

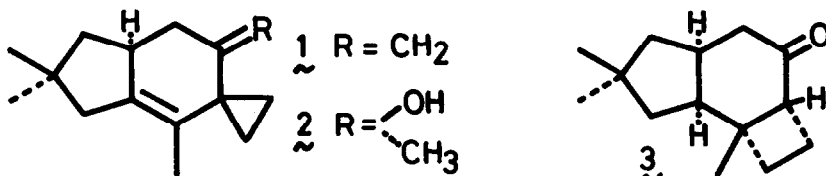
NEW RING CONTRACTION OF CYCLOBUTYL KETONES TO CYCLOPROPYL KETONES
 SYNTHESSES OF $\Delta^{2(3),7(13)}$ -ILLUDADIENE AND $\Delta^{2(3)}$ -7 β -ILLUDENOL

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We should like to describe here a new ring contraction of cyclobutyl ketones to cyclopropyl ketones through probable intermediary formation of 1-acyl cyclobutyl cations, and application of the reaction to the biogenetic-type syntheses of $\Delta^{2(3),7(13)}$ -illudadiene 1^{1,2} and $\Delta^{2(3)}$ -7 β -illudenol 2 from 13-norproto-illudan-7-one 3³.



Bromination of cis-4,4,6-trimethyl-bicyclo[4.2.0]octan-2-one 4⁴ with bromine (CCl_4 , 0°) gave regioselectively 1 β ,3 α - and 1 β ,3 β -bromoketones 5^{5,6} (100%), which on treatment with AgOAc in AcOH (120° , 6hr) afforded spiro[2.5]octenone 6⁵ [57%; oil; nmr(CCl_4) δ 1.04 (2H, m, AA' of an AA' BB' system), 1.06 (6H, s), 1.28 (2H, m, BB'), 1.47 (3H, d, J=1.5Hz), 2.28 (2H, s), 5.50 (1H, m); ir(neat) 3070, 1708, 1655 cm^{-1}] and acetoxy ketone 7⁵ [28%; oil; nmr(CCl_4) δ 1.03 (6H, s),

1.95 (6H, s), 2.15 (4H, s), 2.56, 3.95 (each 2H, A_2X_2 t, $J=7\text{Hz}$); ir(neat) 1745, 1665, 1635cm^{-1}]. The structure of 7 was ascertained by leading 6 to 7 by heating in AcOH (120° , 6hr; 100%), through a Michael type reaction. On bromination of cis-6-methyl-bicyclo[4.2.0]octan-2-one 8⁷ (Br_2 , CCl_4 , 0°), 3-bromoketone 9^{5,6} was obtained (64%). Similar treatment of 9 with AgOAc in AcOH (120° , 6hr) afforded spiro[2.5]octenone 10⁵ [40%; oil; nmr(CCl_4) δ 1.02 (2H, m, AA' of an AA' BB' system), 1.33 (2H, m, BB'), 1.49 (3H, broad s), 2.40 (4H, broad s), 5.16 (1H, m); ir(neat) 3070, 1705cm^{-1}] together with a substitution product 3-acetoxyketone 11⁵ [47%; oil; ir(neat) 1755, 1720cm^{-1}]. The new unusual rearrangement may be explained by assuming primary formation of α -keto carbenium ion⁸ 12, which rearranges to 1-acyl cyclobutyl cation 13 via 1,3-hydride shift (Scheme I).

