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Pinacol-Type Rearrangement of 1-Methoxybicyclo[3.2.2]nona-3,6-dien-2-ols. An Efficient Route to Homobarrelenones

Tadao UYEHARA,* Yoshinori KAWAI, Jun-ichi YAMADA, and Tadahiro KATO
Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980

Pinacol-type rearrangement of 1-methoxybicyclo[3.2.2]nona-3,6-dien-2-ols proceeds preferentially to give bicyclo[3.2.2]nona-6,8-dien-2-ones by treating with TsOH in boiling benzene. This transformation is incorporable in a new synthesis of homobarrelenone and a large number of its derivatives starting from 1-methoxybicyclo-[3.2.2]nona-3,6-dien-2-ones.

Bicyclo[3.2.2]nona-3,6,8-trien-2-one (homobarrelenone, 8d) and its derivatives are important precursors for theoretically interesting reactive intermediates related to bicycloaromaticity(1) and peculiar polycyclic compounds such as barbaralone(2) and 3a,7a-dihydro-1-indenone.(3) The parent compound (8d) has been prepared effectively from cycloheptatrienylacetyl chloride(3) or 2,4,6-cycloheptatrienone (tropone)(4) and the limited derivatives have been provided by Diels-Alder reaction of tropones with acetylenic dienophiles.(5) We now report a new method to prepare homobarrelenone and its derivatives which have alkyl and/or aryl groups at the positions desired.

The pinacol-type rearrangement of 1-methoxybicyclo[3.2.2]non-6-en-2-ols (1) is a selective process to give the bicyclo[3.2.2]non-6-en-2-ones (2) mainly.(6) If this type of selectivity is caused by the difference between the migratory aptitude of the saturated and unsaturated two-carbon bridges, we are able to expect preferential formation of the bicyclo[3.2.2]nona-6,8-dien-2-ones (7), precursors of homobarrelenones (8), from dienols 5 and 6 employing a procedure similar to that used for the rearrangement of 1.

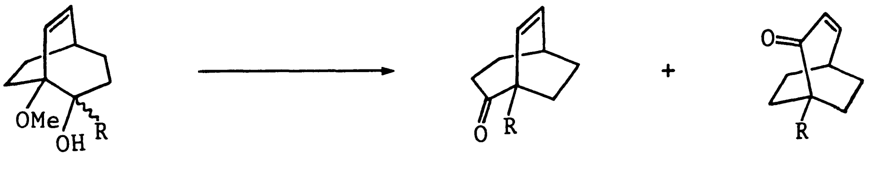
1-Methoxybicyclo[3.2.2]nona-3,6-dien-2-one (4) is the major Diels-Alder adduct of 2-methoxytropone and ethylene.(7) Treatment of 4 with methyllithium gave 5a and 6a in 50% and 31% yields, respectively.(8) The stereochemistry of them was confirmed on the basis of their ^{1}H-NMR spectra.(9)

Pinacol-type rearrangements of these alcohols and the related ones are summarized in Table 1. It is clear that, in the case of the tertiary allylic alcohols, the unsaturated two-carbon bridge migrates exclusively regardless of the stereochemistry of the hydroxyl group (runs 1-4). Therefore, a typical transformation of 4 into 7 has been simplified as follows. A mixture of the allylic alcohols 5 and 6 is derived from 4 and an excess of an organolithium reagent, and the ketone 7 is obtained from the crude mixture by heating under reflux with 10 mol% of p-toluensulfonic acid (TsOH) in benzene (10 ml/ 1mmol of an alcohol) on a preheated oil bath for 2-5 min and purified by a simple silica-gel chromatography (runs 5-7).

The pinacol-type rearrangement of this system is the most selective one among those of the related bridged bicyclic systems. The decrease in the preference of migration of the unsaturated bridge is in the order bicyclo[3.2.2]nona-3,6-dien-2-ols> 3-methylenebicyclo[2.2.2]oct-5-en-2-ols10)> bicyclo[3.2.2]non-6-en-2-ols6)> bicyclo[2.2.2]oct-5-en-2-ols.11) This means the relative migratory aptitude of the unsaturated two-carbon bridges *versus* the saturated two-carbon bridges is larger when the carbocation intermediate is formed more easily and/or the cation is more stable.

When a mixture of 5a and 6a was heated with an equivalent of TsOH for 5 min, the conjugated ketone (9a)7) was obtained along with 7a (run 8). This suggests the possibility of the secondary acid-catalyzed transformation of 7 to 9. In fact, treatment of 7b with TsOH (1 equiv.) gives 9b which is not stable under the reaction conditions (run 9).

Diisobutylaluminium hydride (DIBAH) reduction of 4 gave 5d and 6d in 45% and 23% yields, respectively. Regardless of the stereochemistry of the hydroxyl group, 7d and 9d are derived in the approximate ratio of 2 : 1 (runs 10-11). Thus the pinacol-type rearrangement of the secondary allylic alcohols is relatively slow and less selective. When 7d and TsOH (1 equiv.) were heated under reflux in benzene for 19 h, a 10 : 1 mixture of 7d and 9d was obtained in 61% yield. This means the conversion of 7d into 9d can be ignored under the conditions for the pinacol-type rearrangement. Although the reason for the difference in the selectivity of the rearrangements is essentially uncertain, it is probable that the relative migratory aptitude of the unsaturated bridge of the carbocation derived from the secondary



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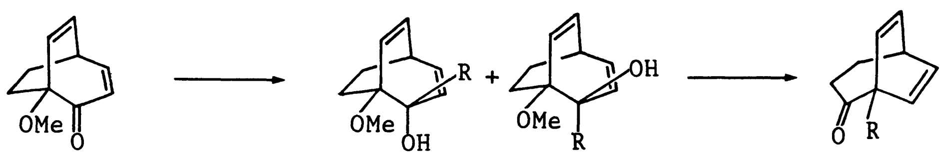
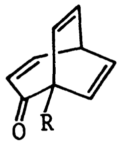


