CHEMISTRY LETTERS, pp. 989-992, 1983.

SYNTHESIS OF BICYCLO[4.3.1]DEC-2-EN-7-ONE *VIA* INTRAMOLECULAR [2+2] PHOTOCYCLOADDITION

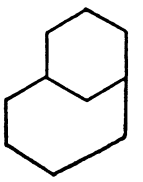
Hideharu SETO,* Shinya HIROKAWA, Yasuo FUJIMOTO, and Takashi TATSUNO

The Institute of Physical and Chemical Research, Hirosawa, Wako, Saitama 351

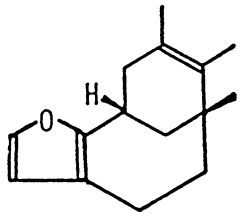
An efficient five step synthesis of bicyclo[4.3.1]dec-2-en-7-one by intramolecular [2+2] photocycloaddition of 1-acetoxy-2-(pent-4-enoyl)cyclopentene and subsequent transformation sequence of the resulting cyclobutane derivative is described.

The bicyclo[4.3.1]decane skeleton (Scheme 1; A) is a novel structural feature of natural products such as nakafuran-9[1] (Scheme 1; B), pallescensin C[2] and pallescensin D[2] which were recently isolated from some marine sponges and nudibranchs. In connection with our work on the total synthesis of these compounds, we required a simple and general method for the synthesis of reasonably functionalized bicyclo[4.3.1]decane ring systems. We wish to report here the synthesis of bicyclo[4.3.1]dec-2-en-7-one (9), a potential intermediate leading to nakafuran-9, by intramolecular [2+2] photocycloaddition of easily prepared 1-acetoxy-2-(pent-4-enoyl)cyclopentene (3) and subsequent conversion of the photoproduct (4a).

