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Reaction of Aliphatic Dicarboxylic Acids with Acyl Chlorides in the Presence of Aluminum Chloride[1)]

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The treatment of succinic acid with lauroyl or stearoyl chloride gave the five-membered β-diketone (II) substituted with a long chain at the α-position, together with a trimer (III) of the acyl chloride. Bicyclo[3.3.1]nonane-2,4-dione (VI) substituted with a methyl or ethyl group at the C_3-position was prepared from cyclohexane-1,3-dicarboxylic acid (V) and propionyl or butyryl chloride, respectively. D-Camphoric acid afforded an unexpected product, 4-acyl-2,2,3-trimethyl-3-cyclopentenecarboxylic acid (IX), on reaction with acyl chloride. Although acetyl chloride gave no product on treatment with succinic acid, it afforded 3-acetylbicyclo[3.2.1]octane-2,4-dione (XI), 3-acetylbicyclo[3.3.1]nonane-2,4-dione (VId), and 2-acetylcyclohexane-1,3-dione (XII) on reaction with the corresponding dicarboxylic acids.

Keywords——β-diketone; cyclic β-diketone; bicyclic β-diketone; dicarboxylic acid; aluminum chloride; acyl chloride; bicyclo[3.*n*.1]alkane-2,4-dione

In the synthesis of cyclic vinylogous esters or vinylogous thioesters, many cyclic β-diketones have been used as starting materials. In particular, alkyl-substituted, five-membered β-diketones (I) were prepared by the reaction of a succinic acid derivative and an appropriate acyl chloride (3 mol eq) in the presence of aluminum chloride (3 mol eq) in nitromethane. This method was found and developed by Schick and his co-workers.[2)] However the scope and limitations of this reaction have not yet been established. If the method can be applied to various dicarboxylic acids and acyl chlorides, it would be a useful tool to obtain β-diketone, which are important intermediates for organic syntheses.[3)]

The reaction of succinic acid with higher acyl halides was examined to obtain cyclopentane-1,3-dione bearing a long chain carbon unit at the C_2-position (II). The treatment of succinic acid with caproyl chloride gave 2-butylcyclopentane-1,3-dione (IIa) in 40.0% yield.[4)] In the case of lauroyl chloride, 2-decylcyclopentane-1,3-dione (IIb) was obtained in 27.4% yield, along with a trimer of lauroyl chloride, 13-decylpentacosane-12,14-dione (IIIb), in 19.6% yield. In the case of stearoyl chloride, 2-hexadecylcyclopentane-1,3-dione (IIc) and 19-hexadecylheptatricontane-1,3-dione (IIIc) were obtained in 15.2 and 13.1% yields, respectively. Compound IIc exhibited a broad carbonyl band at 1540 cm^{-1} in the infrared (IR) spectrum, a parent peak at *m/e* 322 in the mass spectrum (MS), and a singlet signal at δ 2.96 due to the $C_{4,5}$ -methylene protons in the nuclear magnetic resonance (NMR) spectrum. On the other hand, IIIc exhibited carbonyl bands at 1730 (strong) and 1700 (weak) cm^{-1} in the IR spectrum, a parent peak at *m/e* 772 in the MS, and a triplet signal (J=7 Hz) due to the C_{19}-methine proton in the NMR spectrum. Compounds IIb and IIc were weakly positive in the ferric chloride test and gave the corresponding vinylogous esters, 2-decyl-3-methoxy-2-cyclopentenone (IVa) and 2-hexadecyl-3-methoxy-2-cyclopentenone (IVb), on treatment with diazomethane, while IIIb and IIIc were negative in this test, and inert to diazomethane. Thus, the method could be applied to the preparation of cyclopentane-1,3-

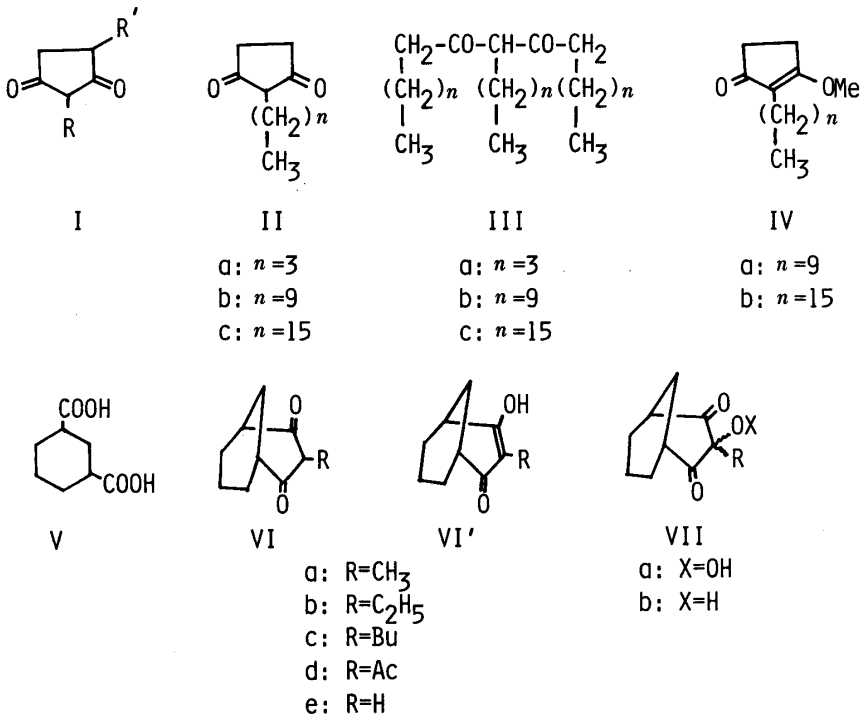

Chart 1

dione bearing a long-chain alkyl group at the C_2-position, but the yields were not satisfactory and the undesired trimers were obtained as a by-product.

