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On the ozonolysis of unsaturated tosylhydrazones as a direct approach to diazocarbonyl compounds†

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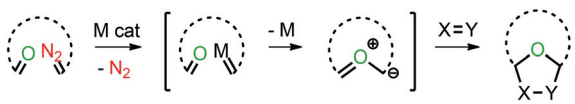
The scope and limitations are described of reacting unsaturated tosylhydrazones with O_3 followed by Et_3N for the generation of 1,4- and 1,5-diazocarbonyl systems. Tosylhydrazones, from tosylhydrazide condensation with readily available δ- and ε-unsaturated α-ketoesters, led in the former case to a 2-pyrazoline whereas the latter cases led to α-diazo-ε-ketoesters, although a terminal alkene produced a tetrahydropyridazinol. Using the ozonolysis–Et_3N strategy, tosylhydrazones from cyclic enones give 2,5- and 2,6-diazoketones with aldehyde or ester functionality at the 1-position; the α-diazoaldehydes prefer the s-*trans* conformation, with a rotation barrier of 74 kJ mol^{-1} at 25 °C determined by NMR. This one-pot ozonolysis/Bamford–Stevens chemistry demonstrates both the tolerance of tosylhydrazones to ozone, and the subsequently added amine playing a dual role to directly transform the intermediate tosylhydrazone ozonides into products containing reactive diazo and ketone functionalities; such adducts are of particular value as precursors to cyclic carbonyl ylides for 1,3-dipolar cycloadditions.

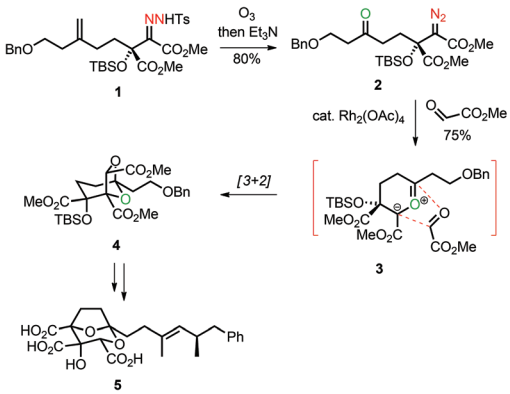
Introduction

Transition metal-catalysed decomposition of diazo functionality in the presence of a carbonyl group provides one of the best ways of accessing carbonyl ylides for application in 1,3-dipolar cycloaddition chemistry (Scheme 1).[1] The use of cyclic carbonyl ylides from diazocarbonyl compounds (usually diazoketones) is particularly popular, due to the typically efficient intramolecular generation of the transient ylide in combination with the subsequent pericyclic step leading overall to concise construction of complex polycycles. It was therefore considered that a method to simultaneously reveal the reactive diazo and ketone functionalities from more readily accessible and compatible functional groups would be of value in the further development of this chemistry.

We were faced with the above issue in the context of our recent asymmetric synthesis of 6,7-dideoxysqualestatin H5 (6,7-DDSQ H5, **5**, Scheme 2), where cogeneration of keto and diazo functionality was achieved through ozonolysis of an unsaturated hydrazone **1**.[2] The resulting diazoketone **2** underwent Rh(II)-catalysed tandem cyclic carbonyl ylide formation **3** and cycloaddition with methyl glyoxylate, giving a cycloadduct **4** that was eventually converted to the natural product **5** through acid-catalysed rearrangement and installation of the



Scheme 1 Carbonyl ylide formation-cycloaddition from diazocarbonyl compounds.



Scheme 2 Chemoselective formation of diazoketone **2** leading to 6,7-DDSQ H5 (**5**).[2]

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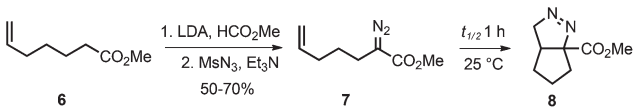
†Electronic supplementary information (ESI) available: Copies of ^{1}H NMR and ^{13}C NMR spectra of all new compounds. NOE and *s-E*/*s*-Z NMR study of **41**. *X*-ray data for compound **35**. CCDC 1815202. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c8ob00435h

full side-chain. Herein we report on the development and scope and limitations of the ozonolytic strategy to diazocarbonyl compounds.

