Rhodium(II)-carbenoid C–H insertion reactions in the synthesis of β-oxospirane systems

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A simple one-pot procedure is described for the preparation of spiro[4.4]nonane-2,7-dione derivatives from open chain bis(α-diazoketones) by two consecutive intramolecular Rh(II)-catalyzed carbenoid insertion reactions. With 1-diazo-4-(3-oxocycloalkyl)butan-2-ones as substrates, the methodology provides 2,7-dioxospiranes with a cyclopentane ring spiroannulated onto a five-, six- or seven-membered cycloalkane.

Introduction

Spiranes constructed from small to medium sized rings are characterized by a stiff framework and may therefore serve as a rigid scaffold for stereocontrol of pharmacophoric groups in bioorganic molecules. Appropriately substituted and enantiomeric spiranes may also be envisaged as chiral auxiliaries in dissymmetric catalytic operations. We have therefore initiated work on the preparation of selected spiranes and some studies of chemical transformations in these systems. In particular, we have reported on the use of α,α′-dioxospiro[3.3.0]nonane as substrates in palladium-catalyzed carbosubstitutions.[1,2] In this report we describe work on the construction of β,β′-dioxocarbospiranes. The products are functionalized substrates which are useful for further manipulations of the spirane system *via* oxo group activations.

Several synthetic routes are available for the preparation of α,α′-diones such as *via* spiro[4.4]nonane-1,6-diones and α,β-unsaturated derivatives thereof.[3,4] In contrast, the spiro[4.4]nonane-2,7-dione system had received little attention when this work was begun. The parent compound **4a** had been prepared by a multistep synthesis involving reductive cyclization of mercurial α,β-unsaturated cyclopentanone derivatives.[5] Part of our initial work on spiro[4.4]spirane-2,7-diones has been disclosed in a recent preliminary report.[6] Another recent report describes the preparation of spiro[4.4]nonane-2,7-dione and spiro[4.5]-decane-2,7-dione by a SmI$_2$ reductive cleavage reaction of appropriate cyclopropane derivatives,[7] and finally the latter compound as well as spiro[5.5]undecane-2,8-dione have been prepared by an acid catalyzed cyclization procedure.[8]

Results and discussion

We have based our construction of spiranes on carbenoid rhodium intramolecular C–H insertion reactions leading to spiroannulations. In Rh(II)-carbenoid C–H insertions the usual order of reactivity observed is methine > methylene > methyl.[9–11] Furthermore, the C–H insertion is normally site selective in that five-membered ring formation is normally favored and will generally take preference over the above considerations.[9,12,13] With this information to hand, we have constructed a convenient and practical method for the preparation of the spiro[4.4]nonane system from aliphatic α,α′-diazo-dicarbonyl reagents in a "one-pot" intramolecular Rh(II)-carbenoid C–H insertion reaction.[6] The substrates for the cyclization reactions, the open chain α,α′-diazo-dicarbonyl derivatives **2** were readily available from the corresponding

dicarboxylic acids, pimelic acid and methyl-substituted homologs by way of their acid chlorides and subsequent reactions with diazomethane or diazoethane in diethyl ether solution (Scheme 1). The diazo ketones **2** were isolated after
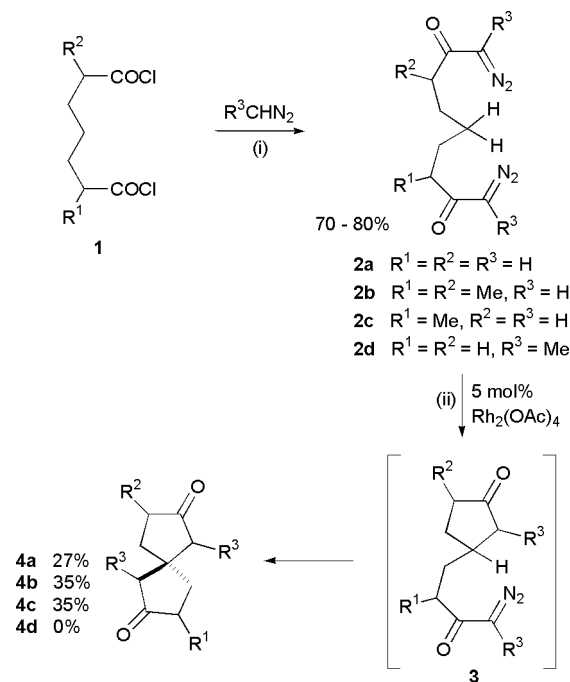
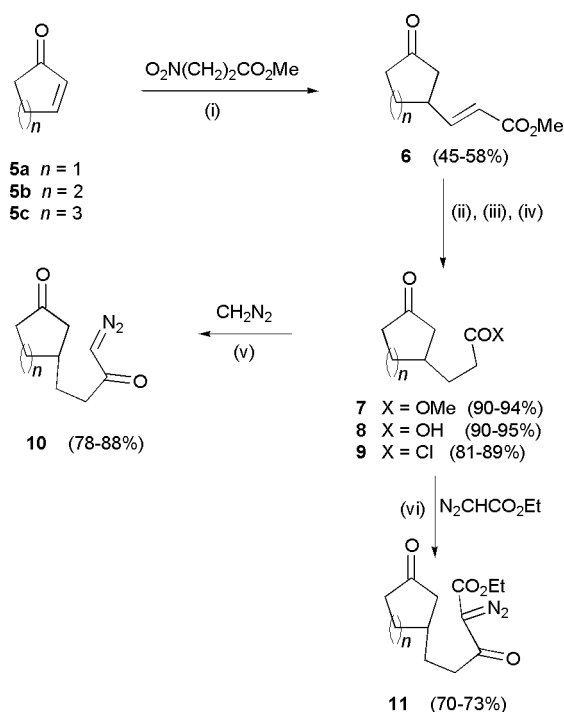**Scheme 1** *Reagents and conditions*: (i) Et$_2$O, 0 °C, 3 h; (ii) CH$_2$Cl$_2$, 20 °C, 14 h.

flash chromatography in good yields. Dirhodium tetraacetate was used as the catalyst for the intramolecular C–H insertion reactions which were run in dichloromethane solutions at ambient temperature. The spiranes **4** were isolated after flash chromatography in 27–35% overall yield. The methyl derivatives **4b** and **4c** were diastereomeric mixtures because racemic methyl-substituted pimeloyl chlorides **1b** and **1c** were used as substrates for exploring the methodology. The spirane **4d**, which has methyl groups in the two α,α′-positions, was not obtained by this procedure presumably because of unfavorable steric interactions in the formation of the spiro center. An α-methyl derivative, however, is available indirectly from an α-carboxylate derivative such as **13a** (see Scheme 4).

Intramolecular Rh(II)-carbenoid insertion into the C–H bond in methylene groups generally favors formation of five-

membered rings (*vide supra*). Therefore the cyclopentanone **3** would be expected to be the first formed product. The latter possesses a methine C–H bond in a position suitable for a second five-membered ring formation, and would be expected to undergo insertion at the methine carbon with spiroannulation faster than formation of the intermediate cyclopentanone **3**. In accordance with this postulate we did not isolate any intermediate corresponding to the cyclopentanone **3**.

