# Regiospecific Functionalization of Dimetalated Isopropenylacetylene, a Synthetic Equivalent of the Isoprene "Anion". An Efficient Synthesis of the Bark Beetle Pheromones (±)-Ipsenol and (±)-Ipsdienol

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Regiospecific (mono)functionalization of dilithiated isopropenylacetylene LiC≡CC(=$CH_2$)$CH_2$Li with a large number of electrophilic reagents ("$E^{+}$") gave the compounds HC≡CC(=$CH_2$)$CH_2$E in high yields. Coupling with $(CH_3)_2CHCH_2CH$=O and $(CH_3)_2C$=CHCH=O, followed by partial reduction of the triple bond with activated zinc powder, gave the bark beetle pheromones ipsenol and ipsdienol, respectively, in >55% overall yields.

## Introduction

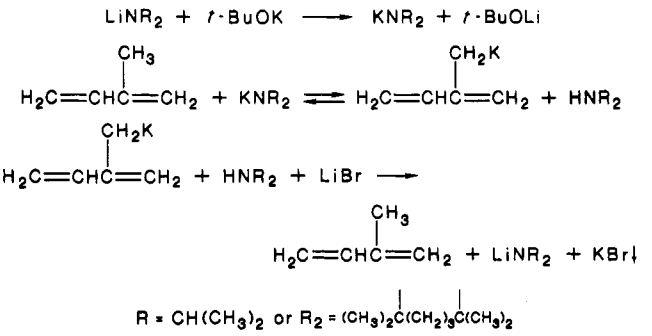
Recently[1] we reported the first successful metalation of isoprene with a 1:1 molar mixture of lithium diisopropylamide (LDA) or lithium tetramethylpiperidine (LTMP) and potassium *tert*-butoxide (*t*-BuOK) in tetrahydrofuran (THF) and hexane. Subsequent addition of alkyl halides or oxirane to the solution of the presumed potassio derivative of isoprene gave the expected products in moderate to good yields, but in the cases of (enolizable) aldehydes or ketones and dialkyl disulfides the results were poor. If, prior to adding these reagents, an equivalent amount of lithium bromide was introduced, no trace of coupling product could be isolated, not even in the reaction with alkyl halides or oxirane. The observed phenomena (see Scheme I) were explained by assuming a deprotonation equilibrium, which is far on the left side if the counterion of the metalating agent is lithium. Attempts at direct *lithiation* of isoprene with LDA or LTMP were also unsuccessful.

Some years ago[2] we reported the dimetalation of 2-methylbutenyne (isopropenylacetylene) with the Lochmann–Schlosser reagent[3,4] BuLi–*t*-BuOK in a THF/hexane mixture and subsequent transformation of the presumed dipotassio derivative into the dilithio compound LiC≡CC(=$CH_2$)$CH_2$Li by exchange with anhydrous lithium bromide. Addition of powdered selenium or tellurium resulted in regiospecific "insertion" of these elements into the $CH_2$–Li bond with formation of LiC≡CC(=$CH_2$)$CH_2$XLi (X = Se or Te). Addition of a proton donor (*t*-BuOH) and a strongly polar cosolvent (HMPT or DMSO) afforded five-membered selenium and tellurium ring compounds.[2]

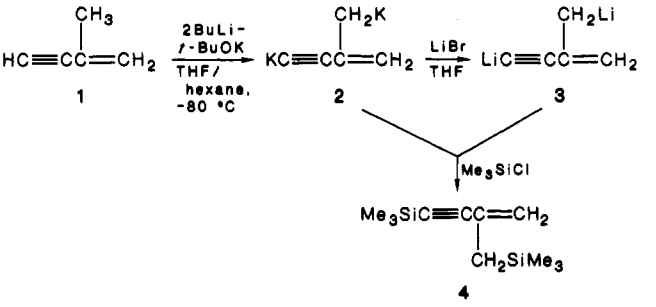
The observed regiospecificity in the reactions with these elements led us to investigate the reaction of dimetalated isopropenylacetylene with other "electrophiles". In the meantime we found that a number of conjugated enynes and diynes could be partially reduced to conjugated dienes and enynes, respectively.[5]

The present paper deals with regiospecific monofunctionalizations of dilithiated isopropenylacetylene and their combination with the reduction method in an efficient synthesis of the bark beetle pheromones ipsenol and ipsdienol.

**Scheme I**




**Scheme II**




## Results and Discussion

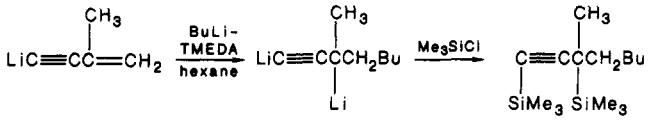
**a. Conditions for the Dimetalation of Isopropenylacetylene.** Following the procedure for the dimetalation,[2] isopropenylacetylene was added at ~−80 °C to a solution of 2 mol equiv of a 1:1 molar mixture of BuLi and *t*-BuOK (Lochmann–Schlosser reagent[3,4]) in THF and hexane. Addition of an excess of trimethylchlorosilane to the yellow suspension afforded the expected disilyl derivative $Me_3SiC$≡CC(=$CH_2$)$CH_2SiMe_3$ (**4**) in greater than 90% yield. The almost pure *crude* product contained only 1% of the monosilyl compound $Me_3SiC$≡CC(=$CH_2$)$CH_3$, which means a degree of dimetalation of 99%! A similar result was obtained when prior to the silylation a solution of 2 equiv of anhydrous lithium bromide in THF was introduced. (See Scheme II.)

Although there is no direct proof, we presume on the basis of experiments of Schlosser et al.[6] and Schleyer et al.[7] that initially dipotassium derivative **2** is formed. The unique properties of the superbasic reagent as a depro-

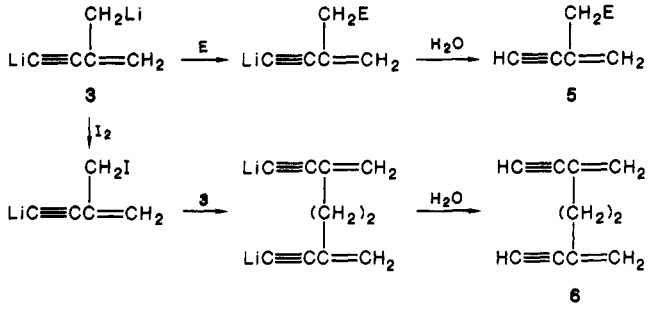
(1) Klusener, P. A. A.; Hommes, H. H.; Verkruijsse, H. D.; Brandsma, L. *J. Chem. Soc., Chem. Commun.* **1985**, 1677.
(2) Kulik, W.; Verkruijsse, H. D.; de Jong, R. L. P.; Hommes, H. H.; Brandsma, L. *Tetrahedron Lett.* **1983**, 2203.
(3) Lochmann, L.; Pospíšil, J.; Lím, D. *Tetrahedron Lett.* **1966**, 257.
(4) Schlosser, M. *J. Organomet. Chem.* **1967**, *8*, 9.
(5) Aerssens, M. H. P. J.; Brandsma, L. *J. Chem. Soc., Chem. Commun.* **1984**, 735.
(6) Schlosser, M.; Hartmann, J. *Angew. Chem.* **1973**, *85*, 544; *Angew. Chem., Int. Ed. Engl.* **1973**, 439.
(7) Pi, R.; Bauer, W.; Brix, B.; Schade, C.; Schleyer, P. v. R. *J. Organomet. Chem.* **1986**, *306*, C1.

