
An Unusual Base-catalysed Rearrangement of an α -Ethoxycarbonylethyl (or α -Cyanoethyl) Cyclic β -Keto Ester

Zhuo-Feng Xie, Izumi Nakamura, Hiroshi Suemune, and Kiyoshi Sakai*
Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka 812, Japan

Treatment of the title compounds (3), (7), and (8) with potassium t-butoxide afforded the unusual rearrangement products (5), (9), and (10).

It is generally accepted that, under basic conditions, a compound with an active methylene at the γ -position to the carbonyl function, *e.g.* (3), may undergo a zip reaction to afford two ring-expanded products *via* the four-membered intermediate (A) (see Scheme 1), instead of retro-Michael cleavage.¹ In continuation of studies on ring-expansion reactions,² we have found a novel, unexpected rearrangement.

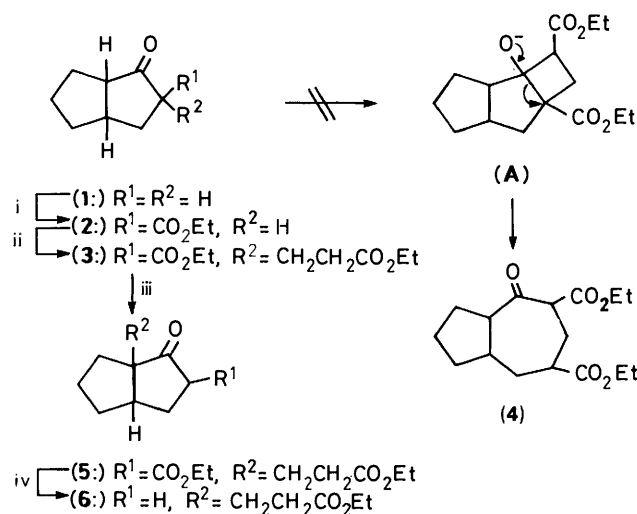
Ethoxycarbonylation of bicyclo[3.3.0]octan-2-one (1)³ with ethyl cyanofornate afforded (2) (70%) which upon Michael addition with ethyl acrylate gave a single product (3). Treatment of the latter with Bu'OK in Me₂SO at 25 °C gave three components two of which were identified as the retro-Michael cleavage product (2) (20%) and unchanged (3) (12%). The ¹H n.m.r. spectrum of the third component (22%), obtained as an inseparable stereoisomeric mixture, showed remarkable differences from that of (3). A newly formed quaternary carbon was observed at 58.92 p.p.m. [(3) 61.80 p.p.m.] in its ¹³C off-resonance n.m.r. spectrum, which suggests that this is not the expected compound (4), but the rearrangement product (5). The g.c.-m.s. analysis also offered additional proof (fragment peak: 225 (*M*⁺ - CO₂Et), 123 [225 - CH₂CH₂CO₂Et] for the assigned structure (5). Decarboxylation⁴ of (5) with NaCl-

Me₂SO-H₂O/150 °C afforded (6) (66%), the structure of which was supported by spectroscopic data g.c.-m.s., 270 MHz ¹H n.m.r., ¹³C n.m.r., and long range 2D ¹H-¹³C COSY spectrum).†

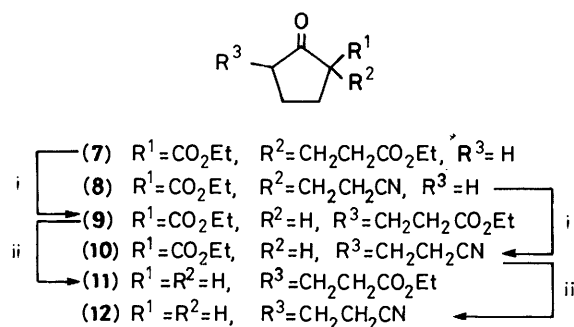
This unprecedented rearrangement was also observed in the cyclopentanone systems (7) and (8) which on treatment with Bu'OK in Me₂SO afforded (9) (57%) and (10) (47%) respectively. These were converted into the corresponding decarboxylated compounds (11) and (12)‡ (Scheme 2). With the six- and seven-membered ring systems (13) and (14), the rearrangement failed to take place, only retro-Michael cleavage

