# SYNTHESES OF ENDO-EXO-TETRACYCLO[3.3.1.0^{2,4}.0^{7,8}]NONAN-9-ONES

AND THE UNUSUAL COURSE OF THEIR KETAL HYDROLYSIS

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The synthesis of endo,exo-tetracyclo [3.3.1.0^{2,4}.0^{7,8}]nonan-9-one has already been described by S.C. CLARKE, K.J. FRAYNE, and B.L. JOHNSON[1]. In the crucial step of this synthetic route, the Simmons-Smith reaction of isomeric tricyclo-[3.2.1.0^{2,4}]oct-6-en-8-ols leads in low yield to a tetracyclic alcohol which is oxidized to the ketone mentioned above. During our attempts to synthesize sub-stituted homotropilidenes[2,3] we found a more effective synthesis of endo,exo-ketones and ketals by direct cyclopropanation of their respective unsaturated precursors[2] with gaseous diazomethane in presence of CuCl[4,5] without using any solvent.
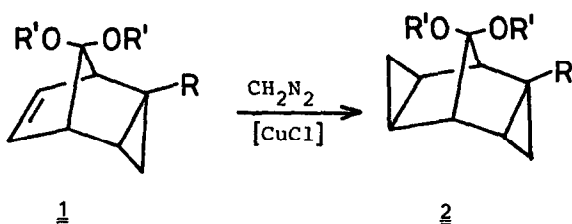
	R	R'	R'
a	H	CH$_3$	CH$_3$
b	CH$_3$	CH$_3$	CH$_3$
c	H	-CH$_2$——CH$_2$-

While compounds 2a[6] and 2b were obtained as colorless liquids (b.p. 110 - 113°/15 mm, yield 61 %, 106-107°/12 mm, yield 80 %) 2c is a crystalline compound (m.p. 47-48°,yield 54 %).

As the acid catalysed hydrolyses of 2 proceeded mostly with rearrangement, we prepared the tetracyclic ketones 4 by the reaction of the unstable[3,8] (decarbo-nylization) ketones 3 with gaseous CH$_2$N$_2$/CuCl at -10°C in CH$_2$Cl$_2$ (3a) and with-out solvent (3b).
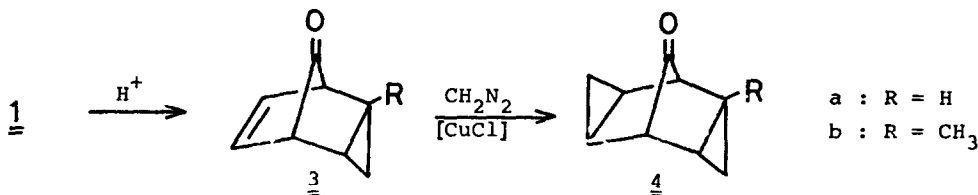

a : R = H
b : R = CH$_3$

Apparently the β,γ-unsaturated ketones 3 reacted only at the olefinic double bond. No spectroscopic evidence for any product resulting from a reaction at the carbonyl group was obtained. Ketone 4a (yield: 41 %) proved to be identical (m.p., ir, nmr) with the ketone described by B.L. JOHNSON et al.[1]. Ketone 4b, a colorless oil, was isolated in a yield of 30 %. The stereospecific exo-cyclopropanations of the ketones 3 were proved by [1]H-nmr spectroscopy[9].

To our knowledge this reaction represents the first example of a direct cyclopropanation of a nonconjugated ketone by diazomethane; for instance a different reaction course was observed by SHECHTER et al.[10] in the reaction of bicyclo-[4.2.1]nona-2,4,7-trien-9-one (5) with CH_2N_2 in methanol-chloroform-ether using LiCl as catalyst. We are now inverstigating the reaction of diazomethane with 5 under the conditions of our reaction.