0022-3263/87/1952-5261$01.50/0 

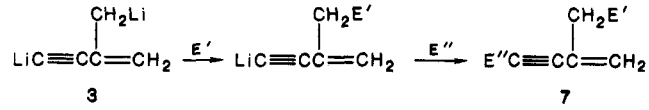
**Scheme III**



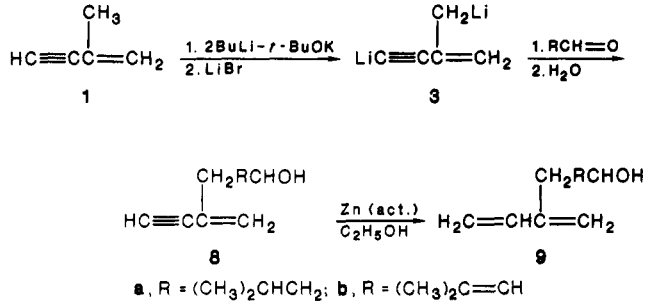
**Scheme IV**



**Scheme V**



**Scheme VI**



tonating base were confirmed by investigatng other conditions for the dimetalation.

Interaction at ~−20 °C during 2 h between 1 and 2 equiv of BuLi, followed by addition of diphenyl disulfide, gave $PhSC{\equiv}CC(=CH_2)CH_3$ in ~60% yield along with BuSPh, indicating that only metalation of the triple bond had occurred. When 1 was reacted at temperatures between −20 and −60 °C with 2 mol equiv of BuLi-*N,N,N′,N′*-tetramethylethylenediamine (TMEDA) in hexane, subsequent quenching with $Me_3SiCl$ (after addition of THF) afforded a mixture of $Me_3SiC{\equiv}CC(=CH_2)CH_3$ (~30% yield) and $Me_3SiC{\equiv}CC(CH_3)(SiMe_3)CH_2Bu$ (~30% yield). A considerable amount of viscous residue remained after the distillation. Thus, in the presence of TMEDA, the second equivalent of BuLi does not deprotonate the methyl group in $LiC{\equiv}CC(=CH_2)CH_3$, but rather adds across the double bond (see Scheme III).

**b. Regiospecific Reaction of Dilithiated Isopropenylacetylene with Electrophilic Reagents.** In preliminary experiments, we reacted the dipotassium compound **2** with a number of electrophiles, including alkyl halides, dialkyl disulfides (RSSR), and carbonyl compounds. Although with 1 equiv of these reagents specific reaction at the $CH_2$ center was observed, yields of the desired products were moderate to low. These unsatisfactory results were ascribed to elimination of hydrogen halides (from alkyl halides), metalation of the initial thioalkylated product to $KC{\equiv}CC(=CH_2)CHKSR$ and subsequent introduction of a second RS group, formation of enolates of the carbonyl compounds, and a second functionalization at the C≡C center. As such undesired processes are generally less serious with lithium compounds, our functionalization reactions were carried out with **3**. As shown in Table I, yields of the derivatives were satisfactory, while the regiospecificity with respect to the $CH_2$ center was perfect, even in the case of the highly reactive aldehydes, ketones, and $CO_2$ (see Scheme IV). Formation of small amounts of difunctionalized compounds occurred in these cases. Since no traces of products monofunctionalized at the C≡C center could be detected, we assume that these minor products are formed by further functionalization of the initial $LiC{\equiv}CC(=CH_2)CH_2E$.

Reaction of **3** with iodine afforded the unstable "dimer" **6**, probably as a result of iodination at the $CH_2$ center and a very fast subsequent coupling of the iodo compound with **3** (Scheme IV).

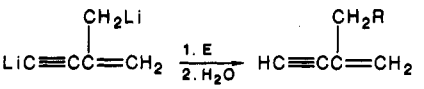
The ideal regiospecificity observed in the monofunctionalization of **3** may be largely due to the enormous difference in the basicity and nucleophilicity of the two reactive centers in **3**. As a model system for the regiospecific functionalization reaction of **3** competition experiments—in which a (soluble) lithium alkynylide $RC{\equiv}CLi$ and isobutenyllithium $H_2C{=}C(CH_3)CH_2Li$ (prepared as described previously[8]) were allowed to compete for a number of electrophiles under the same conditions as in our functionalization experiments—were carried out (though clearly the situation in dimetalated **3** may be more complicated). All electrophiles showed a strong preference for isobutenyllithium. Indeed, acetylides are much less strong nucleophiles than isobutenyllithium.

The regiospecificity in the monofunctionalizations of **3** should allow successful introduction of two different groups E′ and E″ at the $CH_2$ and C≡C centers as shown in Scheme V. As may be expected from the results of Table I, successive functionalizations at the $CH_2$ and C≡C centers can be realized with a variety of combinations of E′ and E″. We carried out two successive functionalizations with pairs of different electrophiles, viz., with bromobutane and acetone and with methyl iodide and cyclohexanone, respectively. In both cases high yields of pure products **7** were obtained.

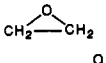
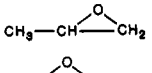
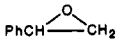
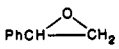
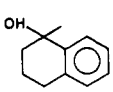
**c. Synthesis of the Bark Beetle Pheromones Ipsenol and Ipsdienol.** Ipsenol (**9a**) and ipsdienol (**9b**) are aggregation pheromones of the bark beetle.[10-15] A number of syntheses have been reported,[16-37] the most recent one

