The CH_2Cl_2 was washed with saturated NaCl solution, dried (K_2CO_3), and concentrated on a rotary evaporator to give 0.69 g (84% crude) of **2**. This was distilled to give 0.31 g (38%) of pure **2**: bp 110 °C (0.07 mm); ^1H NMR ($CDCl_3$) δ 0.95–2.02 (m, 8, H_3, H_6, H_7, and NH_2), 2.12 (broad s, 1, H_1), 2.45 (d, 1, H_4), 2.54–3.14 (m, 2, H_2 and H_5), 7.14 (q, *endo*-py β-H), 7.27 (q, *exo*-py β-H), 8.47 (q, 2, py α-H).

Anal. Calcd for $C_{12}H_{16}N_2$: C, 76.55; H, 8.56; N, 14.87. Found: C, 76.67; H, 8.58; N, 14.90.

Similarly, hydrolysis of 0.1662 g of **1b** in 5 mL of EtOH and 5 mL of concentrated HCl gave 0.1206 g (89% crude) of **2b**: ^1H NMR ($CDCl_3$) δ 0.95–1.95 (m, 8, H_3, H_6, H, and NH_2), 2.08 (broad s, 1, H_1), 2.37 (d, 1, H_4), 2.59 (t, 1, H_{5x}), 2.99 (1, 1, H_{2n}), 7.09 (q, 2, (q, 2, *endo*-py β-H), 8.45 (q, 2, py α-H).

2-*exo*-6-(4-Pyridinyl)bicyclo[2.2.1]heptan-2-amine (4). A solution of 2.17 g (0.00943 mol) of **6** in 30 mL of EtOH and 30 mL of concentrated HCl was heated under reflux for 66 h. Workup in the same manner as the previous experiment gave 1.02 g (58% crude) of an oil which was distilled to give 0.21 g (12%) of **4a**: bp 111 °C (0.07 mm); ^1H NMR ($CDCl_3$) δ 0.95–2.15 (multiplets, 8, H_3, H_5, H_7, and NH_2), 2.35 (broad s, 1, H_4), 2.62 (broad s, 1, H_{6n}), 3.09 (1, J = 5 Hz, 1, H_{2n}), 3.19 (s, 1, H_1), 7.20 (q, 2, py β-H), 8.52 (q, 2, py α-H).

Anal. Calcd for $C_{12}H_{16}N_2$: C, 76.55; H, 8.56; N, 14.87. Found: C, 76.41; H, 8.71; N, 14.80.

2-(4-Pyridinyl)bicyclo[2.2.1]heptane (5). A solution of 10.24 g (0.0602 mol) of **3** in 300 mL of EtOH was hydrogenated with 5% Pd/C on a Parr apparatus at 60 psi. After 1 h, H_2 uptake had ceased and the solution was filtered and concentrated on a rotary evaporator to give 10.14 g of a liquid which was distilled to give **5**: bp 63–83 °C (0.03–0.05 mm); ^1H NMR ($CDCl_3$) δ 1.00–1.70 (m, 7, H_{3x}, H_5, H_6, and H_7), 2.00 (m, 1, H_{3n}), 2.40 (m. 2, H_1 and H_4), 3.20 (m, 1, H_2), 7.14 (q, 2, py β-H), 8.50 (q, 2, py α-H).

Anal. Calcd for $C_{12}H_{15}N$: C, 83.18; H, 8.72; N, 8.08. Found: C, 83.04; H, 8.79; N, 8.26.

Registry No.—**1b**, 69631-86-3; **2a**, 6963-87-4; **2b**, 69631-88-5; **3a**, 69631-89-6; **3a** hydrochloride, 69631-90-9; **3b**, 69631-91-0; **3b** hydrochloride, 69631-92-1; **4a**, 69668-79-7; **5a**, 69631-93-2; **5b**, 69631-94-3; **6a**, 69631-95-4; **7**, 7242-92-4; cyclopentadiene, 542-92-7; 4-vinylpyridine, 100-43-6; acetonitrile, 75-05-8.

References and Notes

(1) J. B. Grutzner, M. Jautelat, J. B. Dence, R. A. Smith, and J. D. Roberts, *J. Am. Chem. Soc.*, **92**, 7107 (1970).
(2) C. J. Cavallito and A. P. Gray, U.S. Patent 3 409 626, 1968.
(3) The chemical shifts for H_{2n} and H_{2x} of the *exo*- and *endo*-*N*-acetylnorbornan-2-amines are δ 3.75 and 4.10.
(4) G. D. Sargent, *Q. Rev., Chem. Soc.*, **20**, 301 (1966).
(5) H. C. Brown, "The Non-Classical Ion Problem", Plenum Press, New York, 1977.