To apply this method to the synthesis of a bicyclic β-diketone, *cis*-cyclohexane-1,3-dicarboxylic acid (V) as a starting material was prepared directly from isophthalic acid by catalytic reduction in the presence of platinum oxide in acetic acid under medium pressure.[5] The acid V was treated with propionyl chloride to give 3-methylbicyclo[3.3.1]nonane-2,4-dione (VIa) in 37.5% yield. In chloroform, VI was found to be in equilibrium with 4-hydroxy-3-methyl-3-bicyclo[3.3.1]nonen-2-one (VI'a) in the ratio of 3:7, while in the solid state this compound was wholly in the enol form. Thus, it was found that this method could be applied to the synthesis of a bicyclic β-diketone. On standing for a long time, this compound was gradually oxidized to its hydroperoxide, 3-hydroperoxy-3-methylbicyclo[3.3.1]nonane-2,4-dione (VIIa), which exhibited hydroxy and carbonyl bands at 3340, 1730, and 1710 cm^{-1} in the IR spectrum and a singlet at δ 1.46 due to the C_3-methyl protons in the NMR spectrum. Compound VIIa was treated with aqueous sodium hydroxide followed by addition of an excess of diazomethane to give dimethyl cyclohexane-1,3-dicarboxylate. In addition, VIIa was reduced quantitatively to 3-hydroxy-3-methylbicyclo[3.3.1]nonane-2,4-dione (VIIb) by using zinc dust in aqueous acetic acid. In a similar manner, 3-ethylbicyclo[3.3.1]nonane-2,4-dione (VIb) was also prepared from V and butyryl chloride in a low yield. An attempt to obtain 3-butylbicyclo[3.3.1]nonane (VIc) from V and caproyl chloride was unsuccessful and a trimer of caproyl chloride, 7-butyltridecane-6,8-dione (IIIa) was obtained.[6] When D-camphoric acid (VIII) was chosen as a substrate, abnormal products was obtained. The reaction with propionyl chloride or with butyryl chloride gave 2,2,3-trimethyl-4-propionyl-3-cyclopentenecarboxylic acid (IXa) or the 4-butyryl homologue (IXb) in 34.0 and 63.8% yields, respectively. Compound IXa exhibited absorption bands at 3600—2400, 1695, 1675 cm^{-1} due to the carboxyl and α,β-unsaturated carbonyl groups in the IR spectrum and an absorption maximum at 248 nm due to the unsaturated ketone in the ultraviolet (UV) spectrum. In the NMR spectrum, the signals due to both of the C_5-protons appeared as a pair of double quartets with geminal (J=14 Hz), vicinal (J=8 Hz), and homoallyl (J=2 and 1.3 Hz in each

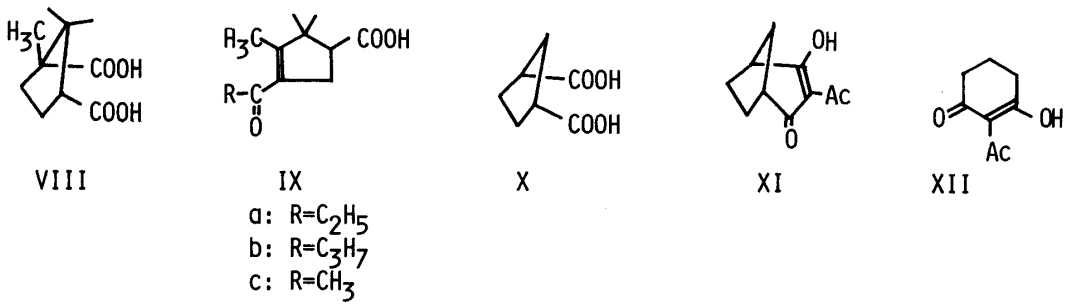

Chart 2

signal) couplings. These products were optically active. They were derived to the corresponding methyl or phenacyl esters, and furthermore the methyl esters were reduced catalytically then treated with 2,4-dinitrophenylhydrazine (2,4-DNPH) to give the corresponding dihydro 2,4-DNPH derivative. Thus, the structures of IXa and IXb were confirmed, though the mechanism of formation of these compounds remains unclear. When cyclopentane-1,3-dicarboxylic acid (X), which was prepared from norbornylene,[7] was treated with propionyl chloride, neither a normal product such as VI nor an abnormal product such as IX could be obtained.

