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Facile Synthesis of Oxatricyclic Systems with Various Ring Sizes and Substituents

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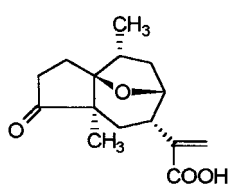
Abstract—A series of α-diazo carbonyl compounds having cyclopentanone, cyclohexanone and substituted cyclohexanone units with different tether lengths have been synthesized using diazomethane solution or methanesulphonyl azide. The above synthesized α-diazo carbonyl compounds with rhodium(II) acetate dimer furnish cyclic five- or six-ring carbonyl ylide dipoles, which undergo facile 1,3-dipolar cycloaddition with different dipolarophiles to furnish the substituted and functionalized oxatricyclic systems having various ring sizes. Two X-ray crystallographic analyses of compounds **8b** and **15a** are reported to firmly establish the stereochemistry of the cycloadducts.

Introduction

Medium-size cyclic ethers are becoming increasingly recognized as common structural units in naturally occurring compounds such as the ionophores,[1] the brevetoxins[2] and other marine natural products.[3] Due to increasing interest in these bio-active molecules and well recognized problems in building medium-sized rings, the synthesis of such systems is a challenging synthetic objective. Moreover, bridging ethers confer structural rigidity to the carbon skeleton which allows highly stereoselective transformations within the six- and seven-membered carbocycles. Medium-size cyclic ethers are generally assembled from an intramolecular Diels–Alder reaction[4] of a furan diene and dipolar cycloaddition of pyrylium ylides.[5] The 1,3-dipolar cycloaddition of carbonyl ylides with π bonds represent an attractive strategy[6,7] for tetrahydrofuran formation. In medium-size cyclic ethers particularly the oxatricylic ring system is very important and present in several natural products such as Ambrosic acid[8] **1**, Smitopsin[9] **2** and Linearol[10] **3** etc. In our quest for the synthesis of sesquiterpenoids containing bridging ethers, starting from cycloalkanone carboxylic acids **4**, we herein wish to report our detailed preliminary studies on the synthesis of substituted and functionalized oxatricyclic systems via five or six-ring carbonyl ylides involving carbocyclic carbonyl groups having different ring sizes and substitutents with various dipolarophiles.



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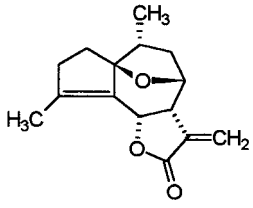

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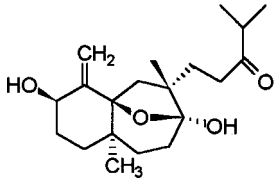

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Results and Discussion

It was envisaged that the reaction of diazo ketones such as **6a–d** and **6e–g/14a–d** with rhodium(II) acetate dimer, can in principle generate five- and six-ring carbonyl ylides, respectively. For investigating the intramolecular formation and intermolecular cycloaddition of these carbonyl ylides **7** and **16**, the requisite starting materials **6** and **14** were assembled from commercially available materials.

Mild hydrolysis of 2-carbethoxy-2-methyl cyclopentanone was carried out using 5% aqueous potassium hydroxide solution at room temperature to afford 1-methyl-2-oxo-cyclopentanecarboxylic acid **4a**. Care was taken in the

Keywords: diazo compounds; carbonyl ylides; cycloaddition; rhodium acetate catalyst.

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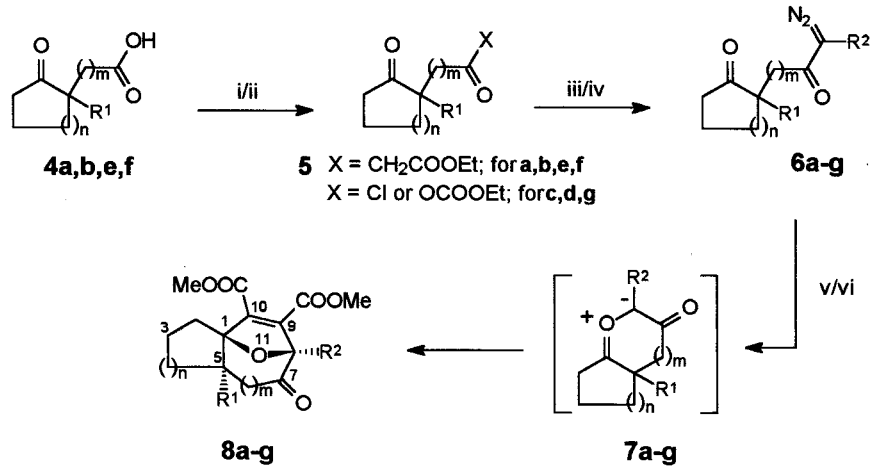
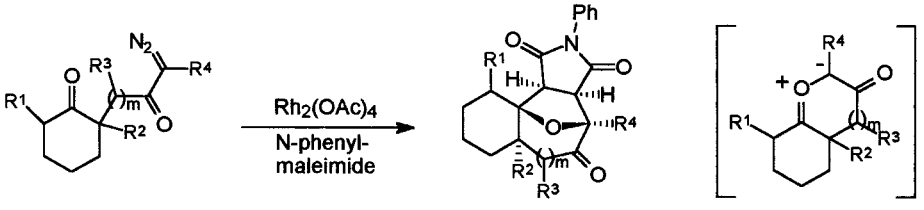


Substrate	n	m	R^1	R^2	Yield[a](%)
a	1	0	CH_3	COOEt	83
b	2	0	CH_3	COOEt	88
c	1	0	CH_3	H	74
d	2	0	CH_3	H	76
e	1	1	H	COOEt	89
f	2	1	H	COOEt	86
g	2	1	H	H	71

[a]Yields (unoptimized) refer to isolated and chromatographically pure compounds of **8a-g**.

Scheme 1. Reagents for substrates **a**,**b**,**e**,**f**: (i) (a) $(COCI)_2$, Ether; (b) *i*-PrMgBr, $EtOOCCH_2COOH$, DCM/THF (1:5); (iii) MsN_3, NEt_3, DCM; (v) $Rh_2(OAc)_4$, DMAD, C_6H_6; Reagents for substrates **c**,**d**,**g**: (ii) $(COCl)_2$, Ether or ClCOOEt, NEt_3, Ether; (iv) CH_2N_2, Ether; (vi) $Rh_2(OAc)_4$, DMAD, DCM.

preparation and further reactions of β-keto acids **4a**,**b** due to their instability under thermal conditions and possible ring opening reactions. Treatment of **4a** with oxalyl chloride furnished the corresponding acid chloride, which on reaction with excess Mg-complex of dianion of monoethyl malonate in a mixture of DCM/THF (1:5) afforded the active methylene compound **5a** in moderate yield as described in the literature.[11] The diazo transfer reaction[12] of **5a** was carried out using mesyl azide-triethylamine to give diazo compound **6a**. The same sequence of reactions on 2-carbethoxy-2-methyl cyclohexanone, ethyl 2-cyclopentanoneacetate and ethyl 2-cyclohexanoneacetate furnished α-diazo ketones **6b**,**e**,**f** (Scheme 1), respectively in very good yields. Treatment of 1-methyl-2-oxocyclopentanecarboxylic acid (**4a**), 1-methyl-2-oxocyclohexanecarboxylic acid (**4b**) and 2-oxocyclohexaneacetic acid (**4f**) with ethyl chloroformate and triethylamine resulted in a white suspension at room temperature and the resulting mixed anhydride was then treated with freshly prepared ethereal diazomethane at 0–10°C to furnish α-diazo ketones **6c**,**d**,**g**, respectively. In order to obtain a better yield of these diazo compounds, the above acids **4a**,**b**,**f** were treated with



Substrate	m	R^1	R^2	R^3	R^4	Yield[a](%)
a	1	CH_3	H	H	COOEt	92
b	1	C_2H_5	H	H	COOEt	93
c	1	CH_3	H	CH_3	COOEt	84
d	1	CH_3	H	H	CH_3	69
e	0	H	CH_3	-	H	88
f	0	H	CH_3	-	COOEt	95

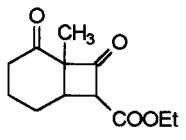
[a]Yields (unoptimized) refer to isolated and chromatographically pure compounds of **15a-f**.

Scheme 2.

oxalyl chloride at room temperature to afford the corresponding acid chlorides. These crude acid chlorides were treated with freshly prepared ethereal diazomethane containing triethylamine at 0°C and furnished the respective α-diazo ketones **6c**,**d**,**g**. Comparatively we obtained better overall yields of diazo ketones from acids by the acid chloride method than the mixed anhydride method. All these diazo compounds were stable for chromatographic purification and spectroscopic characterization purposes.

We next investigated the Rh(II) catalyzed behavior of the above synthesized α-diazo ketones **6**. The reaction of **6a** and dimethyl acetylenedicarboxylate (DMAD) with 1 mol% $Rh_2(OAc)_4$ catalyst in dry benzene was refluxed under an argon atmosphere for 13 h followed by chromatographic purification, product **8a** was obtained in 83% yield. Typically the quantity of the catalyst was maintained at 1 mol% for performing all our experiments. The Rh(II) catalyzed behavior of diazo compounds **6b**–**d** and **6e**–**g** was also studied to form five- and six-ring carbonyl ylides, respectively, which further undergo 1,3-dipolar cycloaddition in the presence of DMAD to furnish the oxatricyclic systems **8b**–**g** in very good yield. The presence of a singlet resonance around δ 4.8 for the bridgehead proton in the ^{1}H NMR spectra, the presence of a signal around δ 85 in the ^{13}C NMR spectra for the tertiary bridgehead carbon atom of compounds **8c**,**d**,**g** and the presence of oxygen attached quaternary carbons around δ 90 in all the products in the ^{13}C NMR spectra clearly established the oxatricyclic system. The above tertiary bridgehead carbon signals are deshielded in the range of δ 7–8 when carbethoxy group is present in compounds **8a**,**b**,**e**,**f**.

Padwa[13] observed a similar oxatricyclic ring system from the decomposition of a diazo carbonyl compound, in which the competition of ylide formation and C–H insertion takes place in the presence of a dipolarophile. Under carefully maintained experimental conditions, we could successfully obtain only the oxatricyclic compound in very good yields without forming any C–H insertion[13,14] product **9** (expected from compound **6b**). Moreover, we have also not isolated any 2:1 cycloadducts like **10** as described in the literature[13] for rhodium catalyzed cycloaddition reactions with excess amount of diazo ketone. We also failed to obtain 2:1 cycloadduct **10a**,**b** by reacting the diazo compounds **6b** as well as **6d** with isolated product **8b** in the presence of rhodium(II) acetate as a catalyst. It may be noted that the rhodium(II) catalyzed reactions of diazo compounds without carbonyl functionality in the cyclopentyl[15] and cyclohexyl[16] ring furnished only a mixture of corresponding cycloalkylacetic acids via Wolff rearrangement and unexpected cycloalkylcarboxylic acids without forming any C–H insertion product.