(8) Brandsma, L.; Verkruijsse, H. D. *Preparative Polar Organometallic Chemistry*; Springer-Verlag: Heidelberg, 1986; Vol. 1.
(9) Heus-Kloos, Y. A.; de Jong, R. L. P.; Verkruijsse, H. D.; Brandsma, L.; Julia, S. *Synthesis* **1985**, 958.
(10) Silverstein, R. M.; Rodin, J. O.; Wood, L. E.; Browne, D. L. *Tetrahedron* **1966**, *22*, 1929.
(11) Silverstein, R. M.; Rodin, J. O.; Wood, D. L. *Science (Washington, D.C.)* **1966**, *154*, 509.
(12) Silverstein, R. M.; Rodin, J. O.; Wood, D. L. *J. Econ. Entomol.* **1967**, *60*, 944.
(13) Silverstein, R. M. *J. Chem. Educ.* **1968**, *45*, 794.
(14) Young, J. C.; Silverstein, R. M.; Birch, M. C. *J. Insect. Physiol.* **1973**, *19*, 2273.
(15) Vité, J. P.; Francke, W. *Naturwissenschaften* **1976**, *63*, 550.
(16) Reece, C. A.; Rodin, J. O.; Brownlee, R. G.; Duncan, W. G.; Silverstein, R. M. *Tetrahedron* **1968**, *24*, 4249.
(17) Vig, O. P.; Anand, R.; Kad, G. L.; Seghal, J. M. *J. Indian Chem. Soc.* **1970**, *47*, 999.
(18) Katzenellenbogen, J. A.; Lenox, R. S. *J. Org. Chem.* **1973**, *38*, 326.
(19) Riley, R. G.; Silverstein, R. M.; Katzenellenbogen, J. A.; Lenox, R. S. *J. Org. Chem.* **1974**, *39*, 1957.
(20) Mori, K. *Agric. Biol. Chem.* **1974**, *38*, 2045.
(21) Mori, K. *Tetrahedron Lett.* **1975**, 2187.
(22) Mori, K. *Tetrahedron Lett.* **1976**, 1609.
(23) Mori, K. *Tetrahedron* **1976**, *32*, 1101.
(24) Kondo, K.; Dobashi, S.; Matsumoto, M. *Chem. Lett.* **1976**, 1077.
(25) Karlsen, S.; Frøyen, P.; Skattebøl, L. *Acta Chem. Scand. Ser. B* **1976**, *B30*, 664.
(26) Haslouin, J.; Rouessac, F. *Bull. Soc. Chim. Fr.* **1977**, 1242.

**Table I. Experimental Data**




3 5

| run no. | electrophile E | product 5, R | yield,[a] % | bp, °C/mmHg | $n^{20}_D$ | reactn time, min/temp, °C |
|---|---|---|---|---|---|---|
| 1 | $CH_3(CH_2)_4Br$ | $CH_3(CH_2)_4$ | 79 | 52/10 | 1.4423 | 20/−70 → −10 |
| 2 | $CH_3(CH_2)_5Br$ | $CH_3(CH_2)_5$ | 83 | 62/10 | 1.4455 | 20/−70 → −10 |
| 3 |  |  | 70 | 70/10 | 1.4778 | 20/−70 → −15 |
| 4 | $CH_3(CH_2)_3OCH_2Cl$ | $CH_3(CH_2)_3OCH_2$ | 80 | 72/10 | 1.4463 | 20/−80 → −40 |
| 5 | $(CH_3)_2CHCH_2(CH_3O)CHCl$ | $(CH_3)_2CHCH_2(CH_3O)CH$ | 64 | 78/10 | 1.4493 | 40/−60 → −20 |
| 6 |  | $HOCH_2CH_2$[d] | 92 | 71/10 | 1.4748 | 30/−50 → −10 |
| 7 |  | $HOCH(CH_3)CH_2$ | 90 | 45/0.1 | 1.4707 | 50/−50 → +20 |
| 8a |  | 67% $HOCH(Ph)CH_2$ | 85 | 105/0.05 | 1.5453 | 30/−50 → +10 |
| 8b |  | 33% $HOCH_2(Ph)CH$ | | | | |
| 9 | $CH_3CH_2CH=O$ | $CH_3CH_2(HO)CH$ | 51 | 65/10 | 1.4665 | 5/−90 → −60[c] |
| 10 | $(CH_3)_2CHCH_2CH=O$[b] | $(CH_3)_2CHCH_2(HO)CH$ | 63 | 47/0.1 | 1.4627 | 20/−70 → −40 |
| 11 | $(CH_3)_2C=CH-CH=O$[b] | $(CH_3)_2C=CH(HO)CH$ | 76 | 57/0.1 | 1.4906 | 10/−70 → −50 |
| 12 | $PhCH=O$ | $Ph(HO)CH$ | 60 | 85/0.01 | 1.5504 | 15/−70 → −50 |
| 13 | $(CH_3)_2C=O$[b] | $(CH_3)_2(HO)C$ | 69 | 58/10 | 1.4647 | 5/−80 → −70 |
| 14 | $CH_3CH_2(CH_3)C=O$[b] | $CH_3CH_2(CH_3)(HO)C$ | 65 | 70/10 | 1.4704 | 5/−100 → −80[c] |
| 15 | $(CH_3)_3C(CH_3)C=O$ | $(CH_3)_3C(CH_3)(HO)C$ | 83 | 78/10 | 1.4710 | 5/−70 → −50[c] |
| 16 |  |  | 61 | 55/0.1 | 1.5004 | 5/−80 → −60[c] |
| 17 |  |  | 55 | 135/0.1 | 1.5683 | 30/−90 → −60 |
| 18 | $O=C=O$[e] | HOOC | 39 | 61/0.01 | 1.4759 | 25/−90 → −80[c] |
| 19 | $(CH_3)_2N(CH_3)C=O$[f] | $CH_3(O=)C$ | 60 | 71/10 | 1.4697 | 30/−90 → 0 |
| 20 | $CH_3SSCH_3$ | $CH_3S$ | 71 | 45/10 | 1.5104 | 15/−60 → −30 |
| 21 | $CH_3SC\equiv N$ | $CH_3S$ | 54 | 45/10 | 1.5104 | 15/−80 → −70 |
| 22 | $CH_3(CH_2)_2SC\equiv N$ | $CH_3(CH_2)_2S$ | 42 | 72/10 | 1.4962 | 20/−70 → −50 |
| 23 | $I_2$ | $HC\equiv CC(=CH_2)CH_2$[d] | 85 | 35/0.5[g] | 1.4781 | 20/−80 → −60 |

[a] Yields after distillation. With carbonyl compounds the difunctionalized products $RC\equiv CC(=CH_2)CH_2R$ were also formed and obtained as high-boiling fractions in up to 10% yield. [b] 0.9 mol equiv of the required amount of electrophile E was used. [c] Cooling with liquid nitrogen was necessary during the addition of the electrophile E. [d] These compounds polymerized during storage at room temperature in daylight after a few months. [e] A weighed amount of solid $CO_2$ was dissolved in THF. [f] After functionalization, the reaction mixture was poured into an acid/water mixture. [g] This product has a very low thermostability!

by Margot and Schlosser.[37] Both pheromones can be synthesized in sizable quantities starting from isopropenylacetylene (see Scheme VI).

The precursors for the pheromones **8a** and **8b** were prepared as indicated previously in section b in 63 and 76% yields, respectively. Treating **8a** and **8b** with powdered zinc (successively activated by treatment with 1,2-dibromoethane and lithium bromocuprate $LiCuBr_2$ in ethanol/THF[5]) under reflux afforded the desired pheromones **9a** and **9b** (±-pairs) in excellent yields.