Results and discussion

Prior to embarking on the above total synthesis, studies were carried out on simpler substrates to assess the viability of the ozonolytic strategy to diazocarbonyl compounds from unsaturated ketones, successively through condensation reaction with tosylhydrazide, then ozonolysis[3] and finally Bamford–Stevens[4] reaction. It was considered that the diazo functionality should not be generated (from hydrazone) before the double bond was subjected to ozonolysis since, even assuming that conditions could be established for the diazo group to survive alkene ozonolysis unscathed (cf, **11** →**12** Scheme 4), Dauben and co-workers had reported that a structurally related unsaturated diazo substrate **7**, prepared from unsaturated ester **6** by α-formylation and deformylative diazo transfer, underwent spontaneous intramolecular dipolar cycloaddition to give a 1-pyrazoline **8** (Scheme 3).[5]

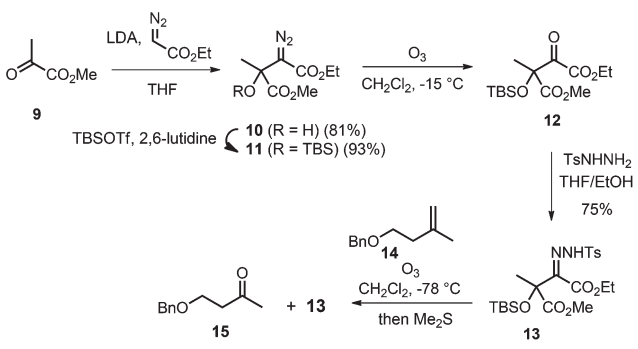


Scheme 3 Formation and instability of diazoalkene **7**.[5]

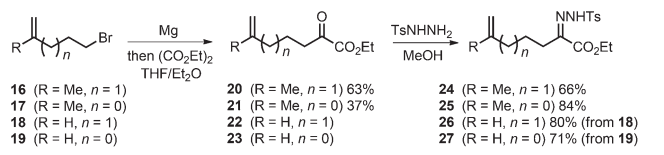
At the outset of these investigations, the tolerance of hydrazone functionality during ozonolysis of an alkene required clarification, since (like diazo compounds)[6] hydrazones are known to be convertible to ketones through such oxidation chemistry.[7,8] However, rendering the hydrazone electron deficient, through ester substitution at the hydrazino carbon and a Ts group on the amino nitrogen, was anticipated to reduce its reactivity to electrophilic attack by ozone.[8] A simplified hydrazone **13** that retained the key features present in the target system **1** (Scheme 2), was straightforwardly synthesised in four steps starting from α-lithiated ethyl diazoacetate[9] and methyl pyruvate (**9**, Scheme 4), then silylation of the resulting tertiary alcohol **10**, ozonolysis of the silyl ether **11** to the substituted α-ketoester **12**, and condensation with tosylhydrazide.