The assumption that the initial product in the overall spirocyclization was a cyclopentanone led us to extend this approach to the use of appropriately substituted five-, six- and seven-membered cycloalkanones **10** and **11** (see Scheme 3) as substrates for the dirhodium(II) tetraacetate catalyzed C–H insertion. Because of the strong tendency for formation of five-membered rings over any other ring size, no attempts were made to prepare side-chains in the cycloalkanone for spiroannulation of smaller or larger rings. The methodology presented provides 2,7-dioxospiranes with a cyclopentane ring spiroannulated onto a five-, six- or seven-membered cycloalkane.

Preparation of intermediate substrates for the spiroannulation is shown in Scheme 2. α,β-Unsaturated cycloalkanones

Scheme 2 *Reagents and conditions*: (i) *t*BuOK, THF, −20 °C; (ii) H₂, 5% Pd/C, AcOH, 20 °C; (iii) LiOH, MeOH, 20 °C; (iv) (COCl)₂, benzene, 40 °C; (v) Et₂O, 0 °C, 4 h; (vi) neat, 40–60 °C, 7 h.

were β-alkylated by a Michael addition reaction using metal-lated 3-nitropropionate. Concurrent elimination to the acrylate **6** occurred under the conditions of the reaction.[14] Saturation of the olefinic double bond by catalytic hydrogenation and ester hydrolysis yielded the propionic acid **8**.[15] Subsequent treatment with oxalyl chloride furnished the acid chlorides **9** which were to become substrates for the formation of the diazoketones **10** and **11** in reactions with diazomethane and diazoacetate, respectively. Diazomethane was more reactive, with ethyl diazoacetate requiring heating in diethyl ether. Both series of diazoketones were obtained in good yields.

The C–H insertion reaction was effected by dirhodium tetraacetate catalysis in dichloromethane (Scheme 3). The yields of the diketospiranes **12** and **13** were all in the range 40–45% irrespective of the presence or absence of the carboxylic ester group. Any stereoselectivity during the spiroannulation remains unknown since the the ester products **13** were partly enolized as judged by NMR. In the two-step process from the acyclic bis(diazo)-substrate **2** in the formation of the
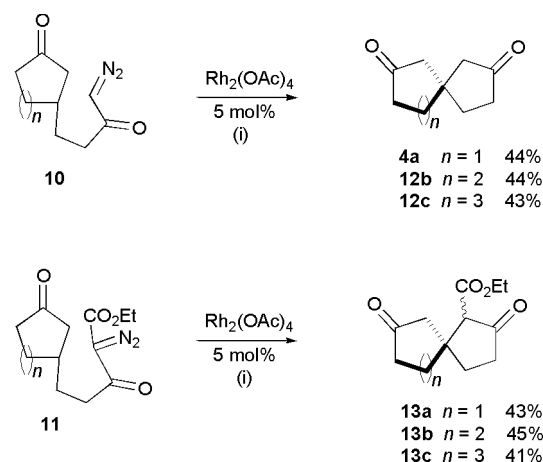
Scheme 3 *Reagents and conditions*: (i) CH₂Cl₂, 20 °C, 12 h.

dioxospiranes **4** (Scheme 1) the overall yields were in the range 27–35%. For the simplest member, **4a**, the yield was 27% which would correspond to an average 52% yield in each cyclization step (**2a**→**3a**→**4a**).

The direct spiroannulation methodology had failed (*vide supra*) to yield the α,α′-dimethyl derivative **4d** (Scheme 1). α-Methylation, however, would seem likely in the carboxylates **13** because the ester group would direct enolate formation towards the α-carbon. Subsequent treatment with an alkylating agent would lead to α-substitution. The monomethyl ester **15** was prepared in this manner from the spiro[4.4]nonane **13a** (Scheme 4). Subsequent ester hydrolysis and decarboxylation provided the monomethyl derivative **16**.
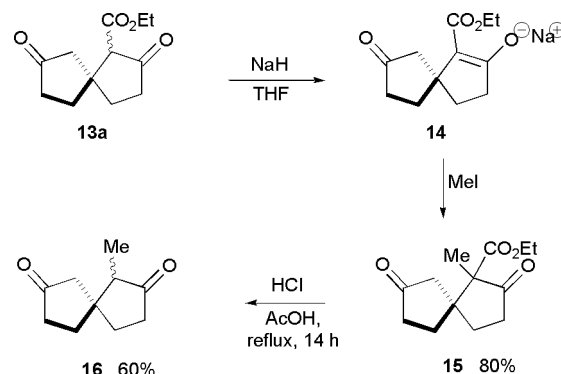
Scheme 4

In conclusion, we have developed a simple "one-pot" procedure for the preparation of spiro[4.4]nonane-2,7-dione derivatives from readily available open chain α,α′-bis(diazo)diketones. The cyclizations are effected by intramolecular Rh(II)-carbenoid insertion into a methylene C–H bond with cyclopentane formation and a subsequent cyclopentane spiroannulation by insertion into a methine C–H bond. In a more general method, the substrates for cyclization by the dirhodium(II) acetate catalyzed C–H insertion were cycloalkanones which were appropriately β-functionalized for spiroannulation onto cyclopentanones.

Experimental

The ¹H NMR spectra were recorded at 200 or 300 MHz, and the ¹³C NMR spectra at 50 or 75 MHz unless otherwise specified. The mass spectra were recorded at 70 eV under electron impact conditions (EI) and are presented as *m/z* (% rel. int.). Dry THF was distilled from sodium and benzophenone. Dry dichloromethane was distilled from calcium hydride. Ethereal diazomethane solution was prepared from Diazald.[16]

1,9-Bisdiazononane-2,8-dione 2a

Compound **2a** was synthesized according to the procedure described in ref. 17.

1,9-Bisdiazo-3,7-dimethylnonane-2,8-dione 2b

DMF (5 drops) was added to 2,6-dimethylpimelic acid[18] (9.0 g, 47 mmol) in thionyl chloride (30 ml) and the mixture heated under reflux for 6 h. Excess thionyl chloride was distilled off. Distillation of the residual material furnished 2,6-dimethyl-pimeloyl chloride (10.33 g, 96%) as a colorless liquid, bp 90–93 °C/0.5 mmHg (HRMS: M 224.0349. $C_9H_{14}Cl_2O_2$ requires 224.0348); ν_{max}(film)/cm^{-1} 1780 (C=O); δ_H(CDCl$_3$) 1.25–1.28 (6 H, d, 2 × CH$_3$), 1.37–1.6 (4 H, m, 2 × CH$_2$), 1.71–1.91 (2 H, m, CH$_2$), 2.76–2.92 (2 H, m, 2 × CH); δ_C(CDCl$_3$) 16.89 (CH$_3$), 23.80 (CH$_2$), 23.90 (CH$_2$), 32.85 (CH$_2$), 32.92 (CH$_2$), 51.07 (CH), 177.2 (C=O); m/z (EI) 224 (M$^+$, 24%), 171 (5), 161 (22), 149 (25), 133 (16), 126 (36), 105 (11), 97 (100), 69 (64).

