz), 7.20 (5H, s)	3365, 1800, 1640, 1598, 1150, 995, 973, 952, 900, 785	225 (ε 24000)	112/2
1d	1.19 (6H, s), 1.62 (3H, s), 1.83 (3H, s), 2.19 (2H, d, J=8.0 Hz), 2.87 (2H, d, J=7.0 Hz), 3.04 (1H, s), 4.83 (2H, s), 5.28 (1H, t), 5.53 (1H, dt, J=16.0 Hz), 6.10 (1H, d)	3490, 3081, 1780, 1601, 1145, 970, 890, 835	239 (ε 25000)	92/3
1e	1.18 (6H, s), 1.73 (3H, s), 1.80 (3H, s), 2.16 (2H, s), 2.82 (2H, t, J=7.0 Hz), 2.94 (1H, s), 4.82 (2H, s), 5.15 (1H, t, J=7.0 Hz), 5.52 (1H, dt, J=16.0 Hz), 6.10 (1H, d)	3495, 3080, 1772, 1601, 1141, 963, 886, 842	239 (ε 24900)	92/3
2	1.18 (6H, s), 2.15 (2H, d, J=2.0 Hz), 2.80—2.91 (6H, m), 3.10 (1H, s), 4.90—5.32 (3H, ABX), 5.51 (2H, q, J=7.0 Hz), 5.60—7.01 (4H, m, J=16.0 Hz)	3365, 1800, 1640, 1598, 1150, 973, 952, 900	229 (ε 85200)	103/3

a) 60 MHz, in CCl_4, s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet. b) Neat. c) Measured in ethanol.



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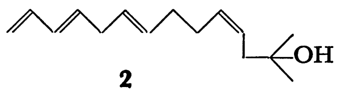
a: $R_1=R_2=R_3=H$, $R_4=R_5=Me$
b: $R_1=R_2=R_3=H$, $R_4=Me$, $R_5=i\text{-}C_3H_7$
c: $R_1=R_2=R_3=H$, $R_4=Me$, $R_5=C_6H_5$
d: $R_1=R_2=R_4=R_5=Me$, $R_3=H$
e: $R_1=R_3=R_4=R_5=Me$, $R_2=H$



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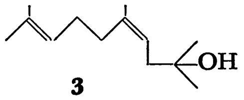

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with acetone was effected with Ni–P (O-*o*-Me-C_6H_4)$_3$ to give a mixture of **1a** and **2** in 62 and 16% yields, respectively (based on reacted 1,3-butadiene). Similar results were obtained using other ligands, such as PPh_3 or $P(OPh)_3$. However, catalyst activity was rather low (65% conversion for PPh_3 and 70% for $P(OPh)_3$) as compared to that of P(O-*o*-Me–C_6H_4)$_3$ (81%). A small amount of 1,3-butadiene dimers and higher products[4] were also formed. The *cis*-geometry of the C4—5 and *trans* geometry of the C7—8 double bonds in **1a** can be deduced from the olefin proton coupling constants, 7, and 16 Hz, respectively. The structure of **2** was deduced from the hydrogenated product; an alkanol obtained was identical with the authentic 2-methyl-2-tetradecanol in their physical and spectral properties. The NMR spectroscopy of **2** showed the presence of two *trans*-double bonds at C8 and C11 (5.60—7.01, 4H, m, $J=16.0$ Hz) and a *cis*-double bond at C4 (5.51, 2H, m, $J=7.0$ Hz). The regioselective linear linkage of three 1,3-butadiene molecules in **2** is noteworthy in view of the unavoidable formation of branched isomers in the catalytic linear oligomerization of the diene. Similarly the reactions of methyl isopropyl ketone and acetophenone with 1,3-butadiene gave **1b** and **1c** in 55 and 52% yields, respectively. Bulkier ketones such as diisopropyl ketone gave no alcohol. No alcohol formation was observed with propionaldehyde. Typical results are given in Table 2.

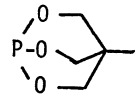
The rate of reaction of isoprene with acetone was small as compared to that of the reaction of 1,3-butadiene.

