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-7one by intramolecular [2+2] photocycloaddition of 1-acetoxy-2-(pent-4-enoy1)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-9¹⁾ (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-4enoy1)cyclopentene (3) and subsequent conversion of the photoproduct (40).

Scheme 1





The starting material, enol acetate (3)³⁾ [a colorless oil, bp 80-83.5 °C/0.08 mmHg], was prepared from the acid chloride (]) 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 x 10^{-2} mol·1⁻¹) 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 (40)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 (40) 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 fragmentation⁵ 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 $(70)^{8}$ [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 (70) 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 ¹H-NMR spectra $[J_{C_2-H}, C_3-H] = 9.5$ Hz in (70) and 3.5 Hz in (7b)]. Tosylation of (70) 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 '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.*, <u>108</u>, 683 (1975); W. Oppolzer and T. Godel. J. Am. Chem. Soc., <u>100</u>, 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., <u>1979</u>, 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) ${}^{13}C-NMR$ (CDCl₃) 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., <u>100</u>, 6519 (1978).
- All compounds gave satisfactory analytical and spectral properties. Selected data for (4a), (4b), (6), (7a), (7b), (8), and (9) are as follows:
 - (4a): IR (CHCl₃) 1724, 1702 cm⁻¹; ¹H-NMR (CDCl₃) δ= 1.52-2.61(12H), 1.99(3H, s), 3.03-3.11(1H, m); ¹³C-NMR (CDCl₃) 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 (CHCl₃) 1724 cm⁻¹; ¹H-NMR (CDCl₃) δ = 1.45–2.77(13H), 1.98(3H, s); ¹⁹C-NMR (CDCl₃) 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 (CHCl₃) 3590, 1710 cm⁻¹; ¹³C-NMR (CDCl₃) 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; ¹H-NMR (CDCl₃) δ = 1.22–2.17(15H), 4.11(1H, br d, J=9.5 Hz).
 - (7b): IR (KBr) 3320, 3270 cm⁻¹; ¹H-NMR (CDCl₃) δ = 1.00–2.22(15H), 3.64(1H, br d, J=3.5 Hz).
 - (8): ¹H-NMR (CDC1_s) 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 (CHCl₃) 1688 cm⁻¹; ¹H-NMR (CDCl₃) 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 Hž), 5.81(1H, d/t, J= 11.5 and 5.5 Hz); ¹³C-NMR (C₆D₆) 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).

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