When acetyl chloride was used as a reagent, the reaction with VIII gave 4-acetyl-2,2,3-trimethyl-3-cyclopentanecarboxylic acid (IXc) in 85.7% yield. Compound IXc showed physical data similar to those for IXa or IXb, and furthermore it exhibited in the ^{13}C-NMR spectrum quartet, triplet, doublet, singlet, and singlet signals at δ 25.91, 33.10, 52.76, 132.05, and 158.54 due to the acetyl methyl, C_5, C_1, C_4 and C_3, respectively. The reaction with V gave 3-acetylbicyclo[3.3.1]nonane-2,4-dione (VId) as an oil in 14.8% yield. Compound VId exhibited IR absorptions at 3430, 1660 and 1550 cm^{-1}. The NMR spectrum indicated that VId was wholly in the enol form (VI'd); that is, a broad singlet at δ 18.00 due to the enol proton (one proton) was observed. Attempts to convert VI'd to bicyclo[3.3.1]nonane-1,3-dione (VIe) were unsuccessful. Compound VI'd was treated with sodium borocyanohydride (SBCH) in methanol to give VIb in good yield. The physical data were nearly identical with those of the product obtained from V and butyryl chloride. In a similar fashion, X gave 3-acetyl-4-hydroxy-3-bicyclo[3.2.1]octen-2-one (XI) in 12.1% yield. Compound XI exhibited in the NMR spectrum a broad singlet (one proton) at δ 17.90 due to the enol proton. Although 2-acetylcyclopentane-1,3-dione could not be detected from the reaction of succinic acid and acetyl chloride, the formation of 2-acetyl-3-hydroxy-2-cyclohexenone (XII)[8] was confirmed in the reaction of glutaric acid with acetyl chloride. In the NMR spectrum, XII exhibited a broad singlet signal at δ 18.26 due to the enol proton. No desired product could be detected from the reaction between succinic acid and phenylacetyl chloride, 3-ethylthiopropionyl chloride or ethylthioacetyl chloride, and the reaction between propionyl chloride and sebacic acid, O-diacetyltartaric acid, or N-acetylglutamic acid was unsuccessful.

These results show that the reaction of aliphatic dicarboxylic acids and acyl chloride in the presence of aluminum chloride can be applied to the synthesis of cyclic β-diketones bearing a long alkyl chain at the α-position and of bicyclic β-diketones. On the other hand, when acetyl chloride was used, only a few cyclic or bicyclic β-diketones substituted with an acetyl group at the α-position could be prepared. Furthermore, it was found that the reaction unexpectedly suffers from strong substituent effects.

Experimental

All melting points (taken on a Kofler block) and boiling points (bath temperature) are uncorrected. IR spectra were determined by using a JASCO A 102 diffraction grating spectrophotometer; absorption data are given in cm^{-1}. UV spectra were obtained in MeOH with a Hitachi 220 spectrometer, and absorption maxima are given in nm. Gas

chromatography (GC) was carried out on a Shimadzu GC-6AM instrument with a stainless steel column packed with 5% SE-30. The N_2 gas flow was 40 ml/min. Optical rotations were taken on a JASCO DIP-140 digital polarimeter and CCl_4 was used as a solvent unless otherwise stated. NMR spectra were recorded on a Varian EM-360, JEOL PMX-60, or Varian XL-200 spectrometer with tetramethylsilane as an internal standard. The chemical shifts and coupling constants (J) are given in δ and Hz, respectively. MS were measured with a JEOL D-200 or D-300 (70 eV, direct inlet system) spectrometer. All solvents were removed by evaporation under reduced pressure after drying of the solution over anhyd. $MgSO_4$ or Na_2SO_4.

2-Butylcyclopentane-1,3-dione (IIa)——Caproyl chloride (6.4 g, 51 mmol) was added to a cooled solution of $AlCl_3$ (6.8 g, 51 mmol) in CH_3NO_2 (10 ml), and then the mixture was stirred at 80 °C for 3 h. The cold solution was poured into ice water to give a precipitate, which was collected by filtration and recrystallized from aq. MeOH. IIa: yield 40%, mp 156—158 °C (lit.[4] mp 155—157 °C).