Bromination of d,1-13-norprotoilludan-7-one 3 with Br_2 in CCl_4 (0°) afforded an epimeric mixture of 7-keto-8-bromides 14 and 15 in 92% yield (14/15=3/1, by nmr) as crystals and repeated recrystallization (n-hexane) of the mixture afforded pure 8α -bromide 14⁵, mp $78\sim 79^\circ$. The detailed conformation of 14 was obtained by X-ray crystallographic analysis⁹ (Fig. I). Conversion of 14 into norilludane skeleton was achieved by treatment with AgOAc in AcOH (120° , 7hr) to give the desired $\Delta^{2(3)}$ -13-norilluden-7-one 16 in 47% yield. Similar treatment of the mixture of 14 and 15 (14/15=3/1) gave the same result. 16⁵; Oil; nmr(CCl_4) δ 0.60, 1.56 (4H, m), 1.04, 1.15 (each 3H, s), 1.38 (3H, broad s, long range coupling with C-9H, $J_{9-12}=2.5\text{Hz}$), 2.02 (1H, q, 8 β H, $J_{8\beta-9}=13\text{Hz}$, $J_{8\alpha-8\beta}=14\text{Hz}$), 2.16 (2H, broad s, 1 α and 1 β H), 2.55 (1H, q, 8 α H, $J_{8\alpha-9}=5\text{Hz}$, $J_{8\alpha-8\beta}=14\text{Hz}$), 2.80 (1H, broad m, 9-H); ir(neat) 1705cm^{-1} . The nmr data¹⁰ suggested for 16 a partial conformation 16a with an axial C-9H. Methylenation of norilludenone 16 with $\text{ph}_3\text{P}=\text{CH}_2$ (from $\text{ph}_3\text{PCH}_2\text{Br}^-\text{tAmONa}$) in benzene (rt, 30min) furnished $\Delta^{2(3),7(13)}$ -illudadiene 1⁵ in 90% yield. 1; Oil; nmr(CCl_4) δ 0.20~1.25 (4H, m), 1.01, 1.10 (each 3H, s), 1.27 (3H, broad s), 4.35 (2H, m); ir(neat) 3080, 1645, 880cm^{-1} . Finally methylation of 16 with MeMgI in ether (0° , 30min and rt, 1hr) afforded stereoselectively $\Delta^{2(3)}$ -7 β -illudenol 2⁵ in 85% yield. 2; Oil; nmr(CCl_4) δ 0.20~1.50 (4H, m), 1.05, 1.07, 1.15 (each 3H, s), 1.23 (3H, m); ir(neat) 3440cm^{-1} . The β orientation of the hydroxyl group of 2 was derived from the lanthanide induced shift data, which indicated one of the C-8 proton with a large S^{11} value ex-

hibits a large J_{8-9} value¹⁰ of 11Hz [Eu(fod)₃/2=0.294; $\delta(\text{CCl}_4)$ 5.05 (S=8.8, 1H, broad m, 9-H), 6.41 (S=17.3, 1H, q, $J_{8\beta-9}$ =11Hz, $J_{8\alpha-8\beta}$ =12Hz, 8BH), 7.10 (S=18.2, 1H, q, $J_{8\alpha-9}$ =6Hz, $J_{8\alpha-8\beta}$ =12Hz, 8aH)].