## Experimental Section

**a. General Procedures.** $^1H$ NMR spectra were recorded on a Varian EM 390 spectrometer of 30% solutions in $CCl_4$ with tetramethylsilane as internal standard and $^{13}C$ NMR spectra on a Varian CFT 20 or on a Bruker WP 200 apparatus of 30% solutions in deuteriochloroform. Mass spectroscopy was performed on a Kratos MS 80 GC–MS combination apparatus.

THF was distilled from lithium aluminum hydride and stored on sodium–lead alloy under nitrogen. Commercial anhydrous lithium bromide was freed from traces of water by heating (in ~100-g portions) in a 1-L round-bottomed flask for 1 h at 150 °C in a vacuum of <1 mmHg.

Potassium *tert*-butoxide and butyllithium (1.5 M hexane solution) are commercially available and were used as such.

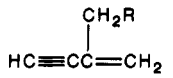
Isopropenylacetylene was prepared on 4.5 M scale as described by Brandsma[38] and stored at −30 °C on molecular sieves (4 Å).

All reactions were carried out in an atmosphere of nitrogen.

**b. Dimetalations of Isopropenylacetylene and Subsequent Functionalizations.** In a 500-mL round-bottomed three-necked flask, equipped with a gas inlet, a dropping funnel, a mechanical stirrer, and a thermometer–gas outlet combination, was placed a mixture of 0.100 mol of freshly distilled isopropenylacetylene[38] and 60 mL of THF. Solutions of 0.220 mol of BuLi in 150 mL

(27) Bertrand, M.; Viala, J. *Tetrahedron Lett.* **1978**, 2575.
(28) Hosomi, A.; Saito, M.; Sakurai, H. *Tetrahedron Lett.* **1979**, 429.
(29) Cheskis, B. A.; Lebedeva, K. V.; Koroleva, T. I.; Kondrat'ev, Yu. A. *Khemoretseptsiya Nasekomykh* **1979**, *n4*, 129; *Chem. Abstr.* **1980**, *93*, 113871y.
(30) Wilson, S. R.; Phillips, L. R. *Tetrahedron Lett.* **1975**, 3047.
(31) Brand, J. M.; Young, J. C.; Silverstein, R. M. *Prog. Chem. Org. Nat. Prod.* **1979**, *37*, 1–190: ipsenol, pp 41–44; ipsdienol, pp 45–50.
(32) Wilson, S. R.; Phillips, L. R.; Natalie, K. J. *J. Am. Chem. Soc.* **1979**, *101*, 3340.
(33) Cazes, B.; Guittet, E.; Julia, S.; Ruel, O. *J. Organomet. Chem.* **1979**, *177*, 67.
(34) Snider, B. B.; Rodini, D. J. *Tetrahedron Lett.* **1980**, *21*, 1815.
(35) Clinet, J. C.; Linstrumelle, G. *Nouv. J. Chim.* **1977**, *1*, 373.
(36) Clinet, J. C. Dissertation, Université P. et M. Curie, Paris, 1980; pp 59, 93, 96.
(37) Margot, C.; Schlosser, M. *Tetrahedron Lett.* **1985**, *26*, 1035.
(38) Brandsma, L. *Preparative Acetylenic Chemistry*; Elsevier: Amsterdam, 1971; p 136. Revised edition, Elsevier: Amsterdam, in press.
(39) Gilman, H.; Gaj, B. J. *J. Org. Chem.* **1957**, *22*, 1165.

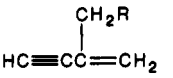
**Table II. $^1$H NMR Data of 5[a]**



| run no. | HC≡C | H$_2$C=C | —CH$_2$— | R (H) |
|---|---|---|---|---|
| 1 | 2.74 | 5.22, 5.34 | 2.13 (t) | 1.2–1.6 (4 CH$_2$), 0.88 (t, CH$_3$) |
| 2 | 2.71 | 5.21, 5.34 | 2.10 (t) | 1.2–1.6 (5 CH$_2$), 0.87 (t, CH$_3$) |
| 3 | 2.68 | 5.08, 5.25 | 1.95 (d) | 0.8–2.0 (11 H, ) |
| 4 | 2.78 | 5.35, 5.40 | 2.35 (t) | 3.50 (t, C*H*$_2$OBu), 3.35 (t, OC*H*$_2$Pr), 1.1–1.7 (2 CH$_2$), 0.90 (t, CH$_3$) |
| 5 | 2.80 | 5.30, 5.40 | 2.23 (m) | 3.35 (m, CHO), 3.28 (s, OCH$_3$), 1.22 (m, CH$_2$), 1.65 (m, CH), 0.89 (d, 2 CH$_3$) |
| 6 | 2.84 | 5.30, 5.38 | 2.21 (t) | 1.75 (m, CH$_2$), 3.56 (t, CH$_2$O), 3.85 (s, OH) |
| 7 | 2.85 | 5.30, 5.35 | 2.22 (t) | 1.65 (m, CH$_2$), 3.76 (m, CH), 1.17 (d, CH$_3$), 3.48 (s, OH) |
| 8a | 2.75 | 5.22, 5.34 | 2.10 (t) | 1.80 (m, CH$_2$), 4.48 (t, CH), 7.2 (Ph), 3.30 (s, OH) |
| 8b | 2.75 | 5.08, 5.28 | 2.15 (d) | 3.00 (tt, CH), 3.55 (d, CH$_2$), 7.2 (Ph), 3.30 (s, OH) |
| 9 | 2.86 | 5.33, 5.46 | 2.22 (d) | 3.72 (m, CH), 1.43 (m, CH$_2$), 0.95 (t, CH$_3$), 2.65 (s, OH) |
| 10 | 2.90 | 5.37, 5.48 | 2.22 (d) | 3.87 (m, C*H*OH), 1.28 (m, CH$_2$), 1.80 (m, CH), 0.95 (d, 2 CH$_3$), 2.71 (s, OH) |
| 11 | 2.84 | 5.33, 5.43 | 2.37, 2.15 (dd) | 4.54 (dt, C*H*OH), 5.13 (dqq, CH=C), 1.68 (d, CH$_3$), 1.70 (d, CH$_3$), 2.63 (s, OH) |
| 12 | 2.81 | 5.18, 5.37 | 2.39 (d) | 4.81 (t, CH), 7.2 (Ph), 2.72 (s, OH) |
| 13 | 2.90 | 5.31, 5.52 | 2.28 (s) | 1.20 (s, CH$_3$), 2.43 (s, OH) |
| 14 | 2.91 | 5.34, 5.52 | 2.27 (s) | 1.12 (s, C*H*$_3$COH), 1.43 (m, CH$_2$), 0.88 (t, CH$_3$), 2.90 (s, OH) |
| 15 | 2.91 | 5.33, 5.57 | 2.21, 2.46 (d) | 1.12 (s, CH$_3$), 0.93 (s, 3 CH$_3$), 1.85 (s, OH) |
| 16 | 2.90 | 5.48, 5.30 | 2.26 (s) | 2.30 (s, OH), 1.4–1.6 (10 H,  ) |
| 17 | 2.84 | 5.31, 5.52 | 2.57 (s) | 2.71 (m, C*H*$_2$Ph), 1.7–2.2 (7, C*H*$_2$C*H*$_2$), 7.46 (m, *o*-*Ph*COH), 6.9–7.1 (3H, Ph), 2.38 (s, OH) |
| 18 | 2.87 | 5.48, 5.60 | 3.19 (s) | 11.87 (COOH) |
| 19 | 2.92 | 5.36, 5.54 | 3.12 (s) | 2.15 (s, CH$_3$) |
| 20 | 2.85 | 5.41, 5.49 | 3.14 (s) | 1.98 (s, CH$_3$) |
| 22 | 2.82 | 5.30 | 3.07 (s) | 2.40 (m, SCH$_2$), 1.55 (m, CH$_2$), 0.95 (t, CH$_3$) |
| 23 | 2.78 | 5.30, 5.40 | 2.36 (s) | |

