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A NOVEL METHOXYLATION OF ALLYLIC ALCOHOLS VIA ALLYLIC REARRANGEMENT USING DICHLOROBIS(TRIPHENYLPHOSPHINE)PLATINUM(II)-TIN(II)CHLORIDE DIHYDRATE COMPLEX CATALYST

Yoshiyuki ICHINOHE, Hiroshi SAKAMAKI, and Noriyuki KAMEDA
Department of Chemistry, Faculty of Science and Engineering
Nihon University, Narashinodai, Funabashi, Chiba 274

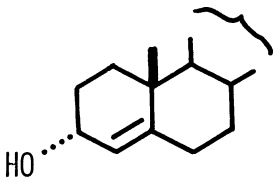
Several allylic steroidal alcohols give rearranged allyl methyl ethers by dichlorobis(triphenylphosphine)platinum(II)-tin(II)chloride dihydrate complex catalyst in methanol.

Allylic alcohol-type compounds exist frequently as important natural products and that their pyrophosphates are biosynthetically key intermediates[1].

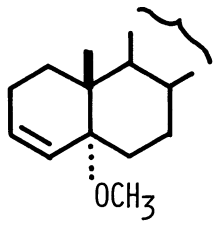
Although transition metal-catalyzed isomerization of allylic-type compounds are known[2], methoxylation of allylic alcohol via allylic rearrangement using metal complex has not yet been reported. Several years ago, we reported that methanol used as the solvent reacted with cholest-4-en-3β-ol (II) in the presence of dichlorobis(triphenylphosphine)platinum(II)-tin(II)chloride complex catalyst under a hydrogen pressure (30-40 kg/cm^2) at 30-35°C[3]. We also found[3] that ethanol, 2-propanol or t-butyl alcohol etc. did not participate in the reaction. In this paper, we wish to describe results obtained for this novel isomerization-methoxylation reaction of several steroidal allylic systems, as we were able to isolate unstable products by carrying the reaction under milder conditions (room temperature and ordinary pressure).

4-Cholesten-3α-ol (I) (50 mg) reacted with methanol (4 ml) giving, almost quantitatively, glassy 5β-methoxy-3-cholestene (IV) $[\alpha]_D^{26°}$+71.1° (c=4.10, abs. EtOH), IR (KBr): ν 1665 (C=C), 1085 cm^{-1} (OCH_3); NMR[4] ($CDCl_3$): δ 5.39 (2H, br. s., C<u>H</u>=C<u>H</u>), 3.28 (3H, s., O<u>CH</u>$_3$) upon treatment with the complex catalyst (390 mg) in THF or benzene (6 ml) at 15°C under ordinary pressure for 1 h., while the reaction of 4-cholesten-3β-ol (II) under similar conditions for 4 h. gave 5α-methoxy-3-cholestene (III), mp 70-70.5°C, $[\alpha]_D^{26°}$-38.5° (c=0.87, abs. EtOH), IR (KBr): ν 1665 (C=C),

1085 cm^{-1} (OCH_3); NMR ($CDCl_3$): δ 5.64 (2H, br. d., C<u>H</u>=C<u>H</u>), 3.35 (3H, s., OC<u>H</u>$_3$) in ca. 75% yield (39 mg), and 5β-methoxy-3-cholestene (IV) in ca. 25% yield (13 mg). 3,5-Cholestadiene (IX) mp 77-78°C, $[\alpha]_D^{25°}$-118° (c=0.56, abs. EtOH), IR (KBr): ν 1650 cm^{-1} (C=C) was isolated in a poor yield of ca. 10% after prolonged reaction (12 h.) for both cases.



(I)



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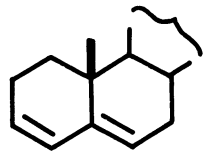
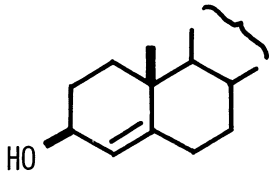
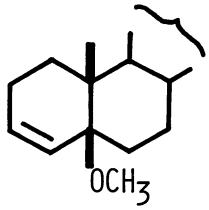


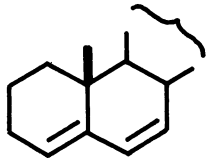
(IX)



(II)



(IV)



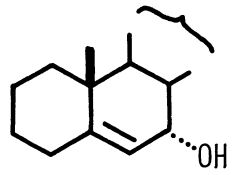
(X)