2-Decylcyclopentane-1,3-dione (IIb) and 13-Decylpentacosane-12,14-dione (IIIb)——Under the general conditions mentioned above, a solid material was obtained from succinic acid (2 g, 17 mmol), lauroyl chloride (11.1 g, 51 mmol), and $AlCl_3$ (6.8 g, 51 mmol). It was collected by filtration and recrystallized from hexane. IIb: yield 1.11 g (27.4%), mp 136—138 °C. IR (Nujol): $\nu_{C=O}$ 1530 (br). NMR ($CDCl_3$): 0.88 (3H, t, J=6, CH_3), 1.2—1.6 (16H, m, $CH_2\times8$), 2.32 (2H, t, J=7, CH_2), 3.02 (4H, s, -$COCH_2CH_2$-). MS m/e (%): 238 (M^+, 20), 112 (2-methylcyclopentane-1,3-dione, 100), 99 (CH_3-$(CH_2)_5CH_2^+$, 23). *Anal.* Calcd for $C_{15}H_{26}O_2\cdot1/10\ H_2O$: C, 75.02; H, 11.01. Found: C, 75.06; H, 11.08. The filtrate was extracted with benzene and the organic layer was concentrated. The residue was purified through an SiO_2 column. Compound IIIb was eluted with benzene. IIIb: 3.70 g (19.6%). mp 25—28 °C (recrystallized from hexane or MeOH). IR (Nujol): $\nu_{C=O}$ 1730 (s). NMR ($CDCl_3$): 0.88 (9H, t, J=7, CH_3), 1.24 (48H, br s, CH_2), 1.4—1.7 (4H, m), 1.7—1.9 (2H, m), 2.42 (4H, t, J=8, –CH_2–CO–), 3.62 (1H, t, J=8, –CO–CH–CO–). MS m/e (%): 520 (M^+, 7), 183 ($CH_3(CH_2)_{10}C\equiv O^+$, 100), 57 ($CH_3$-$(CH_2)_2CH_2^+$, 90), 43 (Et–$CH_2^+$, 88). *Anal.* Calcd for $C_{35}H_{68}O_2$: C, 80.70; H, 13.16. Found: C, 80.73; H, 13.39. 2-Decyl-3-methoxy-2-cyclopentenone (IVa): NMR (CCl_4): 0.94 (3H, t, J=6, CH_3), 1.27 (16H, nearly s, CH_2), 2.07 (2H, t, J=6, vinyl CH_2), 2.2—2.5 and 2.5—2.8 (each 2H, pair of m, succinyl CH_2). MS m/e (%): 252 (M^+, 50), 221 (M^+ – MeO, 30), 153 (61), 139 (59), 126 (3-methoxy-2-methyl-2-cyclopentenone, 100).

2-Hexadecylcyclopentane-1,3-dione (IIc) and 19-Hexadecyltricontaheptane-18,20-dione (IIIc)——In the same manner as described in the case of lauroyl chloride, IIc (15.2%) and IIIc (13.1%) were obtained from stearoyl chloride and succinic acid. IIc: mp 106—109 °C (recrystallized from hexane). IR (Nujol): $\nu_{C=O}$ 1540 (br). NMR ($CDCl_3$): 0.87 (3H, t, J=6, CH_3), 1.1—1.5 (28H, m, $CH_2\times14$), 2.28 (2H, t, J=7, CH_2), 2.96 (4H, s, –CO–CH_2–CH_2–). MS m/e (%): 322 (M^+, 14), 112 (2-methylcyclopentane-1,3-dione, 100). *Anal.* Calcd for $C_{21}H_{38}O_2\cdot1/4\ H_2O$: C, 77.13; H, 11.87. Found: C, 77.22; H, 11.62. IIIc: mp 51—53 °C (recrystallized from hexane). IR (Nujol): $\nu_{C=O}$ 1730 (s), 1700 (w). NMR ($CDCl_3$): 0.97 (9H, t, J=6, $CH_3\times3$), 1.22 (88H, s, $CH_2\times44$), 1.58 (2H, m, CH_2), 2.42 (4H, t, J=7, $2\times CH_2$), 3.60 (1H, t, J=7, –CO–CH–CO–). MS m/e (%): 772 (M^+, 9), 743 (M^+ – Et, 16), 714 (M^+ – 2Et, 13), 531 (77), 503 (71), 57 (Et–$CH_2CH_2^+$, 71), 42 ($CH_3CH=CH_2$, 100). *Anal.* Calcd for $C_{53}H_{104}O_2$: C, 82.31; H, 13.55. Found: C, 82.42; H, 13.43. 2-Hexadecyl-3-methoxy-2-cyclopentenone (IVb): NMR (CCl_4): 0.90 (3H, t, J=6, CH_3), 1.26 (28H, nearly s, CH_2), 2.2—2.4 and 2.5—2.8 (each 2H, pair of m, succinyl CH_2), 3.92 (3H, s, OMe). MS m/e (%): 336 (M^+, 27), 307 (M^+ – Et, 29), 305 (M^+ – OMe, 18), 153 (59), 139 (63), 126 (3-methoxy-2-methyl-2-cyclopentenone, 100).

3-Methylbicyclo[3.3.1]nonane-2,4-dione (VIa)——A mixture of cyclohexane-1,3-dicarboxylic acid (V, nearly pure *cis*-acid, 25 g, 145 mmol),[5] $AlCl_3$ (58 g, 435 mmol), and EtCOCl (40 g, 435 mmol) in CH_3NO_2 (20 ml) was stirred and worked up according to the general procedure. The solid material was collected by filtration and the filtrate was extracted with benzene. The benzene layer was extracted with 10% NaOH solution. The solid obtained by acidification of the aq. layer was collected, combined with the former product, and recrystallized from benzene to give pure VIa. Yield 9.0 g (37.5%), mp 177—179 °C. IR (Nujol): ν_{OH} 3100, $\nu_{C=O}$ 1600. NMR ($CDCl_3$): 1.20 (3H, d, J=7, C_3-CH_3), 1.76 (s, C_3-CH_3), 2.58 and 2.76 (br s, bridgehead H), 3.72 (q, J=7, C_3-H). MS m/e (%): 166 (M^+, 100), 111 (58), 98 (53), 67 (54), 57 (70). *Anal.* Calcd for $C_{10}H_{14}O_2$: C, 72.01; H, 8.37. Found: C, 72.26; H, 8.49.