† All compounds gave satisfactory spectroscopic data. For selected data: (6); $\delta_{\text{H}}(\text{CDCl}_3)$ 1.24 (t, *J* 7.1 Hz, 3-H), 1.45–2.50 (m, 15 H), 4.11 (q, *J* 7.1 Hz, 2-H); $\delta_{\text{C}}(\text{CDCl}_3)$ 14.2 (q), 24.9 (t), 25.3 (t), 30.3 (t), 31.0 (t), 33.4 (t), 35.9 (t), 37.5 (t), 46.3 (d), 59.3 (s), 60.3 (t), 173.4 (s), and 224.5 (s); $\nu_{\text{max}}(\text{neat})$ 2 950 and 1 730 cm⁻¹; *m/z* (e.i.-m.s.) 224 (*M*⁺), 196, 179, and 123 (Found: *M*⁺, 224.1407. Calc. for C₁₃H₂₀O₃: 224.2992).

‡ Chemical and spectroscopic characteristics are in full agreement with that of the authentic samples prepared by alkylation of pyrrolidin-1-ylcyclopentene with ethyl acrylate and acrylonitrile, respectively, see G. Stork, A. Brizzolara, H. Landesman, J. Szmuszowicz, and R. Terrell, *J. Am. Chem. Soc.*, 1963, **85**, 207.



Scheme 1. Reagents and conditions: i, EtOCOCN–lithium di-isopropylamine (LDA)/THF, $-78^\circ C$, 70%; ii, Bu^tOK/Bu^tOH, ethyl acrylate, $25^\circ C$, 65%; iii, Bu^tOK/Me₂SO, $25^\circ C$, 22%; iv, NaCl–Me₂SO–H₂O, $150^\circ C$, 66%.



Scheme 2. Reagents and conditions: i, Bu^tOK/Me₂SO, $25^\circ C$, (9) (57%), (10) (63%); ii, NaCl–Me₂SO–H₂O, $150^\circ C$: (11) 46% and (12) 76%.

products (15) and (16) being isolated (Scheme 3). This finding suggests that the reaction may involve an intramolecular rearrangement. We believe that the quasi-axial bond of the side chain in the five-membered ring (7) plays an important role in suppressing the retro-Michael reaction.* In addition, this bond can adopt an appropriate trajectory⁵ for a reverse [3.3] sigmatropic rearrangement⁶ to the proximal carbonyl to

* It seems to be reasonable to assume that methoxycarbonyl ethyl (or cyanoethyl) function in six- and seven-membered rings occupies the axial configuration, and the overlap between the carbonyl π -orbital and the σ^* -orbital of C_a–C_b should then facilitate cleavage of the C_a–C_b bond (see Figure).

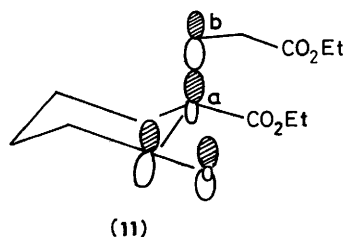
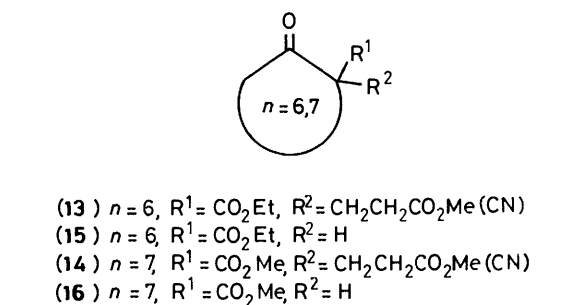
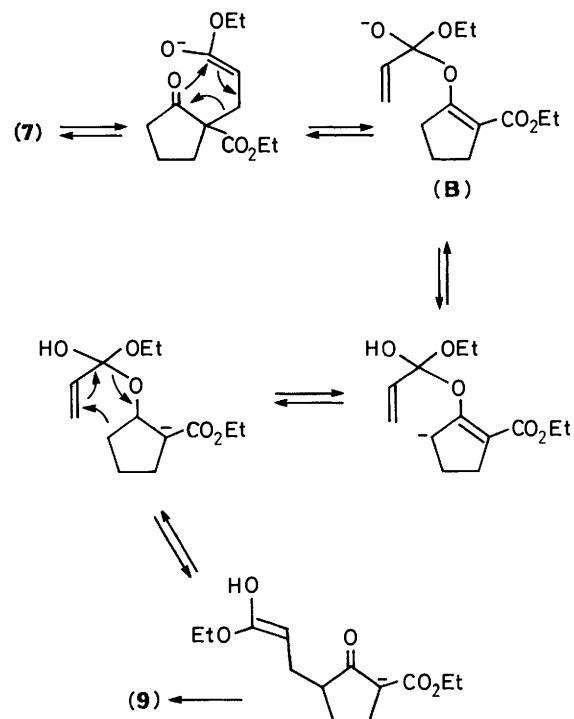