The acid chloride **1b** (1.32 g, 0.58 mmol) in dry diethyl ether (100 ml) was added dropwise with stirring to a solution of diazomethane (1.0 g, 2.4 mmol) in diethyl ether (100 ml) at 0 °C. The reaction was allowed to proceed at 0 °C for 4 h before the solvent and excess reagent were removed by evaporation at reduced pressure. The residual material was subjected to flash chromatography using hexane–EtOAc 1:2. The product (1.09 g, 80%) was a yellowish, partly crystalline, oily material (HRMS: M 236.1302. $C_{11}H_{16}N_4O_2$ requires 236.1313); ν_{max}(film)/cm^{-1} 2100 (C=N$_2$), 1621 (C=O); δ_H(CDCl$_3$) 0.85–0.97 (6 H, d, 2 × CH$_3$), 1.0–1.3 (4 H, m, 2 × CH$_2$), 1.4–1.55 (2 H, m, 2 × CH$_2$), 2.0–2.3 (2 H, m, 2 × CH); 5.2 (2 H, s, 2 × CH=N$_2$); δ_C(CDCl$_3$) 17.3 (CH$_3$), 17.5 (CH$_3$), 24.9 (CH$_2$), 25.2 (CH$_2$), 33.5 (CH$_2$), 33.6 (CH$_2$), 44.5 (CHN$_2$), 53.5 (CO*C*HCH$_3$), 53.55 (2 × CH), 198 (C=O); m/z (EI) 236 (M$^+$, 0.8%), 109 (10), 98 (19), 81 (14), 69 (100), 55 (50), 41 (80).

1,9-Bisdiazo-3-methylnonane-2,8-dione 2c

2-Methylpimelic acid was prepared from diethyl methyl-malonate and ethyl 5-bromovalerate,[18] and then converted into its acid chloride,[19] which was subsequently reacted with diazomethane to yield the diazoketone **2c** as above. The product (1.11 g, 70%) was obtained as a yellowish oily material after flash chromatography using hexane–EtOAc 1:2. The product could be kept for a few days in the dark in the refrigerator (HRMS: M 222.1119. $C_{10}H_{14}N_4O_2$ requires 222.1117); ν_{max}(film)/cm^{-1} 2080 (C=N$_2$), 1650 (C=O); δ_H(CDCl$_3$) 1.00–1.04 (3 H, d, CH$_3$), 1.17–1.59 (6 H, m, 3 × CH$_2$), 2.10–2.37 (3 H, m, C*H*CH$_3$ and C*H$_2$*CO), 5.20 (1 H, s, CH=N$_2$); δ_C(CDCl$_3$) 17.2 (CH$_3$), 24.9 (CH$_2$), 26.7 (CH$_2$), 33.3 (CH$_2$), 40.5 (CHN$_2$), 44.7 (CHN$_2$), 53.6 (CH), 54.25 (CH), 195.5 (*C*OCHN$_2$), 199.4 (*C*OCHN$_2$); m/z (EI) 222 (M$^+$, 0.92%), 137 (6), 123 (5), 109 (11), 98 (21), 81 (20), 64 (84), 55 (100).

2,10-Bisdiazoundecane-3,9-dione 2d

Pimeloyl chloride (1.32 g, 5.8 mmol) in dry diethyl ether (100 ml) was added dropwise with stirring to a solution of diazoethane[20] (1.5 g, 2.6 mmol) in diethyl ether (100 ml) at 0 °C. The reaction was allowed to proceed at 0 °C for 3 h before the solvent and excess reagent were removed by evaporation at reduced pressure. The residual material was subjected to flash chromatography using hexane–EtOAc 1:1 (R_f 0.3) which gave a yellow oily material (0.8 g, 60%) (HRMS: M 236.1288. $C_{11}H_{16}N_4O_2$ requires 236.1278); ν_{max}(film)/cm^{-1} 2060 (C=N$_2$), 1630 (C=O); δ_H(CDCl$_3$) 1.21–1.35 (2 H, m, CH$_2$), 1.48–1.65 (4 H, m, 2 × CH$_2$), 1.85 (6 H, s, 2 × CH$_3$), 2.33–2.40 (4 H, t, 2 × CH$_2$); δ_C(CDCl$_3$) 7.9 (CH$_3$), 24.2 (CH$_2$), 28.6 (CH$_2$), 37.1 (CH$_2$), 61.95 (C=N$_2$), 194.25 (C=O); m/z (EI) 181 (29), 165 (14), 137 (13), 123 (5), 109 (20), 95 (38), 81 (25), 69 (45), 55 (100).

General procedure for the preparation of spiro[4.4]nonane-2,7-diones 4

The 1,9-bisdiazononane-2,8-dione **2** (6.0 mmol) was dissolved in dry dichloromethane (600 ml) under nitrogen and a solution of Rh$_2$(OAc)$_4$ (0.13 g, 5 mol%) in dichloromethane (10 ml) added. The mixture was stirred at ambient temperature for 12 h. Nitrogen gas was evolved and the color of the mixture changed from yellow to a bright emerald green. The mixture was filtered, the solvent distilled off and the residue subjected to flash chromatography.

Spiro[4.4]nonane-2,7-dione 4a. The product **4a**, obtained after flash chromatography using EtOAc–CH$_2$Cl$_2$ 1:3 (R_f 0.44), was further purified by sublimation at 65 °C/0.1 mmHg and was isolated as a white crystalline solid (27%) with mp 84–85 °C (CH$_2$Cl$_2$) (HRMS: M 152.0832. $C_9H_{12}O_2$ requires 152.0837); ν_{max}(KBr)/cm^{-1} 1730 (C=O); δ_H(CDCl$_3$) 1.98 (4 H, t, 2 × CH$_2$), 2.25 (4 H, s, 2 × CH$_2$), 2.29–2.39 (4 H, m, 2 × CH$_2$); δ_C(CDCl$_3$) 35.3 (CH$_2$), 38.1, (CH$_2$), 44.6 (C), 51.1 (CH$_2$), 216.92 (C=O); m/z (EI) 152 (M$^+$, 100%), 123 (21), 109 (27), 96 (51), 81 (42), 67 (64).

3,8-Dimethylspiro[4.4]nonane-2,7-dione 4b. The crude product was subjected to flash chromatography using EtOAc–CH$_2$Cl$_2$–hexane 4:4:5 (R_f 0.5) and further purified by sublimation at 74 °C/0.1 mmHg. The product **4b** was obtained as a white solid (35%), mp 90–92 °C (Found: C, 73.44; H, 8.73. $C_{11}H_{16}O_2$ requires C, 73.33; H, 8.88%) (HRMS: M 180.1155. $C_{11}H_{16}O_2$ requires 180.1150); ν_{max}(KBr)/cm^{-1} 1720 (C=O); δ_H(CDCl$_3$) 1.03–1.12 (6 H, d, 2 × CH$_3$), 1.3–2.5 (10 H, m, 5 × CH$_2$); δ_C(CDCl$_3$) 14.0 (CH$_3$), 14.35 (CH$_3$), 39.4 (C), 39.7 (C), 42.7 (CH), 43.2 (CH), 43.8 (CH$_2$), 44.2 (CH$_2$), 44.7 (CH$_2$), 50.1 (CH$_2$), 50.4 (CH$_2$), 218.0 (C=O), 219.0 (C=O); m/z (EI) 180 (M$^+$, 96%), 152 (26), 137 (65), 123 (17), 110 (56), 95 (33), 82 (100), 67 (98).

