Tetrahedron Letters, Vol. 33, No. 21, pp. 2987-2990, 1992
Printed in Great Britain

0040-4039/92 $5.00 + .00
Pergamon Press Ltd

A Simple Preparative Method for Isopropenyl and Vinyl Groups from Ketones

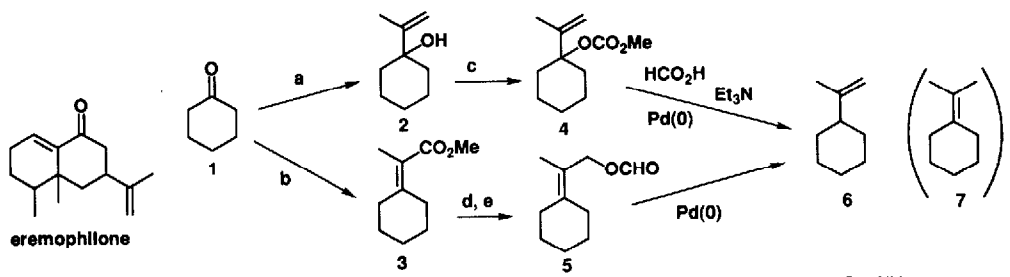
Tadakatsu Mandai,* Sadahiro Suzuki, Taro Murakami, Mitsugu Fujita, Mikio Kawada, Jiro Tsuji*

Department of Applied Chemistry, Okayama University of Science, Ridai-cho, Okayama, 700, Japan

Key words.
Palladium-catalyzed hydrogenolysis with formic acid, Allyl formates, Allyl carbonates

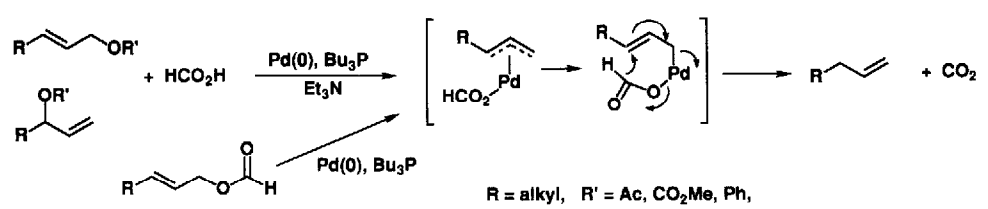
Abstracts: The palladium-catalyzed regioselective hydrogenolysis is applied to a simple preparation of isopropenyl and vinyl groups from ketones.

Isopropenyl group is present abundantly in naturally occurring terpenoids such as eremophilone, isoplegol, and picrotoxinin. There are a number of synthetic methods for this important functional group,[1] but sometimes facile double bond isomerization to the more stable isopropylidene group during the preparation poses a serious problem and further elaboration is required. We now wish to report a simple preparative method for this functional group from ketones as shown by the following scheme.



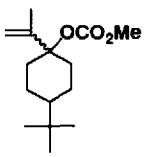
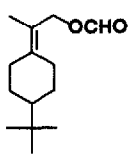
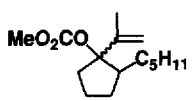
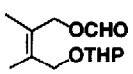
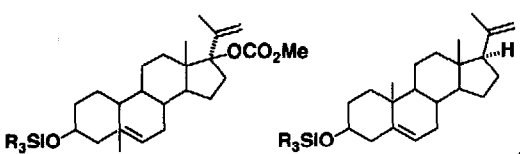
(a) isopropenyllithium, (b) $(EtO)_2P(O)CHMeCO_2Me$, (c) n-BuLi, $ClCO_2Me$, (d) i-Bu_2AlH, (e) acetic formic anhydride

In this method, palladium-catalyzed regioselective hydrogenolysis of allylic compounds with formate to give terminal olefins shown below is a key reaction.[2]



In this methodology, the ketone **1** was treated with isopropenyllithium to give the allylic alcohol **2**, which was converted to methyl carbonate **4**. On the other hand, **1** was converted to **3** and its reduction and formylation afforded the allylic formate **5**. The palladium-catalyzed reaction of **4** with formic acid and triethylamine at room temperature in benzene gave isopropenylcyclohexane (**6**) regioselectively in 85% yield without forming isopropylidenecyclohexane (**7**). The reaction of the allylic formate **5** with the palladium catalyst proceeded rapidly to afford **6**. Results of the application of this method are shown in Table 1.

TABLE 1

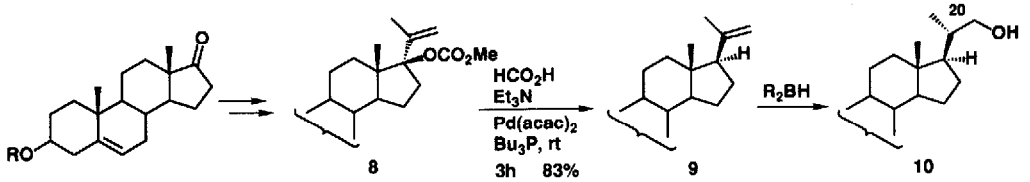
Entry	Product	Time, h	Yield (%)
1		3	82
2		0.5	88
3		0.5	82
4		0.5	86
5		3	83

Typical experimental procedure is as follows.