3-Hydroperoxy-3-methylbicyclo[3.3.1]nonane-2,4-dione (VIIa)——Solid VIa (6.9 g) gradually changed on standing at room temperature for about 3 months. The crude mixture was recrystallized from benzene to give pure VIa (5.4 g). From the mother liquor, VIIa was obtained by concentration. Yield 0.5 g, mp 136—139 °C. IR (Nujol): ν_{OH} 3340, $\nu_{C=O}$ 1730, 1710, 1600. NMR ($CDCl_3$): 1.46 (3H, s, CH_3), 1.4—1.6 (1H, m), 1.78 (1H, dd, J=7, 3), 1.86 (1H, t, J=4), 1.97 (2H, dt, J=14, 3), 2.25 (2H, d, J=12), 2.58 (1H, d, J=14), 2.85 (2H, t, J=3, C_1- and C_5-H), 9.43 (1H, OH). MS m/e (%): 198 (M^+, null), 182 (M^+ – O, 8), 181 (13), 153 (23), 135 (58), 81 (100). *Anal.* Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.58; H, 7.06.

This compound (0.1 g) was warmed with 10% NaOH (3 ml) for 1 h. After being acidified with 5% HCl, the mixture was extracted several times with AcOEt. The residue obtained after evaporation of the extracts was esterified with an excess of CH_2N_2. The product was purified through an SiO_2 column to give dimethyl cyclohexane-1,3-dicarboxylate (60 mg) from the benzene–AcOEt (9 : 1) fraction. GC (200 °C), t_R: 1.1 min. NMR (CCl_4): 1.1—2.6 (10H, m), 3.60 (6H, s, OMe). MS m/e (%): 200 (M^+, 7), 169 (M^+ – OMe, 34), 168 (43), 140 (56), 109 (31), 108 (35), 81 (100). This compound was identified as dimethyl cyclohexane-1,3-dicarboxylate by comparison with an authentic sample prepared from V.

Zinc dust (1 g) was added to a solution of VIIa (0.1 g) in 10% aq. AcOH at room temperature. After being stirred overnight, the mixture was filtered and the filtrate was extracted with AcOEt. The organic layer was dried and concentrated. The crystalline residue was recrystallized from CCl_4 to give pure 3-hydroxy-3-methylbicyclo[3.3.1]nonane-2,4-dione (VIIb). mp 109—113 °C, 90 mg. IR (Nujol): ν_{OH} 3500, $\nu_{C=O}$ 1700, 1710, 1730. NMR ($CDCl_3$): 1.0—1.4 (1H, m), 1.56 (3H, s, CH_3), 1.5—1.7 (1H, m), 1.7—2.0 (2H, m), 2,0 (1H, dt, J=14, 2.5), 2.20 (2H, dm, J=12), 2.68 (1H, dm, J=14), 2.8—3.0 (2H, m, C_1- and C_3-H), 3.71 (1H, s, OH). MS *m/e* (%): 182 (M^+, 51), 140 (M^+-42, 75), 100 (62), 43 ($CH_3C\equiv O^+$, 100). *Anal.* Calcd for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.72; H, 7.57.

3-Ethylbicyclo[3.3.1]nonane-2,4-dione (VIb)——A mixture of V (0.7 g, 4 mmol), $AlCl_3$ (1.7 g, 12 mmol), and butyryl chloride (1.5 g, 12 mmol), in CH_3NO_2 (5 ml) was stirred and worked up according to the general procedure. The solid material was collected and recrystallized from water. Yield 57 mg (7.9%). mp 188—192 °C. IR (Nujol): ν_{OH} 3300—2300, $\nu_{C=O}$ 1560, δ_{CO} 1090. NMR ($CDCl_3$): 0.8—1.1 (3H, m, $CH_2\underline{CH_3}$), 1.4—2.1 (7.4H, m), 2.32 (1.2H, q, J=8, $\underline{CH_2}CH_3$), 2.1—2.3 (1.4H, m), 2.4—2.9 (2H, m, bridgehead H), 3.56 (0.4H, t, J=4, C_3-H), 5.84 (0.6H, br s, OH). MS *m/e* (%): 180 (M^+, 100), 165 (M^+-CH_3, 23), 112 (78), 97 (44), 55 (67). *Anal.* Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.33; H, 8.83. Compound VIb was treated with an excess of CH_2N_2–Et_2O. The product was microdistilled. bp < 150 °C (12 mmHg). GC (150 °C), t_R: 6.7 min. NMR ($CDCl_3$); 0.95 (3H, t, J=7, $\underline{CH_3}CH_2$), 1.4—1.9 (8H, m), 2.19 (1H, dm, J=12), 2.31 (2H, q, J=7, $\underline{CH_2}CH_3$), 2.45 and 2.98 (each 1H, nearly s, C_1- and C_5-H, respectively), 3.83 (3H, s, OMe). MS *m/e* (%): 195 (M^++1, 59), 194 (M^+, 100), 179 (M^+-CH_3, 72), 140 (41), 111 (51). *Anal.* Calcd for $C_{12}H_{18}O_2\cdot 1/3\ H_2O$: C, 71.96; H, 9.40. Found: C, 72.00; H, 9.13.