A 1 : 1 mixture of hydrazone **13** and benzylated isoprenol **14**[10] (the latter to mimic the alkene present in **1**) in CH_2Cl_2 underwent controlled ozonolysis at −78 °C in the presence of Sudan red 7B as an end-point indicator.[11] Ozonolysis was halted as soon as the colour of the reaction mixture changed from red to light pink. Following treatment with Me_2S, ^1H NMR analysis of the reaction mixture indicated that alkene **14** was completely oxidised to corresponding ketone **15**[12] but, pleasingly, hydrazone **13** survived.[13] No evidence of formation of ketoester **12** was detected by ^{13}C NMR analysis of the crude reaction mixture (diagnostic α-keto carbon EtO_2C-*C*=O signal at ∼190 ppm[2] absent). Unfortunately, direct transfer of these promising conditions to unsaturated hydrazone **1** (Scheme 2), although leading to complete consumption of the alkene functionality did not allow successful isolation of the corresponding keto hydrazone **2** (NNHTs instead of N_2); despite various attempts, partial decomposition on purification by silica gel chromatography was observed and clean keto hydrazone was not obtained. To overcome this problematic step, it was proposed that if the intermediate ozonide from unsaturated hydrazone **1** was treated with Et_3N instead of Me_2S, this should also lead to the desired ketone functionality,[14] with the additional bonus of converting the hydrazone moiety to a diazo group[4,15] in a one-pot ozonolysis/Bamford–Stevens process. Application of this strategy proved successful (Scheme 2),[2] and it was subsequently found that the end-point indicator could be dispensed with, provided ozonolysis was halted as soon as the reaction mixture turned blue [diketone **2** (C=N_2 replaced by C=O) was observed if ozonolysis was prolonged]; however, the scope and limitations of this process remained to be explored.

Unsaturated tosylhydrazones **24–27** (Scheme 5), lacking the β-siloxy and β-ester functionality that could be providing additional steric and/or electronic "protection" of the hydrazone to ozonolysis in **1** and **13**, were made by tosylhydrazide condensation with δ- and ε-unsaturated α-ketoesters **20–23**. The latter were readily prepared by addition to diethyl oxalate of the relevant Grignard reagents available from the corresponding unsaturated bromides **16–19**.[16]

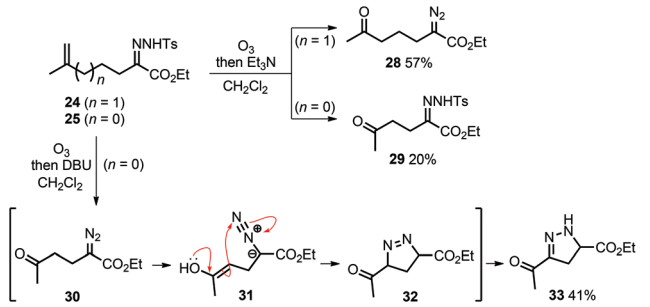


Scheme 4 Synthesis and tolerance to ozonolysis of hydrazone **13**.



Scheme 5 Synthesis of unsaturated tosylhydrazones **24–27**.

Of the unsaturated tosylhydrazones **24–27**, only **24** could be successfully converted to the corresponding diazocarbonyl compound **28** though the ozonolysis/Bamford–Stevens process (Scheme 6). Diazocarbonyl compound **28** has

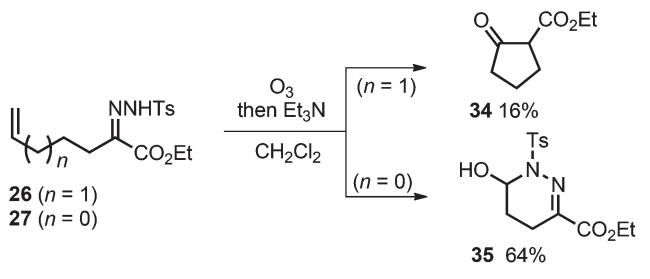


Scheme 6 Ozonolysis followed by base treatment of unsaturated tosylhydrazones **24** and **25**.

previously been prepared by Padwa and co-workers (in 3 steps from α-acetylbutyrolactone), and shown to be a viable substrate for carbonyl ylide formation – cycloaddition chemistry (for example with DMAD as the dipolarophile, in 73% yield).[17,18]