3-Methylspiro[4.4]nonane-2,7-dione 4c. The product **4c**, obtained after flash chromatography using EtOAc–CH$_2$Cl$_2$ 6:1 (R_f 0.52) and sublimation at 69 °C/0.2 mmHg, was a white solid (35%) with mp 70–72 °C (Found: C, 72.13; H, 8.48. $C_{10}H_{14}O_2$ requires C, 72.28; H, 8.43%) (HRMS: M 166.1002. $C_{10}H_{14}O_2$ requires 166.1001); ν_{max}(KBr)/cm^{-1} 1720 (C=O); δ_H(CDCl$_3$) 1.07–1.11 (3 H, d, CH$_3$), 1.59–1.71 (1 H, m, CH), 1.88–2.05 (2 H, m, CH$_2$), 2.21–2.38 (8 H, m, 4 × CH$_2$); δ_C(CDCl$_3$) 14.3 (CH$_3$), 14.5 (CH$_3$), 34.5 (CH$_2$), 35.6 (CH$_2$), 37.1 (C), 42.9 (CH), 43.0 (CH), 43.5 (CH$_2$), 43.6 (CH$_2$), 49.55 (CH$_2$), 49.8 (CH$_2$), 50.9 (CH$_2$), 51.0 (CH$_2$), 217.4 (C=O), 218.7 (C=O); m/z (EI) 166 (M$^+$, 100%), 146 (5), 138 (12), 123 (33), 109 (20), 96 (36), 82 (44), 67 (57).

1,6-Dimethylspiro[4.4]nonane-2,7-dione 4d. When the reaction with 2,10-bisdiazoundecane-3,9-dione (**2d**) was run under the above conditions polymeric products were obtained from which no identified product was isolated.

Methyl 3-(3-oxocyclopentyl)acrylate 6a[14]

A 1.2 M solution of potassium *tert*-butoxide in THF (8 ml, 10 mmol) was added dropwise to a solution of methyl 3-nitropropionate[15] (1.3 g, 10 mmol) in dry THF (20 ml) at −20 °C. The mixture was stirred at this temperature for 15 min, cooled to −20 °C and cyclopent-2-enone (9.96 g, 10 mmol) added slowly. The mixture was stirred for 30 min and allowed to reach ambient temperature during 3 h. Methanol (1.76 ml) was then added and the mixture stirred at ambient temperature for 4 days. The reaction was stopped by addition of 2 M HCl (70 ml) and the product extracted into diethyl ether for further purification as described in the reference given.

Methyl 3-(3-oxocyclohexyl)acrylate 6b

The product **6b**, obtained after flash chromatography using

hexane–Et$_2$O 1:1, was a colorless oil (50%) (HRMS: *M* 182.0944. C$_{10}$H$_{14}$O$_3$ requires 182.0943); ν_{max}(film)/cm^{-1} 2980 (C–H), 1710, 1650 (C=O); δ_H(CDCl$_3$) 1.38–1.79 (2 H, m, CH$_2$), 1.87–2.47 (6 H, m, 3 × CH$_2$), 2.56–2.73 (1 H, m, CH), 3.67 (3 H, s, OCH$_3$), 5.71–5.80 (1 H, dd, J_1 1.5, J_2 16, CH=C*H*CO$_2$Me), 6.78–6.88 (1 H, dd, J_1 6.6, J_2 16, C*H*=CHCO$_2$Me); δ_C(CDCl$_3$) 24.9 (CH$_2$), 30.2 (CH$_2$), 40.7 (CH$_2$), 45.7 (CH), 45.8 (CH$_2$), 51.4 (CO$_2$*C*H$_3$), 119.7 (*C*H=CHCO$_2$Me), 149.9 (CH=*C*HCO$_2$-Me), 166.1 (*C*O$_2$Me), 208.5 (*C*=O, ketone); *m/z* (EI) 182 (M$^+$, 74%), 167 (47), 150 (42), 139 (9), 123 (100), 111 (44), 95 (62), 81 (46).

Methyl 3-(3-oxocycloheptyl)acrylate 6c

Product **6c**, obtained after flash chromatography using hexane–Et$_2$O 1:1, was a colorless oil (45%) (HMRS: *M* 196.1098. C$_{11}$H$_{16}$O$_3$ requires 196.1099); ν_{max}(film)/cm^{-1} 2910, 2850 (C–H), 1710, 1640 (C=O); δ_H(CDCl$_3$) 1.37–1.98 (6 H, m, 3 × CH$_2$), 2.43–2.6 (5 H, m, CH$_2$COCH$_2$ and CH), 3.67 (3 H, s, OCH$_3$), 5.71–5.79 (1 H, dd, J_1 7.0, J_2 16.0, C*H*=CHCO$_2$Me), 6.78–6.90 (1 H, dd, J_1 1.0, J_2 16.0, CH=C*H*CO$_2$Me); δ_C(CDCl$_3$) 23.9 (CH$_2$), 28.3 (CH$_2$), 35.90 (CH$_2$), 38.6 (CH$_2$), 43.95 (CH), 47.9 (CH$_2$), 51.6 (OCH$_3$), 119.4 (*C*H=CHCO$_2$Me), 151.6 (CH=*C*HCO$_2$Me), 166.7 (*C*O$_2$Me), 212.0 (*C*=O, ketone); *m/z* (EI) 196 (M$^+$, 9%), 164 (44), 136 (100), 122 (7), 107 (26), 94 (23), 87 (9), 81 (24).

Methyl 3-(3-oxocyclopentyl)propionate 7a

Compound **7a** was prepared according to the procedure described in ref. 14.

Methyl 3-(3-oxocyclohexyl)propionate 7b

A solution of methyl 3-(3-oxocyclohexyl)acrylate (**6b**) (1.5 g, 8.2 mmol) in acetic acid (15 ml) was hydrogenated over 10% palladium-on-charcoal (0.5 g) at atmospheric pressure for 6 h. The catalyst was removed by filtration through a plug of Celite, the filtrate evaporated at reduced pressure and the residual material subjected to flash chromatography using hexane–Et$_2$O 1:1. The product (1.42 g, 94%) was a colorless oil (HRMS: *M* 184.1086. C$_{11}$H$_{16}$O$_3$ requires 184.1091); ν_{max}(film)/cm^{-1} 2910 (C–H), 1720, 1690 (C=O); δ_H(CDCl$_3$) 1.18–1.38 (2 H, m, CH$_2$), 1.44–2.0 (6 H, m, 3 × CH$_2$), 2.11–2.39 (5 H, m, 2 × CH$_2$, CH), 3.62 (3 H, s, OCH$_3$); δ_C(CDCl$_3$) 21.2 (CH$_2$), 25.4 (CH$_2$), 31.2 (CH$_2$), 31.6 (CH$_2$), 38.6 (CH), 41.4 (CH$_2$), 47.75 (CH$_2$), 51.8 (OCH$_3$), 172.85 (*C*O$_2$CH$_3$), 210.0 (C=O, ketone); *m/z* (EI) 184 (M$^+$, 10%), 153 (21), 124 (7), 110 (100), 97 (98), 82 (13), 74 (18).

Methyl 3-(3-oxocycloheptyl)propionate 7c

Compound **7c** was prepared from methyl 3-(3-oxocycloheptyl)-acrylate (**6c**) (2.02 g, 10 mmol) as above. Flash chromatography using hexane–Et$_2$O 1:1 gave the product **7c** (1.85 g, 90%) as a colorless oil (HRMS: *M* 198.1265. C$_{11}$H$_{18}$O$_3$ requires 198.1256); ν_{max}(film)/cm^{-1} 2900, 2870 (C–H), 1750, 1680 (C=O); δ_H(CDCl$_3$) 1.15–1.60 (4 H, m, 2 × CH$_2$), 1.78–1.84 (3 H, m, CH$_2$, CH), 2.23–2.43 (6 H, m, 3 × CH$_2$), 3.6 (3 H, s, OCH$_3$); δ_C(CDCl$_3$) 24.2 (CH$_2$), 28.2 (CH$_2$), 31.5 (CH$_2$), 31.9 (CH$_2$), 35.3 (CH$_2$), 36.4 (CH$_2$), 43.75 (CH$_2$), 49.3 (CH$_2$), 51.5 (OCH$_3$), 173.0 (*C*O$_2$CH$_3$), 213.7 (C=O, ketone); *m/z* (EI) 198 (M$^+$, 11%), 167 (25), 155 (6), 138 (29), 124 (68), 111 (100), 96 (26), 83 (25).