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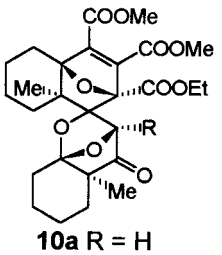


10a R = H
10b R = COOEt

After studying various ring systems, we were interested in further illustrating the scope and synthetic utility of the tandem cyclization–cycloaddition sequence. Thus, we synthesized α-diazo ketones **14** in order to obtain oxatricyclic systems with various subtituents. C-Alkylation of ethyl 2-cyclohexanoneacetate with methyl iodide, ethyl iodide was carried out by the Stork-enamine method as described[17] in the literature to afford ethyl 3-methyl-2-cyclohexanoneacetate (**11a**) and ethyl 3-ethyl-2-cyclohexanoneacetate (**11b**), respectively. The above reaction was carried out with 2-methylcyclohexanone and ethyl 2-bromopropionate to afford ethyl 2-(3-methyl-2-oxocyclohexyl) propionate (**11c**). Hydrolysis of the above substrates **11a**–**c** using 5% aqueous potassium hydroxide solution afforded 3-methyl-2-cyclohexanoneacetic acid (**12a**), 3-ethyl-2-cyclohexanoneacetic acid (**12b**) and 2-(3-methyl-2-oxocyclohexyl)propionic acid (**12c**), respectively. Further reactions of acids **12a**–**c** were carried out as described above for substrate **6a** to obtain α-diazo ketones **14a**–**c**, respectively (Scheme 2). Reaction of the acid chloride of **12a** and diazoethane solution afforded diazo ketone **14d**. In these cases, the exclusive products were the *exo*-isomers of the oxatricyclic compounds **15a**–**f** in the presence of *N*-phenylmaleimide as a dipolarophile. The assignment of stereochemistry was made upon inspection of the ^{1}H NMR spectra; the bridgehead proton (R^4=H) of compound **15e** showed a singlet without any coupling. No products resulting from potential competitive C–H insertion[14] could be detected.

All the active methylene compounds **5a**,**b**,**e**,**f** and **13a**–**c** prepared in this work exist in 5–10% enolic form based on the presence of characteristic peaks around δ 5.0 (olefinic proton) and δ 12.0 (enol proton) in ^{1}H NMR and around δ 90 for olefinic carbon (C=*C*H) in ^{13}C NMR. Typically, the presence of strong absorption around 2100 cm^{-1} in infrared spectra, the singlet resonance around δ 5.3 in compounds **6c**,**d**,**g** and **14e** in ^{1}H NMR spectra and a quaternary carbon atom around δ 75 in compounds **6a**,**b**,**e**,**f** and **14a**–**c** in ^{13}C NMR spectra established the presence of the diazo functionality. Due to very long relaxation times, the resonance for the above quaternary carbon atom adjacent to the diazo functional group was usually less intense for diazo compounds **6a**,**b**,**e**,**f** and **14a**–**c**.

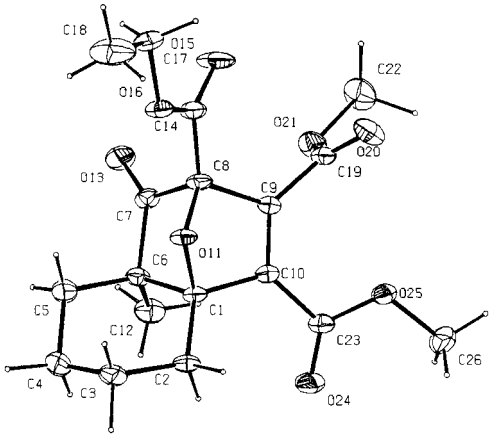


Figure 1. ORTEP view of the compound **8b**.

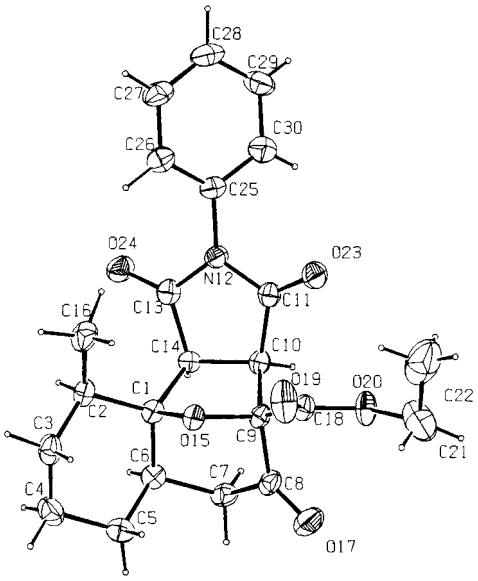
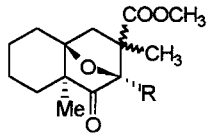


Figure 2. ORTEP view of the compound **15a**.

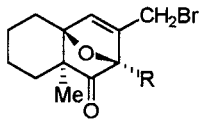
The diazo substrates **6a**,**b**,**e**,**f**/**14a**–**c** and **14d** were obtained by diazo transfer reactions and diazoethane reactions. The rhodium induced carbonyl ylide formation process is highly dependent on the electronic nature[18] of the substituent attached to the diazo carbon atom. Irrespective of five- or six-ring carbonyl ylide formation, the yield of cycloadducts **8a**,**b**,**e**,**f** and **15a**–**c**,**f** increased when the electrophilicity of the intermediate rhodium carbenoid was increased (when R^2=COOEt in compounds **6** and R^4=COOEt in compounds **14**). The methyl substituent in the diazo compounds **6a**–**d**, **14e**,**f** was required because the apparently highly stabilized dipole **7a**–**d**, **16e**,**f** transfers a proton at a faster rate than bimolecular cycloaddition. This phenomenon[19] is not observed in diazo substrates **6e**–**g** and **14a**–**d**.

The stereochemical assignments of compounds **8b** (Fig. 1) and **15a** (Fig. 2) were unambiguously established by X-ray crystallography. The presence of the methyl group at the ring juncture in the compound **8b**, *endo* with respect to the oxido bridge is tentatively assigned for other products based on their similarity in spectral data. The angle of oxa-bridge (C–O–C) was observed as 97.2 and 106.7° in six- and seven-membered carbocyclic systems **8b** and **15a**, respectively. The dihedral angle between H10 and C18 showed 88.5° in compound **15a** and this prediction agrees well with the absence of coupling between the H9 proton and the bridgehead proton (H8) in compound **15e**. Moreover, the crystal structure confirms the complete diastereoselectivity and is the result of *exo*-cycloadduct **15a**.

To widen the synthetic utility, the carbenoid cyclization–cycloaddition sequence was extended to unsymmetrical dipolarophiles, so as to probe the regiochemical aspects of the reaction. To this end, diazo ketones **6b** and **6d** were allowed to react with methyl methacrylate. Cycloaddition products **17a**,**b** and **17c**,**d** were formed regioselectively as diastereomeric mixtures (ratio of 1:5 and 1:2) in good yields, respectively. The distereomeric mixtures were separated by column chromatography for full spectral characterization. The diazo ketones **6b** and **6d** were also subjected to propargyl bromide in the presence of rhodium-(II) catalyst affording the regioselective products **18a** and **18b** in moderate yield. The assigned regio- and stereochemistry of the products follow from the above studies and ^{1}H NMR spectra, which showed a singlet for the bridgehead proton (H-8) in products **17a**, **17b** and **18a**. The cycloaddition does proceed, however, with high regioselectivity producing a single regioisomer in both cases.



17a,b R = H
17c,d R = COOEt



18a R = H
18b R = COOEt

The above results show that the mechanism by which **6a**–**d**/**14e**–**f** were converted into **8a**–**d**/**15e**–**f**, respectively involves rapid cyclization of the rhodium carbenoid onto the neighboring ring carbonyl group to give five-ring carbonyl ylides **7a**–**d** and **16e**–**f**. The length of the tether that links the carbonyl and diazo ketone functionalities in compounds **6e**–**g** and **14a**–**d** involves six-ring carbonyl ylides as intermediates **7e**–**g**/**16a**–**d** followed by a subsequent [3+2]-cycloaddition with dipolarophiles takes place. Similar efficiency of this cyclization–cycloaddition strategy was observed with both five- or six-ring carbonyl ylides and provides the basic sesquiterpenoids skeleton having a cyclic ether bridge.

In conclusion, we have demonstrated the high efficiency of rhodium carbenoid induced cyclization of diazo ketones. Coupled with the simplicity of the procedure, the method promises to provide an effective route to a variety of the substituted and functionalized oxatricyclic systems in a single step operation. Further, the oxa-bridge serves as a latent hydroxyl substitutent of defined stereochemistry upon reductive cleavage to a targeted family of hydroxylated bicyclic carbocyclic systems. As a consequence of its practical simplicity and high efficiency, this method is expected to have wide synthetic utility for the synthesis of oxapolycyclic and carbocyclic systems. Currently, we are investigating the application of this methodology in the synthesis of natural products.

Experimental

Melting points are uncorrected. IR spectra were recorded on a Perkin–Elmer Spectrum GX FT-IR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX 200 (200 and 50 MHz, respectively) spectrometer and referenced to TMS. Carbon types were determined from DEPT ^{13}C NMR experiments. Mass analyses were performed on a Finnigan MAT 8230 mass spectrometer with an ionizing voltage of 70 eV. Elemental analyses were performed on a Perkin Elmer Model 2400 analyser. X-Ray crystallographic analyses were carried out in a Enraf Nonius CAD-4 diffractometer with Mo K_α radiation. All solvents were purified by distillation. Thin layer chromatography was performed on silica or alumina plates and components were visualized by observation under iodine or by sulphuric acid charring.

Column chromatography was performed on Silica Gel 100–200 mesh and neutral alumina. All air sensitive reactions were conducted in flame-dried glassware under a positive pressure of Argon with magnetic stirring. Reagents were added via syringes through septa. Care has been taken to avoid light during the course of reaction in the synthesis of diazo compounds and its further conversion.

General procedure for the synthesis of diazo ketones 6 and 14

Acid chloride method: Cycloalkanone ester (12 mmol) was carefully hydrolyzed using 5% aqueous potassium hydroxide solution (20 ml) with stirring at room temperature. The reaction was monitored by TLC and continued till the disappearance of starting material. The reaction mixture was extracted with ether, the aqueous layer acidified and extracted with ethyl acetate. The organic phase was concentrated under reduced pressure at room temperature to obtain the corresponding keto acids **4**. Freshly distilled oxalyl chloride (20 mmol) was added dropwise to a stirring solution of 10 mmol of appropriate acid in 15 ml of dry ether at 25°C, and the stirring was continued for 2 h under an argon atmosphere. The solution was evaporated under reduced pressure, the crude residual acid chloride was dissolved in 100 ml freshly prepared dry ether and used for next step without further purification. The crude acid chloride solution was added dropwise over a 0.5 h period to stirring solution of 13 mmol of freshly prepared diazomethane and 10 mmol of freshly distilled triethylamine in 50 ml of dry ether at 0°C, and the stirring was continued for 2 h under an argon atmosphere. The mixture was filtered and the filtrate evaporated. Chromatography of the residue through a silica gel column (prewashed by ethyl acetate) led to the corresponding diazo ketone with 10% ethyl acetate–hexane elution.