Scheme 1



A

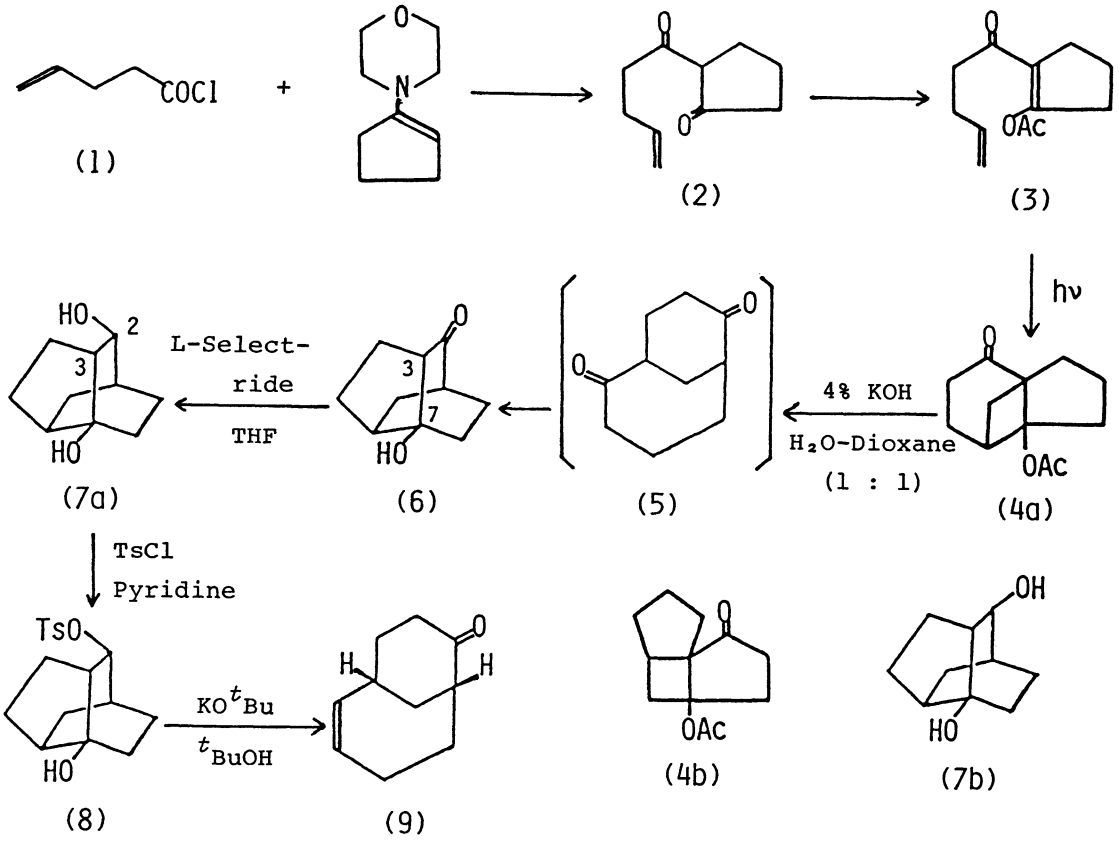


B

The starting material, enol acetate (3)[3] [a colorless oil, bp 80–83.5 °C/0.08 mmHg], was prepared from the acid chloride (1) by the usual way in 65% overall yield [i, 1.2 equiv. of 1-morpholinocyclopentene, 1.2 equiv. of triethylamine, chloroform, r.t., overnight, then 36% hydrochloric acid, water, reflux, 5 h; ii, 1.5 equiv. of acetyl chloride, pyridine, 0 °C, 4 h]. Irradiation of (3)[4] (1.4×10^{-2} mol·l^{-1}) in diethyl ether with a 300 W medium-pressure mercury lamp equipped with Pyrex filter under an argon stream at -60 – -50 °C for *ca.* 40 h afforded the desired "crossed"

cycloaddition product (4a)[8] in high isolated yield [colorless prisms, mp 73.5–74 °C (lit.,[4] 74–75 °C), 74.8%] together with the "straight" adduct (4b)[8] [colorless prisms, mp 78.5–79 °C (lit., [4] 78–79 °C), 7.8%]. These photoproducts were easily separated by column chromatography on silica gel. Hydrolytic cleavage of the acetoxy group of (4a) with 4% potassium hydroxide in dioxane/water, 1:1, at r.t. for 1.5 h gave directly the ketol (6)[8] [colorless needles, mp 121–123 °C, 86.6%] instead of forming desired bicyclo[4.3.1]decan-2,7-dione (5) which was presumably the transient intermediate. However, it is expected that the cleavage of the C_3–C_7 bond in (6) leading to bicyclo[4.3.1]decane skeleton can be readily accomplished by Grob fragmentation[5] of diol monotosylate (8), because the C_2–tosyloxy leaving group and the C_3–C_7 bond are arranged in antiperiplanar on the basis of Dreiding model consideration. In fact, this expectation proved to be true as follows.