3-(3-Oxocyclopentyl)propionic acid 8a

Compound **8a** was prepared in 96% yield by following the procedure described in ref. 20.

3-(3-Oxocyclohexyl)propionic acid 8b

Compound **8b** was prepared in 98% yield by following the procedure described in ref. 21.

3-(3-Oxocycloheptyl)propionic acid 8c

Compound **8c** was prepared in 98% yield by following the procedure described in ref. 22.

3-(3-Oxocyclopentyl)propionyl chloride 9a

A solution of oxalyl chloride (11.4 mmol) in benzene (5 ml) was added to a solution of 3-(3-oxocyclopentyl)propionic acid (**8a**) (7.6 mmol) in dry benzene (20 ml) with ice-cooling. The resultant solution was stirred at ambient temperature for 1 h, and at 50 °C for 1 h, before the solution was evaporated to dryness. The acid chloride was isolated after distillation, bp 88 °C/0.3 mmHg, yield 81–82% (HRMS: *M* 170.0447. C$_8$H$_{11}$ClO$_2$ requires 174.0448); ν_{max}(film)/cm^{-1} 2960 (C–H), 1780, 1720 (C=O); δ_H(CDCl$_3$) 1.3–1.92 (5 H, m, 2 × CH$_2$, CH), 2–2.45 (4 H, m, 2 × CH$_2$), 2.84–2.97 (2 H, m, CH$_2$COCl); δ_C(CDCl$_3$) 29.1 (CH$_2$), 30.5 (CH$_2$), 35.9 (CH$_2$), 38.3 (CH), 44.5 (CH$_2$), 45.4 (CH$_2$), 173.4 (COCl), 218.1 (C=O, ketone); *m/z* (EI) 174.8 (M$^+$, 3%), 174 (22), 145 (6), 139 (44), 111 (8), 96 (24), 83 (14), 55 (100).

3-(3-Oxocyclohexyl)propionyl chloride 9b

Compound **9c** was obtained as above from oxalyl chloride in 85–89% yield, bp 89–92 °C/0.3 mmHg (HRMS: *M* 188.0587. C$_9$H$_{13}$ClO$_2$ requires 188.0582); ν_{max}(film)/cm^{-1} 2950 (C–H), 1780, 1700 (C=O); δ_H(CDCl$_3$) 1.18–2.13 (8 H, m, 4 × CH$_2$), 2.16–2.33 (3 H, m, CH$_2$, CH), 2.78–2.85 (2 H, t, CH$_2$COCl); δ_C(CDCl$_3$) 24.4 (CH$_2$), 30.2 (CH$_2$), 30.8 (CH$_2$), 37.2 (CH$_2$), 40.6 (CH), 43.9 (CH$_2$), 46.8 (CH$_2$), 172.4 (COCl), 209.2 (C=O, ketone); *m/z* (EI) 188 (M$^+$, 25%), 153 (38), 145 (41), 124 (16), 116 (5), 110 (100), 97 (78), 89 (20), 82 (50), 69 (35), 55 (96).

3-(3-Oxocycloheptyl)propionyl chloride 9c

Compound **9c** was obtained as above from oxalyl chloride in 81–83% yield, bp 90–92 °C/0.3 mmHg (HRMS: *M* 202.0758. C$_{10}$H$_{15}$ClO$_2$ requires 202.0760); ν_{max}(film)/cm^{-1} 2910, 2860 (C–H), 1770, 1680 (C=O); δ_H(CDCl$_3$) 1.25–1.91 (9 H, m, 4 × CH$_2$, CH), 2.39–2.48 (4 H, m, 2 × CH$_2$), 2.88–2.95 (2 H, t, CH$_2$COCl); δ_C(CDCl$_3$) 24.1 (CH$_2$), 27.95 (CH$_2$), 31.7 (CH$_2$), 34.8 (CH$_2$), 36.3 (CH$_2$), 43.8 (CH), 44.7 (CH$_2$), 49.0 (CH$_2$), 173.6 (COCl), 213.3 (C=O, ketone); *m/z* (EI) 202 (M$^+$, 0.6%), 184 (18), 166 (10), 138 (27), 124 (44), 111 (100), 96 (23), 83 (30), 55 (95).

1-Diazo-4-(3-oxocyclopentyl)butan-2-one 10a

A solution of 3-(3-oxocyclopentyl)propionyl chloride (**9a**) (6 mmol) in anhydrous diethyl ether (10 ml) was added drop-wise over 30 min to a solution of diazomethane (12 mmol) in anhydrous diethyl ether (50 ml) with stirring at 0 °C. The solution was stirred at this temperature for 3 h before the solvent was evaporated. The residual oil was subjected to flash chromatography using hexane–EtOAc 1:3; the product was a yellow oily material (0.864 g, 80%) (HRMS (*M* − N$_2$) 152.0829. C$_9$H$_{12}$O$_2$ (*M* − N$_2$) requires 152.0838); ν_{max}(film)/cm^{-1} 3030, 2900 (C–H), 2094 (C=N$_2$), 1720, 1630 (C=O); δ_H(CDCl$_3$) 1.20–1.80 (4 H, m, C*H*$_2$CH$_2$COCHN$_2$ and C*H*$_2$CH$_2$CO), 2.07–2.35 (7 H, m, C*H*$_2$COCHN$_2$, C*H*$_2$COC*H*$_2$ and C*H*), 5.25 (1 H, s, CHN$_2$); δ_C(CDCl$_3$) 29.2 (CH$_2$), 30.4 (CH$_2$), 36.5 (CH$_2$), 38.4 (CH), 38.9 (CH$_2$), 44.8 (CH$_2$), 54.5 (CHN$_2$), 194.0 (*C*OCHN$_2$), 218.7 (C=O, ring); *m/z* (EI) 152 (M$^+$ − N$_2$, 17%), 123 (51), 109 (14), 95 (27), 84 (65), 67 (26), 55 (100).

1-Diazo-4-(3-oxocyclohexyl)butan-2-one 10b

Compound **10b** was obtained as above from 3-(3-oxocyclohexyl)propionyl chloride (**9b**) as a yellow oil (88%) (HRMS (*M* − N$_2$) 166.0986. C$_9$H$_{12}$O$_2$ (*M* − N$_2$) requires 166.0994); ν_{max}(film)/cm^{-1} 3010, 2910, 2880 (C–H), 2100 (C=N$_2$), 1700, 1630 (C=O); δ_H(CDCl$_3$) 1.15–1.40 (2 H, m, CH$_2$), 1.51–2.06

(8 H, m, 4 × CH$_2$), 2.18–2.42 (5 H, m, 2 × CH$_2$, CH), 5.23 (1 H, s, CHN$_2$); δ_C(CDCl$_3$) 25.1 (CH$_2$), 31.2 (CH$_2$), 31.4 (CH$_2$), 38.0 (CH$_2$), 38.6 (CH), 41.3 (CH$_2$), 47.8 (CH$_2$), 54.5 (CHN$_2$), 194.15 (COCHN$_2$), 211.1 (C=O, ring); *m/z* (EI) 166 (M$^+$ − N$_2$, 2%), 138 (35), 123 (48), 109 (23), 95 (19), 84 (99), 55 (100).