Mixed anhydride method: To a solution containing 1 equiv. of appropriate (10 mmol) keto acid in 100 ml of freshly prepared dry ether was added 1.2 equiv. of freshly distilled ethyl chloroformate followed by the slow addition of 1.5 equiv. of dry triethylamine. The resulting mixture was stirred at room temperature for 45 min and the solid that formed was filtered under inert atmosphere. The filtrate was added to 20 mmol of freshly prepared ethereal diazomethane solution and then the mixture stirred for 12 h at 0°C, after this duration allowed to warm till 10°C for a period of 2 h under an argon atmosphere. Then at the end of this time the solvent was removed under reduced pressure and the residue was purified as described above.

Diazo transfer method: To a solution of freshly distilled monoethyl malonate (35 mmol) in dry dichloromethane (8 ml) under an argon atmosphere was added dropwise a solution of isopropylmagnesium bromide (70 mmol) in tetrahydrofuran (50 ml) until propane has been evolved. The temperature rises to 40–50°C. The green-colored solution was then cooled in an ice/salt bath and crude appropriate acid chloride obtained from the corresponding acid (14 mmol) in dichloromethane (2 ml) was added dropwise with efficient stirring. The stirring was continued for an hour after removing from the cooling bath and the resultant mixture was poured into cold 10% hydrochloric acid (20 ml). After cessation of carbon dioxide evolution the clear solution was extracted with ethyl acetate, washed with saturated sodium bicarbonate and brine solution. The organic phase was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography on silica gel to afford the corresponding active methylene compound.

To a solution containing 1 equiv. of the appropriate active methylene compound and 1.2 equiv. of freshly distilled methanesulphonyl azide in 5 ml of dry acetonitrile or methylenechloride was added 2 equiv. of freshly distilled triethylamine under an argon atmosphere at room temperature. The reaction was monitored by TLC till the disappearance of the starting material. The solvent was removed under reduced pressure at room temperature and the residue subjected to short neutral alumina column chromatography to get pure diazo ketone with 15% ethyl acetate–hexane elution.

Preparation of 2-diazo-3-(1-methyl-2-oxocyclopentyl)-3-oxopropanoic acid ethyl ester (6a). Hydrolysis of 2.5 g of 2-carbethoxy-2-methyl cyclopentanone was carried out for 5 h to afford the acid **4a** (1.9 g) in 90% yield. Treatment of 1.5 g (10.6 mmol) of acid **4a** with oxalyl chloride (2.2 ml, 21.2 mmol) furnished the crude acid chloride. Further reaction of crude acid chloride with DCM/THF (1:5) solution of dianion of monoethyl malonate, prepared from monoethyl malonate (3.5 g, 26.5 mmol) and isopropylmagnesium bromide (8.0 g, 53.0 mmol) gave active methylene compound **5a** (1.2 g) in 55% yield as a colorless liquid; ν_{max} (neat) 2978, 1741, 1708, 1648, 1459, 1408, 1320, 1263, 1157, 1029 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.16 (2H, q, J=7.2 Hz, OCH_2), 3.74 (1H, d, J=16.0 Hz), 3.56 (1H, d, J=16.0 Hz), 2.76–2.66 (1H, m), 2.39–2.30 (2H, m), 2.00–1.85 (2H, m), 1.78–1.68 (1H, m), 1.34 (3H, s, CCH_3), 1.26 (3H, t, J=7.2 Hz, CH_2CH_3); δ_C (50 MHz, $CDCl_3$) 217.0 (C=O), 201.0 (C=O), 168.0 (COO), 64.3 (CCH$_3$), 61.9 (OCH$_2$), 45.2 (CH$_2$), 38.7 (CH$_2$), 34.1 (CH$_2$), 21.3 (CH$_3$), 19.9 (CH$_2$), 14.7 (CH$_2$$CH_3$).

The reaction of the compound **5a** (330 mg, 1.6 mmol), mesyl azide (230 mg, 1.7 mmol) and triethylamine (0.44 ml, 3.2 mmol) afforded **6a** (333 mg) in 90% yield as a thick yellow oil; [Found: C, 55.61; H, 6.01; N, 11.70. $C_{11}H_{14}N_2O_4$ requires C, 55.46; H, 5.92; N, 11.76%]; ν_{max} (neat) 2982, 2142, 1738, 1715, 1643, 1372, 1323, 1170 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.23 (2H, q, J=7.2 Hz, OCH_2), 2.87–1.69 (6H, m), 1.30 (3H, s, CCH_3), 1.29 (3H, t, J=7.2 Hz, CH_2CH_3); δ_C (50 MHz, $CDCl_3$) 216.5 (C=O), 191.0 (C=O), 160.9 (COO), 76.0 (C=N$_2$), 62.0 (OCH$_2$), 61.7 (CCH$_3$), 36.1 (CH$_2$), 34.9 (CH$_2$), 19.8 (CH$_3$), 19.75 (CH$_2$), 14.8 (CH$_3$).

Preparation of 2-diazo-3-(1-methyl-2-oxocyclohexyl)-3-oxopropanoic acid ethyl ester (6b). Hydrolysis of 2.0 g of 2-carbethoxy-2-methyl cyclohexanone was carried out for 6 h to afford the acid **4b** (1.5 g) in 88% yield. Treatment of 1.4 g (9.0 mmol) of acid **4b** with oxalyl chloride (1.9 ml, 18.0 mmol) furnished the crude acid chloride. Further reaction of crude acid chloride with DCM/THF (1:5) solution of dianion of monoethyl malonate, prepared from monoethyl malonate (3.0 g, 22.4 mmol) and

isopropylmagnesium bromide (7.0 g, 44.8 mmol) gave active methylene compound **5b** (1.3 g) in 63% yield as a colorless liquid; ν_{max} (neat) 2978, 1742, 1710, 1648, 1458, 1407, 1372, 1329, 1263, 1028 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.21 (2H, q, J=7.2 Hz, OCH_2), 3.52 (1H, d, J=16.0 Hz), 3.42 (1H, d, J=16.0 Hz), 2.58–2.38 (3H, m), 2.04–1.39 (5H, m), 1.31 (3H, s, CCH_3), 1.27 (3H, t, J=7.2 Hz, CH_2CH_3); δ_C (50 MHz, $CDCl_3$) 209.7 (C=O), 201.8 (C=O), 166.8 (COO), 63.9 (CCH_3), 61.3 (OCH_2), 44.6 (CH_2), 41.0 (CH_2), 36.1 (CH_2), 27.0 (CH_2), 21.8 (CH_2), 20.4 (CH_3), 13.9 (CH_2CH_3).

The reaction of the compound **5b** (385 mg, 1.7 mmol), mesyl azide (250 mg, 2.0 mmol) and triethylamine (0.48 ml, 3.4 mmol) afforded **6b** (355 mg) in 83% yield as a thick yellow oil; [Found: C, 57.35; H, 6.13; N, 10.87. $C_{12}H_{16}N_2O_4$ requires C, 57.13; H, 6.39; N, 11.10%]; ν_{max} (neat) 2947, 2876, 2147, 1712, 1646, 1453, 1375, 1320, 1156, 1031 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.21 (2H, q, J=7.2 Hz, OCH_2), 2.45–2.19 (4H, m), 1.85–1.77 (3H, m), 1.62–1.56 (1H, m), 1.35 (3H, s, CCH_3), 1.28 (3H, t, J=7.2 Hz, CH_2CH_3); δ_C (50 MHz, $CDCl_3$) 209.0 (C=O), 192.7 (C=O), 161.2 (COO), 75.3 (C=N_2), 61.3 (OCH_2), 60.5 (CCH_3), 37.7 (CH_2), 34.3 (CH_2), 24.0 (CH_2), 20.5 (CH_3), 20.1 (CH_2), 13.5 (CH_3).

Preparation of 1-diazo-2-(1-methyl-2-oxocyclopentyl)-ethan-2-one (6c). A solution containing 600 mg (4.2 mmol) of acid **4a** in dry ether was treated with 0.48 ml (5.0 mmol) of ethyl chloroformate, 0.9 ml (6.4 mmol) of triethylamine to afford the mixed anhydride **5c** and followed by treatment with 8.5 mmol of diazomethane solution gave the diazo ketone **6c** (440 mg) in 65% yield.

A solution containing 500 mg (3.5 mmol) of acid **4a** in dry ether was treated with 0.73 ml (7.0 mmol) of oxalyl chloride to afford the acid chloride **5c** which on treatment with 4.6 mmol diazomethane solution containing 0.5 ml (3.5 mmol) of triethylamine gave the diazo ketone **6c** (497 mg) in 85% yield as a thick yellow bright oil; [Found: C, 57.69; H, 6.05; N, 16.78. $C_8H_{10}N_2O_2$ requires C, 57.82; H, 6.07; N, 16.85%]; ν_{max} (neat) 2962, 2875, 2109, 1733, 1631, 1458, 1351, 1277, 1199, 1043 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 5.65 (1H, s, CHN_2), 2.52–2.31 (3H, m), 2.03–1.86 (3H, m), 1.30 (3H, s, CH_3); δ_C (50 MHz, $CDCl_3$) 216.1 (C=O), 194.0 (C=O), 56.2 (CCH_3), 54.0 (CHN_2), 38.0 (CH_2), 36.3 (CH_2), 19.8 (CH_2), 19.7 (CH_3).

Preparation of 1-diazo-2-(1-methyl-2-oxocyclohexyl)-ethan-2-one (6d). A solution containing 320 mg (2.1 mmol) of acid **4b** in dry ether was treated with 0.23 ml (2.5 mmol) of ethyl chloroformate, 0.43 ml (3.2 mmol) of triethylamine to afford the mixed anhydride **5d** and followed by treatment with 4.0 mmol of diazomethane solution gave the diazo ketone **6d** (250 mg) in 68% yield.

A solution containing 1.4 g (8.9 mmol) of acid **4b** in dry ether was treated with 1.9 ml (17.9 mmol) of oxalyl chloride to afford the acid chloride **5d** which on treatment with 11.7 mmol diazomethane solution containing 1.3 ml (8.9 mmol) of triethylamine gave the diazo ketone **6d** (1.5 g) in 92% yield as a thick yellow oil; [Found: C, 60.15; H, 6.67; N, 15.42. $C_9H_{12}N_2O_2$ requires C, 59.99; H, 6.71; N, 15.55%]; ν_{max} (neat) 2942, 2870, 2110, 1757, 1721, 1453, 1355, 1266, 1126, 1018 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 5.27 (1H, s, CHN_2), 2.59–2.41 (2H, m), 2.07–1.35 (6H, m), 1.24 (3H, s, CH_3); δ_C (50 MHz, $CDCl_3$) 211.0 (C=O), 193.7 (C=O), 61.9 (CCH_3), 53.8 (CHN_2), 41.8 (CH_2), 37.3 (CH_2), 27.6 (CH_2), 22.8 (CH_2), 22.7 (CH_3).

