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A NOVEL SYNTHESIS OF METHYL dl-JASMONATE[1]

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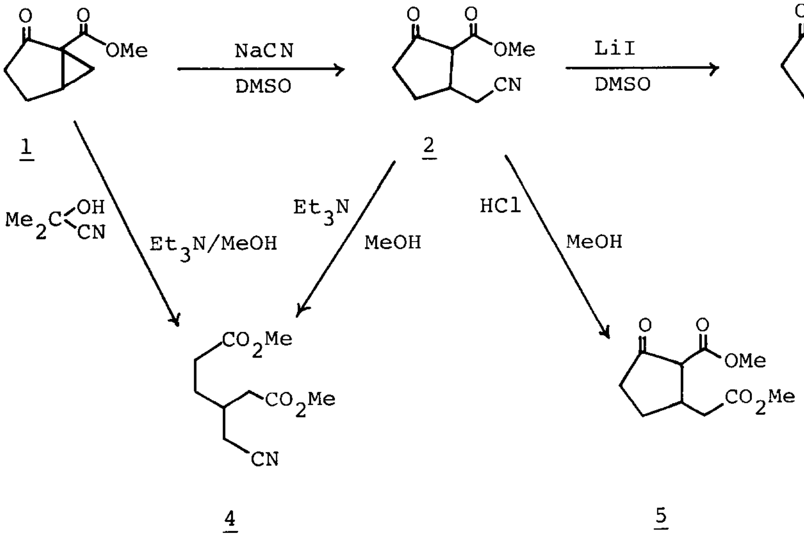
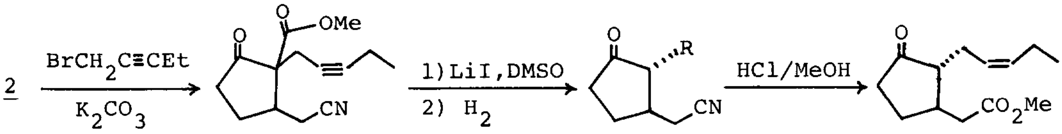
Considerable interest has recently been focused on the nucleophilic ring-opening reaction of geminally activated cyclopropanes[2] and the reactions with thiols[3] or amines[4] were utilized as a crucial step for construction of complex molecules. In this paper, we wish to report the ring-opening reaction of 2-oxobicyclo[3.1.0]hexane-1-carboxylate with cyanide anion[5] and an application of the reaction to the synthesis of methyl dl-jasmonate[6] which is an essential constituent found in jasmine oil[7].

The starting methyl 2-oxobicyclo[3.1.0]hexane-1-carboxylate (1) was prepared from methyl 3-oxo-6-heptenoate through diazotization and then intramolecular carbenoid addition[3a]. When 1 was treated with acetone cyanohydrin in methanol in the presence of triethylamine for 12 hrs at 100° in a sealed tube, there was obtained dimethyl 3-cyanomethyladipate (4) [bp 130∿135°/0.2 mmHg, ν_{max} 2240, 1740 cm^{-1}; nmr (CCl_4) δ1.43∿2.70 (m, 9H), 3.62, 3.65 (s, 2x3H)] in almost quantitative yield. This means that though the desired ring-opening of cyclopropane moiety in 1 occurs, the cleavage of cyclopentanone ring[8] in the resulting product also proceeds under the reaction conditions. After several trials, a suitable condition leading to the desired ring-opening product was found. Thus the bicyclo ester 1 was treated with 1.1 equivalent of sodium cyanide in dimethyl sulfoxide (DMSO) at 10∿20° for 24 hrs and then the reaction mixture was quenched with acetic acid-water (1:1). Thin layer chromatography of the resulting mixture indicated the presence of single product. However, this product was found to be too soluble in aqueous layer. Thus, without washing with water, the mixture was directly submitted to column chromatography (silica gel : ethyl acetate-n-hexane) to afford methyl 5-cyanomethyl-2-oxo-cyclopentane-1-carboxylate 2 in 69% yield; mp 49∿50°; ν_{max} 2250, 1755, and 1725 cm^{-1}. As the nmr spectrum of 2 was too complex to be analyzed due to the presence of keto-enol equilibrium and possibly cis-trans isomerism, its structure was finally confirmed by following reactions.



Decarboxylation of 2 by heating in DMSO in the presence of lithium iodide afforded 3-cyanomethyl-cyclopentanone 3 in 76% yield: bp 85∿86°C/0.1 mmHg; ν_{max} 2245, 1740 cm^{-1}, thus supporting the presence of cyclopentanone ring in 2. This observation is rather important for our purpose, because simple cyclopropane derivatives are known to be attacked by nucleophiles to the more substituted carbon[9]. Treatment of 2 with dry hydrogen chloride in methanol followed by hydrolysis of the resulting imino ester hydrochloride with water[10] gave the diester 5 in 59% yield. The diester 5 has already been prepared by S. Torii et al.[5h] and was used as a precursor to methyl dl-jasmonate[5a]. The cleavage of cyclopentanone ring was confirmed by treating 2 in methanol in the presence of triethylamine under reflux for 12 hrs to afford the nitrile diester 4 (96% yield).