As mentioned above the acid catalyzed hydrolyses of the ketals 2 proceed mostly with rearrangement. This is remarkable because the ketones are formed in hydrolyzing the ketals 6 [1,4,11], 7 [4], and 8 [1,4,8,11].

| 6 | 7 | 8 |

R = H
R = Cl
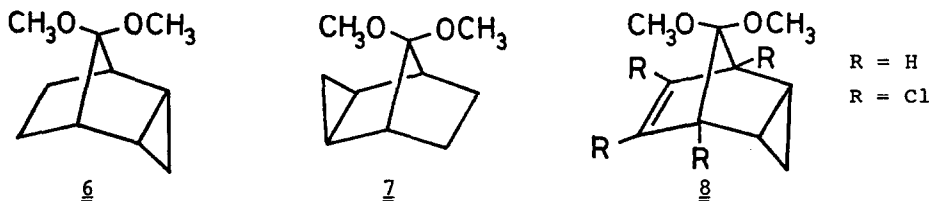
The hydrolysis of ketal 2a with 3N $HClO_4$ in water or methanol leads completely to the rearranged compounds 9a and 9b, respectively. On performing the reaction in dioxane/water or acetone/water with 3N $HClO_4$, ketone 4a was also formed in addition to 9a in a ratio of 4a : 9a = 35 : 65.

a:X = OH
b:X = OCH_3

| 2a | 9 | 4a |
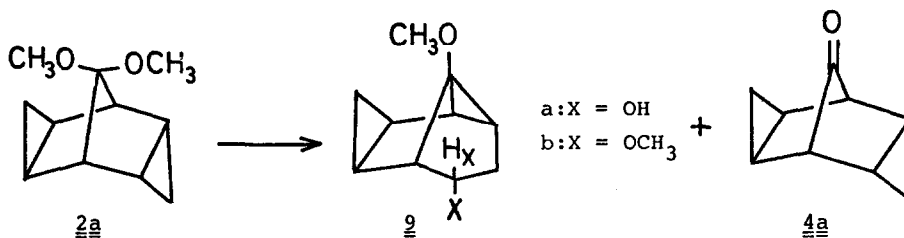
Our observation of rearranged products is in contrast to a recent investigation of G. LAMATY et al.[7] who studied the kinetics of the HCl catalyzed hydrolyses of ketals in the 7-norbornyl series in dioxane/water measuring the uv absorption of the ketones formed. They do not report any rearranged product in the case of 2a. Hydrolyzing the methyl derivative 2b we did not succeed in shifting the reaction course towards ketone formation; only rearranged products of type 10 could be isolated. The endo-position of X in the rearranged product 9 was confirmed by the characteristic multiplet of H_x[11,12,13] and in the alcohol 10a

using Eu(fod)$_3$ as a paramagnetic shift reagent[2].

a : X = OH
b : X = OCH$_3$
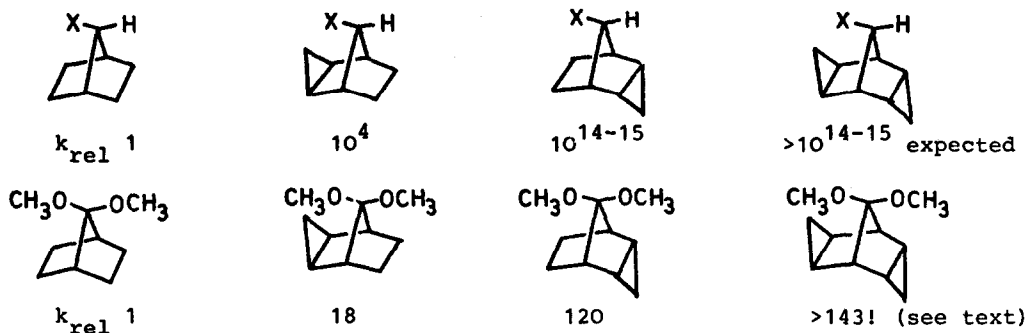c : X = OCCH$_3$ (with O below, doubly bonded)
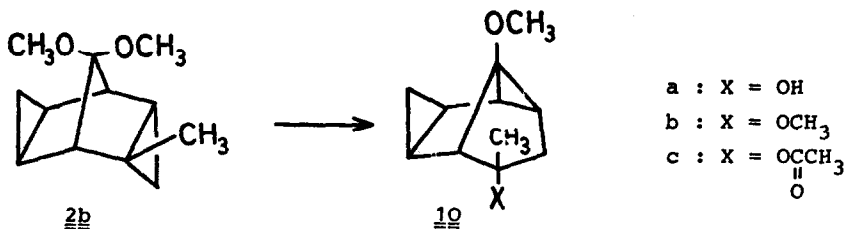
To discuss this unusual reaction course one must consider the nature of the in-
termediate carbonium ion which occurs during ketal hydrolyses. It seems likely
that there exist two competitive stabilization possibilities of the positive
charge, via the carbonium-oxonium ion and via the anchimeric effect of the ske-
leton. The formed products depend on the mode of attack of a nucleophile on the
intermediate carbonium ion which can proceed by the ways A - C.