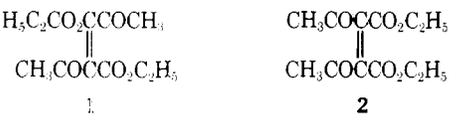
Synthesis and Structure Proof of Diethyl Diacetylmaleate and Diethyl Diacetylfumarate

Subhash C. Airy, Craig Martin, and John M. Sullivan*

Department of Chemistry, Eastern Michigan University, Ypsilanti, Michigan 48197

Received November 20, 1978

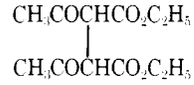
When we became interested in obtaining diethyl diacetylfumarate (**1**) as a synthetic intermediate, we found that it was first reported in 1885[1] and in three subsequent publications.[2-4] All of these procedures involved the dimerization of an ethyl acetoacetate moiety, usually via an α-monosubstituted or a α,α-disubstituted intermediate. In all of these syntheses, yields were quite low and no support was offered for the assigned trans stereochemistry. We therefore undertook the task of repeating the synthesis of this alleged fumarate, of synthesizing the previously unreported diethyl diacetylmaleate (**2**), and of obtaining proof of the stereochemistry of these compounds from their vibrational spectra.



1

2

The alleged fumarate (**1**) was readily obtained by the method of Tronov et al.,[4] and its trans stereochemistry was verified and will be discussed shortly. The maleate (**2**) was synthesized quite by accident by the oxidation of diethyl diacetylsuccinate (**3**). The latter compound, prepared as a possible precurser for **1** and **2**, surprisingly showed no evidence of enolization in the IR or NMR. In order to see whether a degree of enolization too small to show in the IR and NMR spectra was occurring, an attempt was made to induce H/D exchange for the methine hydrogens by adding a small amount of D_2O and H_2SO_4 to the CCl_4 solution used for the NMR spectrum. Although this did result in the disappearence of the methine signal from the NMR spectrum, a repetition of the experiment using H_2O–H_2SO_4 also caused the methine signal to disappear! Further investigation revealed that oxidation of the diethyl diacetylsuccinate (**3**) to diethyl diacetylmaleate (**2**) and not H/D exchange was the cause of the methine hydrogens' disappearence. Evidence for the structure of **2** included readily rationalized IR, Raman, mass, and NMR spectra and elemental analysis. This unusual acid-catalyzed oxidation would not occur in ether–H_2SO_4 or in CCl_4–concentrated HCl. Thus the strong acid H_2SO_4 and not the weaker H_3O^+ or protonated ether is needed. Normal dehydrogenation conditions such as heating with platinum or palladium failed to induce the reaction.



3

The vibrational spectra of **1** and **2** corroborated their stereochemistries. Comparing the C=C stretching peaks at 1600–1645 cm^{-1} gave the expected results; i.e., this peak was much more intense in **2**, which has no center of symmetry, than in **1** which has a center of symmetry. In the Raman spectra this peak was intense for both compounds. A similar result occurred in the 900–1050 cm^{-1} region. **2** shows moderate skeletal absorptions at 940 and 1030 cm^{-1} in both the IR and Raman spectra. **1** also shows moderate peaks at 940 and 1030 cm^{-1} in the Raman spectrum, but these peaks are extremely weak in the IR specturm. Another tetrasubstituted ethylene, diethylstilbesterol, has been reported to show similar results in the 900–1050 cm^{-1} region when its cis and trans isomers are compared.[5]

Experimental Section

Instrumentation. Melting points are uncorrected and were determined on a Mel-Temp instrument. IR spectra were recorded on Beckman Models IR-8 and IR-12, NMR spectra on a JEOL C-60 HL, Raman spectra on a Cary-83, and mass spectra on a Dupont 21-490. Elemental analyses were obtained from Spang Microanalytical Laboratory, Eagle Harbor, Mich.