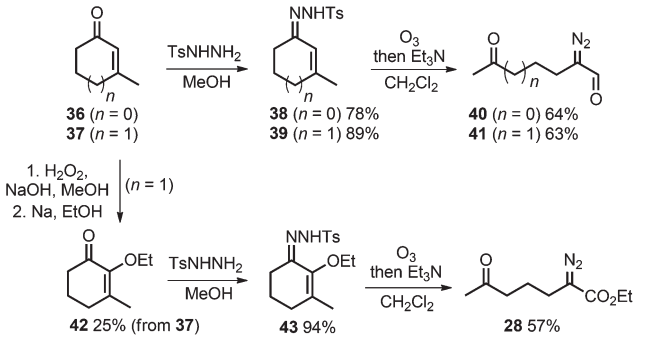
Surprisingly, following ozonolysis and addition of Et_3N, unsaturated tosylhydrazone **25** was only converted as far as the keto hydrazone **29**, in low yield (20%, Scheme 6). Switching to DBU[19] as a stronger base after ozonolysis of tosylhydrazone **25** led to the 2-pyrazoline **33** (41%). Presumably, DBU does facilitate generation of the anticipated diazoketone **30**, but under the reaction conditions the corresponding enol **31** undergoes cyclisation with the proximal diazo functionality followed by regioselective tautomerisation from 1-pyrazoline **32**.[20]

Terminal alkene-containing hydrazones **26** and **27** (Scheme 7) were anticipated to lead to diazoaldehydes following ozonolysis and base treatment. However, in both cases the greater reactivity of the aldehyde group, compared to ketone functionality earlier, led to cyclisation chemistry at the aldehyde. With hydrazone **26**, only β-ketoester **34** was isolated (16%), likely arising from intramolecular aldolisation of the diazoaldehyde followed by 1,2-hydride shift with expulsion of N_2.[9c] For hydrazone **27**, tetrahydropyridazinol **35** was obtained (64%, structure confirmed by X-ray crystallographic analysis[21]). The latter proved recalcitrant to conversion to the corresponding diazoaldehyde, being inert to separate treatment with Et_3N or NaOEt whereas significant decomposition was observed on exposure to DBU.



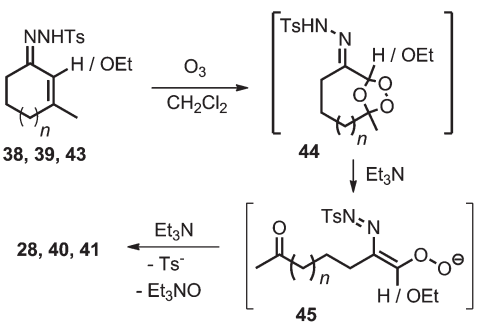
Scheme 7 Ozonolysis followed by base treatment of unsaturated tosylhydrazones **26** and **27**.

α,β-Unsaturated hydrazones from 3-methylcyclopentenone (**36**) and 3-methylcyclohexenone (**37**) allow access to 1,4- and 1,5-diazoketones **40** and **41** using the ozonolysis–Et_3N strategy. The α-diazo-ε-ketoester **28**, made earlier (Scheme 6), was also accessible *via* 2-ethoxy-3-methylcyclohexenone (**42**, prepared from the epoxide of 3-methylcyclohexenone (**37**) by α-ring-opening/β-elimination using NaOEt[22]) (Scheme 8).[23]



Scheme 8 1,4- and 1,5-Diazoketones **40**, **41** and **28** from cyclic enones.

Generation of diazo carbonyl compounds **40**, **41** and **28** from the corresponding, α,β-unsaturated hydrazones **38**, **39** and **43** indicates that, if the reactions were to proceed through formation of an ozonide **44**, then the Et_3N acts as a reductant; although for the potential ozonides derived from **38** and **39** bridgehead deprotonation might be expected on the basis of direct analogy with previous studies on simple (cyclo) alkenes,[14] leading to carboxylic acid functionality through anionic cycloreversion, rather than the aldehyde functionality observed. However, in these systems, the proximity of the adjacent hydrazone functionality, aside from likely dictating (through stabilisation) carbonyl oxide generation on the proximal, rather than distal carbon in the first formed molozonide, could also lead through NH deprotonation to intermediate **45**. The latter, following elimination of Ts^-, could undergo reduction by Et_3N (Scheme 9).