[a] δ values downfield of SiMe$_4$, added as an internal standard.

**Table III. $^{13}$C NMR Data of 5[a]**

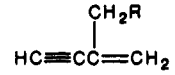


| run no. | HC≡C | HC≡*C* | *C*=CH$_2$ | C=*C*H$_2$ | —CH$_2$— | R (C) |
|---|---|---|---|---|---|---|
| 1 | 76.54 | 84.04 | 131.06 | 122.13 | 36.97 | 27.88 (=CCH$_2$*C*H$_2$), 28.57 (CH$_2$), 31.65 (*C*H$_2$CH$_2$CH$_3$), 22.59 (*C*H$_2$CH$_3$), 13.94 (CH$_3$) |
| 2 | 76.54 | 84.07 | 130.98 | 122.19 | 36.89 | 27.85 (=CCH$_2$*C*H$_2$), 28.78 and 28.99 (*C*H$_2$H$_2$), 31.72 (*C*H$_2$CH$_2$CH$_3$), 22.54 (*C*H$_2$CH$_3$), 13.90 (CH$_3$) |
| 3 | 76.58 | 84.19 | 129.54 | 123.30 | 44.80 | 35.91 (CH), 32.82 (2 CHCH$_2$), 26.14 (2 CHCH$_2$CH$_2$), 26.48 (CHCH$_2$CH$_2$CH$_2$) |
| 4 | 76.82 | 83.21 | 127.30 | 123.58 | 36.88 | 68.20 (=CCH$_2$*C*H$_2$), 70.23 (OCH$_2$), 31.37 (OCH$_2$*C*H$_2$), 18.91 (*C*H$_2$CH$_3$), 13.39 (CH$_3$) |
| 5 | 77.05 | 83.77 | 127.69 | 124.61 | 43.12 | 77.42 (CHO), 56.58 (OCH$_3$), 41.70 (CH$_2$), 24.43 (CH), 23.06 and 22.12 (CH$_3$) |
| 6 | 76.95 | 83.41 | 129.71 | 122.31 | 32.69 | 30.19 (*C*H$_2$CH$_2$O), 60.70 (CH$_2$OH) |
| 7 | 76.89 | 83.63 | 130.03 | 122.39 | 32.84 | 36.1 (CH$_2$), 66.53 (CH), 22.95 (CH$_3$) |
| 8a | 77.14 | 83.52 | 129.66 | 122.64 | 32.68 | 36.63 (CH$_2$), 72.72 (CH), 144.11 (Ph, C$_1$), 125.53 (Ph, 2 C$_2$), 127.90 (Ph, 2 C$_3$), 126.92 (Ph, C$_4$) |
| 8b | 77.14 | 83.52 | 129.66 | 124.12 | 39.10 | 46.00 (CH), 65.58 (CH$_2$), 141.13 (Ph, C$_1$), 126.22 (Ph, 2 C$_2$), 127.90 (Ph, 2 C$_3$), 126.92 (Ph, C$_4$) |
| 9 | 77.33 | 83.52 | 127.31 | 124.89 | 44.25 | 70.58 (CH), 29.03 (CH$_2$), 9.45 (CH$_3$) |
| 10 | 77.46 | 83.52 | 127.28 | 124.81 | 45.38 | 67.18 (CHOH), 45.25 (CH$_2$), 24.12 (CH), 23.05 and 21.60 (CH$_3$) |
| 11 | 77.14 | 83.54 | 126.75 | 124.79 | 44.83 | 66.23 (CHOH), 126.81 (=CH), 134.39 (CH=*C*), 25.21 (*E*-CH$_3$), 17.78 (*Z*-CH$_3$) |
| 12 | 77.85 | 83.36 | 126.54 | 125.46 | 46.41 | 71.67 (CH), 143.25 (Ph, C$_1$), 125.58 (Ph, 2 C$_2$), 127.89 (Ph, 2 C$_3$), 127.05 (Ph, C$_4$) |
| 13 | 77.88 | 84.89 | 126.50 | 126.84 | 50.14 | 70.40 (COH), 28.86 (3 CH$_3$) |
| 14 | 77.69 | 84.77 | 126.23 | 126.73 | 47.76 | 72.23 (COH), 33.85 (CH$_2$), 25.59 (*C*H$_3$COH), 7.82 (CH$_3$) |
| 15 | 77.97 | 85.15 | 127.00 | 126.74 | 43.25 | 75.51 (COH), 37.44 (*C*Me$_3$), 24.88 (3 CH$_3$), 21.08 (CH$_3$) |
| 16 | 77.65 | 84.91 | 125.76 | 126.53 | 48.70 | 70.76 (COH), 36.77 (2 HOCCH$_2$), 21.64 (2 HOCCH$_2$CH$_2$), 25.26 (HOCCH$_2$CH$_2$*C*H$_2$) |
| 17[b] | 77.86 | 84.80 | 126.21 | 126.79 | 48.77 | 72.11 (COH), 35.23 (*C*H$_2$COH), 19.68 (CH$_2$CH$_2$CH$_2$), 29.30 (*C*H$_2$Ph), 136.03 + 127.43 + 128.41 + 125.82 + 141.54 (Ph) |
| 18[c] | 78.43 | 83.26 | 124.39 | 125.86 | 41.65 | 170.79 (COOH) |
| 19 | 77.86 | 82.51 | 123.21 | 126.10 | 50.55 | 203.80 (C=O), 28.41 (CH$_3$) |
| 20 | 77.18 | 82.55 | 126.46 | 123.81 | 39.44 | 14.30 (CH$_3$) |
| 22 | 77.18 | 82.55 | 127.13 | 123.40 | 40.58 | 32.80 (SCH$_2$), 22.02 (CH$_2$), 12.96 (CH$_3$) |
| 23 | 77.13 | 83.45 | 129.29 | 123.17 | 35.19 | |