TABLE 2. REACTIONS[a] OF 1,3-BUTADIENE WITH CARBONYL COMPOUNDS

No.	Carbonyl compound[b]	Conversion (%)	Dimers (%)	Alcohols (%)[c]	Higher products (%)
1.	Me_2CO	81	15	**1a**(62) **2** (16)	7
2.	$i\text{-}C_3H_7COMe$	55	21	**1b**(55)	24[d]
3.	$MeCOC_6H_5$	61	23	**1c**(52)	25[d]
4.	$(i\text{-}C_3H_7)_2CO$	12	91	—	9
5.	CH_3CH_2CHO	7	100	—	

a) Conditions: 5 mol% of $Ni(acac)_2$, P(O-*o*-Me–C_6H_4)$_3$ and $AlEt_3$ (1: 1: 5) based on 1,3-butadiene at 70 °C for 10 h. b) The ratio of 1,3-butadiene to carbonyl compounds was 4: 1. c) Based on reacted 1,3-butadiene. d) Alcohols were detected by IR and TLC.

TABLE 3. REACTIONS OF ISOPRENE WITH ACETONE[a]

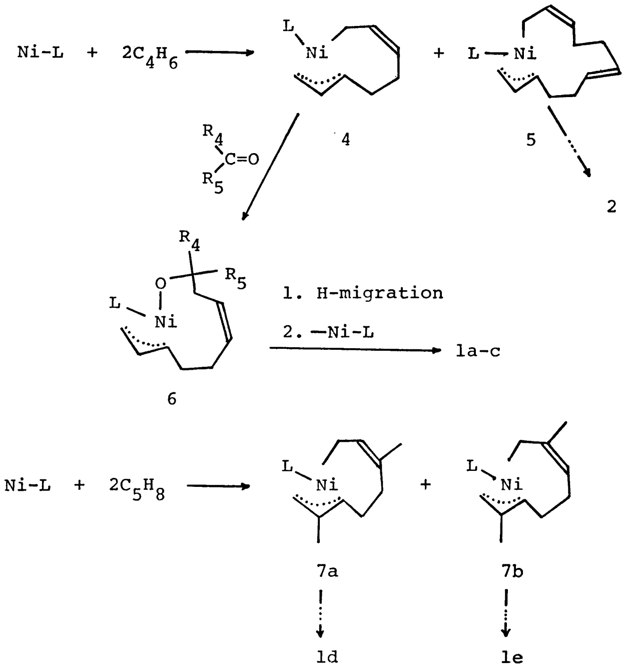
No.	Ligand	Conversion (%)	Dimers (%)	Alcohols (**1d**+**1e**) (%)[b]	Higher products (%)	Ratio[c] **1d**/**1e**
1.	P(O-*o*-MeC_6H_4)$_3$	62	12	72	16	15/85
2.	$P(O\text{–}C_6H_5)_3$	57	20	61	19	21/79
3.		47	10	52	38	55/45
4.	$P(C_6H_5)_3$	35	37	48	15	75/25
5.	$PPh(NEt_2)_2$	35	31	45	24	59/41
6.	P(*n*-C_4H_9)$_3$	22	70	0	30	

a) Reaction conditions: $Ni(COD)_2$/ligand/isoprene/acetone 1/1/200/70 at 70 °C for 10 h. b) Based on reacted isoprene. c) Calculated by VPC.

The reaction with isoprene gave two isomeric alcohols **1d** and **1e**, together with a relatively large amount of the dimers. The structure of **1d** is related to that of terpenoids. (*Z*)-2,5,9-Trimethyl-4,8-decadien-2-ol (**3**), for example, can be readily derived from partial hydrogenation of **1d**.

The nature of the ligand affects the activity and regioselectivity. As shown in Table 3, electron-donating trialkylphosphines, like P(*n*-C_4H_9)$_3$, completely suppress the reaction, while electron-accepting phosphites facilitate the reaction. The bulkier the phosphite ligand, the higher the selectivity for **1e**.

The requirement of a phosphite ligand suggests the importance of the low valence state of nickel in the catalysis. This is in contrast to the linear trimerization of isoprene[5] where a Ni(II) species, formation of which is assisted by coordination of an electron-donating ligand, plays an important role. One conspicuous feature of the products is the *cis*-configuration of the inner double bond nearest to the alcohol carbon. This leads to a reaction scheme involving a nucleophilic



attack of the carbanionic allyl end of the dimer or the trimer ligand on the carbonyl carbon in intermedates **4**, **7a**, or **7b** and **5**. The subsequent step will be the formation of **6**, where hydrogen migration from a methylene group, adjucent to the π-allyl group, to the carbonyl oxygen atom will take place to give the alcohols and to regenerate the catalyst. Baker *et al.*[6] observed a similar insertion of an aldehydic carbonyl group into a metal–allyl bond of dodecatrienyl nickel complex in the stoichiometric reaction. However, because of hydrolysis of the product they isolated alcohols of dodecatrienyl derivatives.