Preparation of 2-diazo-4-(2-oxocyclopentyl)-3-oxobutanoic acid ethyl ester (6e). Hydrolysis of 4.0 g of ethyl 2-cyclopentanoneacetate was carried out for 8 h to afford the acid **4e** (3.2 g) in 96% yield. Treatment of 2.8 g (19.7 mmol) of acid **4e** with oxalyl chloride (4.0 ml, 39.4 mmol) furnished the crude acid chloride. Further reaction of crude acid chloride with DCM/THF (1:5) solution of dianion of monoethyl malonate, prepared from monoethyl malonate (6.5 g, 49.3 mmol) and isopropylmagnesium bromide (14.5 g, 98.6 mmol) gave active methylene compound **5e** (2.4 g) in 57% yield as a colorless liquid; ν_{max} (neat) 2977, 1738, 1715, 1643, 1447, 1371, 1322, 1190, 1133, 1054 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.19 (2H, q, J=7.2 Hz, OCH_2), 3.62 (1H, d, J=16.1 Hz), 3.52 (1H, d, J=16.1 Hz), 2.76–2.66 (1H, m), 2.48–2.03 (6H, m), 1.84–1.58 (2H, m), 1.26 (3H, t, J=7.2 Hz, CH_3); δ_C (50 MHz, $CDCl_3$) 219.5 (C=O), 202.1 (C=O), 167.1 (COO), 61.2 (CH_2), 50.1 (CH_2), 46.2 (CH), 37.8 (CH_2), 34.4 (CH_2), 29.7 (CH_2), 20.9 (CH_2), 14.6 (CH_3).

The reaction of the compound **5e** (420 mg, 2.0 mmol), mesyl azide (290 mg, 2.4 mmol) and triethylamine (0.56 ml, 4.0 mmol) afforded **6e** (395 mg) in 84% yield as a thick yellow oil; [Found: C, 55.40; H, 5.89; N, 11.75%. $C_{11}H_{14}N_2O_4$ requires C, 55.46; H, 5.92; N, 11.76%]; ν_{max} (neat) 2981, 2148, 1740, 1707, 1644, 1374, 1320, 1267, 1156, 1029 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.20 (2H, q, J=7.1 Hz, OCH_2), 2.72–2.61 (1H, m), 2.52–2.08 (6H, m), 1.89–1.50 (2H, m), 1.27 (3H, t, J=7.1 Hz, CH_3); δ_C (50 MHz, $CDCl_3$) 217.0 (C=O), 192.0 (C=O), 161.9 (COO), 75.9 (C=N_2), 62.0 (OCH_2), 46.1 (CH), 37.1 (CH_2), 34.3 (CH_2), 29.8 (CH_2), 21.0 (CH_2), 14.7 (CH_3).

Preparation of 2-diazo-4-(2-oxocyclopentyl)-3-oxobutanoic acid ethyl ester (6f). Hydrolysis of 4.0 g of ethyl 2-cyclohexanoneacetate was carried out for 7.5 h to afford the acid **4f** (3.2 g) in 94% yield. Treatment of 2.7 g (17.3 mmol) of acid **4f** with oxalyl chloride (3.5 ml, 34.6 mmol) furnished the crude acid chloride. Further reaction of crude acid chloride with DCM/THF (1:5) solution of dianion of monoethyl malonate, prepared from monoethyl malonate (5.7 g, 43.3 mmol) and isopropylmagnesium bromide (13.4 g, 86.5 mmol) gave active methylene compound **5f** (2.4 g) in 61% yield as a colorless liquid; ν_{max} (neat) 2976, 1739, 1712, 1456, 1409, 1373, 1317, 1209, 1148, 1020 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.19 (2H, q, J=7.2 Hz, OCH_2), 3.58 (1H, d, J=15.4 Hz), 3.48 (1H, d, J=15.4 Hz), 3.08–2.91 (2H, m), 2.45–2.16 (3H, m), 2.14–2.07 (2H, m), 1.87–1.76 (1H, m), 1.75–1.32 (3H, m), 1.28 (3H, t, J=7.2 Hz, CH_3); δ_C (50 MHz, $CDCl_3$) 211.8 (C=O), 202.8 (C=O), 167.9 (COO), 61.9 (OCH_2), 50.5 (CH_2), 47.4 (CH), 43.2 (CH_2), 42.4 (CH_2), 34.5 (CH_2), 28.4 (CH_2), 25.9 (CH_2), 14.8 (CH_3).

The reaction of the compound **5f** (300 mg, 1.3 mmol), mesyl azide (195 mg, 1.6 mmol) and triethylamine (0.37 ml, 2.6 mmol) afforded **6f** (298 mg) in 89% yield as a thick yellow oil; [Found: C, 57.55; H, 6.33; N, 10.82. $C_{12}H_{16}N_2O_4$ requires C, 57.13; H, 6.39; N, 11.10%]; ν_{max} (neat) 2949, 2148, 1714, 1646, 1375, 1320, 1125, 1031 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.20 (2H, q, J=7.2 Hz, OCH_2), 3.04–2.93 (2H, m), 2.41–2.27 (3H, m), 2.16–2.08 (2H, m), 1.72–1.32 (4H, m), 1.28 (3H, t, J=7.2 Hz, CH_3); δ_C (50 MHz, CD_3CN) 211.8 (*C*=O), 202.8 (*C*=O), 167.9 (*C*OO), 76.9 (*C*=N_2), 62.0 (O*C*H_2), 47.4 (*C*H), 43.2 (*C*H_2), 42.4 (*C*H_2), 34.6 (*C*H_2), 28.4 (*C*H_2), 25.8 (*C*H_2), 14.8 (*C*H_3).

Preparation of 1-diazo-3-(2-oxocyclohexyl)propan-2-one (6g). A solution containing 1.0 g (6.4 mmol) of acid **4f** in dry ether was treated with 0.73 ml (7.7 mmol) of ethyl chloroformate, 1.4 ml (9.6 mmol) of triethylamine to afford the mixed anhydride **5g** and followed by treatment with 12.8 mmol of diazomethane solution gave the diazo ketone **6g** (810 mg) in 70% yield. A solution containing 1.0 g (6.4 mmol) of acid **4f** in dry ether was treated with 1.3 ml (12.8 mmol) of oxalyl chloride to afford the acid chloride **5g** which on treatment with 8.3 mmol diazomethane solution containing 0.9 ml (6.4 mmol) of triethylamine gave the diazo ketone **6g** (1.1 g) in 95% yield as a thick yellow bright oil; [Found: C, 60.22; H, 6.66; N, 15.37. $C_9H_{12}N_2O_2$ requires C, 59.99; H, 6.71; N, 15.55%]; ν_{max} (neat) 2938, 2864, 2108, 1713, 1450, 1371, 1277, 1132, 1030 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 5.34 (1H, s, C*H*N_2), 2.92–2.70 (2H, m), 2.43–2.35 (2H, m), 2.20–1.86 (3H, m), 1.79–1.38 (4H, m); δ_C (50 MHz, $CDCl_3$) 212.0 (*C*=O), 193.7 (*C*=O), 53.9 (*C*HN_2), 47.5 (*C*H), 42.2 (*C*H_2), 34.8 (*C*H_2), 34.3 (*C*H_2), 28.2 (*C*H_2), 25.6 (*C*H_2).

Preparation of 2-diazo-4-(3-methyl-2-oxocyclohexyl)-3-oxobutanoic acid ethyl ester (14a). A toluene solution (50 ml) of ethyl 2-cyclohexanoneacetate (5.0 g, 27.2 mmol) and pyrrolidine (5.7 ml, 68.0 mmol) was refluxed under a water separator in the presence of catalytic amount of *p*-toluenesulphonic acid for 15 h. The solvent and excess pyrrolidine were removed under reduced pressure and the crude pyrrolidine enamine was taken in dry benzene (50 ml). To the reaction mixture methyl iodide (2.5 ml, 41.0 mmol) was added at room temperature with stirring and refluxed for 10 h. The solvent was removed and the residue refluxed with 30 ml of water–methanol (1:5) mixture for an hour. Removal of solvent and extraction with ether, washing with dilute hydrochloric acid gave ethyl 3-methyl-2-cyclohexanoneacetate (**11a**) (1.94 g) in 36% yield.

Hydrolysis of the ester **11a** (370 mg, 1.9 mmol) with 5% aqueous potassium hydroxide solution for 4 h afforded the acid **12a** (300 mg) in 96% yield. Treatment of 270 mg (1.6 mmol) of acid **12a** with oxalyl chloride (0.33 ml, 3.2 mmol) furnished the crude acid chloride. Further reaction of crude acid chloride with DCM/THF (1:5) solution of dianion of monoethyl malonate, prepared from monoethyl malonate (525 mg, 4.0 mmol) and isopropylmagnesium bromide (1.17 g, 8.0 mmol) gave active methylene compound **13a** (183 mg) in 48% yield as a colorless liquid; ν_{max} (neat) 2979, 1738, 1713, 1457, 1408, 1372, 1312, 1262, 1202, 1141, 1112, 1108, 1029 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.20 (2H, q, J=7.2 Hz, OCH_2), 3.60 (1H, d, J=15.4 Hz), 3.48 (1H, d, J=15.4 Hz), 3.05–2.95 (2H, m), 2.47–2.08 (4H, m), 1.87–1.77 (2H, m), 1.42–1.33 (2H, m), 1.28 (3H, t, J=7.2 Hz, CH_2CH_3), 0.99 (3H, d, J=6.4 Hz); δ_C (50 MHz, $CDCl_3$) 213.0 (*C*=O), 202.3 (*C*=O), 167.8 (*C*OO), 61.8 (O*C*H_2), 50.4 (*C*H_2), 47.4 (*C*H), 45.8 (*C*H), 43.2 (*C*H_2), 37.6 (*C*H_2), 35.3 (*C*H_2), 25.9 (*C*H_2), 15.0 (*C*H_3), 14.7 (*C*H3).

The reaction of the compound **13a** (120 mg, 0.5 mmol), mesyl azide (73 mg, 0.6 mmol) and triethylamine (0.14 ml, 1.0 mmol) gave **14a** (130 mg) in 98% yield as a thick yellow oil; [Found: C, 58.65; H, 6.78; N, 10.48. $C_{13}H_{18}N_2O_4$ requires C, 58.62; H, 6.81; N, 10.52%]; ν_{max} (neat) 2931 2137, 1714, 1654, 1368, 1304, 1169, 1137, 1031 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.17 (2H, q, J=7.2 Hz, OCH_2), 3.04–2.94 (2H, m), 2.32–2.08 (4H, m), 1.87–1.77 (2H, m), 1.37–1.33 (2H, m), 1.28 (3H, t, J=7.2 Hz, CH_2CH_3), 0.99 (3H, d, J=6.4 Hz); δ_C (50 MHz, $CDCl_3$) 213.0 (*C*=O), 202.3 (*C*=O), 167.8 (*C*OO), 76.0 (*C*=N_2), 61.8 (O*C*H_2), 47.3 (*C*H), 45.8 (*C*H), 43.2 (*C*H_2), 37.6 (*C*H_2), 35.3 (*C*H_2), 25.9 (*C*H_2), 15.0 (*C*H_3), 14.7 (*C*H_3).

Preparation of 2-diazo-4-(3-ethyl-2-oxocyclohexyl)-3-oxobutanoic acid ethyl ester (14b). Pyrrolidine enamine of ethyl 2-cyclohexanoneacetate (4.0 g, 21.7 mmol) was prepared as described above. To the crude enamine reaction mixture in dry benzene (50 ml), ethyl iodide (2.6 ml, 32.5 mmol) was added at room temperature with stirring and refluxed for 8 h. The reaction mixture was worked-up as above to obtain ethyl 3-ethyl-2-cyclohexanoneacetate **11b** (1.88 g) in 41% yield.