[a] δ values downfield of SiMe$_4$ and CDCl$_3$ as solvent and internal standard. [b] δ values reported for the CH=CH$_2$ group and the phenyl group may be interchanged. [c] (CD$_3$)$_2$C=O was used as solvent and internal standard.

of hexane and 0.220 mol of *t*-BuOK in 60 mL of THF were successively added at −80 °C (occasional cooling in a bath with liquid nitrogen was necessary). A yellow precipitate was formed gradually. After an additional 30 min at −70 °C the temperature was allowed to rise to +5 °C (note 1), and after the mixture was stirred for 10 min at this temperature (note 2), a solution of 0.220 mol of anhydrous lithium bromide in 60 mL of THF was added at −20 °C. After the mixture was stirred for an additional 10 min,

**Table IV. Mass Spectral Data of 5**



| run no. | molecular ion M⁺, m/e | molecular ion % | base peak, m/e | five other high peaks, m/e (%) |
|---|---|---|---|---|
| 1 | 136 | 0.2 | 93 | 121 (24), 107 (35), 79 (59), 66 (70), 55 (16) |
| 2 | 150 | 0.1 | 93 | 135 (10), 121 (21), 107 (31), 79 (47), 66 (42) |
| 3 | 148 | 2.0 | 55 | 133 (73), 119 (45), 105 (69), 91 (50), 83 (78) |
| 4 | 152 | 0.02 | 57 | 151 (0.1), 137 (6), 109 (6), 80 (35), 77 (24) |
| 5[a] | | | | |
| 6 | 110 | 1.3 | 91 | 109 (9), 95 (24), 81 (23), 77 (26), 68 (45) |
| 7 | 124 | 1.5 | 79 | 109 (32), 91 (92), 65 (28), 58 (41), 43 (92) |
| 8a | 186 | 3.9 | 107 | 167 (6), 155 (10), 120 (18), 104 (60), 79 (82) |
| 8b | 186 | 2.3 | 155 | 167 (43), 121 (63), 103 (81), 91 (48), 77 (43) |
| 9 | 124 | 78 | 95 | 109 (48), 81 (21), 66 (59), 59 (46), 41 (31) |
| 10 | 152 | 8.2 | 69 | 137 (5), 109 (17), 95 (38), 87 (33), 85 (34) |
| 11 | 150 | 0.5 | 117 | 132 (45), 103 (26), 91 (64), 85 (20), 77 (18) |
| 12 | 172 | 4.9 | 107 | 153 (3), 128 (3), 115 (2), 179 (38), 77 (21) |
| 13 | 124 | 1.4 | 59 | 109 (10), 91 (4), 79 (3), 66 (10), 43 (51) |
| 14 | 138 | 2.4 | 73 | 123 (5), 105 (12), 91 (10), 55 (32), 43 (73) |
| 15 | 166 | 6.1 | 43 | 133 (6), 109 (67), 101 (55), 83 (25), 57 (21) |
| 16 | 164 | 82 | 121 | 149 (25), 135 (24), 107 (54), 99 (75), 81 (72) |
| 17 | 212 | 8.7 | 147 | 194 (10), 179 (9), 165 (10), 129 (32), 91 (36) |
| 18[a] | | | | |
| 19 | 108 | 26 | 43 | 93 (9), 65 (12), 50 (4), 39 (12) |
| 20 | 112 | 90 | 61 | 111 (37), 97 (77), 66 (40), 45 (21), 39 (26) |
| 22 | 140 | 100 | 140 | 125 (37), 111 (65), 97 (79), 89 (33), 74 (83) |
| 23 | 130 | 33 | 91 | 115 (10), 102 (2), 77 (3), 65 (14), 51 (5) |

[a] Decomposed in the GC column of the GC–MS apparatus.

derivatization reactions were carried out with an excess of trimethylchlorosilane (0.280 mol) or iodine (0.050 mol in 30 mL of THF) and with the reagents (0.100 or 0.090 mol) mentioned in Table I.

The workup was carried out by adding 70 mL of a saturated aqueous solution of ammonium chloride (after the reaction with dimethyl disulfide only water was used) at −40 °C. In the case of the carboxylation with $CO_2$ the reaction mixture was poured into a mixture of 60 g of concentrated hydrochloric acid (36%) and 200 mL of water. The products were extracted with diethyl ether and the organic solutions dried over $MgSO_4$. After concentration of these solutions under reduced pressure, the remaining liquids were distilled in vacuo. For additional experimental and spectral data see Tables I–IV.

Note 1: This warming up to +5 °C was necessary to eliminate the excess of butylpotassium—formed by the reaction of BuLi with *t*-BuOK[7]—with THF to give ethene and HC≡CHOK; compare ref 39.

Note 2: The efficiency of the dimetalation was demonstrated by adding trimethylchlorosilane (0.280 mol, excess) at −50 °C after the reaction with BuLi–*t*-BuOK and after the exchange reaction with lithium bromide. After the addition, the temperature was allowed to rise to +10 °C. Water (100 mL) was added, and after separation of the layers, extractions with diethyl ether were carried out. The organic solutions were dried over $MgSO_4$ and subsequently concentrated under reduced pressure. Distillation of the remaining liquid gave the disilylated enyne **4**: bp 76 °C (10 mmHg); $n^{20}_D$ 1.4572; ~90% yield.

**c. Successive Functionalizations of Dilithiated Isopropenylacetylene.** To 0.100 mol of a suspension of **3** in THF, prepared as described in section b, was added 0.100 mol of bromobutane or methyl iodide at −60 °C. Then, after the temperature was allowed to rise to −10 °C in ca. 10 min, 0.150 mol of acetone (p.a.) or cyclohexanone was added. After the reaction mixture was stirred for an additional 10 min at +30 °C, it was cooled to −20 °C. Workup as described previously in section b gave the following compounds.

$(CH_3)_2C(OH)C{\equiv}CC(=CH_2)(CH_2)_4CH_3$ (2-methyl-5-methylene-3-decyn-2-ol): 88% yield; bp 60 °C (0.10 mmHg); $n^{20}_D$ 1.4668; $^1$H NMR δ 0.84 ($CH_3CH_2$, t, $J$ = 6 Hz), 1.0–1.6 ($CH_2CH_2CH_2CH_3$, m), 1.47 ($(CH_3)_2COH$, s), 3.80 (OH, s), 5.0–5.1 ($CH_2$=C, m).