4 5 6 7



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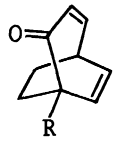

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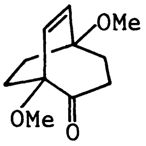
a) R=Me
b) R=*n*-Bu
c) R=Ph
d) R=H



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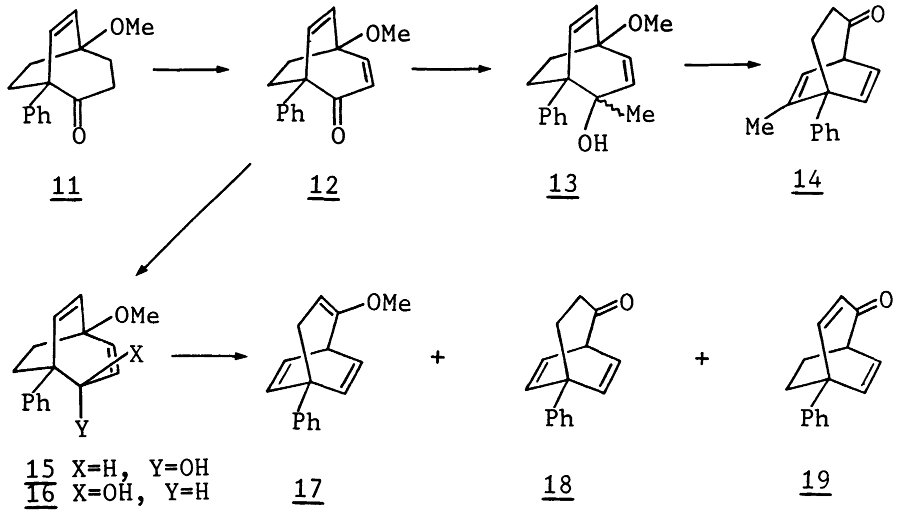
allylic alcohols is smaller than that derived from the tertiary allylic alcohols. When a mixture of 5d and 6d was heated with an equivalent of TsOH, the ratio of 7d and 9d was increased up to 3.8 : 1 (run 12).

Table 1. Pinacol-type rearrangement of 1-methoxybicyclo[3.2.2]nona-3,6-dien-2-ols and the related reactions a)

Run	Substrate	TsOH equiv.	Temp b) °C	Time min	Products (yield/%)
1	5a	0.1	21.5	120	7a (74)
2	6a	0.1	20.5	60	7a (53)
3	5a	0.1	80	5	7a (62)
4	6a	0.1	80	5	7a (61)
5	5a+6a	0.1	80	5	7a (82) c)
6	5b+6b	0.1	80	2	7b (68) c)
7	5c+6c	0.1	80	5	7c (92) c)
8	5a+6a	1.0	80	5	7a (37), c) 9a (40) c)
9	7b	1.0	80	45	9b (87) d)
10	5d	0.1	80	30	7d (34), 9d (17)
11	6d	0.1	80	30	7d (39), 9d (23)
12	5d+6d	1.0	80	3	7d (50), 9d (13)
13	13	0.1	80	2	14 (75)
14	15	0.1	80	60	17 (38), 18 (14), 19 (14)
15	16	0.1	80	120	17 (31), 18 (11), 19 (11)

a) All the ractions were carried out in dry benzene (10 ml/ 1 mmol) with TsOH (monohydrate). The products were isolated by chromatography on silica gel.
b) The reaction at 80 °C means that under gentle reflux. c) Overall yield from 4.
d) Determined by VPC.



1,5-Dimethoxybicyclo[3.2.2]non-6-en-2-one (10) has been prepared[12] as a synthetic intermediate for C-5 substituted homobarrelenones. The reaction of 10 and phenyllithium followed by treatment with TsOH (0.5 equiv.) in boiling benzene for 30 min gave 11 in 74% yield. The ketone 11 was converted into 12 by palladium catalyzed oxidation[13] of the allyl enol carbonate of 11 in 55% yield. It is noteworthy that this dehydrogenation procedure is applicable to the preparation of other derivatives of 4 from 1-methoxybicyclo[3.2.2]non-6-en-2-ones.[12]

The reaction of 12 with methyllithium to yield 13 followed by acid treatment (run 13) gave only the 5,6-disubstituted dienone 14. DIBAH reduction of 12 afforded alcohols 15 and 16. Upon treatment with TsOH, each of the secondary allylic alcohols gave the methyl enol ether 17 and ketones 18 and 19 (runs 14-15). Thus, we have demonstrated an *extended pinacol-type rearrangement* of a 4-alkoxy-2-buten-1-ol system.

Dienones 7 are convertible into the corresponding homobarrelenones (8) with ease; α-phenylselenenylation of the lithium enolates of 7a-7d with phenylselenenyl bromide followed by oxidation with sodium metaperiodate in the presence of sodium hydrogen carbonate gave homobarrelenones (8a, 56%; 8b, 64%; 8c, 71%; and 8d, 57%).

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8) All new compounds reported here exhibit satisfactory spectral (IR and NMR) and analytical and/or mass spectral characteristics.

9) Upon irradiation of the tertiary methyl protons of 5a at δ=1.27, significant enhancement was observed of the H-3 (δ=5.24) and H-7 (δ=5.94) signals. The spectra of 5a show an unusual low-field signal at δ=2.43 due to the H-8-*endo* which is close to the oxygen of the hydroxyl group. The signals due to the methylene protons of 6a are observed in the range of δ=1.5-2.1.

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