1-Diazo-4-(3-oxocycloheptyl)butan-2-one 10c

Compound **10c** was obtained as above from 3-(3-oxocyclo-heptyl)propionyl chloride (**9c**) as a yellow oil (78%) (HRMS (*M* − N$_2$) 180.1141. C$_{10}$H$_{14}$O$_2$ (*M* − N$_2$) requires 180.1148); ν_{max}(film)/cm^{-1} 3060, 2910, 2860 (C–H), 2080 (C=N$_2$), 1680, 1620 (C=O); δ_H(CDCl$_3$) 1.18–1.7 (6 H, m, 3 × CH$_2$), 1.76–1.91 (3 H, m, CH$_2$, CH), 2.27–2.43 (6 H, m, 3 × CH$_2$), 5.22 (1 H, s, CHN$_2$); δ_C(CDCl$_3$) 24.1 (CH$_2$), 28.0 (CH$_2$), 31.8 (CH$_2$), 35.3 (CH$_2$), 36.6 (CH$_2$), 38.1 (CH), 43.7 (CH$_2$), 49.1 (CH$_2$), 54.4 (CHN$_2$), 194.3 (COCHN$_2$), 213.8 (C=O, ring); *m/z* (EI) 180 (M$^+$ − N$_2$, 4%), 151 (21), 137 (3), 123 (27), 109 (19), 95 (21), 84 (83), 55 (100).

Ethyl 2-diazo-3-oxo-5-(3-oxocyclopentyl)pentanoate 11a

3-(3-Oxocyclopentanyl)propionyl chloride (**9a**) (6 mmol) and ethyl diazoacetate (13 mmol) were mixed. The mixture was stirred at ambient temperature for 30 min; the stirring was continued at 40 °C for 1 h and at 60 °C for 6 h. Excess ethyl diazoacetate and the ethyl chloroacetate, which was formed in the reaction, were removed by distillation under reduced pressure. The residual oily material was purified by flash chromatography using hexane–EtOAc 2:1. The product (1.05 g, 70%) was a yellow oil (HRMS (*M* − N$_2$) 224.1103. C$_{12}$H$_{16}$O$_4$ (*M* − N$_2$) requires 224.1111); ν_{max}(film)/cm^{-1} 2899 (C–H), 2120 (C=N$_2$), 1740, 1700, 1640 (C=O); δ_H(CDCl$_3$) 1.20–1.27 (3 H, t, C*H$_3$*CH$_2$O), 1.39–1.80 (4 H, m, C*H$_2$*CH$_2$COCN$_2$CO, C*H$_2$*-CH$_2$CO), 2.0–2.4 (5 H, m, CH$_2$COCH$_2$, CH), 2.78–2.86 (2 H, m, C*H$_2$*COCN$_2$), 4.15–4.26 (2 H, q, CH$_3$C*H$_2$*O); δ_C(CDCl$_3$) 14.8 (CH$_3$), 29.8 (CH$_2$), 30.3 (CH$_2$), 37.6 (CH$_2$), 39.3 (CH), 39.4 (CH$_2$), 45.9 (CH$_2$), 54.1 (C=N), 62.1 (CH$_3$*C*H$_2$O), 160.7 (*C*O$_2$Et), 191.4 (CN$_2$*C*O), 217.8 (C=O, ring); *m/z* (EI) 224 (M$^+$ − N$_2$, 0.63%), 178 (33), 156 (44), 150 (16), 139 (15), 122 (24), 109 (11), 99 (42), 83 (20), 55 (100).

Ethyl 2-diazo-3-oxo-5-(3-oxocyclohexyl)pentanoate 11b

Compound **11b** was obtained as above from 3-(3-oxocyclo-hexyl)propionyl chloride (**9b**) as a yellow oil (73%) (HRMS (*M* − N$_2$) 238.1196. C$_{13}$H$_{18}$O$_4$ (*M* − N$_2$) requires 238.1205); ν_{max}(film)/cm^{-1} 2910, 2890 (C–H), 2110 (C=N$_2$), 1700, 1650 (C=O); δ_H(CDCl$_3$) 1.25–1.32 (3 H, t, OCH$_2$C*H$_3$*), 1.47–2.42 (11 H, m, 5 × CH$_2$, CH), 2.77–2.86 (2 H, m, C*H$_2$*COCN$_2$), 4.18–4.28 (2 H, q, CH$_3$C*H$_2$*O); δ_C(CDCl$_3$) 14.9 (CH$_3$), 25.6 (CH$_2$), 31.2 (CH$_2$), 31.5 (CH$_2$), 37.8 (CH$_2$), 39.0 (CH), 41.8 (CH$_2$), 48.3 (CH$_2$), 53.2 (C=N$_2$), 61.8 (CH$_3$*C*H$_2$O), 161.2 (*C*O$_2$Et), 192.2 (*C*OCN$_2$), 211.1 (C=O, ring); *m/z* (EI) 238 (M$^+$ − N$_2$, 3%), 210 (11), 192 (25), 164 (44), 156 (87), 135 (18), 123 (21), 110 (28), 99 (55), 55 (100).

Ethyl 2-diazo-3-oxo-5-(3-oxocycloheptyl)pentanoate 11c

Compound **11c** was obtained as above from 3-(3-oxocyclo-heptyl)propionyl chloride (**9c**) as a yellow oil (72%) (HRMS (*M* − N$_2$) 252.1350. C$_{14}$H$_{20}$O$_4$ (*M* − N$_2$) requires 252.1361); ν_{max}(film)/cm^{-1} 2900 (C–H), 2120 (C=N$_2$), 1700–1640 (C=O); δ_H(CDCl$_3$) 1.19–1.39 (5 H, m, OCH$_2$C*H$_3$*, CH$_2$), 1.40–1.68 (4 H, m, 2 × CH$_2$), 1.79–1.88 (3 H, m, CH$_2$, CH), 2.37–2.50 (4 H, m, 2 × CH$_2$), 2.80–2.87 (2 H, t, C*H$_2$*COCN$_2$), 4.20–4.31 (2 H, q, CH$_3$C*H$_2$*O); δ_C(CDCl$_3$) 14.4 (CH$_3$), 24.4 (CH$_2$), 28.5 (CH$_2$), 31.5 (CH$_2$), 35.6 (CH$_2$), 36.5 (CH$_2$), 37.7 (CH), 43.9 (CH$_2$), 49.6 (CH$_2$), 54.6 (C=N$_2$), 61.4 (CH$_3$*C*H$_2$O), 160.95 (CO$_2$Et), 192.1 (CN$_2$*C*O), 213.5 (C=O, ring); *m/z* (EI) 252 (M$^+$ − N$_2$, 8%), 206 (17), 195 (5), 188 (13), 178 (19), 167 (21), 156 (100), 149 (18), 135 (15), 99 (47).