$(CH_2)_5C(OH)C{\equiv}CC(=CH_2)CH_2CH_3$: 76% yield; bp 62 °C (0.10 mmHg) $n^{20}_D$ 1.5028; $^1$H NMR δ 1.10 ($CH_3$, t, $J$ = 7 Hz), 1.2–1.8 ($(CH_2)_5$, m), 2.10 ($CH_2CH_3$, q, $J$ = 7 Hz), 3.30 (OH, s), 5.0–5.1 ($CH_2$=C, m).

**d. Reduction of 2-Methyl-6-methylene-7-octyn-4-ol (8a) with Activated Zinc; Preparation of Ipsenol (9a).** To a stirred suspension of 15 g of zinc powder (Merck, p.a.) in 20 mL of 100% ethanol was added 1 mL of 1,2-dibromoethane. The suspension was heated under reflux until the evolution of ethene stopped. Then another 1 mL of 1,2-dibromoethane was added through the reflux condenser, and refluxing was continued for an additional 5 min. The suspension was cooled to 45–50 °C, and a solution of 6.0 g of anhydrous lithium bromide and 5.0 g of copper(I) bromide in 20 mL of THF was added with stirring. After being refluxed for an additional 15 min, the suspension was cooled to ~40 °C, and 0.050 mol of **8a** was added in one portion. The temperature rose to ~70 °C without external heating. The mixture was heated under reflux for an additional 1 h, and then 100 mL of a saturated aqueous solution of $NH_4Cl$ was added. The zinc was filtered off and thoroughly rinsed with six portions of diethyl ether. After separation of the organic layer, the aqueous phase was extracted four times with diethyl ether. The unwashed combined organic layers were dried over $MgSO_4$ and subsequently concentrated in vacuo. Distillation gave 2-methyl-6-methylene-7-octen-4-ol (ipsenol, **9a**): bp 45 °C (0.1 mmHg); $n^{20}_D$ 1.4633; 84% yield; $^1$H NMR δ 0.92 and 0.96 (2 $CH_3$, 2 d, $J$ = 6.6 Hz), 1.20–1.40 ($CHCH_2CH$, m), 1.85 ($CHCH_3$, m), 2.28 and 2.31 ($CH_2C$=, 2 dd, $J_{gem}$ = 1.2 Hz, $J_a$ = 7.2 Hz, $J_b$ = 5.4 Hz), 2.77 (OH, s), 3.76 (CHOH, dddd, $J_a$ = 7.4 Hz, $J_b$ = 5.6 Hz, $J_c$ = 8.5 Hz, $J_d$ = 4.4 Hz), 4.95–5.35 (2 $H_2C$=, m), 6.34 ($H_2C$=C$H$, dd, $J_{trans}$ = 17.7 Hz, $J_{cis}$ = 10.5 Hz); $^{13}$C NMR δ 21.50 ($CH_3$), 23.08 ($CH_3$), 24.08 ($CHCH_3$), 40.22 ($CHCH_2CH$), 45.99 ($CH_2C$=), 67.06 (CHOH), 113.25 ($H_2C$=C), 117.66 ($H_2C$=CH), 138.34 ($H_2C$=CH), 142.78 ($H_2C$=C); mass spectrum, m/e (% of base peak) no $M^+$ (154), 136 (2.4, $M^+ - H_2O$), 121 (2.1), 93 (9), 85 (19), 79 (12), 68 (100), 53 (15), 43 (30).

The $^1$H NMR and mass spectral data of our product correspond with those of ipsenol recorded in the literature.[10,13,16,18,21,23,32] The ipsenol molecule contains diastereotopic protons and carbon atoms, and therefore some signals in the NMR spectra are double.

**e. Reduction of 2-Methyl-6-methylene-7-octyn-2-en-4-ol (8b) with Activated Zinc; Preparation of Ipsdienol (9b).** The reduction of **8b** was carried out in a way similar to that used for **8a**. After concentration of the combined organic layers in vacuo almost pure (according to the $^1$H NMR and $^{13}$C NMR spectra) **9b** remained. The yield was virtually quantitative. Chromatography through a 40-cm column of $Al_2O_3$ (deactivated with 20% of water) and diethyl ether gave pure 2-methyl-6-methylene-2,7-octadien-4-ol (ipsdienol, **9b**): $n^{20}_D$ 1.4898; 80% yield; $^1$H NMR δ 1.65 and 1.72 (2 $CH_3$, 2 S), 2.30 and 2.58 ($CH_2$, 2 dd, $J_{gem}$ = 13.5 Hz, $J_a$ = 6.7 Hz), 3.95–4.45 (OH), 4.95 (CHOH, ddd, 2 $J_a$ = 6.7 Hz, $J_b$ = 9.2 Hz), 5.00–5.40 (2 $H_2C$= and $HC$=$C(CH_3)_2$, m), 6.43 ($HC$=$CH_2$, dd, $J_{cis}$ = 11.3 Hz, $J_{trans}$ = 18.0 Hz); $^{13}$C NMR δ 18.23 ($CH_3$), 25.53 ($CH_3$), 39.68 ($CH_2$), 67.54 (CHOH), 113.80 ($H_2C$=C), 118.60 ($H_2C$=CH), 126.59 ($C$=$C(CH_3)_2$), 125.86 (=$C(CH_3)_2$), 138.38 ($H_2C$=CH), 142.13 ($H_2C$=$C$); mass spectrum, m/e (% of base peak) 152 ($M^+$, 0.13), 150 (0.35), 134 (55), 119 (100), 105 (32), 91 (95), 79 (80), 65 (11), 53 (15), 41 (23).

The spectral data of our product correspond with those of ipsdienol recorded in the literature.[12,16,19,20,22]

**f. Preparation of 3-Methyl-2-butenal.** To a stirred solution of 0.200 mol of the $(CH_3)_2C{=}CHMgBr$ in 200 mL of THF—prepared from 20 g of magnesium and 0.200 mol of $(CH_3)_2C{=}CHBr$[8]—was added dropwise 0.240 mol of dimethylformamide. After this addition, which was carried out at −70 °C, the temperature was allowed to rise to −30 °C. The solution was then added over 15 min to a stirred mixture of 56 g of concentrated hydrochloric acid (36%) and 350 mL of an aqueous saturated $NH_4Cl$ solution at −10 °C. The aqueous layer was extracted four times with diethyl ether. The combined solutions were dried over $MgSO_4$ after which the solvent was carefully removed at reduced pressure. The remaining crude product was warmed to 30 °C, and the pressure was reduced to 0.10 mmHg. The product was collected in an acetone/$CO_2$-cooled trap. This yielded 73% of 3-methyl-2-butenal: $n^{20}_D$ 1.4525; lit.[19] bp 133 °C (760 mmHg); $^1H$ NMR $\delta$ 1.97 and 2.17 (2 $CH_3$, d, $J$ = 1.2 Hz), 5.80 (HC=, dqq, $J$ = 8 Hz, 2 $J$ = 1.2 Hz), 9.96 (HC=O, d, $J$ = 7.2 Hz).