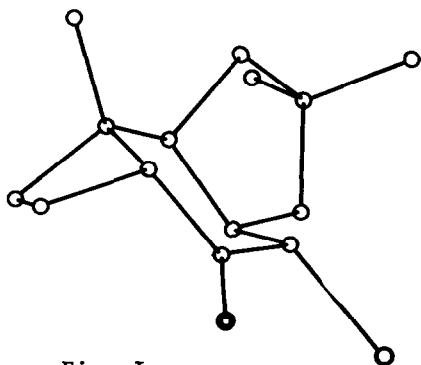
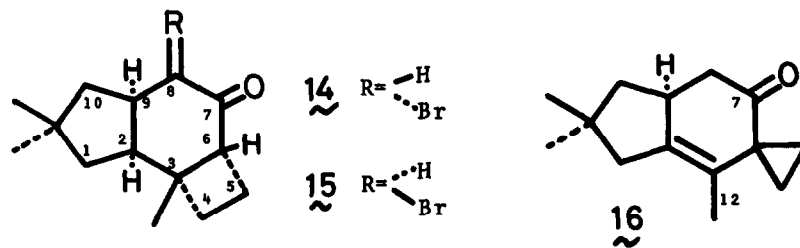
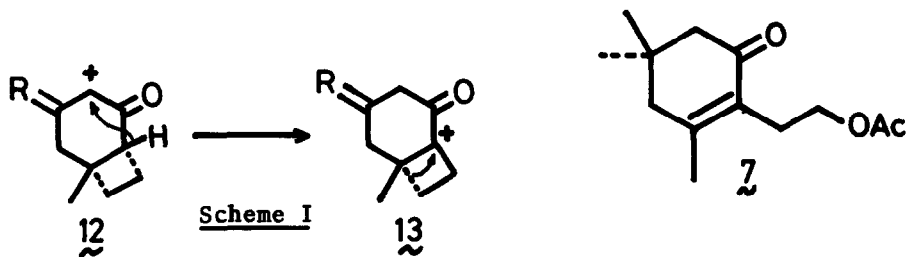
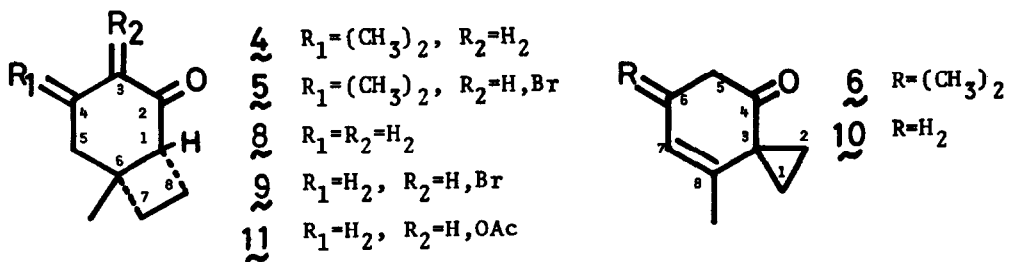
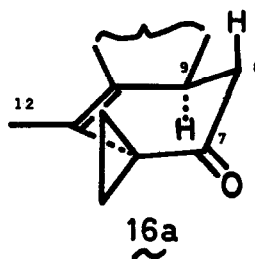


Fig. I



References and footnotes

1. $\Delta^{2(3)}$ -7-Illudenyli cation, which in turn is derived through a protoilludane compound, has been suggested as a biosynthetic precursor for illudins²; M. Anchel, T.C. McMorris and P. Singh, *Phytochemistry*, 9, 2339 (1970); J.R. Hanson, T. Marten and R. Nyfeler, *J.C.S., Perkin I*, 876 (1976).
2. T. Matsumoto, H. Shirahama, A. Ichihara, Y. Fukuoka, T. Mori and M. Watanabe, *Tetrahedron*, 21, 2671 (1965) and references cited. See also G.A. Cordell, *Chem. Rev.*, 76, 425 (1976).
3. Y. Ohfuné, H. Shirahama and T. Matsumoto, *Tetrahedron Lett.*, 4377 (1975).
4. D.C. Owsley and J.J. Bloomfield, *J.C.S., C*, 3445 (1971).
5. Satisfactory ir, nmr and mass spectral data as well as elementary analytical data were obtained.
6. Obtained as a mixture of epimers at C-3 position and used in the next step as such. The epimer was readily epimerized (AcOH/ Δ or chromatography on SiO₂) to give an equilibrium mixture. $\delta(\text{CCl}_4)$: Major isomer 5a; 1.12, 1.25, 1.38 (each s), 3.92 (s): minor isomer 5b; 4.06 (broad s). 5a/5b=3/1. Major isomer 9a; 1.25 (s), 4.26 (t, J=6Hz): minor isomer 9b; 1.40 (s), 4.20 (dd, J=3 and 4Hz). 9a/9b=1.8/1.
7. Y. Yamada, H. Uda and K. Nakanishi, *Chem. Commun.*, 423 (1966).
8. Formation of α -keto carbenium ions under special conditions; J.P. Bégue, D. Bonnet, M. Charpentier-Morize and C. Pardo, *Tetrahedron*, 31, 2505 (1975).
9. This is the first demonstration of the detailed conformation of the cis-anti-cis protoilludane skeleton. The details of the X-ray analysis will be published elsewhere.
10. The peaks were assigned as shown in the parentheses by extensive decoupling experiments.
11. A.F. Cockerill and D.M. Rackham, *Tetrahedron Lett.*, 5149 (1970).