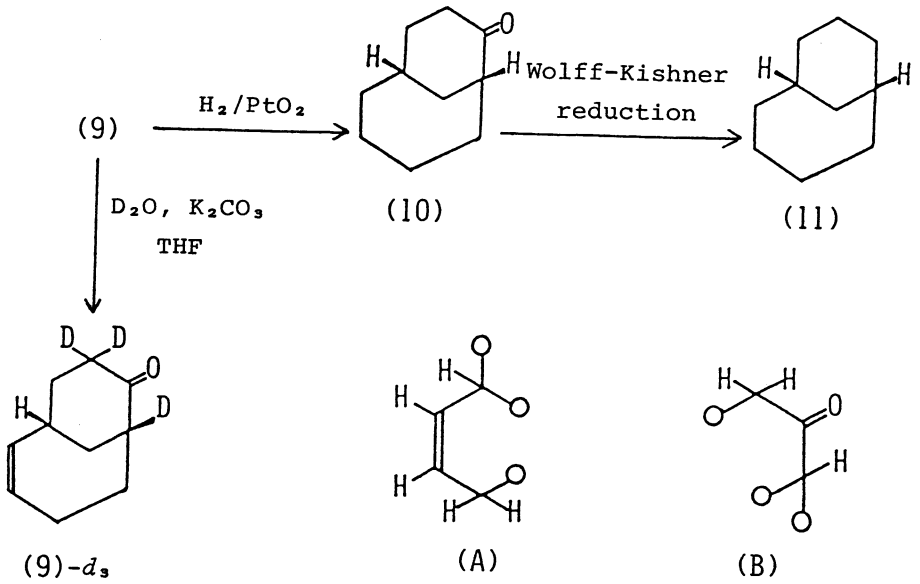
Scheme 2



Reduction of (6) with 2.5 equiv. of L-Selectride in tetrahydrofuran at −78 °C for 3 h occurred exclusively from the sterically less hindered side to afford the diol (7a)[8] [colorless needles, mp 143–144 °C, 93.7%]. On the other hand, sodium borohydride reduction of (6) in ethanol at 0 °C led to a 5:2 mixture of (7a) and (7b)[8] [colorless granules, mp 142–143.5 °C, total yield 90.4%] which were separated

by column chromatography on silica gel. The stereochemical evidence of each diols were obtained from their ^{1}H-NMR spectra [$J_{C_2\text{-}H,\ C_3\text{-}H}$ = 9.5 Hz in (7a) and 3.5 Hz in (7b)]. Tosylation of (7a) with 1.3 equiv. of *p*-toluenesulfonyl chloride in pyridine at r.t. for overnight gave the diol monotosylate (8)[8] [colorless needles, mp 98–99.5 °C, 92.4%]. Finally, when (8) was treated with 3.0 equiv. of potassium *t*-butoxide in *t*-butyl alcohol at 40 °C for 1 h, to meet to our expectation, the Grob fragmentation proceeded smoothly to afford bicyclo[4.3.1]dec-2-en-7-one (9)[8] [a colorless oil, 81.9%]. The structure of (9) was established as follows (Scheme 3).

Scheme 3



Catalytic hydrogenation of (9) [1 atm hydrogen, platinum oxide, diethyl ether, r.t.] followed by Wolff-Kishner reduction of the resulting ketone (10)[8] [10% hydrazine monohydrate, cat. amount of acetic acid, diethylene glycol, 80–90 °C, then potassium hydroxide, 190–200 °C] afforded a known hydrocarbon, bicyclo[4.3.1]-decane (11)[6], confirming the carbon skeleton. Deuteration of (9) [potassium carbonate, deuterium oxide, tetrahydrofuran, reflux] gave (9)-d_3[8], suggesting the partial structure B. The partial structure A was given by the coupling pattern of the vinyl protons of its ^{1}H-NMR spectrum [δ: 5.71(1H, d/d/d/d, J= 11.5, 7, 3, and 1.5 Hz), 5.81(1H, d/t, J= 11.5 and 5.5 Hz)]. Moreover, the signal pattern of the allylic protons unchanged on deuteration indicated that A and B units were not adjacent to each other. Thus, the structure (9) was sole possible one for this compound.

As described, the synthesis of bicyclo[4.3.1]dec-2-en-7-one (9) was achieved in five steps and 46% overall yield from readily available enol ester (3). Further

studies on generalization of this route to a variety of substituted bicyclo[4.3.1]-dec-2-en-7-one derivatives and on the conversion of (9) into (±)-nakafuran-9 are in progress.