Scheme 9 Proposed pathway to diazocarbonyl compounds **28**, **40** and **41**.

The α-diazoaldehydes **40** and **41** display s-*cis*/*trans* isomerism, arising from partial double bond character in the N_2C–CHO bond. This phenomenon has been observed for diazoacetaldehyde (the simplest α-diazoaldehyde), α-diazoketones and other α-diazo carbonyl compounds.[24,25] In solution, diazoacetaldehyde and monosubstituted α-diazoketones ($RCOCHN_2$) prefer the *Z*-form, whereas disubstituted open-chain α-diazo carbonyl compounds exist exclusively as, or prefer, the *E*-form. NOE studies on α-diazoaldehyde **41** recorded at −40 °C (to eliminate exchange between isomers) indicated that the predominant form was *E*- (analogously for **40**; *E*- : *Z*- both ~85 : 15).[13] Stabilisation by weak H-bonding between β C–H on the (*cis*-) alkyl chain and the aldehyde may contribute to the preference for the *E*-form.[26] For α-diazoaldehyde **41**, variable temperature ^{1}H NMR studies in $CDCl_3$ and 1D EXSY analyses were used to obtain exchange rate constants and hence estimate rotational activation parameters ($\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$), from which the activation energy ($\Delta G^{\ddagger}$) barrier to rotation was calculated as 74 kJ mol^{-1} at 25 °C.[13] The latter value lies at the upper end of the range of barriers so far determined for α-diazo carbonyl compounds, and likely reflects greater electron delocalisation into the aldehyde compared with α-diazo-ketone (and -ester) systems.

Conclusions

In summary, the scope and limitations of reacting unsaturated tosylhydrazones with O_3 followed by Et_3N for the direct generation of diazocarbonyl systems were examined. Here, the Et_3N facilitates two processes: ozonide conversion to keto and/or aldehyde functionality,[14] and tosylhydrazone to ketone in a Bamford–Stevens reaction.[4,15] The chemistry is viable to α-diazo-ε-ketoesters, but an α-diazo-δ-ketoester underwent cyclisation to a 2-pyrazoline under the basic reaction conditions following ozonolysis. Terminal alkene hydrazones did not produce diazoaldehydes, as the later proved too reactive in the presence of tethered hydrazone or diazo functionality, although the chemistry did provide an interesting route to a tetrahydropyridazine ring system. Finally, cyclic α,β-unsaturated hydrazones are shown to undergo ozonolytic ring-cleavage and Bamford–Stevens reaction to give 2,5- and 2,6-diazoketones with aldehyde or ester functionality at the 1-position.