7-Butyltridecane-6,8-dione (IIIa)——The acid V (2.0 g, 12 mmol), caproyl chloride (4.8 g, 36 mmol), and $AlCl_3$ (4.8 g, 36 mmol) were reacted in CH_3NO_2 under the general conditions. The reaction mixture was poured into ice-water. The starting material was recovered by filtration of this solution and then the filtrate was extracted with benzene. The organic layer was washed with aq. $NaHCO_3$ and brine, and then concentrated. The oily residue was purified through an SiO_2 column. Compound IIIa was eluted from benzene. Yield 840 mg (26.9%). bp < 120 °C (5 mmHg, lit[6] bp 131—132 °C (2 mmHg)). GC (200 °C), t_R: 2.9 min. IR (film): $\nu_{C=O}$ 1720, 1695. NMR (CCl_4): 0.86 (9H, t, J=6, CH_3), 2.36 (4H, t, J=6, CH_2CO), 3.50 (1H, t, J=6, CO–CH–CO). MS *m/e* (%): 268 (M^+, 2), 170 (31), 99 ($BuCH_2C\equiv O^+$, 100).

2,2,3-Trimethyl-4-propionyl-3-cyclopentenecarboxylic Acid (IXa)——D-Camphoric acid (VIII, 1.4 g, 7 mmol), propionyl chloride (2.0 g, 22 mmol), and $AlCl_3$ (2.8 g, 21 mmol) were reacted in CH_3NO_2 (6 ml) under the general conditions. The reaction mixture was extracted with benzene and AcOEt. The residue obtained after concentration of the combined organic solution was purified through an SiO_2 column. From the fraction eluted with AcOEt, IXa was obtained. Yield 0.5 g (34.0%). mp 112—114 °C (recrystallized from Et_2O–hexane). IR (Nujol): ν_{OH} 3600—2450 (br), $\nu_{C=O}$ 1695, 1675, $\nu_{C=C}$ 1635. UV λ_{max}: 248, $\lambda_{max}^{MeOH-OH^-}$: 254. NMR ($CDCl_3$): 0.99 and 1.29 (each 3H, s, C_2-CH_3), 1.07 (3H, t, J=6, $CH_2\underline{CH_3}$), 1.98 (3H, br s, C_3-CH_3), 2.53 (2H, q, J=6, CH_2CO), 2.70 (1H, dd, J=14, 8, 1.3, C_5-H), 2.85 (1H, t, J=8, C_1-H), 3.04 (1H, ddq, J=14, 8, 2, C_5-H). MS *m/e* (%): 210 (M^+, 42), 181 (M^+ – Et, 100). *Anal.* Calcd for $C_{12}H_{18}O_3\cdot 1/3\ H_2O$: C, 66.65; H, 8.70. Found: C, 66.64; H, 8.56. Methyl ester: mp 37—45 °C (recrystallized from aq. MeOH). UV λ_{max} (ε): 247 (9630). $[\alpha]_D^{22}$ −57.6 (c=1.075). *Anal.* Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.73; H, 9.13.

4-Butyryl-2,2,3-trimethyl-3-cyclopentenecarboxylic Acid (IXb)——The acid VIII (1.4 g, 7 mmol), butyryl chloride (2.0 g, 19 mmol), and $AlCl_3$ (2.8 g, 21 mmol) were reacted in CH_3NO_2 (10 ml) under the general conditions. Compound IXb was obtained after work-up in a manner similar to that described for the preparation of IXa. The crude oily product was purified by micro-distillation. bp < 200 °C (5 mmHg). Yield 1.0 g (63.8%). GC (270 °C), t_R: 0.8 min. NMR ($CDCl_3$): 0.94, 1.66, and 2.50 (butyryl), 1.01 and 1.30 (each 3H, s, C_2-CH_3), 1.99 (3H, br s, C_3-CH_3), 2.6—2.8 and 2.9—3.2 (each 1H, m, C_5-H), 2.86 (1H, t, J=8, C_1-H). MS *m/e* (%): 224 (M^+, 26), 181 ($M^+-C_3H_7$, 100). Methyl ester: GC (170 °C), t_R: 4.1 min. $[\alpha]_D^{22}$ −46.7 (c=2.665). NMR ($CDCl_3$): 0.94 and 1.30 (each 3H, s, C_2-CH_3), 2.6—2.8 and 3.0—3.2 (each 1H, m, C_5-H), 2.86 (1H, t, J=9, C_1-H), 3.77 (3H, s, OMe). MS *m/e* (%): 238 (M^+, 27), 195 ($M^+-C_3H_7$, 83), 107 ($C_8H_{11}^+$ 100). *Anal.* Calcd for $C_{14}H_{22}O_3$: C, 70.55; H, 9.31. Found: C, 70.26; H, 9.23. 2,4-DNPH of the methyl ester: mp 134—137 °C (recrystallized from EtOH). MS *m/e* (%): 418 (M^+, 100), 287 (89), 107 (83). *Anal.* Calcd for $C_{20}H_{26}N_4O_6$: C, 57.40; H, 6.26; N, 13.39. Found: C, 57.42; H, 6.39; N, 13.58. Phenacyl ester: GC (270 °C), t_R: 5.3 min. $[\alpha]_D^{22}$ −6.7 (c=3.99). NMR ($CDCl_3$): 0.92, 1.61, and 2.47 (butyryl), 1.03 and 1.33 (each 3H, s, C_2-CH_3), 1.97 (3H, br s, C_3-CH_3), 2.6—2.8 (1H, m, C_5-H), 2.9—3.2 (2H, m, C_1- and C_5-H), 5.33 and 5.48 (each 1H, d, J=16, CH_2O), 7.4—7.7 (3H, m), 7.9—8.0 (2H, m). MS *m/e* (%): 342 (M^+, 11), 299 ($M^+-C_3H_7$, 32), 178 ($M^+-PhCOCH_2-CO$, 71), 135 (*m/e* 178 − C_3H_7, 100), 107 ($C_8H_{11}^+$, 81), 105 ($PhC\equiv O^+$, 63), 71 ($C_3H_7C\equiv O^+$, 86). *Anal.* Calcd for $C_{21}H_{26}O_4\cdot 1/5\ H_2O$: C, 72.89; H, 7.69. Found: C, 72.92; H, 7.59.