Hydrolysis of the ester **11b** (1.0 g, 4.7 mmol) with 5% aqueous potassium hydroxide solution for 5 h afforded the acid **12b** (798 mg) in 94% yield. Treatment of 525 mg (2.9 mmol) of acid **12b** with oxalyl chloride (0.6 ml, 5.8 mmol) furnished the crude acid chloride. Further reaction with monoethyl malonate (950 mg, 7.2 mmol) and isopropylmagnesium bromide (2.12 g, 14.4 mmol) as described above gave active methylene compound **13b** (183 mg) in 58% yield as a colorless liquid; ν_{max} (neat) 2978, 2975, 1737, 1712, 1458, 1433, 1376, 1346, 1262, 1200, 1149, 1108, 1028 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.19 (2H, q, J=7.2 Hz, OCH_2), 3.56 (1H, d, J=16.0 Hz), 3.44 (1H, d, J=16.0 Hz), 3.07–2.94 (2H, m), 2.39–1.98 (4H, m), 1.85–1.77 (2H, m), 1.38–1.34 (2H, m), 1.27 (3H, t, J=7.2 Hz, CH_2CH_3), 1.03–0.96 (2H, m), 0.90 (3H, t, J=7.5 Hz, CH_2CH_3); δ_c (50 MHz, $CDCl_3$) 212.9 (*C*=O), 202.0 (*C*=O), 167.8 (*C*OO), 61.7 (O*C*H_2), 50.3 (*C*H_2), 47.4 (*C*H), 44.5 (*C*H), 43.9 (*C*H_2), 37.5 (*C*H_2), 35.2 (*C*H_2), 26.0 (*C*H_2), 15.1 (*C*H_3), 14.9 (*C*H_2), 14.7 (*C*H_3).

The reaction of the compound **13b** (300 mg, 1.2 mmol), mesyl azide (172 mg, 1.4 mmol) and triethylamine (0.33 ml, 2.4 mmol) afforded **14b** (319 mg) in 96% yield as a thick yellow oil; [Found: C, 59.86; H, 7.16; N, 10.06. $C_{14}H_{20}N_2O_4$ requires C, 59.99; H, 7.19; N, 9.99%]; ν_{max} (neat) 2930, 2137, 1713, 1655, 1362, 1309, 1179, 1135, 1031 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.18 (2H, q, J=7.2 Hz, OCH_2), 3.08–2.84 (2H, m), 2.38–2.00 (4H, m), 1.87–1.75 (2H, m), 1.38–1.35 (2H, m), 1.27 (3H, t, J=7.2 Hz,

CH_2CH_3), 1.0–0.96 (2H, m), 0.91 (3H, t, J=7.5 Hz); δ_C (50 MHz, $CDCl_3$) 213.0 (*C*=O), 202.3 (*C*=O), 167.7 (*C*OO), 76.1 (*C*=N_2), 61.9 (O*C*H_2), 47.4 (*C*H), 45.9 (*C*H), 43.0 (CH_2), 36.7 (CH_2), 35.3 (CH_2), 25.7 (CH_2), 15.0 (CH_3), 14.9 (CH_2), 14.2 (CH_3).

Preparation of 2-diazo-4-methyl-4-(3-methyl-2-oxocyclohexyl)-3-oxobutanoic acid ethyl ester (14c). Pyrrolidine enamine of 2-methylcyclohexanone (5.0 g, 44.6 mmol) was prepared as described above. To the crude enamine reaction mixture in dry benzene (50 ml), ethyl 2-bromopropionate (11.6 ml, 89.2 mmol) was added at room temperature with stirring and refluxed for 15 h. The reaction mixture was worked-up as above to obtain ethyl 2-(3-methyl-2-oxocyclohexyl)propionate **11c** (3.15 g) in 33% yield.

Hydrolysis of the ester **11c** (2.0 g, 9.4 mmol) with 5% aqueous potassium hydroxide solution for 8 h afforded the acid **12c** (1.57 g) in 90% yield. Treatment of 1.25 g (6.8 mmol) of acid **12c** with oxalyl chloride (1.4 ml, 13.6 mmol) furnished the crude acid chloride. Further reaction with monoethyl malonate (2.25 g, 17.0 mmol) and isopropylmagnesium bromide (5.0 g, 34.0 mmol) as described above gave active methylene compound **13c** (810 mg) in 47% yield as a colorless liquid; ν_{max} (neat) 2978, 1739, 1710, 1649, 1458, 1407, 1378, 1332, 1267, 1102 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.21 (2H, q, J=7.2 Hz, OCH_2), 3.58 (1H, d, J=15.5 Hz), 3.46 (1H, d, J=15.5 Hz), 3.10–2.90 (2H, m), 2.59–2.10 (3H, m), 1.87–1.70 (2H, m), 1.42–1.33 (2H, m), 1.27 (3H, t, J=7.2 Hz, CH_2CH_3), 1.17 (3H, d, J=6.2 Hz), 0.98 (3H, d, J=6.3 Hz); δ_C (50 MHz, $CDCl_3$) 213.2 (*C*=O), 202.8 (*C*=O), 167.5 (*C*OO), 61.8 (O*C*H_2), 53.2 (*C*H), 50.3 (CH_2), 47.2 (*C*H), 39.6 (*C*H), 31.2 (CH_2), 27.6 (CH_2), 25.1 (CH_2), 15.0 (CH_3), 14.7 (CH_3), 14.1 (CH_3).

The reaction of the compound **13c** (400 mg, 1.6 mmol), mesyl azide (230 mg, 1.9 mmol) and triethylamine (0.45 ml, 3.2 mmol) afforded **14c** (425 mg) in 96% yield as a thick yellow oil; [Found: C, 59.92; H, 7.23; N, 9.95. $C_{14}H_{20}N_2O_4$ requires C, 59.99; H, 7.19; N, 9.99%]; ν_{max} (neat) 2942, 2139, 1716, 1658, 1362, 1348, 1307, 1183, 1029 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.19 (2H, q, J=7.2 Hz, OCH_2), 3.12–2.89 (2H, m), 2.53–2.12 (3H, m), 1.92–1.73 (2H, m), 1.45–1.30 (2H, m), 1.28 (3H, t, J=7.2 Hz, CH_2CH_3), 1.18 (3H, d, J=6.3 Hz), 0.99 (3H, d, J=6.3 Hz); δ_C (50 MHz, CD_3CN) 212.0 (*C*=O), 203.0 (*C*=O), 167.9 (*C*OO), 76.4 (*C*=N_2), 62.0 (O*C*H_2), 53.3 (*C*H), 47.4 (*C*H), 39.8 (*C*H), 31.3 (CH_2), 27.8 (CH_2), 25.3 (CH_2), 15.2 (CH_3), 14.8 (CH_3), 14.2 (CH_3).

Preparation of 2-diazo-4-(3-methyl-2-oxocyclohexyl)-3-oxobutane (14d). A solution containing 850 mg (5.1 mmol) of acid **12a** in dry ether was treated with 1.1 ml (10.6 mmol) of oxalyl chloride to afford the corresponding acid chloride which on treatment with 6.5 mmol diazoethane solution containing 0.7 ml (5.0 mmol) of triethylamine gave the diazo ketone **14d** (755 mg) in 71% yield as a thick yellow bright oil; [Found: C, 63,27; H, 7.53; N, 13.71. $C_{11}H_{16}N_2O_2$ requires C, 63.44; H, 7.74; N, 13.45%]; ν_{max} (neat) 2953, 2083, 1710, 1640, 1382, 1228, 1123, 1028 cm^{-1}.

General procedure for the rhodium catalyzed cycloaddition reaction of diazo ketones 6 and 14 with dipolarophiles

Method A: In a flame-dried flask, a solution containing 2 equiv. of dipolarophile and 1 mol% of rhodium acetate dimer in 10 ml of dry dichloromethane (dried over phosphorous pentoxide) was degassified under an argon atmosphere. To this reaction mixture a solution of 1 equiv. of appropriate diazo ketone in dry dichloromethane was added dropwise slowly for 1 h period under an argon atmosphere at room temperature. The reaction mixture was allowed to stir and followed by TLC till the disappearance of the starting material. The solvent was removed under reduced pressure and the residue purified by neutral alumina/silica column to afford the respective cycloadduct.

Method B: The procedure was followed as in method A using dry benzene (dried over sodium) instead of dichloromethane. The diazo ketone was added dropwise over 1 h to the refluxing reaction mixture under an argon atmosphere.

5-Methyl-6-oxo-10-oxatricyclo(5,2,1,$0^{1,5}$)dec-8-ene-7,8,9-tricarboxylic acid 7-ethyl ester 8,9-dimethyl ester (8a). A mixture of DMAD (180 mg, 1.3 mmol) and 2.8 mg of $Rh_2(OAc)_4$ in benzene (5 ml) was allowed to react with a benzene solution (2 ml) of diazo ketone **6a** (150 mg, 0.6 mmol) for 15 h at reflux according to the general method B to afford 184 mg (83%) of **8a** as a white solid, mp 84–86°C (chloroform/hexane); [Found: C, 57.89; H, 5.76. $C_{17}H_{20}O_8$ requires C, 57.95; H, 5.72%]; ν_{max} (KBr) 2961, 1782, 1747, 1728, 1659, 1443, 1262, 1179, 1016, 851 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.35 (2H, q, J=7.2 Hz, OCH_2), 3.86 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 2.77–2.68 (1H, m), 2.26–2.02 (4H, m), 1.76–1.66 (1H, m), 1.30 (3H, t, J=7.2 Hz, CH_2CH_3), 1.09 (3H, s, *tert*-CH_3); δ_C (50 MHz, $CDCl_3$) 203.3 (*C*=O), 163.5 (*C*OO), 163.0 (*C*OO), 162.2 (*C*OO), 145.6 (*C*=C), 141.1 (*C*=C), 102.0 (*C*–O), 92.1 (*C*–O), 63.3 (O*C*H_2), 53.5 (O*C*H_3), 53.3 (O*C*H_3), 50.4 (C-5), 34.3 (*C*H2), 26.6 (CH_2), 24.0 (CH_2), 21.8 (CH_3), 14.7 (CH_3); *m/z* 352 (M^+, 8), 308 (30), 251 (30), 149 (33), 112 (52), 85 (100%).

6-Methyl-7-oxo-11-oxatricyclo(6,2,1,$0^{1,6}$)undec-9-ene-8,9,10-tricarboxylic acid 8-ethyl ester 9,10-dimethyl ester (8b). A mixture of DMAD (225 mg, 1.6 mmol) and 3.5 mg of $Rh_2(OAc)_4$ in benzene (7 ml) was allowed to react with a benzene solution (3 ml) of diazo ketone **6b** (200 mg, 0.8 mmol) for 18 h at reflux according to the general method B to afford 253 mg (88%) of **8b** as a white solid, mp 82–83°C (chloroform/hexane); [Found: C, 58.92; H, 6.01. $C_{18}H_{22}O_8$ requires C, 59.01; H, 6.05%]; ν_{max} (KBr) 2941, 1779, 1752, 1727, 1634, 1441, 1320, 1268, 1183, 1011, 963 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.30 (2H, q, J=7.2 Hz, OCH_2), 3.80 (3H, s, OCH_3), 3.76 (3H, s, OCH_3), 2.56–2.48 (1H, m), 2.20–2.08 (1H, m), 1.76–1.50 (6H, m), 1.27 (3H, t, J=7.2 Hz, CH_2CH_3), 1.13 (3H, s, *tert*-CH_3); δC (50 MHz, $CDCl_3$) 204.0 (*C*=O), 162.5 (*C*OO), 162.4 (*C*OO), 161.6 (*C*OO), 144.0 (*C*=C), 143.4 (*C*=C), 92.0 (*C*–O), 91.3 (*C*–O), 62.5 (O*C*H_2), 52.7 (O*C*H_3), 52.5 (O*C*H_3), 41.6 (C-6), 32.1 (CH_2), 25.0 (CH_2), 20.9 (CH_2), 20.2 (CH_2), 19.3 (CH_3), 13.9 (CH_3); *m/z* 366 (M^+, 30), 334 (100), 306 (38), 274 (48), 251 (57), 232 (44%).