Experimental

General information

All reactions requiring anhydrous conditions were carried out under an atmosphere of argon in flame-dried glassware. Tetrahydrofuran (THF), dichloromethane (DCM), ether (Et_2O) and ethyl acetate (EtOAc) were obtained from Grubbs' drying stills.[27] MeOH was dried over 4 Å MS for at least 24 h. Petrol (petroleum ether) 30–40 °C was used in flash column chromatography. The latter was carried out using silica gel (VWR chemicals, BDH) in accordance with Still's method,[28] monitored by thin-layer chromatography (TLC) (Merck 60 F_{254}) plates. TLC plates were viewed using ultraviolet light (λ_{max} = 254/365 nm) and immersion in $KMnO_4$, anisaldehyde or vanillin stains, followed by heating. Except where stated otherwise, commercially available reagents were used as received. Melting points (m.p.s) were obtained using an electrothermal melting point apparatus to the nearest 1 °C and are uncorrected. Infrared spectra were obtained using a PerkinElmer FT-IR spectrometer (Universal ATR Sampling Accessory), with absorption maxima quoted in wavenumbers (cm^{-1}). Peak intensities are described as broad (br), weak (w), medium (m) or strong (s). Nuclear magnetic resonance (^{1}H NMR and ^{13}C NMR) spectra were recorded on Bruker Avance DPX 200, AVIIIHD 400, AVII 500, and AVIIIHD 500 spectrometers in $CDCl_3$, referenced to residual $CHCl_3$ singlet at δ 7.27 for ^{1}H NMR spectra, and to the central line of $CDCl_3$ triplet at δ 77.16 for ^{13}C NMR spectra. Chemical shifts are quoted in parts per million (ppm). Coupling constants (*J*) are measured to the nearest 0.5 Hertz (Hz). The splittings are quoted as singlet (s), doublet (d), triplet (t), quartet (q), or multiplet (m). The ^{13}C NMR peaks were assigned by standard methods using HSQC. X-ray crystallography data were collected with (Rigaku) Oxford Diffraction SuperNova A diffractometer at 150 K. Low-resolution mass spectra were obtained using electrospray ionisation (ESI) or chemical ionisation (CI). High-resolution mass spectra were obtained by electrospray ionisation (ESI) or chemical ionisation (CI) using tetraoctylammonium bromide or sodium dodecyl sulfate as the lock mass.

4-Ethyl 1-methyl 3-diazo-2-hydroxy-2-methylsuccinate (10). To a solution of ethyl diazoacetate (571 mg, 5.0 mmol) and methyl pyruvate **9** (510 mg, 5.0 mmol) in THF (10 mL) at −78 °C was added dropwise over 30 min LDA [5.0 mmol, freshly prepared by adding dropwise *n*-BuLi (3.35 mL, 1.5 M in hexanes, 5.0 mmol) to a solution of freshly distilled i-Pr_2NH (0.73 mL, 5.25 mmol) in THF (5 mL) at 0 °C]. The solution was stirred for 3 h at −78 °C and a solution of acetic acid (0.28 mL, 5.0 mmol) in THF (1 mL) at −50 °C was then added dropwise and the reaction mixture allowed to warm to rt. Sat. aq NaCl (20 mL) was added, the organic layer separated and the aq layer extracted with Et_2O (3 × 20 mL). The combined organic layers were dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by column chromatography (25% Et_2O in petrol) to give tertiary alcohol **10** (876 mg, 81%) as a yellow liquid; R_f 0.29 (25% Et_2O in petrol); IR (film, ν_{max} cm^{-1}) 3488 m, 2950 m, 2075 s, 1750 s and 1719 s; ^{1}H NMR (200 MHz; $CDCl_3$) δ 4.30–4.10 (3H, m, CH_2CH_3 and OH), 3.83 (3H, s, CO_2Me), 1.60 (3H, d, *J* 0.5, CH_3), 1.28 (3H, t, *J* 7.0, OCH_2CH_3); ^{13}C NMR (50 MHz; $CDCl_3$) δ 174.5 (CO_2Me), 166.0 (CO_2Et), 71.8 ($HOCCO_2Me$), 64.3 (CN_2), 61.6 (CH_2CH_3), 53.8 (CO_2Me), 24.0 (CH_2CH_3), 14.7 (CH_3); HRMS (CI) *m*/*z* ($M + NH_4^+$), found 234.1087, $C_8H_{16}O_5N_3$ requires 234.1090.