References

1) G. Schulte, P. J. Schever, and O. J. McConell, *Helv. Chim. Acta*, 63, 2159 (1980).
2) G. Cimino, S. De Stefano, A. Guerriero, and L. Minal, *Tetrahedron Lett.*, 1975, 1425.
3) (3) contained large amount of the corresponding *exo*-cyclic enol esters; however, this appeared not to affect the subsequent photoaddition, because these enol esters were equilibrated on irradiation and the *endo*-isomer (3) was selectively trapped by photoaddition; for a close analogy, see E. Wachsen and K. Hartke, *Chem, Ber.*, 108, 683 (1975); W. Oppolzer and T. Godel. *J. Am. Chem. Soc.*, 100, 2583 (1978).
4) The same photolysis in hexane has been published independently by Pattenden *et al.* who obtained (4a) and (4b) in a ratio of 3:2 ; M. J. Begley, M. Mellor, and G. Pattenden, *J. Chem. Soc., Chem. Commun.*, 1979, 235. We examined the effect of temperature and solvent on this photolysis, and found that above conditions were optimum to obtain (4a) selectively. These regiochemical outcome will be reported elsewhere.
5) C. A. Grob and P. W. Schiess, *Angew. Chem., Int. Ed. Engl.*, 6, 1 (1967); C. A. Grob, *ibid.*, 8, 535 (1969); mechanisms and stereochemistry are discussed therein.
6) ^{13}C-NMR ($CDCl_3$) δ= 34.6(t), 32.7(t), 32.1(t), 30.5(d), 27.9(t), and 19.4(t) (lit.,[7] 34.55, 32.66, 32.01, 30.37, 27.86, and 19.31).
7) K. J. Shea and S. Wise, *J. Am. Chem. Soc.*, 100, 6519 (1978).
8) All compounds gave satisfactory analytical and spectral properties. Selected data for (4a), (4b), (6), (7a), (7b), (8), and (9) are as follows:
(4a): IR ($CHCl_3$) 1724, 1702 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ= 1.52–2.61(12H), 1.99(3H, s), 3.03–3.11(1H, m); ^{13}C-NMR ($CDCl_3$) δ= 20.9(q), 22.8, 25.2, 26.7, 27.4, 32.8, and 36.3(each t), 39.2(d), 67.9, 88.6, 169.7, and 210.5(each s).
(4b): IR ($CHCl_3$) 1724 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ= 1.45–2.77(13H), 1.98(3H, s); ^{13}C-NMR ($CDCl_3$) δ= 21.2(q), 24.9, 27.1, 30.1, 37.7, 37.9, and 38.6(each t), 33.1(d), 62.2, 85.6, 169.5, and 216.3(each s).
(6): IR ($CHCl_3$) 3590, 1710 cm^{-1}; ^{13}C-NMR ($CDCl_3$) δ= 24.3, 26.1, 26.7, 31.5, and 32.1(each t), 40.5, 40.9, and 58.4(each d), 80.4 and 218.1(each s).
(7a): IR (KBr) 3260 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ= 1.22–2.17(15H), 4.11(1H, br d, J=9.5 Hz).
(7b): IR (KBr) 3320, 3270 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ= 1.00–2.22(15H), 3.64(1H, br d, J=3.5 Hz).
(8): ^{1}H-NMR ($CDCl_3$) δ= 1.15–2.11(14H), 2.45(3H, s), 4.76(1H, br d, J=10 Hz), 7.33(2H, d, J= 8 Hz), 7.79(2H, d, J=8 Hz).
(9): IR ($CHCl_3$) 1688 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ= 1.79(1H, d/d/d/d, J=14.5, 10, 6, and 4.5 Hz), 1.84–2.13(5H, m), 2.15(1H, d/t/d, J=14, 3, and 2 Hz), 2.28(1H, d/m, J=16 Hz), 2.43(1H, t/t/t, J=12, 5.5, and 1.5 Hz), 2.51(1H, d/d/d, J=16, 13.5, and 6.5 Hz), 2.71(1H, m), 2.77(1H, br q, J=5.5 Hz), 5.71(1H, d/d/d/d, J=11.5, 7, 3, and 1.5 Hz), 5.81(1H, d/t, J= 11.5 and 5.5 Hz); ^{13}C-NMR (C_6D_6) δ= 26.1, 31.6, 31.6, 34.1, and 37.0(each t), 34.3, 47.3 , 130.3, and 133.8(each d), 212.0(s).

(Received April 13, 1983)