5-Methyl-6-oxo-10-oxatricyclo(5,2,1,0^{1,5})dec-8-ene-8,9-dicarboxylic acid 8,9-dimethyl ester (8c). A mixture of DMAD (170 mg, 1.2 mmol) and 2.7 mg of $Rh_2(OAc)_4$ in dichloromethane (7.0 ml) was allowed to react with a dichloromethane solution (3 ml) of diazo ketone **6c** (100 mg, 0.6 mmol) at room temperature for 5 h according to the general method A to afford 125 mg (74%) of **8c** as a thick oil; [Found: C, 60.07; H, 5.98. $C_{14}H_{16}O_6$ requires C, 59.99; H, 5.75%]; ν_{max} (neat) 2960, 1764, 1727, 1632, 1439, 1325, 1271, 1145, 1117 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.82 (1H, s, C*H*), 3.79 (3H, s, OCH_3), 3.75 (3H, s, OCH_3), 2.24–1.19 (6H, m), 1.02 (3H, s, *tert*-CH_3); δ_C (50 MHz, $CDCl_3$) 209.6 (*C*=O), 163.9 (*C*OO), 161.9 (*C*OO), 149.2 (*C*=C), 140.7 (*C*=C), 104.7 (C-1), 84.3 (C-7), 53.09 (O*C*H$_3$), 53.04 (O*C*H$_3$), 50.6 (C-5), 34.0 (*C*H$_2$), 26.6 (*C*H$_2$), 23.7 (*C*H$_2$), 21.3 (*C*H$_3$).

6-Methyl-7-oxo-11-oxatricyclo(6,2,1,0^{1,6})dec-9-ene-9,10-dicarboxylic acid 9,10-dimethyl ester (8d). A mixture of DMAD (475 mg, 3.3 mmol) and 7.3 mg of $Rh_2(OAc)_4$ in dichloromethane (10 ml) was allowed to react with a dichloromethane solution (5 ml) of diazo ketone **6d** (300 mg, 1.7 mmol) at room temperature for 3 h according to the general method A to afford 371 mg (76%) of **8d** as a white solid, mp 87–88°C (dichloromethane/hexane); [Found: C, 61:05; H, 6.35. $C_{15}H_{18}O_6$ requires C, 61.22; H, 6.16%];ν_{max} (KBr) 2955, 1761, 1732, 1650, 1440, 1318, 1259, 1202, 1131 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 5.00 (1H, s), 3.85 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 2.58–2.41 (1H, m), 2.12–1.99 (1H, m), 1.83–1.51 (6H, m), 1.18 (3H, s, *tert*-CH_3); δ_C (50 MHz, $CDCl_3$) 210.8 (*C*=O), 164.2 (*C*OO), 161.5 (*C*OO), 153.4 (*C*=C), 138.4 (*C*=C), 94.3 (C-1), 84.0 (C-8), 58.7 (C-6), 53.1 (O*C*H$_3$), 53.0 (O*C*H$_3$), 32.2 (*C*H$_2$), 25.4 (*C*H$_2$), 22.4 (*C*H$_2$), 21.4 (*C*H$_2$), 19.3 (*C*H$_3$); *m/z* 294 (M$^+$, 32), 262 (100), 234 (70), 202 (56), 179 (87), 166 (29), 91 (24%).

7-Oxo-11-oxatricyclo(6,2,1,0^{1,5})undec-9-ene-8,9,10-tricarboxylic acid 8-ethyl ester 9,10-dimethyl ester (8e). A mixture of DMAD (300 mg, 2.1 mmol) and 4.6 mg of $Rh_2(OAc)_4$ in benzene (10 ml) was allowed to react with a benzene solution (3 ml) of diazo ketone **6e** (250 mg, 1.1 mmol) for 14 h at reflux according to the general method B to afford 330 mg (89%) of **8e** as a thick oil; [Found: C, 58.08; H, 5.67. $C_{17}H_{20}O_8$ requires C, 57.95; H, 5.72%]; ν_{max} (neat) 2958, 1740, 1733, 1728, 1645, 1435, 1263, 1096, 1029, 978, 782 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.31 (2H, q, *J*=7.2 Hz, OCH_2), 3.84 (3H, s, OCH_3), 3.82 (3H, s, OCH_3), 2.99 (1H, dd, J_1=17.8 Hz, J_2=8.0 Hz), 2.67 (1H, dd, J_1=17.9 Hz, J_2=4.0 Hz), 2.60–2.35 (2H, m), 2.15–1.94 (3H, m), 1.82–1.70 (2H, m), 1.33 (3H, t, *J*=7.2 Hz, CH_3); δ_C (50 MHz, $CDCl_3$) 194.6 (*C*=O), 163.3 (*C*OO), 163.0 (*C*OO), 161.8 (*C*OO), 141.1 (*C*=C), 140.9 (*C*=C), 95.8 (*C*–O), 92.3 (*C*–O), 62.5 (O*C*H$_2$), 52.61 (O*C*H$_3$), 52.62 (O*C*H$_3$), 44.2 (C-5), 40.2 (*C*H$_2$), 33.0 (*C*H$_2$), 32.9 (*C*H$_2$), 24.1 (*C*H$_2$), 13.9 (*C*H$_3$).

8-Oxo-12-oxatricyclo(7,2,1,0^{1,6})dodec-10-ene-9,10,11-tricarboxylic acid 9-ethyl ester 10,11-dimethyl ester (8f). A mixture of DMAD (100 mg, 0.7 mmol) and 1.5 mg of $Rh_2(OAc)_4$ in benzene (7 ml) was allowed to react with a benzene solution (3 ml) of diazo ketone **6f** (90 mg, 0.4 mmol) for 11 h at reflux according to the general method B to afford 112 mg (86%) of **8f** as a thick liquid; [Found: C, 59.23; H, 6.26. $C_{18}H_{22}O_8$ requires C, 59.01; H, 6.05%]; ν_{max} (neat) 2936, 1741, 1739, 1732, 1645, 1436, 1372, 1264, 1154, 1108, 1037 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.30 (2H, q, *J*=7.2 Hz, OCH_2), 3.83 (6H, s, OCH_3), 3.12 (1H, dd, J_1=16.8 Hz, J_2=7.6 Hz), 2.41–2.28 (1H, m), 2.22–2.14 (1H, m), 2.09 (2H, d, *J*=17.0 Hz), 1.84–1.63 (4H, m), 1.43–1.36 (2H, m), 1.31 (3H, t, *J*=7.2 Hz, CH_2CH_3); δ_C (50 MHz, $CDCl_3$) 195.7 (*C*=O), 164.2 (*C*OO), 164.1 (*C*OO), 162.6 (*C*OO), 143.2 (*C*=C), 140.2 (*C*=C), 94.4 (*C*–O), 90.1 (*C*–O), 63.0 (O*C*H$_2$), 53.36 (O*C*H$_3$), 53.34 (O*C*H$_3$), 41.1 (*C*H$_2$), 40.5 (*C*H), 31.9 (*C*H$_2$), 31.0 (*C*H$_2$), 25.8 (*C*H$_2$), 21.3 (*C*H$_2$), 14.6 (*C*H$_3$), *m/z* 366 (M$^+$, 40), 334 (95), 306 (84), 274 (95), 246 (44), 233 (100), 201 (48), 115 (29%).

8-Oxo-12-oxatricyclo(7,2,1,0^{1,6})dodec-10-ene-10,11-dicarboxylic acid 10,11-dimethyl ester (8g). A mixture of DMAD (475 mg, 3.3 mmol) and 7.3 mg of $Rh_2(OAc)_4$ in dichloromethane (10 ml) was allowed to react with a dichloromethane solution (5 ml) of diazo ketone **6g** (300 mg, 1.7 mmol) at room temperature for 5 h according to the general method A to afford 348 mg (71%) of **8g** as a white solid, mp 84–86°C (dichloromethane/hexane); [Found; C, 61.11; H, 6.12. $C_{15}H_{18}O_6$ requires C, 61.22; H, 6.16%]; ν_{max} (KBr) 2930, 2861, 1731, 1654, 1440, 1273, 1200, 1142, 1013, 947 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.84 (1H, s), 3.90 (3H, s, OCH_3), 3.78 (3H, s, OCH_3), 3.02 (1H, dd, J_1=17.6 Hz, J_2=7.8 Hz), 2.33–2.21 (1H, m), 2.04 (2H, d, *J*=16.4 Hz), 1.81–1.25 (7H, m); δ_C (50 MHz, $CDCl_3$) 200.3 (*C*=O), 164.7 (*C*OO), 161.6 (*C*OO), 148.6 (*C*=C), 135.6 (*C*=C), 90.5 (C-1), 86.8 (C-9), 53.22 (O*C*H$_3$), 53.02 (O*C*H$_3$), 40.8 (*C*H$_2$), 38.4 (C-6), 31.9 (*C*H$_2$), 30.9 (*C*H$_2$), 25.6 (*C*H$_2$), 20.9 (*C*H$_2$); *m/z* 294 (M$^+$, 5), 278 (38), 261 (48), 233 (76) 201 (57), 167 (33), 149 (100), 91 (32%).

2-Methyl-8,11,13-trioxo-12-phenyl-15-oxa-12-azatetracyclo[7.5.1.0^{1,6}.0^{10,14}]pentadecane-9-carboxylic acid ethyl ester (15a). A mixture of *N*-phenyl maleimide (76 mg, 0.4 mmol) and 1.0 mg of $Rh_2(OAc)_4$ in dry benzene (7 ml) was allowed to react with a benzene solution (3 ml) of diazo ketone **14a** (60 mg, 0.2 mmol) for 10 h at reflux according to the general method B to afford 83 mg (92%) of **15a** as a white solid, mp 194–196°C (ethyl acetate/hexane); [Found: C, 67.26; H, 6.03; N, 3.36. $C_{23}H_{25}NO_6$ requires C, 67.14; H, 6.12; N, 3.40%]; ν_{max} (KBr) 2965, 1774, 1741, 1715, 1499, 1452, 1212, 1074, 1017, 851 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.51–7.43 (3H, m, Arom-*H*), 7.27–7.25 (2H, m, Arom-*H*), 4.39 (2H, q, *J*=7.2 Hz, OCH_2), 3.87 (1H, d, *J*=8.2 Hz), 3.57 (1H, d, *J*=8.2 Hz), 2.90 (1H, dd, J_1=12.5 Hz, J_2=7.4 Hz), 2.34–2.20 (5H, m), 1.70–1.50 (4H, m), 1.34 (3H, t, *J*=7.2 Hz, CH_2CH_3), 0.96 (3H, d, *J*=6.2 Hz, CH_3); δ_C (50 MHz, $CDCl_3$) 197.9 (*C*=O), 175.1 (N*C*O), 175.0 (N*C*O), 172.5 (*C*OO), 132.1 (*quat*-C), 129.9 (Arom-*C*H), 129.6 (Arom-*C*H), 126.8 (Arom-*C*H), 89.4 (*C*–O), 89.1 (*C*–O), 62.5 (O*C*H$_2$), 53.7 (*C*H), 52.3 (*C*H), 49.5 (*C*H), 42.0 (*C*H$_2$), 34.5 (*C*H), 32.9 (*C*H$_2$), 29.6 (*C*H$_2$), 25.5 (*C*H$_2$), 17.1 (*C*H$_3$), 14.6 (*C*H$_3$); *m/z* 411 (M$^+$, 32), 383 (40), 338 (25), 281 (43), 238 (100), 175 (83), 93 (37%).