4-Butyryl-2,2,3-trimethylcyclopentanecarboxylic Acid——The methyl ester of IXb was hydrogenated in the presence of PtO_2 under medium pressure (3—4 atm) of H_2 for 2 h to give a crude dihydro compound. UV, only end absorption. MS *m/e* (%): 240 (M^+, 27), 208 (M^+ – MeOH, 31), 197 ($M^+-C_3H_7$, 42), 137 ($M^+-CO_2-CH_4$, 91), 109 ($C_8H_{13}^+$, 100). This product was converted into its 2,4-DNPH, which was purified on an SiO_2 column. NMR ($CDCl_3$): 0.74 (3H, s, C_2-β-Me), 1.20 (3H, s, C_2-α-Me), 0.91 (3H, t, J=9, $\underline{CH_3}$-CH_2), 1.68 (2H, m, $\underline{CH_2}$-CH_2), 1.81 (1H, m, C_5-β-H), 2.03 (1H, qd, J=7, 3), 2.39 (2H, t, J=9, CH_2-CO-), 2.55 (1H, t, J=9.5, C_4-H), 2.6—2.8 (1H, m, C_5-α-H), 2.69

(1H, ddd, J=13.5, 9.5, 3, C_4-H), 3.73 (3H, s, OMe). MS *m/e* (%): 420 (M^+, 17), 389 ($M^+ - HNO$, 13), 41 ($C_3H_5^+$, 100). High-resolution MS: Calcd for $C_{20}H_{28}N_4O_6$: 420.201. Found: 420.196.

4-Acetyl-2,2,3-trimethyl-3-cyclopentenecarboxylic Acid (IXc)——The acid VIII (1 g, 5 mmol), acetyl chloride (1.2 g, 15 mmol), and $AlCl_3$ (2.0 g, 15 mmol) were reacted in CH_3NO_2 (10 ml) under the general conditions. The crude product obtained after usual work-up was fractionated through an SiO_2 column. IXc was eluted with benzene–AcOEt (24 : 1), and recrystallized from Et_2O–cyclohexane. mp 125—128 °C. Yield 0.84 g (85.7%). IR (Nujol): ν_{OH} 3400—2400, $\nu_{C=O}$ 1730, 1695, 1660, ν 1605. $[\alpha]_D^{22}$ −69.06 (c=1.285, CH_2Cl_2). ^{1}H-NMR ($CDCl_3$): 1.00 and 1.30 (each 3H, s, C_2-CH_3), 1.98 (3H, t, J=1, C_3-CH_3), 2.25 (3H, s, Ac), 2.6—2.8 and 2.9—3.1 (each 1H, m, C_5-H), 2.85 (1H, t, J=9, C_1-H). ^{13}C-NMR ($CDCl_3$): 12.62 and 20.38 (each q, C_2-CH_3), 25.91 (q, $\underline{C}H_3CO$), 30.33 (q, C_3-CH_3), 33.10 (t, C_5), 51.20 (s, C_2), 52.76 (d, C_1), 132.05 (s, C_4), 158.54 (s, C_3), 178.93 (s, COOH), 199.10 (s, $CH_3\underline{C}O$). MS *m/e* (%): 196 (M^+, 32), 181 ($M^+ - CH_3$, 21), 163 (*m/e* 181 − H_2O, 16), 135 (*m/e* 163 − CO, 32), 43 ($CH_3C{\equiv}O^+$, 100). *Anal.* Calcd for $C_{11}H_{16}O_3$: C, 67.52; H, 8.22. Found: C, 67.54; H, 8.32. Methyl ester of IXc: bp < 130 °C (2 mmHg). IR (film): $\nu_{C=O}$ 1730, 1680, 1650, $\nu_{C=C}$ 1610. NMR ($CDCl_3$): 0.90, 1.26, 2.25 (each 3H, s, CH_3), 1.96 (3H, t, J=1, C_3-Me), 2.55—2.75 and 2.94—3.16 (each 1H, m, C_5-H), 2.82 (1H, t, J=8, C_1-H), 3.74 (3H, s, OMe). MS *m/e* (%): 210 (M^+, 18), 195 ($M^+ - CH_3$, 6), 135 ($C_8H_{11}C{\equiv}O^+$, 19), 107 ($C_8H_{11}^+$, 21). *Anal.* Calcd for $C_{12}H_{18}O_3 \cdot 1/8\ H_2O$: C, 67.82; H, 8.65. Found: C, 67.58; H, 8.36.