Spiro[4.4]nonane-2,7-dione 12a (4a)

A solution of 1-diazo-4-(3-oxocyclopentyl)butan-2-one (**10a**) (0.63 g, 3.5 mmol) in dry dichloromethane (100 ml) was added dropwise over 1 h to a stirred suspension of Rh$_2$(OAc)$_4$ (0.074 g, 0.17 mmol) in dry methylene chloride (60 ml) under nitrogen at ambient temperature. The mixture was stirred at this temperature for 14 h. Filtration, evaporation of the filtrate and flash chromatography of the residual material using EtOAc–CH$_2$Cl$_2$ 1:3 gave the product as a white crystalline solid (0.234 g, 44%) with mp 84–85 °C (sublimed at 65 °C/0.1 mmHg) (HRMS: *M* 152.0832. C$_9$H$_{12}$O$_2$ requires 152.0837); ν_{max}(KBr)/cm^{-1} 2980 (C–H), 1730 (C=O); δ_H(CDCl$_3$) 1.98 (4 H, t, 2 × CH$_2$), 2.25 (4 H, s, CH$_2$), 2.29–2.39 (4 H, m, 2 × CH$_2$); δ_C(CDCl$_3$) 35.3 (CH$_2$), 38.1 (CH$_2$), 44.6 (C), 51.1 (CH$_2$), 216.9 (C=O); *m/z* (EI) 152 (M$^+$, 100%), 123 (21), 109 (27), 96 (51), 81 (42), 67 (64).

Spiro[4.5]decane-2,7-dione 12b

Compound **12b** was obtained as above from 1-diazo-4-(3-oxo-cyclohexyl)butan-2-one (**10b**). After flash chromatography using CH$_2$Cl$_2$–EtOAc 12:1 the product **12b** was obtained as an oily material (44%) (Found: C, 72.06; H, 8.44. C$_{10}$H$_{14}$O$_2$ requires C, 72.28; H, 8.43%) (HRMS: *M* 166.1000. C$_{10}$H$_{14}$O$_2$ requires 166.0994); ν_{max}(KBr)/cm^{-1} 2980 (C–H), 1730, 1700 (C=O); δ_H(CDCl$_3$) 1.73–2.04 (6 H, m, 3 × CH$_2$), 2.10–2.17 (2 H, m, CH$_2$), 2.25–2.42 (6 H, m, 3 × CH$_2$); δ_C(CDCl$_3$) 23.4 (CH$_2$), 34.4 (CH$_2$), 36.15 (CH$_2$), 36.7 (CH$_2$), 41.3 (CH$_2$), 44.8 (C), 50.7 (CH$_2$), 52.45 (CH$_2$), 208.35 (7-C=O), 215.7 (2-C=O); *m/z* (EI) 167 (M$^+$, 100%), 148 (7), 138 (38), 123 (42), 110 (50), 95 (33), 82 (43), 67 (80), 55 (91).

Spiro[4.6]undecane-2,7-dione 12c

Compound **12c** was obtained as above from 1-diazo-4-(3-oxocycloheptyl)butan-2-one (**10c**). Flash chromatography using CH$_2$Cl$_2$–EtOAc 6:1 gave a colourless oil (43%) (HRMS: *M* 180.1157. C$_{11}$H$_{16}$O$_2$ requires 180.1150); ν_{max}(KBr)/cm^{-1} 2910–2900 (C–H), 1730, 1680 (C=O); δ_H(CDCl$_3$) 1.58–1.90 (8 H, m, 4 × CH$_2$), 2.06–2.08 (2 H, d, CH$_2$), 2.21–2.32 (2 H, d, CH$_2$), 2.36–2.44 (2 H, m, CH$_2$), 2.58–2.61 (2 H, d, CH$_2$); δ_C(CDCl$_3$) 23.9 (CH$_2$), 25.4 (CH$_2$), 34.5 (CH$_2$), 36.3 (CH$_2$), 41.3 (C), 42.2 (CH$_2$), 44.1 (CH$_2$), 51.6 (CH$_2$), 53.8 (CH$_2$), 212.4 (7-C=O), 217.9 (2-C=O); *m/z* (EI) 180 (M$^+$, 59%), 162 (51), 152 (18), 137 (16), 122 (93), 109 (72), 96 (100), 81 (53), 67 (53).

Ethyl 2,7-dioxospiro[4.4]nonane-1-carboxylate 13a

A solution of ethyl 2-diazo-3-oxo-5-(3-oxocyclopentyl)pentano-ate (0.882 g, 3.5 mmol) in dry dichloromethane (100 ml) was added dropwise over 1 h to a stirred suspension of Rh$_2$(OAc)$_4$ (0.074 g, 0.17 mmol) in dry dichloromethane (60 ml) under nitrogen at ambient temperature. The mixture was stirred at this temperature for 14 h. Filtration, evaporation of the filtrate and flash chromatography of the residual material using CH$_2$Cl$_2$–EtOAc 6:1 gave the product (0.31 g, 43%) as a colorless oil (Found: C, 64.22; H, 7.48. C$_{12}$H$_{16}$O$_4$ requires C, 64.28; H, 7.14%) (HRMS: *M* 224.1044. C$_{12}$H$_{16}$O$_4$ requires 224.1048); ν_{max}(film)/cm^{-1} 2910 (C–H), 1740, 1700, 1635, 1600 (C=O); δ_H(500 MHz; CDCl$_3$) 1.22–1.36 (3 H, m, OCH$_3$CH$_2$), 1.61–2.64 (10 H, m, 5 × CH$_2$), 2.76, 2.79, 3.08, 3.11 (1 H, 4 × s), 4.13–4.36 (2 H, m, OCH$_2$CH$_3$) 10.87 (1 H, s, OH enol); δ_C(125 MHz; CDCl$_3$) 14.1, 14.25 (OCH$_2$CH$_3$), 29.55, 29.6, 29.8, 30.4, 30.5 (5 × CH$_2$), 33.3, 33.5, 33.5, 34.0, 34.3, 34.45, 34.7, 34.9 (8 × CH$_2$), 36.1, 36.4, 36.5, 36.6, 36.6, 36.8, 37.0, 37.3 (8 × CH$_2$), 44.5, 44.8, 46.3, (3 × CH$_2$), 48.2, 48.2, 49.2 (3 × C), 50.2, 50.3, 50.5, 50.9, 51.1 (6 × CH$_2$), 60.2, 61.6, 61.6 (OC*H$_2$*CH$_3$), 63.0, 63.1, 63.2, 63.75 (*C*HCO$_2$), 84.6, 104.6 (C–OH, enol), 167.95, 168.1, 169.4, 169.85, 169.95, 175.9, 177.5 (*C*O$_2$Et), 210.6, 212.1, 216.1–216.3, 217.35, 219.4 (C=O); *m/z* (EI) 224 (M$^+$, 61%), 206 (19), 195 (20), 178 (61), 168 (24), 160 (15), 149 (41), 136 (25), 122 (100).