2-Ethyl-8,11,13-trioxo-12-phenyl-15-oxa-12-azatetracyclo-[7.5.1.0^{1,6}.0^{10,14}]pentadecane-9-carboxylic acid ethyl ester (15b). A mixture of *N*-phenyl maleimide (90 mg, 0.5 mmol) and 1.2 mg of $Rh_2(OAc)_4$ in benzene (7 ml)

was allowed to react with a benzene solution (3 ml) of diazo ketone **14b** (75 mg, 0.3 mmol) for 8 h at reflux according to the general method B to afford 98 mg (82%) of **15b** as a white solid, mp 204–206°C (ethyl acetate/hexane); [Found: C, 67.61; H, 6.13; N, 3.20. $C_{24}H_{27}NO_6$ requires C, 67.75; H, 6.39; N, 3.29%]; ν_{max} (KBr) 2941, 1779, 1740, 1714, 1389, 1319, 1214, 1078, 1012, 996 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.48–7.36 (3H, m, Arom-*H*), 7.29–7.23 (2H, m, Arom-*H*), 4.38 (2H, q, *J*= 7.2 Hz, OCH_2), 3.87 (1H, d, *J*=8.2 Hz), 3.57 (1H, d, *J*= 8.2 Hz), 2.91 (1H, dd, J_1=14.2 Hz, J_2=7.4 Hz), 2.32–2.08 (5H, m), 1.76–1.30 (4H, m), 1.34 (3H, t, *J*=7.2 Hz, CH_2CH_3), 1.03–0.97 (2H, m), 0.92 (3H, t, *J*=7.5 Hz, CH_3); δ_C (50 MHz, $CDCl_3$) 198.0 (*C*=O), 175.1 (N*C*O), 172.5 (N*C*O), 169.8 (*C*OO), 132.1 (*quat*-C), 130.1 (Arom-*C*H), 129.5 (Arom-*C*H), 126.9 (Arom-*C*H), 89.5 (*C*–O), 89.3 (*C*–O), 62.9 (OCH_2), 53.9 (*C*H), 52.6 (*C*H), 47.6 (*C*H), 42.1 (CH_2), 34.6 (*C*H), 33.0 (CH_2), 29.7 (CH_2), 25.6 (CH_2), 16.0 (CH_3), 14.9 (CH_2), 14.2 (CH_3).

2,7-Dimethyl-8,11,13-trioxo-12-phenyl-15-oxa-12-azatetracyclo[7.5.1.0^{1,6}.0^{10,14}]pentadecane-9-carboxylic acid ethyl ester (15c). A mixture of *N*-phenyl maleimide (280 mg, 1.6 mmol) and 3.5 mg of $Rh_2(OAc)_4$ in dry benzene (7 ml) was allowed to react with a benzene solution (3 ml) of diazo ketone **14c** (225 mg, 0.8 mmol) for 11 h at reflux according to the general method B to afford 287 mg (84%) of **15c** as a white solid, mp 203–204°C (ethyl acetate/hexane); [Found: C, 67.67; H, 6.32; N, 3.26. $C_{24}H_{27}NO_6$ requires C, 67.75; H, 6.40; N, 3.29%]; ν_{max} (KBr) 2933, 1775, 1742, 1716, 1652, 1393, 1319, 1218, 1028 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.48–7.38 (3H, m, Arom-*H*), 7.29–7.23 (2H, m, Arom-*H*), 4.28 (2H, q, *J*=7.2 Hz, OCH_2), 3.89 (1H, d, *J*=8.3 Hz), 3.59 (1H, d, *J*=8.3 Hz), 2.92–2.87 (1H, m), 2.38–2.09 (4H, m), 1.81–1.34 (4H, m), 1.37 (3H, t, *J*= 7.2 Hz, CH_2CH_3), 1.23 (3H, d, *J*=6.3 Hz), 0.95 (3H, d, *J*=6.2 Hz, CH_3); δ_C (50 MHz, $CDCl_3$) 198.3 (*C*=O), 176.1 (N*C*O), 173.0 (N*C*O), 168.2 (*C*OO), 132.1 (*quat*-C), 130.2 (Arom-*C*H), 129.5 (Arom-*C*H), 127.2 (Arom-*C*H), 89.9 (*C*–O), 89.7 (*C*–O), 62.7 (OCH_2), 53.8 (*C*H), 52.9 (*C*H), 48.2 (*C*H), 40.2 (*C*H), 35.3 (*C*H), 32.8 (CH_2), 29.3 (CH_2), 25.9 (CH_2), 17.2 (CH_3), 14.6 (CH_3), 14.2 (CH_3).

2,9-Dimethyl-8,11,13-trioxo-12-phenyl-15-oxa-12-azatetracyclo[7.5.1.0^{1,6}.0^{10,14}]pentadecane (15d). A mixture of *N*-phenyl maleimide (375 mg, 2.2 mmol) and 4.8 mg of $Rh_2(OAc)_4$ in dichloromethane (15 ml) was allowed to react with a dichloromethane solution (5 ml) of diazo ketone **14d** (225 mg, 1.1 mmol) at room temperature for 9 h according to the general method A to afford 263 mg (69%) of **15d** as a white solid, mp 182–183°C (ethyl acetate/hexane); [Found: C, 71.46; H, 6.43; N, 3.84. $C_{21}H_{23}NO_4$ requires C, 71.37; H, 6.56; N, 3.96%]; ν_{max} (KBr) 2938, 2863, 1768, 1707, 1598, 1493, 1386, 1237, 1120, 990 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.52–7.40 (3H, m, Arom-*H*), 7.28–7.24 (2H, m, Arom-*H*), 3.52 (1H, d, *J*=8.0 Hz), 3.37 (1H, d, *J*=8.0 Hz), 2.92 (1H, dd, J_1=14.2 Hz, J_2=7.8 Hz), 2.40–2.01 (5H, m), 1.79–1.31 (4H, m), 1.51 (3H, s, CH_3), 0.97 (3H, d, *J*=6.4 Hz, CH_3); δ_C (50 MHz, $CDCl_3$) 199.1 (*C*=O), 175.2 (N*C*O), 172.9 (N*C*O), 132.0 (*quat*-C), 129.9 (Arom-*C*H), 129.3 (Arom-*C*H), 126.6 (Arom-*C*H), 89.4 (*C*–O), 86.2 (*C*–O), 53.8 (*C*H), 52.3 (*C*H), 47.2 (*C*H), 42.2 (CH_2), 34.7 (*C*H), 32.9 (CH_2), 29.2 (CH_2), 25.6 (CH_2), 23.2 (CH_3), 16.8 (CH_3).

6-Methyl-7,10,12-trioxo-11-phenyl-14-oxa-11-azatetracyclo[6.5.1.0^{1,6}.0^{9,13}]tetradecane (15e). A mixture of *N*-phenyl maleimide (105 mg, 0.6 mmol) and 1.3 mg of $Rh_2(OAc)_4$ in dichloromethane (7 ml) was allowed to react with a dichloromethane solution (3 ml) of diazo ketone **6d** (55 mg, 0.3 mmol) at room temperature for 3 h according to the general method A to afford 88 mg (88%) of **15e** as a white solid, mp 170–172°C (ethyl acetate/hexane); [Found: C, 70.26; H, 5.83; N, 4.24. $C_{19}H_{19}NO_4$ requires C, 70.14; H, 5.89; N, 4.30%]; ν_{max} (KBr) 2934, 2864, 1768, 1709, 1595, 1498, 1385, 1199, 1160, 992 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.51–7.42 (3H, m, Arom-*H*), 7.28–7.23 (2H, m, Arom-*H*), 4.89 (1H, s, O*CH*), 3.21 (2H, s, C*H*), 2.07–1.87 (2H, m), 1.80–1.59 (3H, m), 1.49–1.16 (3H, m), 1.09 (3H, s, *tert*-CH_3); δ_C (50 MHz, $CDCl_3$) 213.4 (*C*=O), 174.1 (N*C*O), 131.6 (*quat*-C), 129.2 (Arom-*C*H), 128.9 (Arom-*C*H), 126.4 (Arom-*C*H), 90.7 (*C*–O), 82.4 (O*C*H), 49.6 (CCH_3), 47.9 (*C*H), 47.0 (*C*H), 30.4 (CH_2), 25.7 (CH_2), 21.9 (CH_2), 19.9 (CH_2), 16.2 (CH_3).

6-Methyl-7,10,12-trioxo-11-phenyl-14-oxa-11-azatetracyclo[6.5.1.0^{1,6}.0^{9,13}]tetradecane-8-carboxylic acid ethyl ester (15f). A mixture of *N*-phenyl maleimide (142 mg, 0.8 mmol) and 1.8 mg of $Rh_2(OAc)_4$ in benzene (7 ml) was allowed to react with a benzene solution (3 ml) of diazo ketone **6b** (103 mg, 0.4 mmol) for 8 h at reflux according to the general method B to afford 150 mg (95%) of **15f** as a white solid, mp 215–217°C (ethyl acetate/hexane); [Found: C, 66.05; H, 5.81; N, 3.47. $C_{22}H_{23}NO_6$ requires C, 66.49; H, 5.83; N, 3.52%]; ν_{max} (KBr) 2933, 1774, 1741, 1715, 1393, 1317, 1212, 1074 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.49–7.39 (3H, m, Arom-*H*), 7.26–7.22 (2H, m, Arom-*H*), 4.40 (2H, q, *J*=7.2 Hz, OCH_2), 3.51 (1H, d, *J*=8.0 Hz), 3.29 (1H, d, *J*=8.0 Hz), 2.09–1.67 (6H, m), 1.38 (3H, t, *J*=7.2 Hz, CH_2CH_3), 1.46–1.34 (2H, m), 1.23 (3H, s, *tert*-CH_3); δ_C (50 MHz, $CDCl_3$) 207.6 (*C*=O), 173.5 (N*C*O), 172.4 (N*C*O), 163.3 (*C*OO), 132.1 (*quat*-C), 129.7 (Arom-*C*H), 129.5 (Arom-*C*H), 127.0 (Arom-*C*H), 90.1 (*C*–O), 89.7 (*C*–O), 62.9 (OCH_2), 50.4 (*quat*-C), 49.7 (*C*H), 49.1 (*C*H), 31.3 (CH_2), 26.1 (CH_2), 22.2 (CH_2), 20.3 (CH_2), 16.9 (CH_3), 14.7 (CH_3); *m/z* 397 (M^+, 48), 351 (43), 305 (100), 204 (44), 175 (30), 149 (54), 115 (21), 98 (25%).