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**Registry No.** **4**, 90753-25-6; **5** (R = $CH_3(CH_2)_4$), 110316-86-4; **5** (R = $CH_3(CH_2)_5$), 110316-87-5; **5** (R = cyclohexyl), 110316-88-6; **5** (R = $CH_3(CH_2)_3OCH_2$), 110316-89-7; **5** (R = $(CH_3)_2CHCH_2(CH_2O)CH$), 110316-90-0; **5** (R = $HOCH_2CH$), 110316-91-1; **5** (R = $HOCH(CH_3)CH_2$), 110316-92-2; **5** (R = $HOCH(Ph)CH_2$), 110316-93-3; **5** (R = $CH_3CH_2(HO)CH$), 110316-94-4; **5** (R = $(CH_3)_2CHCH_2(HO)CH_2$), 110316-95-5; **5** (R = $(CH_3)_2C{=}CH(HO)CH$), 110316-96-6; **5** (R = $Ph(HO)CH$), 110316-97-7; **5** (R = $(CH_3)_2(HO)C$), 110316-98-8; **5** (R = $CH_3CH_2(CH_3)(HO)C$), 110316-99-9; **5** (R = $(CH_3)_3C(CH_3)(HO)C$), 110317-00-5; **5** (R = 1-hydroxycyclohexyl), 110317-01-6; **5** (R = 1-hydroxytetrahydronaphthalyl), 110317-02-7; **5** (R = HOOC), 110317-03-8; **5** (R = $CH_3CO$), 110317-04-9; **5** (R = $CH_3S$), 110317-05-0; **5** (R = $CH_3(CH_2)_2S$), 110317-06-1; **5** (R = $HC{\equiv}CC(=CH_2)CH_2$), 110317-07-2; **5** (R = $HOCH_2(Ph)CH$), 110330-25-1; **9a**, 60894-96-4; **9b**, 54809-53-9; $PhSC{\equiv}CC(=CH_2)CH_3$, 35346-80-6; $Me_3SiC{\equiv}CC(=CH_2)CH_3$, 18387-60-5; $Me_3SiC{\equiv}CC(CH_3)CH_3$, 110330-26-2; $(CH_3)_2C(OH)C{\equiv}CC(=CH_2)(CH_2)_4CH_3$, 110317-08-3; $(CH_2)_5C(OH)C{\equiv}C(=CH_2)CH_2CH_3$, 110317-09-4; $(CH_3)_2C{=}CHMgBr$, 38614-36-7; $CH_3(CH_2)_4Br$, 110-53-2; $CH_3(CH_2)_5Br$, 111-25-1; $CH_3(CH_2)_3OCH_2Cl$, 2351-69-1; $(CH_3)_2CHCH_2(CH_3O)CHCl$, 86213-40-3; $CH_3CH_2CH{=}O$, 123-38-6; $(CH_3)_2CHCH_2CH{=}O$, 590-86-3; $(CH_3)_2C{=}CHCH{=}O$, 107-86-8; $PhCH{=}O$, 100-52-7; $(CH_3)_2C{=}O$, 67-64-1; $CH_3CH_2(CH_3)C{=}O$, 78-93-3; $(CH_3)_3C(CH_3)C{=}O$, 75-97-8; $(CH_3)_3N(CH_3)C{=}O$, 127-19-5; $CH_3SSCH_3$, 624-92-0; $CH_3SC{\equiv}N$, 556-64-9; $CH_3(CH_2)_2SC{\equiv}N$, 4251-16-5; bromocyclohexane, 108-85-0; oxirane, 75-21-8; methyloxirane, 75-56-9; phenyloxirane, 96-09-3; cyclohexanone, 108-94-1; tetralone, 529-34-0; isopropenylacetylene, 78-80-8.

# Amidation of Chloroalkenes Catalyzed by Tertiary Phosphine Complexes of Palladium(0)

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Tertiary phosphine complexes of palladium(0) catalyze the amidation of vinyl chloride (VCl) with carbon monoxide and amines. The reaction is surprisingly fast and gives high yields of the Michael adduct derived from the amine with the corresponding acrylamide. The high rate with VCl is unusual among monochloroalkenes, being orders of magnitude greater than all three of the chloropropenes. The reaction is also stereospecific, with *cis*- and *trans*-1-chloropropene giving the propenamides with retention of configuration and no adduct formation. Basicity of the amine, coordination stereochemistry of the ligand, and the concentration of carbon monoxide and amine all influence the reaction rate in ways that are sometimes unexpected, in both degree and direction. Like bromoalkenes and arenes, chloroalkenes undergo amidation through oxidative addition. This conclusion is based on the stereospecificity and the quantitative coupling of VCl to 1,3-butadiene when carbon monoxide is absent. Catalyst deactivation can occur and is mainly caused by the loss of ligand through conjugate addition with acrylamide. The rate of that reaction is controlled by the nucleophilicity of both the phosphine and the amine with which it competes. It is greatly suppressed in the presence of dimethylamine where amidation occurs with high catalyst turnover.

## Introduction

Despite its low cost and abundant supply, the only commercial use of vinyl chloride (VCl) today is in the production of poly(vinyl chloride). Recently, we examined several hypothetical process concepts based on VCl. They included the preparation of acrylamide and N-substituted acrylamides by catalytic carbonylation with amines. Such an amidation process appeared to have commercial promise if it could be achieved with high rate, yield, and turnover.

There are only a few reports describing VCl carbonylation in the presence of alcohols. Saturated esters (propionate and 2-chloroprionate) are the main products when catalyzed by $Pd(PPh_3)_2Cl_2$.[1] Similarly, stoichiometric $PdCl_2$ in methanol gives methyl 2,2-dichloropropionate.[2] However, ethyl acrylate has been reported when $SnCl_2$ is used together with $Pd(PPh_3)Cl_2$, though large amounts of catalyst are required and few turnovers achieved.[1] Moreover, it is unclear if the acrylate forms directly or is an elimination product of the chloropropionate.

The classic studies by Heck, Schoenberg, and Bartoletti on the $Pd(PPh_3)_2X_2$-catalyzed amidation[3] and carbalkoxylation[4] of several halogen-substituted arenes and alkenes are the most comprehensive reported. Together with a complementary mechanistic study by Heck and Garrou[5]

(1) Knifton, J. U.S. Pat. 3 991 101, Nov. 9, 1976.

(2) Tsuji, J.; Morikawa, M.; Kiji, J. *J. Am. Chem. Soc.* **1968**, *86*, 4851.
(3) Schoenberg, A.; Heck, R. F. *J. Org. Chem.* **1974**, *39*, 3327.
(4) Schoenberg, A.; Bartoletti, I.; Heck, R. F. *J. Org. Chem.* **1974**, *39*, 3318.
(5) Garrou, P. E.; Heck, R. F. *J. Org. Chem.* **1976**, *98*, 4115.

0022-3263/87/1952-5266$01.50/0 