3-Acetyl-4-hydroxy-3-bicyclo[3.3.1]nonen-2-one (VI'd)——The acid V (1.2 g, 7 mmol) was added portionwise to a solution of $AlCl_3$ (2.8 g, 21 mmol) in CH_3NO_2 (10 ml). Acetyl chloride (1.5 ml, 21 mmol) was added to the homogeneous mixture using a syringe. Compound VI'd (201 mg, 14.8%) was obtained from the benzene fraction of the residue from the AcOEt layer. bp < 130 °C (2.5 mmHg). IR (film): ν_{OH} 3430, $\nu_{C=O}$ 1660, 1550 (br), δ_{C-O} 1005. NMR ($CDCl_3$): 1.2—2.1 (6H, m), 2.1—2.3 (2H, m), 2.60 and 2.78 (each 1H, br s, bridgehead H), 2.65 (3H, s, Ac), 18.00 (1H, s, OH). MS *m/e* (%): 194 (M^+, 100), 179 ($M^+ - CH_3$, 36), 126 ($C_6H_{11}COCH_3^+$, 75), 43 ($CH_3C{\equiv}O^+$, 97). *Anal.* Calcd for $C_{11}H_{14}O_3 \cdot 1/5\ H_2O$: C, 66.79; H, 7.34. Found: C, 66.91; H, 7.08.

VIb from VId——A pinch of bromocresol green was added to a methanolic solution of VId (154 mg, 0.79 mmol), then $NaBH_3CN$ (SBCH, 100 mg, 1.6 mmol) was added. A 1 M methanolic HBr solution was added dropwise over 1 h, maintaining a yellow color in the mixture. The mixture was stirred at room temperature for an additional 1 h, then diluted with water and extracted with AcOEt. The extract was dried and concentrated, and the residue was purified by recrystallization from benzene. Yield 137 mg (96.3%). mp 197—200 °C. The physical data were identical with those of an authentic sample.

3-Acetyl-4-hydroxy-3-bicyclo[3.2.1]octen-2-one (XI)——Cyclopentane-1,3-dicarboxylic acid (X, 1.1 g, 7 mmol), prepared from norbornylene,[7] was added portionwise to a solution of $AlCl_3$ (2.8 g, 21 mmol) in CH_3NO_2 (10 ml). Acetyl chloride (1.5 ml, 21 mmol) was added to the homogeneous mixture using syringe. Compound XI (153 mg, 12.1%) was obtained from the benzene fraction by column chromatography of the residue derived from a usual work-up using benzene extraction. bp < 130 °C (2 mmHg). IR (film): ν_{OH} 3350 (br), $\nu_{C=O}$ 1650 (br), 1550 (br). GC (130 °C), t_R: 6.7 min. (170 °C), t_R: 2.8 min. NMR ($CDCl_3$): 1.6—2.0 (3H, m), 2.0—2.3 (3H, m), 2.56 (3H, s, Ac), 2.9—3.1 (2H, m, bridgehead H), 17.90 (1H, br s, OH). MS *m/e* (%): 180 (M^+, 60), 165 ($M^+ - CH_3$, 26), 139 ($M^+ - CH_2{=}C{=}O + H$, 100), 43 ($CH_3C{\equiv}O^+$, 72). *Anal.* Calcd for $C_{10}H_{12}O_3 \cdot 1/6\ H_2O$: C, 65.56; H, 6.78. Found: C, 65.54; H, 6.59.

2-Acetyl-3-hydroxy-2-cyclohexenone (XII)——Glutaric acid (0.92 g, 7 mmol) was added portionwise to a solution of $AlCl_3$ (2.8 g, 21 mmol) in CH_3NO_2 (10 ml). Acetyl chloride (1.5 ml, 21 mmol) was added to the homogeneous mixture using a syringe. The residue obtained from the AcOEt extract was purified through an SiO_2 column to give pure XII. Yield 115 mg (10.3%). bp < 120 °C (10 mmHg). IR (film): ν_{OH} 3600—2400 (br), $\nu_{C=O}$ 1660, $\nu_{C=C}$ 1560, δ_{C-O} 1190. NMR (CCl_4): 1.9—2.4 (2H, m, C_5-H), 2.70 (3H, s, Ac), 2.4—3.0 (4H, m, C_4- and C_6-H), 18.26 (1H, br s, OH). MS *m/e* (%): 154 (M^+, 64), 98 (68), 43 ($CH_3C{\equiv}O^+$, 100). *Anal.* Calcd for $C_8H_{10}O_3 \cdot 1/3\ H_2O$: C, 59.99; H, 6.71. Found: C, 59.85; H, 6.41.

References and Notes

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