6,9-Dimethyl-7-oxo-11-oxatricyclo(6,2,1,0^{1,6})undecane-9-carboxylic acid 9-methyl ester (17a,b). A mixture of methyl methacrylate (122 mg, 1.2 mmol) and 2.7 mg of $Rh_2(OAc)_4$ in dichloromethane (7 ml) was allowed to react with a dichloromethane solution (3 ml) of diazo ketone **6d** (110 mg, 0.6 mmol) for 4 h according to the general method A afforded the diasteromers **17a** (16 mg, 10%) and **17b** (83 mg, 53%) as a thick liquid. **17a**: [Found: C, 66.60; H, 7.82. $C_{14}H_{20}O_4$ requires C, 66.65; H, 7.99%]; ν_{max} (neat) 2938, 2867, 1746, 1741, 1452, 1377, 1277, 1208, 1164, 1119, 998 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.12 (1H, s, H-8), 3.68 (3H, s, OCH_3), 2.70 (1H, d, *J*=13.2 Hz), 1.93–1.67 (6H, m), 1.63–1.26 (3H, m), 1.25 (3H, s, CH_3), 1.09 (3H, s, CH_3); δ_C (50 MHz, $CDCl_3$) 216.8 (*C*=O), 176.5 (*C*OO), 89.3 (C-1), 87.2 (C-8), 53.5 (OCH_3), 51.5 (*quat*-C), 50.3 (*quat*-C), 43.0 (CH_2), 32.0 (CH_2), 29.3 (CH_2), 22.8 (CH_2), 21.0 (CH_2), 20.6 (CH_3), 16.6 (CH_3); **17b**: [Found: C, 66.59; H, 7.94. $C_{14}H_{20}O_4$ requires C, 66.65; H, 7.99%]; ν_{max} (neat) 2937, 2867, 1743, 1741, 1453, 1378,

1278, 1207, 1169, 1120, 995 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.64 (1H, s, H-8), 3.75 (3H, s, OCH_3), 2.32 (1H, d, J=13.2 Hz), 1.90–1.78 (1H, m), 1.75–1.62 (6H, m), 1.43–1.25 (2H, m), 1.22 (3H, s, CH_3), 1.08 (3H, s, CH_3); δ_C (50 MHz, $CDCl_3$) 216.8 (*C*=O), 176.4 (*C*OO), 89.2 (C-1), 87.3 (C-8), 53.4 (O*C*H_3), 51.4 (*quat*-C), 50.3 (*quat*-C), 42.6 (*C*H_2), 31.3 (*C*H_2), 29.2 (*C*H_2), 22.8 (*C*H_2), 20.9 (*C*H_2), 20.6 (*C*H_3), 16.5 (*C*H_3).

6,9-Dimethyl-7-oxo-11-oxatricyclo(6,2,1,0^{1,6})undecane-8,9-dicarboxylic acid 8-ethyl ester 9-methyl ester (17c,d). A mixture of methyl methacrylate (60 mg, 0.6 mmol) and 1.32 mg of $Rh_2(OAc)_4$ in benzene (7 ml) was allowed to react with a benzene solution (3 ml) of diazo ketone **6b** (75 mg, 0.3 mmol) for 11 h at reflux according to the general method B afforded the diasteromers **17c** (24 mg, 25%) and **17d** (59 mg, 61%) as a thick liquid which solidified on standing. **17c**: mp 87–89°C (dichloromethane/hexane); [Found: C, 62.86; H, 7.37. $C_{17}H_{24}O_6$ requires C, 62.95; H, 7.46%]; ν_{max} (KBr) 2941, 2867, 1751, 1746, 1744, 1452, 1377, 1300, 1187, 1145 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.31 (2H, q, J=7.2 Hz, OCH_2), 3.72 (3H, s, OCH_3), 2.59 (1H, d, J=13.0 Hz), 1.91 (1H, d, J=13.0 Hz), 1.79–1.33 (8H, m), 1.36 (3H, s, CH_3), 1.31 (3H, t, J=7.2 Hz, CH_2CH_3), 1.27 (3H, s, CH_3); δ_C (50 MHz, $CDCl_3$) 209.3 (*C*=O), 173.6 (*C*OO), 165.3 (*C*OO), 94.4 (*C*–O), 87.6 (*C*–O), 62.4 (O*C*H_2), 54.6 (C-6), 52.9 (O*C*H_3), 49.9 (*quat*-C), 46.8 (*C*H_2), 32.4 (*C*H_2), 29.5 (*C*H_2), 22.7 (*C*H_2), 22.0 (*C*H_3), 20.8 (*C*H_2), 16.4 (*C*H_3), 14.7 (*C*H_3); *m*/*z* 324 (M^+, 5), 219 (100), 204 (11), 149 (21), 123 (11), 109 (25%). **17d**: mp 86–88°C (dichloromethane/hexane); [Found: C, 62.83; H, 7.45. $C_{17}H_{24}O_6$ requires C, 62.95; H, 7.46%]; ν_{max} (KBr) 2938, 2867, 1767, 1732, 1461, 1282, 1201, 1133, 1103, 1033, 960 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.34 (2H, q, J=7.2 Hz, OCH_2), 3.71 (3H, s, OCH_3), 2.17 (1H, d, J=13.4 Hz), 1.92 (1H, d, J=13.4 Hz), 1.99–1.62 (5H, m), 1.44 (3H, s, CH_3), 1.42–1.20 (3H, m), 1.34 (3H, t, J=7.2 Hz, CH_2CH_3), 1.05 (3H, s, CH_3); δ_C (50 MHz, $CDCl_3$) 210.3 (*C*=O), 174.8 (*C*OO), 165.9 (*C*OO), 93.2 (*C*–O), 85.8 (*C*–O), 62.1 (O*C*H_2), 53.6 (C-6), 53.2 (O*C*H_3), 50.4 (*quat*-C), 45.7 (*C*H_2), 31.6 (*C*H_2), 28.9 (*C*H_2), 22.4 (*C*H_2), 21.2 (*C*H_3), 20.7 (*C*H_2), 16.7 (*C*H_3), 14.7 (*C*H_3).

9-Bromomethyl-6-methyl-7-oxo-11-oxatricyclo(6,2,1,0^{1,6})-undec-9-ene (18a). A mixture of propargyl bromide (160 mg, 1.3 mmol) and 3.0 mg of $Rh_2(OAc)_4$ in dichloromethane (10 ml) was allowed to react with a dichloromethane solution (3 ml) of diazo ketone **6d** (121 mg, 0.7 mmol) for 4.5 h according to the general method A to afford 102 mg (56%) of **18a** as a thick oil; [Found: C, 53.18; H, 5.62. $C_{12}H_{15}BrO_2$ requires C, 53.16; H, 5.58%]; ν_{max} (neat) 2935, 2869, 1734, 1651, 1458, 1384, 1327, 1268, 1128, 1088, 1036 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 6.43 (1H, s, C=C*H*), 4.64 (1H, s, H-8), 4.21 (2H, s, CH_2Br), 2.28–2.15 (1H, m), 1.99–1.58 (5H, m), 1.40–1.39 (2H, m), 1.04 (3H, s, CH_3); δ_C (50 MHz, $CDCl_3$) 206.8 (*C*=O), 143.7 (*C*-10), 141.8 (*C*-9), 92.7 (*C*–O), 84.0 (*C*–O), 55.7 (C-6), 32.4 (*C*H_2), 26.8 (*C*H_2), 24.7 (*C*H_2), 21.6 (*C*H_2), 21.1 (*C*H_3), 20.8 (*C*H_2).

9-Bromomethyl-6-methyl-7-oxo-11-oxatricyclo(6,2,1,0^{1,6})-undec-9-ene-8-carboxylic acid 8-ethyl ester (18b). A mixture of propargyl bromide (108 mg, 0.9 mmol) and 2.0 mg of $Rh_2(OAc)_4$ in benzene (7 ml) was allowed to react with a benzene solution (3 ml) of diazo ketone **6b** (113 mg, 0.5 mmol) for 13 h at reflux according to the general method B to afford 97 mg (63%) of **18b** as a thick dark yellow liquid; [Found: C, 52.57; H, 5.61. $C_{15}H_{19}BrO_4$ requires C, 52.49; H, 5.58%]; ν_{max} (neat) 2935, 2868, 1743, 1650, 1459, 1383, 1327, 1267, 1124, 1087 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 6.44 (1H, s, C=C*H*), 4.35 (2H, q, J=7.2 Hz, OCH_2), 4.20 (2H, s, CH_2Br), 2.22–2.15 (1H, m), 1.95–1.52 (5H, m), 1.49–1.30 (2H, m), 1.38 (3H, t, J=7.2 Hz, CH_2CH_3), 1.09 (3H, s, CH_3); δ_C (50 MHz, $CDCl_3$) 206.8 (*C*=O), 164.5 (*C*OO), 143.7 (C-10), 142.2 (C-9), 92.0 (*C*–O), 89.0 (*C*–O), 62.9 (OCH_2), 55.1 (C-6), 32.2 (*C*H_2), 26.8 (*C*H_2), 24.6 (*C*H_2), 21.5 (*C*H_2), 21.2 (*C*H_3), 20.8 (*C*H_2), 14.7 (*C*H_3).

X-Ray crystal structure analysis

Crystal data for the compound ***8b****:* $C_{18}H_{22}O_8$, M=366.36, 0.30×0.25×0.30 mm^3, Triclinic, P-1, a=8.964(3) Å, b=9.955(4) Å, c=11.952(5) Å, α=74.98(3)°, β=76.96(3)°, γ=64.99(3)°, V=925.3(6) $Å^3$, T=293(2) K, R_1=0.0956, wR_2=0.2216 on observed data, z=2, $D_{calc.}$=1.315 Mg m^{-3}, F(000)=388, Absorption coefficient=0.104 mm^{-1}, λ=0.7107 Å, 2428 reflections were collected on a CAD-4 diffractometer, 1837 observed reflections ($I \geq 2\sigma(I)$). The largest difference peak and hole=0.396 and −0.518e $Å^{-3}$, respectively. *Crystal data for the compound* ***15a****:* $C_{23}H_{25}NO_6$, M=411.44, 0.16×0.08×0.03 mm, Monoclinic, $P2_1/n$, a=8.547(8) Å, b=20.395(14) Å, c=12.074(8) Å, β=106.49(7)°, V=2018(3) $Å^3$, T=293(2) K, R_1=0.0603, wR_2=0.1446 on observed data, z=4, $D_{calc.}$=1.354 Mg m^{-3}, F(000)=872, Absorption coefficient=0.098 mm^{-1}, λ=0.7107 Å, 2613 reflections were collected on a CAD-4 diffractometer, 1636 observed reflections ($I \geq 2\sigma(I)$). The largest difference peak and hole=0.450 and −0.383e $Å^{-3}$, respectively. The structure was solved by direct methods and refined by full-matrix least squares on F^2 using SHELX-97.[20] All non-hydrogen atoms were refined anisotropically. Some hydrogens were located on a difference Fourier map and some were stereochemically fixed. Atomic coordinates, thermal parameters, bond lengths and angles have been deposited at the Cambridge Crystallographic Data Center.

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