Diethyl Diacetylsuccinate (3). This compound was synthesized by a modification of the method reported by Dann et al.[3] Sodium ethyl acetoacetate was prepared by reacting sodium metal (2.2 g, 0.096 mol) with freshly distilled ethyl acetoacetate (13.0 g, 0.1 mol) in dry benzene at 6 °C. The contents were warmed until the benzene solution was clear, and ethyl 2-chloroacetoacetate (16.5 g, 0.1 mol) was added dropwise with stirring over a 15-min period. The reaction mixture was then refluxed overnight. The sodium chloride precipitate that formed during the reaction was filtered off. The filtrate was allowed to sit in an open beaker, and after several days crystals of **3** separated and were recrystallized from petroleum ether. The yield was 3.5 g (13.5%): mp 89 °C (lit.[6] mp 88–89 °C); NMR (CCl_4Me_4Si) δ 1.28 (t, 6 H, J = 7.8 Hz), 2.33 (s, 6 H), 4.15 (q, 4 H, J = 7.8 Hz), 4.6 (s, 2 H); IR (mineral oil) 1725, 1360, 1282, 1242, 1169, 1136 (sh), 1031, 1014, 866 cm^{-1}; MS *m/e* (rel intensity) 258 (3), 213 (18), 174 (20), 173 (100), 167 (62), 166 (56), 145 (42), 128 (20), 127 (100), 125 (28), 117 (22), 99 (59), 97 (20).

0022-3263/79/1944-1891$01.00/0

Diethyl Diacetylmaleate (2). To **3** (0.10 g, 0.39 mmol) dissolved in CCl_4 (3 mL) was added concentrated H_2SO_4 (0.2 g), and the mixture was agitated for 2 min. Water (7 mL) was added, and the CCl_4 layer was washed three times with water and dried over anhydrous Na_2SO_4. After evaporation of the solvent, a viscous liquid was obtained in quantitative yield: bp 119–122 °C (0.5 mm); NMR (CCl_4–Me_4Si) δ 1.28 (t, 6 H, J = 7.7 Hz), 2.40 (s, 6 H), 4.2 (q, 4 H, J = 7.7 Hz); IR (mineral oil) 1725, 1605 (strong), 1418, 1390, 1380, 1305, 1280 (sh), 1210, 1090, 1025, 940, 900, 845, 780, 777 (sh), 740 cm^{-1}; MS *m/e* (rel intensity) 256 (25), 210 (36), 209 (93), 183 (54), 182 (100), 154 (25), 89 (86), 44 (100). Anal. Calcd for $C_{12}H_{16}O_6$: C, 56.24; H, 6.29. Found: C, 56.31; H, 6.32.

Diethyl Diacetylfumarate (1). This compound was prepared in 10% yield by the method of Tronov et al.:[4] mp 94 °C (lit.[1] 95.5–96 °C); NMR (CCl_4–Me_4Si) δ 1.28 (t, 6 H, J = 7.7 Hz), 2.40 (s, 6 H), 4.2 (q, 4 H, J = 7.7 Hz); IR (mineral oil) 1728, 1635 (weak), 1450, 1415, 1360, 1300 (sh), 1250, 1100, 1050, 1025, 950, 800 cm^{-1}. Anal. Calcd for $C_{12}H_{16}O_6$: C, 56.24; H, 6.29. Found: C, 56.02; H, 6.13.

Registry No.—**1**, 69622-58-8; **2**, 69622-59-9; **3**, 2049-86-7; sodium ethyl acetoacetate, 19232-39-4; ethyl 2-chloroacetoacetate, 609-15-4.

References and Notes

(1) F. Just, *Ber.*, **18**, 2636 (1885).
(2) H. Lohaus, *Justus Liebigs Ann. Chem.*, **50**, 130 (1934).
(3) O. Dann, E. Pietschmann, and W. Dimmling, *Arch. Pharm. Ber. Dtsch. Pharm. Ges.*, **292**, 508 (1959).
(4) B. V. Tronov and V. M. Aksencko, *J. Gen. Chem. USSR (Engl. Transl.)*, **26**, 1569 (1956).
(5) S. C. Airy and J. E. Sinsheimer, unpublished work, College of Pharmacy, University of Michigan, Ann Arbor, Mich. 48109.
(6) A. P. Terentev and L. A. Yanovskaya, *J. Gen. Chem. USSR (Engl. Transl.)*, **18**, 1159 (1948).