On the other hand, under a similar condition, 5-cholesten-7α-ol (V)[5] gave 5α-methoxy-6-cholestene (VII), mp 77-78°, $[\alpha]_D^{25°}$-103.1° (c=0.52, abs. EtOH); IR (KBr): ν 1665 (C=C), 1085 cm^{-1} (OCH_3); NMR ($CDCl_3$): δ 5.64 (2H, br. d., C<u>H</u>=C<u>H</u>), 3.35 (3H, s., OC<u>H</u>$_3$), 5β-methoxy-6-cholestene (VIII), mp 90-90.5°C, $[\alpha]_D^{25°}$+22.8° (c=0.36, abs. EtOH), IR (KBr): ν 1670 (C=C), 1098 cm^{-1} (OCH_3); NMR ($CDCl_3$): δ 5.28 (2H, br. s., C<u>H</u>=C<u>H</u>), 3.20 (3H, s., OC<u>H</u>$_3$), and 4,6-cholestadiene (X), mp 87-88°C, $[\alpha]_D^{26°}$-7.5° (c=0.64, abs. EtOH), in 20, 60, and 20% yields after 3 h. respectively. 5-Cholesten-7β-ol (VI) also gave 5α-methoxy-6-cholestene (VII), 5β-methoxy-6-cholestene (VIII), and 4,6-cholestadiene (X) in ca. 60, 20, and 20% yields after 4 h. When the reaction is conducted with only tin(II)chloride as catalyst, both of 4-cholesten-3α-ol (I) and 4-cholesten-3β-ol (II) gave 3,5-cholestadiene (IX) in almost quantative yield after prolonged reaction (12 h.). These results are summarized as the following Table.

	Products. (Yield; %)				
	(III)	(IV)	(VII)	(VIII)	(X)
(I)	0	100	—	—	—
(II)	25	75	—	—	—
(V)	—	—	20	60	20
(VI)	—	—	60	20	20

Attempts to synthesize these new unsaturated methyl ethers by methylation of the corresponding α,β-unsaturated alcohols[5] with methyl halides under alkaline conditions were unsuccessful[6].

The structural assignments were made based on the optical rotation method[7] and catalytic hydrogenation (ruthenium catalyst, atmospheric pressure, room temperature, t-butyl alcohol as solvent[8]). 5α-Methoxy-3-cholestene (III) gave 5α-methoxycholestane (XI), mp 79-80°C, $[\alpha]_D^{26°}$+24.8°, (c=0.46, abs. EtOH), IR (KBr): ν 1105 cm^{-1} (OCH_3); NMR ($CDCl_3$): δ 3.28 (3H, s., $OC\underline{H}_3$) in an excellent yield (98%). Moreover, 5β-methoxy-6-cholestene (VIII) gave 5β-methoxycholestane (XII), mp 77-78°C, $[\alpha]_D^{25°}$+60.2°, (c=0.43, abs. EtOH), IR (KBr): ν 1103 cm^{-1} (OCH_3); NMR ($CDCl_3$): δ 3.19 (3H, s., $OC\underline{H}_3$) in a good yield (95%). Hydrogenation of 5β-methoxy-3-cholestene (IV) and 5α-methoxy-6-cholestene (VII) under similar conditions also provided (XII) and (XI), respectively.



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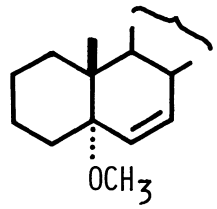
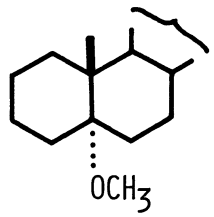
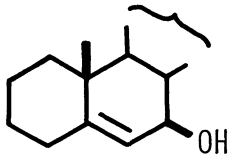


(VII)



(XI)



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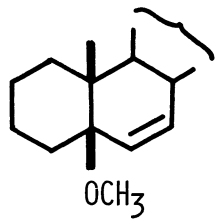

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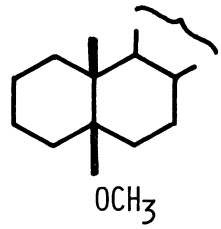

(XII)

Catalytic hydrogenation of (IV) and (VII) in t-butyl alcohol containing a trace of glacial acetic acid[8,9] over Adams' platinum gave 5α-cholestane (XIII) and 5β-cholestane (XIV) in a high yield[10].

The catalytic conversion of (I) into (IV) appears to imply an SN_2'-type reaction. However, the difference in product ratio in the reaction of (II), (V) and (VI) suggests a steric factor is operating between steroidal substrates and organometallic catalyst. Although the reaction mechanism remains to be elucidated, it might involve a π-allyl metal complex intermediate. The methoxylation of π-allyl ligands is known[11].

Extension of this novel methoxylation to other natural allylic alcohols, especially, terpenoids and alkaloids etc. is in progress.

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References and Notes.

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