a : Y = H
b : Y = OCH$_3$

a : R = H
b : R = CH$_3$
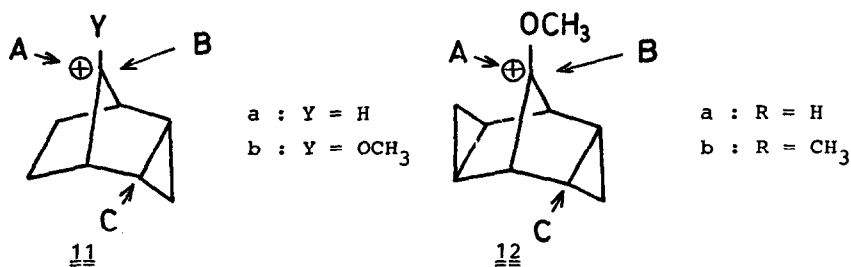
According to the solvolytic studies[12,14] of acyloxy derivatives in the norbonyl
series the attack of a nucleophile on 11a by way B is not observed due to the
stabilizing effect of the endo-cyclopropane ring. The reaction proceeds via A
(retention) and via C (rearrangement). In 11b the more efficient stabilization
of the carbonium ion center by OCH$_3$ enables a normal path of hydrolysis to the
ketone, most probably by way A. In contrast to 11b the attack A is rendered more
difficult in 12 by the exo cyclopropane ring. Thus in 12a way C is now favored
over ketone formation. 12b reacts only by rearrangement due to the hyperconju-
gative or inductive effect of the methyl group. Since one does not observe way
B in the solvolysis of 11a, we believe that A is still dominating over B in the
ketone formation of 12a.

Recently G. LAMATY et al.[7] investigated the rates of ketal hydrolyses in the
norbornyl series and compared them with the solvolytic rates of the correspon-
ding acyloxy compounds. As the rate-determining step of ketal hydrolysis is the
formation of the strongly stabilized carbonium-oxonium ion the influence of the
skeleton on the rates is much smaller in the ketal series. Because of the neg-
lect of the side reaction leading to the rearranged product 9 the relative hydro
lysis rate of 2a determined by G. LAMATY seems to be wrong. The rate constant
for the rate-determining step 2a → 12a should be greater by a factor of nearly
three (see product ratio 9a : 4a).

$$X \overset{H}{\underset{k_{rel} \ 1}{\diagdown}} \qquad X \overset{H}{\underset{10^4}{\diagdown}} \qquad X \overset{H}{\underset{10^{14-15}}{\diagdown}} \qquad X \overset{H}{\underset{>10^{14-15} \ \text{expected}}{\diagdown}}$$

$$CH_3O \overset{OCH_3}{\underset{k_{rel} \ 1}{\diagdown}} \qquad CH_3O \overset{OCH_3}{\underset{18}{\diagdown}} \qquad CH_3O \overset{OCH_3}{\underset{120}{\diagdown}} \qquad CH_3O \overset{OCH_3}{\underset{>143! \ \text{(see text)}}{\diagdown}}$$

To solve the question[7,12,15], whether the syn or anti OCH_3-group to the endo cyclopropane ring is leaving in the first step, we plan to study mixed ketals. The kinetics of the solvolysis of 2a and 2b is under investigation.

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