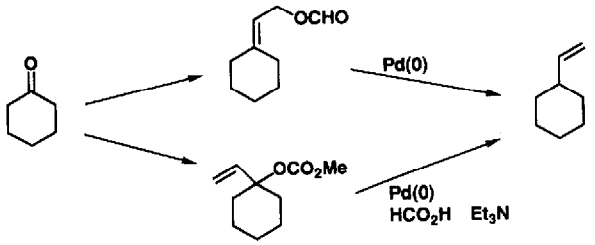
Entry 1: A yellowish solution of the catalyst was prepared by mixing $Pd(acac)_2$ (0.1 mmol) and n-Bu_3P (0.1mmol) in benzene (3 ml). Then a mixed solution of HCO_2H and Et_3N (5 mmol each) in benzene (5 ml), and 1-isopropenyl-4-t-butylcyclohexyl methyl carbonate (a mixture of stereoisomers) (1mmol) were added. The solution was stirred at room temperature for 3 h. After addition of water (40 ml), the mixture was extracted with hexane. The solution was dried and evaporated to give a crude product, which was purified by column chromatography to give an inseparable mixture of *cis*- and *trans* -1-isopropenyl-4-t-butylcyclohexane (ca. 1 : 1, 148 mg, 82%). The presence of isopropylidenecyclohexane was not detected by ^{13}C NMR and GLC (capillary column, 0.2 mm x 25 m). Formation of a small amount of 1-isopropenyl-4-t-butylcyclohexene formed by the palladium-catalyzed elimination was confirmed (3 %).

Entry 2: 2-(4-t-Butylcyclohexylidene)propyl formate (1 mmol) was treated with the same palladium catalyst (0.1 mmol) in benzene (6 ml) at room temperature for 1 h. The reaction mixture was diluted with hexane and concentrated after filtration to give a crude product, which was purified by column chromatography to give 1-isopropenyl-4-t-butylcyclohexane (*cis* and *trans* ca. 1 : 1 mixture, 166 mg, 88%).

The reaction is completely regioselective but not stereoselective, because hydride transfer from terminal σ-allylpalladium formate to give terminal olefin proceeds nonselectively from both sides, and degree of stereoselectivity is dependent on steric hindrance. Mixtures of *cis* and *trans* isomers were obtained in entries 1-3. On the other hand, the stereoselective reaction took place with a rather congested steroid (entry 5). The hydrogenolysis of steroidal 17β–carbonate **8** proceeds from the less hindered side to give 17-β–isopropenyl derivative **9**, which was identified by comparing its ^{1}H and ^{13}C NMR spectra with those of an authentic sample prepared by Wittig reaction of pregnenolone t-butyldimethylsilyl ether. It is known that the correct stereochemistry of C-20 in steroid **10** can be generated by the hydroboration of the isopropenyl group.[4]



As a further extension, ketones can be converted to a vinyl group by the application of similar methodology, and some results are shown in Table 2.

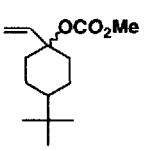
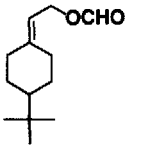
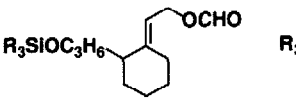
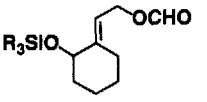
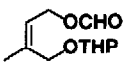
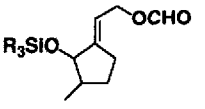
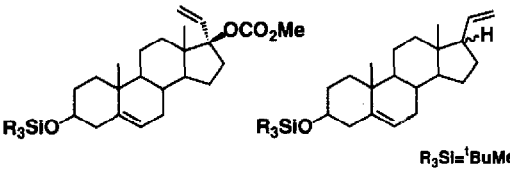


In entries 1-4 and 6, mixtures of *cis* and *trans* isomers of different ratios were obtained. For example, the product of entry 4 was a mixture of *cis* and *trans* isomers (12 : 1). The major product was the *cis* isomer, which was identified by comparing ^{1}H and ^{13}C NMR spectra with those of an authentic sample prepared by the reaction of cyclohexene oxide with vinylmagnesium bromide. This result shows that the hydride attack takes place from the less hindered, opposite side of the silyl group. A *cis* and *trans* mixture of 2 : 1 ratio was obtained in entry 3. The reaction of the steroid afforded the 17β-vinyl as a major product, but not completely stereoselective (17α : 17β = 1 : 6). In all cases, formation of conjugated dienes by elimination of β–hydrogen was less than 5%.

References

1. Heathcock, C. H.; Graham, S. L.; Pirrung, M. C.; Plavac, F.; White, C. T. " *The total synthesis of sesquiterpenes*" in J. ApSimon "*Total synthesis of natural products*" Vol. 5, **1983**, John Wiley & Sons.
2. Tsuji, J.: Yamakawa, T.; *Tetrahedron Lett.*, **1979**, 613-616. Tsuji, J.; Shimizu, I.; Minami, I.; *Chem. Lett.*, **1984**, 1017-1020; *Synthesis*, **1986**, 623-627.
3. The purity of n-Bu3P is crucial for reproducibility of the catalytic reaction. n-Bu3P in a "Sure-seal" bottle purchased from Aldrich was used. A freshly prepared yellowish catalyst solution should be used.
4. Midland, M. M.; Kwon, Y. C. *J. Am. Chem. Soc.*, **1983**, *105*, 3725-3727.

TABLE 2

Entry	Product	Time, h	Yield (%)
1		4	80
2		0.5	82
3		1	86
4		0.5	82
5		0.5	72
6		0.5	92
7		1	94

$R_3Si = {}^tBuMe_2Si$

(Received in Japan 10 February 1992)