S-Nucleoside Photorearrangement. Access to Pyridine Pseudonucleosides

Jean-Louis Fourrey* and Patrick Jouin

Institut de Chimie des Substances Naturelles, C.N.R.S., 91190 Gif sur Yvette, France

Received August 14, 1978

Among the naturally occurring pseudonucleosides (*C*-nucleosides),[1] a few examples of pyridine *C*-nucleosides are known.[2] An understanding of the behavior of this structure type is relevant in light of the recently observed antibiotic character of pyridine nucleosides.[3] We report on the synthesis of pyridine *C*-nucleosides via an application of the thionucleoside photorearrangement.[4]

Preliminary experiments established that the (benzylthio)pyridines **1a** and **4a**[5] undergo photorearrangement to give the *C*-benzyl isomers. Thus, irradiation of **1a** afforded a mixture which on treatment with diazomethane gave 3-benzyl-2-(methylthio)pyridine (**2a**) and 5-benzyl-2-(methylthio)pyridine (**3a**) in yields of 26 and 14%, respectively. The structural assignments for the isomers **2a** and **3a** are based on NMR data. The H-6 proton in the isomer **3a** is a broad singlet (8.2 ppm), while the H-6 proton in **2a** is a quartet centered at 8.14 ppm with $J_{5,6}$ = 5 Hz and $J_{4,6}$ = 2 Hz, respectively. Similarly, irradiation of **4a** and subsequent methylation of the photoproducts gave 3-benzyl-4-(methylthio)pyridine (**5a**, 30%), the structure of which was evident from inspection of its NMR spectrum. This spectrum shows H-2 as a singlet (8.18 ppm) and the two other ring protons as doublets ($J_{5,6}$ = 5 Hz) centered at 8.30 (H-6) and 6.95 ppm (H-5), respectively.

Reaction of 2-mercaptopyridine (**1b**) with 1,2,3,5-tetra-*O*-acetyl-D-ribofuranose (BF_3:Et_2O, dichloroethane, 0 °C) yielded the thionucleoside **1c** (85%). A β configuration is proposed for **1c** from consideration of the method of synthesis.[6] Irradiation of **1c** afforded a mixture of pyridinethiones and nucleoside **6c** (5%). Deacetylation of the latter (NaOMe–MeOH) gave the known β nucleoside **6** (R = ribofuranosyl).[7] The other constituents of the mixture were separated and characterized after methylation (CH_2N_2), deoxyacetylation, and treatment with 2,2-dimethoxypropane (acetone, TsOH). Two anomeric pairs of isomeric pyridine pseudonucleoside acetonides **2d** (9%) and **3d** (5%) were obtained. Inspection of the spectral data (MS, UV, NMR) indicated that derivatives **2d** and **3d** were disubstituted pyridines resulting from a photoinduced migration of the ribosyl moiety from sulfur toward C-3 and C-5, respectively. In addition to the *S*-methyl signals, the NMR spectra of the two anomers **2d** display three quartets due to H-4, H-5, and H-6 with the following coupling constants: $J_{5,6}$ = 5.0 Hz, $J_{4,5}$ = 7.6 Hz, and $J_{4,6}$ = 1.75 Hz. In the case of derivatives **3d**, the lowest field signals are due to H-6 and appear as doublets with a small coupling constant ($J_{4,6}$ < 2.6 Hz).

To establish the configuration at C-1′[8] of the four isomeric pseudonucleosides, we have used a combination of the three following criteria:[9] (i) the chemical shift differences for the acetonide methyls ($\Delta\delta_{CH_3}$),[10] (ii) the respective chemical shifts for the anomeric protons,[11] and (iii) the signal pattern (multiplet or triplet) of the H-4′ proton.[12] Although application to pseudonucleosides of these criteria devised in the nucleoside series might be hazardous, they do give in our case, where both the α and β anomers are available, good evidence to make a reasonable configurational assignment. In fact, the differences of chemical shift ($\Delta\delta_{CH_3}$) due to the acetonide methyls were 0.18 and 0.09 ppm for the α-**2d** and β-**2d** anomers, respectively. Expectedly, the H-1′ signal for the α anomer **2d** is found at lower field than that for the β anomer, and the H-4′ signal appears as a triplet in the case of the α derivative and as a multiplet in the other. For compounds **3d** the acetonide methyl resonance criterion could not be used as the methyl shift difference was higher than 0.15 ppm for both anomers. The tentative attribution has been made on the basis of the H-1′ and H-4′ criteria. Thus, the amorphous compound **3d**, which exhibits H-1′ at 4.82 ppm and H-4′ as a multiplet, was given the β configuration while its crystalline isomer, which shows H-1′ at 5.02 ppm and H-4′ as a triplet, favors an α configuration. For the β and α anomers the $\Delta\delta_{CH_3}$ values were 0.24 and 0.18 ppm, respectively.

As nucleoside **6c** was obtained as the β anomer, it would suggest that the photorearrangement takes place with retention of chirality at C-1′. In the cases of the C-3 and C-5

0022-3263/79/1944-1892$01.00/0