As an alternative and new approach to methyl dl-jasmonate, we have examined the following reaction sequence.



6

7, R=CH$_2$C≡C·Et

8, R=CH$_2$CH$\overset{cis}{=}$CH·Et

9

The β-keto ester 2 was condensed with 1-bromo-2-pentyne[11] in acetone in the presence of potassium carbonate under reflux to afford the corresponding C-alkylated product 6 in 85% yield: mp 100∿101°C; ν_{max} 2250, 1753, 1730 cm^{-1}; nmr (CDCl$_3$) δ1.10 (t, J=6.5Hz, 3H), 1.90∿3.09 (m, 11H), 3.67 (s, 3H). The ester 6 was decarboxylated by treatment with lithium iodide in DMSO at 130°C for 3 hrs to give the *trans*-2,3-disubstituted cyclopentanone 7 in 85% yield: bp 133∿135°C/0.5 mmHg; ν_{max} 2250, 1749 cm^{-1}; nmr (CDCl$_3$) δ1.09 (t, J=6.5Hz, 3H) 1.06∿2.88 (m, 12H). Partial hydrogenation of 7 over Lindlar catalyst in methanol produced 8 in 90% yield: bp 110∿112°C/0.2 mmHg; ν_{max} 2248, 1748 cm^{-1}; nmr (CCl$_4$) δ0.97 (t, J=7Hz, 3H), 1.52∿3.00 (m, 12H), 4.95∿5.80 (m, 2H). The cyano group in 8 was finally converted into methyl ester function by treatment with dry hydrogen chloride in methanol followed by hydrolysis and there was obtained the desired methyl dl-jasmonate 9 in 84% yield: bp 116∿119°C/0.5 mmHg. All spectral data of the resulting jasmonate were exactly identical with those reported[6].

REFERENCES

1) Presented at the 34th Annual Meeting of Japan Chemical Society, Hiratsuka, Japan, April, 1976.

2) S. Danishefsky and R. K. Singh, J. Amer. Chem. Soc., **97**, 3239 (1975), and references cited therein.

3) (a) K. Kondo, E. Hiro, and D. Tunemoto, Tetrahedron Letters, 4489 (1976); (b) D. Tunemoto, N. Araki, and K. Kondo, ibid., 109 (1977); (c) K. Kondo, T. Umemoto, Y. Takahatake, and D. Tunemoto, ibid., 113 (1977).

4) S. Danishefsky, R. Doehner, ibid., 3031 (1977), and references cited therein.

5) (a) S. M. Roberts, Chem. Commun., 948 (1974); (b) J. C. Gilbert, T. Luo, and R. E. Dauis, Tetrahedron Letters, 2545 (1975).

6) (a) E. Demole and M. Stoll, Helv. Chim. Acta, 45, 692 (1962); (b) K. Sisido, S. Kurozumi, and K. Utimoto, J. Org. Chem., 34, 2661 (1969); (c) L. Givaudan et Cie, S. A. Genève, Brevet Ouest Allemand 2,008,878 (1970); Chem. Abstr., 73, 109363d (1970); (d) G. Büchi and B. Egger, J. Org. Chem., 36, 2021 (1971); (e) A. I. Meyers and N. Nazarenko, ibid., 38, 175 (1973); (f) P. Ducos and F. Rouessac, Tetrahedron, 29, 3233 (1973); (g) H. Tanaka and S. Torii, J. Org. Chem., 40, 462 (1975); (h) S. Torii, H. Tanaka, and T. Mandai, ibid., 40, 2221 (1975); (i) F. Johnson, K. G. Paul, and D. Favara, German Patent 2,508,295 (1975); Chem. Abstr., 84, 59783v (1976); (j) A. E. Greene and P. Crabbé, Tetrahedron Letters, 4867 (1976); (k) T. Kitahara, T. Warita, K. Mori, and M. Matsui, The Abstract of the 1977th Meeting of the Agricultural Chemical Society of Japan, p352 (1977); (e) H. J. Monteiro, J. Org. Chem., 42, 2324 (1977).

7) E. Demole, E. Lenderer, and D. Mercier, Helv. Chim. Acta, 45,675 (1962).

8) H. O. House, "Modern Synthetic Reactions", 2nd edition, W. A. Benjamin, INC., Menlo Park, California, 1972, p514.

9) S. Danishefsky and G. Rovnyak, J. Org. Chem., 40, 114 (1975).

10) For example, see B. M. Trost, M. Preckel, and L. M. Leichter, J. Amer. Chem. Soc., 97, 2224 (1975).

11) A. A. Kraevskii, I. K. Sarycheva, and N. A. Preobrazhenskii, Zh. Obshch. Khim., 33, 1831 (1963); Chem. Abstr., 61, 14518 (1964).