Ethyl 2,7-dioxospiro[4.5]decane-1-carboxylate 13b

Compound **13b** was prepared as above from ethyl 2-diazo-3-oxo-5-(3-oxocyclohexyl)pentanoate (**11b**). The product (45%) was a colorless oily material (Found: C, 65.27; H, 7.48. $C_{13}H_{18}O_4$ requires C, 65.54; H, 7.56%) (HRMS: M 238.1213. $C_{13}H_{18}O_4$ requires 238.1205); ν_{max}(film)/cm^{-1} 2190 (C–H), 1740, 1700, 1635, 1600 (C=O); δ_H(500 MHz; CDCl$_3$) 1.22–1.25, 1.28–1.31 (3 H, t, CH_3CH$_2$O), 1.5–1.79 (4 H, m, 2 × CH$_2$), 1.8–2.1 (4 H, m, 2 × CH$_2$), 2.26–2.32 (2 H, m, CH$_2$), 2.4–2.5 (2 H, m, CH$_2$), 2.82, 2.87, 2.99 (1 H, 3 × s), 4.13–4.17, 4.23–4.35 (2 H, q, CH$_3$CH_2O), 10.84 (1 H, s, OH enol); δ_C(125 MHz; CDCl$_3$) 14.0, 14.1, 14.1, 14.25 (CH$_3$CH$_2$O), 21.6, 22.1, 22.2 (3 × CH$_2$), 24.95, 25.0, 25.9, 30.2, 30.8, 30.85, 31.2, 31.3, 31.45, 31.5 (10 × CH$_2$), 34.9, 35.5, 35.7, 35.7 (4 × CH$_2$), 40.5, 40.7, 40.75, 40.8, 40.85, 41.2, 41.25 (7 × CH$_2$), 47.6, 47.65, 47.8 (3 × C), 48.1, 49.55, 51.4, 51.9, 52.1 (5 × CH$_2$), 60.0, 61.3, 61.3, 61.35 (CH$_3$CH$_2$O), 64.2, 64.84, 65.8 (CHCO$_2$Et), 106.45 (C–OH, enol), 167.7, 167.8, 169.2, 169.6, 177.25 (CO$_2$Et), 208.85, 209.2, 210.8, 211.15, 211.3, 211.4 (C=O); m/z (EI) 238 (M$^+$, 61%), 220 (11), 192 (100), 181 (59), 164 (43), 149 (77), 135 (92), 122 (77), 108 (37).

Ethyl 2,7-dioxospiro[4.6]undecane-1-carboxylate 13c

Compound **13c** was prepared as above from ethyl 2-diazo-3-oxo-5-(3-oxocycloheptyl)pentanoate (**11c**). The product (41%) was a colorless oily material (HRMS: M 252.1368. $C_{14}H_{20}O_4$ requires 252.1362); ν_{max}(film)/cm^{-1} 2900, 2850 (C–H), 1750, 1720, 1680, 1640, 1600 (C=O); δ_H(500 MHz; CDCl$_3$) 1.20–1.25, 1.28–1.31 (3 H, m, CH$_3$CH$_2$O), 1.49–1.9 (8 H, m, 4 × CH$_2$), 2.0–2.52 (6 H, m, 3 × CH$_2$), 2.84, 2.86, 2.89, 2.91, 2.98 (1 H, 5 × s), 4.11–4.18, 4.21–4.24 (2 H, m, CH$_3$CH$_2$O), 10.74 (1 H, s, OH); δ_C(125 MHz; CDCl$_3$) 14.0, 14.1, 14.25 (3 × CH$_3$CH$_2$O), 23.3–23.5, 24.5, 24.6, 28.9, 30.4, 30.8, 31.7, 35.35, 35.6, 37.6, 40.0, 42.2, 43.8, 43.9, 44.2, 44.8, 45.0 (18 × CH$_2$), 46.35, 48.7 (2 × C), 51.95, 53.2, 53.8, 59.9 (4 × CH$_2$), 61.1, 61.2, 61.3 (4 × CH$_3$CH$_2$O), 65.4, 65.9 (2 × CHCO$_2$Et), 109.0 (C–OH, enol), 167.2, 167.9, 169.2, 169.5, 176.35 (5 × CO$_2$Et), 211.0, 211.2, 211.3, 211.9, 213.4, 213.9 (6 × C=O); m/z (EI) 252 (M$^+$, 56%), 206 (89), 194 (68), 188 (28), 178 (35), 164 (54), 135 (36), 122 (100), 109 (25), 95 (36).

Ethyl 1-methyl-2,7-dioxospiro[4.4]nonane-1-carboxylate 15

A solution of ethyl 2,7-dioxospiro[4.4]nonane-1-carboxylate (**13a**) (0.140 g, 0.66 mmol) in dry THF (3 ml) was added dropwise over 10 min to a stirred suspension of NaH (30 mg, 0.75 mmol) in dry THF (5 ml) under nitrogen at 0 °C. The mixture was allowed to reach ambient temperature before a solution of methyl iodide (0.093 g, 0.66 mmol) in THF (2 ml) was added. The mixture was stirred at ambient temperature for 10 h when the reaction was acidified with HCl. The mixture was extracted with diethyl ether, the ethereal solution dried (MgSO$_4$), evaporated and the residual material subjected to flash chromatography using CH$_2$Cl$_2$–EtOAc 6 : 1. The product (0.110 g, 80%) was a colorless oil (HRMS: M 238.1214. $C_{13}H_{18}O_4$ requires 238.1205); ν_{max}(film)/cm^{-1} 2915 (C–H), 1735, 1688, 1630, 1605 (C=O); δ_H(CDCl$_3$) 1.17 (3 H, s, CH$_3$), 1.20–1.25 (3 H, m, CH$_3$CH$_2$O), 1.71–2.45 (10 H, m, 5 × CH$_2$), 4.05–4.19 (2 H, m, CH$_3$CH$_2$O); δ_C(CDCl$_3$) 14.45, 14.5 (2 × CH$_3$), 15.0, 15.5 (CH$_3$CH$_2$O), 29.3, 31.35, 31.5, 36.0, 36.1, 36.55, 36.6, 46.9, 48.3 (9 × CH$_2$), 51.0, 51.4 (2 × C) 61.3, 61.35 (2 × EtO$_2$-CCCH$_3$), 61.8, 61.9 (2 × CH$_3$CH$_2$O), 171.2, 171.5 (2 × EtO$_2$C),

214.7, 214.8, 215.9, 216.0 (4 × C=O); m/z (EI) 238 (M$^+$, 92%), 210 (44), 193 (30), 155 (33), 137 (80), 123 (41), 109 (100), 95 (50), 81 (47), 67 (43), 55 (78), 41 (56), 29 (84).

1-Methylspiro[4.4]nonane-2,7-dione 16

A solution of ethyl 1-methyl-2,7-dioxospiro[4.4]nonane-1-carboxylate (**15**) (0.110 g, 0.46 mmol) in acetic acid (2 ml) and HCl (6 ml; 20%) was heated under reflux for 14 h. The cold reaction mixture was extracted with diethyl ether (3 × 10 ml), the combined ethereal solutions washed with water and aq. 20% NaHCO$_3$, dried (MgSO$_4$), the ether distilled off and the residual material subjected to flash chromatography using CH$_2$Cl$_2$–EtOAc 6 : 1. The product (0.046 g, 60%) was a white solid with mp 71–72.5 °C (sublimed at 60–62 °C/0.1 mmHg) (Found: C, 72.18; H, 8.46. $C_{10}H_{14}O_2$ requires C, 72.28; H, 8.44%) (HRMS: M 166.1003. $C_{10}H_{14}O_2$ requires 166.1001); ν_{max}(KBr)/cm^{-1} 1726 (C=O); δ_H(CDCl$_3$) 1.01–1.07 (3 H, t, CH$_3$), 1.19–1.27 (1 H, m, CHCH$_3$), 1.96–2.43 (10 H, m, CH$_2$); δ_C(CDCl$_3$) 8.7, 8.9 (2 × CH$_3$), 27.3, 32.7, 33.9, 35.2, 35.4, 36.85, 37.0 (7 × CH$_2$), 47.9, 49.8 (2 × C), 52.15, 52.3 (2 × CHCH$_3$), 217.4, 218.2 (2 × C=O); m/z (EI) 166 (M$^+$, 100%), 155 (13), 137 (46), 123 (45), 109 (92), 95 (45), 67 (77).

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