Figure.



Scheme 3.



Scheme 4.

generate the intermediate (B). Thus, subsequent rearrangement⁷ as shown in Scheme 4 may afford (9).

Experimental

1 β -Ethoxycarbonyl ethyl-3-ethoxycarbonyl-5 β H-bicyclo-[3.3.0]octan-2-one (5).—Compound (3) (180 mg, 0.61 mmol) in Me₂SO (1.5 ml) was added dropwise with stirring to Bu^tOK (82 mg, 0.73 mmol) in dry Me₂SO (2 ml) at $20^\circ C$. Stirring was continued for 40 min at $20^\circ C$ after which the reaction was quenched by acetic acid (0.25 ml). The reaction mixture was diluted with brine and extracted with AcOEt. The AcOEt extract was washed with 5% aqueous NaHCO₃ and brine, dried, and evaporated under reduced pressure to leave an oil, which was purified by flash column chromatography on silica gel. The fraction eluted with 5% AcOEt in hexane (v/v) afforded (2) (24 mg, 20%), (5) (40 mg, 22%) as a colourless oil, and recovered (3) (22 mg, 12%). For (5): ν_{max} (neat) 3 400, 1 730, and 1 680 cm^{-1} ; δ (CDCl₃) 4.21, 4.20 (3:2) (2 H, q, J 7.1 Hz), 4.11 (2 H, q, J 7.1 Hz), 3.37 (3 H, t, J 8.6 Hz), 2.80–1.61 (13 H, m), 1.30, 1.26 (3:2) (3 H, t, J 7.1 Hz), and 1.24 (3 H, t, J 7.1 Hz); 296 (M^+), 250, 196, 179, and 122.

References

- 1 M. Susse, J. Hajicek, and M. Hesse, *Helv. Chim. Acta*, 1985, **68**, 1986; P. Dowd and S.-C. Choi, *J. Am. Chem. Soc.*, 1987, **109**, 6548; T. Sugawara and I. Kuwajima, *Tetrahedron Lett.*, 1985, **26**, 5571.
- 2 Z.-F. Xie, H. Suemune, and K. Sakai, *J. Chem. Soc., Chem. Commun.*, 1988, 612; Z.-F. Xie, H. Suemune, and K. Sakai, *ibid.*, 1988, 1638.
- 3 N. Jones and H. T. Taylor, *J. Chem. Soc., Chem. Commun.*, 1959, 4017.
- 4 A. P. Krapcho, *Synthesis*, 1982, 805.
- 5 J. E. Baldwin, *J. Chem. Soc., Chem. Commun.*, 1976, 734.
- 6 For retro-Claisen rearrangements, see M. T. Hughes and R. O. Williams, *J. Chem. Soc., Chem. Commun.*, 1968, 587; A. D. Baxter, S. M. Roberts, F. Scheinmann, B. J. Wakefield, and R. D. Cockroft, *J. Am. Chem. Soc.*, 1969, **91**, 2815; E. J. Corey and J. E. Munroe, *ibid.*, 1982, **104**, 6129.
- 7 For recent reviews on [3.3] sigmatropic rearrangements, see F. E. Ziegler, *Acc. Chem. Res.*, 1988, **88**, 1423; M. J. S. Dewar and C. Jie, *J. Am. Chem. Soc.*, 1989, **111**, 511.

Received 15th March 1989

(Accepted 18th July 1989); Paper 9/03035B