The stereoselective formation of the *cis*-double bond in the alkoxy ligand of **6** is accounted for by the preferential insertion of the carbonyl group into the σ-allylic end of **4**. The *anti*-configuration of the π-allylic part in **6** appears to be responsible for the *trans* configuration of the conjugated part of the products.

Although regioselective head to tail coupling of isoprene for the linear oligomerization has been achieved with suitable ligands such as trialkylarsines or aminophosphines,[5] no such regioselectivity was achieved in this reaction (run 5, Table 3).

Experimental

Reaction of 1,3-Butadiene with Carbonyl Compounds. Typical Procedure: To a mixture of Ni(acac)$_2$ (5.0 mmol) and P(O-*o*-Me-C$_6$H$_4$)$_3$ (5.0 mmol) in 65 ml (*ca.* 0.8 mol) of 1,3-butadiene was added a hexane solution of AlEt$_3$ (25 mmol) at −10 °C and subsequently 0.2 mol of a carbonyl compound. After being heated at 70 °C for 10 h, the catalyst was deactivated with a small portion of methanol and the whole reaction mixture was fractionally distilled. The dimer fraction (bp 50—65 °C/30 Torr) consists of 4-vinylcyclohexene, 1,5-cyclooctadiene and 1,3,6-octatriene (VPC, capillary column, PEG 2000, 45 m×0.2 mm). The main fraction consists of **1a**—**c** and **2**. The analytical samples were obtained by preparative VPC (PEG 4000 on Chromosorb W, 3 m×2 cm).

Hydrogenation of (4Z,8E,11E)-2-Methyl-4,8,11,13-tetradecatetraen-2-ol. Catalytic hydrogenation (Pd on charcoal, 10 kg/cm^2, 25 °C in AcOEt) of **2** gave 2-methyl-2-tetradecanol, *m/e* 228 (2%, M$^+$), 210 (98%, M$^+$−H$_2$O), which was identical with an authentic sample prepared by the reaction of *n*-C$_{12}$H$_{25}$-MgBr with Me$_2$CO in IR and VPC (capillary column, PEG 2000, 45 m×0.2 mm).

Reaction of Isoprene with Acetone. General Procedure: To a solution of bis(cyclooctadieneyl)nickel(0) (1 mmol) and ligand (1 mmol) in 20 ml (*ca.* 0.2 mol) of isoprene was added 4 ml (*ca.* 0.08 mol) of acetone at 0 °C. The mixture was stirred at 80 °C for 10 h. After deactivation of the catalyst with methanol, the reaction products were distilled to give isoprene dimers, a mixture of C$_{13}$ alcohols and the higher products.[4] Isoprene dimer fraction for every case consisted of dipentene, 1,5-dimethyl-5-vinyl-1-cyclohexene and 1,5- and 1,6-dimethyl-1,5-cyclooctadiene. Preparative VPC (PEG 4000 on 60—80 Chromosorb W, 3 m×2 cm) was used to separate the mixture of **1d** and **1e**.

(Z)-2,5,9-Trimethyl-4,8-decadien-2-ol (Dimethylnerylcarbinol) (3). Partial hydrogenation of 150 mg of **1d** was carried out (10 wt.% of PtO$_2$, 755 mmHg, 21 °C) to give **3** as an oil, bp 85 °C/5 Torr: IR (neat) cm^{-1}; 3490 and 1145 (alcohol), 842 (*cis*-C=CH–); *m/e* 196 (2%, M$^+$), 178 (95%, M$^+$−H$_2$O); NMR (CCl$_4$) δ, 1.18 (6H, s), 1.62—1.79 (6H, s), 2.19 (2H, d, J=7.0 Hz), 2.75—2.82 (4H, m), 3.45 (1H, s), 5.28 (1H, t, J=8.0 Hz) and 5.95—6.05 (1H, m). These data and the retention time of VPC (capillary column) were identical with those of the authentic sample prepared by treating (*Z*)-4,8-dimethyl-3,7-nonadienoic acid with an excess of MeMgI.

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4) Full analysis of the higher products has not been carried out. However, alcohols and no hydrocarbon were detected by TLC and IR spectroscopy.

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