4-Ethyl 1-methyl 2-((*tert*-butyldimethylsilyl)oxy)-3-diazo-2-methylsuccinate (11). To a solution of 2,6-lutidine (1.4 mL, 12 mmol) in CH_2Cl_2 (10 mL) was added TBSOTf (1.4 mL, 6.0 mmol) dropwise at 0 °C. After 30 min, a solution of tertiary

alcohol **10** (865 mg, 4.0 mmol) in CH_2Cl_2 (5 mL) was added dropwise and the mixture warmed to rt and stirred for 48 h. Brine (20 mL) was then added and the aq layer extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by column chromatography (5% Et_2O in petrol) to give silyl ether **11** (876 mg, 93%) as a colourless oil; R_f 0.30 (5% Et_2O in petrol); IR (film, ν_{max} cm^{-1}); 3496 m 2956 m, 2930 m, 2078 s, 1742 s; ^1H NMR (200 MHz; $CDCl_3$) δ 4.20 (1H, q, *J* 7.0, 1 H of CH_2CH_3), 4.19 (1H, q, *J* 7.0, 1H of CH_2CH_3), 3.76 (3H, s, CO_2Me), 1.68 (3H, s, CH_3), 1.26 (3H, t, *J* 7.0, OCH_2CH_3), 0.88 (9H, s, $Si(CH_3)_2C(CH_3)_3$), 0.12 (3H, s, $Si(CH_3)_2C(CH_3)_3$), 0.10 (3H, s, $Si(CH_3)_2C(CH_3)_3$); ^{13}C NMR (50 MHz; $CDCl_3$) δ 172.5 (CO_2Me), 171.0 (CO_2Et), 73.5 (TBSOCCO_2Me), 60.9 (CH_2CH_3), 52.8 (CO_2Me), 25.9 ($Si(CH_3)_2C(CH_3)_3$), 25.7 ($Si(CH_3)_2C(CH_3)_3$), 18.4 (CH_2CH_3), 14.6 (TBSOCCH_3), −3.07 ($Si(CH_3)_2C(CH_3)_3$), −3.63 ($Si(CH_3)_2C(CH_3)_3$) [CN_2 not observed]; HRMS *m*/*z* (M + Na^+), found 353.1508, $C_{14}H_{26}N_2NaO_5Si$ requires 353.1509.

4-Ethyl 1-methyl (*Z*)-2-((*tert*-butyldimethylsilyl)oxy)-2-methyl-3-(2-tosylhydrazineylidene)succinate (13). A solution of silyl ether **11** (660 mg, 2.0 mmol) in CH_2Cl_2 (40 mL) was cooled to −15 °C. A stream of O_3 in oxygen was bubbled through the solution. After 1 h, ozone treatment was terminated (monitored by the disappearance of IR stretch at 2078 cm^{-1}). The excess O_3 was removed by bubbling N_2 through the reaction mixture and warmed to rt. The residue was concentrated under reduced pressure to give α-ketoester **12** which was used directly in the next step. A solution of α-ketoester **12** and $TsNHNH_2$ (540 mg, 2.9 mmol) in THF/EtOH (6 mL, 1 : 1) was heated to reflux. After 24 h, the residue was concentrated under reduced pressure and purified by column chromatography (50% Et_2O in petrol) to give *Z*[29]-hydrazone **13** (478 mg, 75% from **11**) as a colourless oil; R_f 0.52 (50% Et_2O in petrol); IR (film, ν_{max} cm^{-1}); 2924 s, 1767 s, 1460 m; ^1H NMR (200 MHz; $CDCl_3$) δ 11.58 (1H, s, NH), 7.83 (2H, d, *J* 8.0, 2xArCH), 7.31 (2H, d, *J* 8.0, 2xArCH), 4.33–4.07 (2H, m, CH_2CH_3), 3.66 (3H, s, CO_2Me), 2.42 (3H, s, Ar*Me*), 1.52 (3H, s, TBSOCCH_3), 1.25 (3H, t, *J* 7.0, CH_2CH_3), 0.75 (9H, s, $Si(CH_3)_2C(CH_3)_3$), 0.03 (3H, s, $Si(CH_3)_2C(CH_3)_3$) and −0.18 (3H, s, $Si(CH_3)_2C(CH_3)_3$); ^{13}C NMR (50 MHz; $CDCl_3$) δ 173.5 (CO_2Me), 161.3 (CO_2Et), 144.4 (ArC), 138.0 (ArC), 135.3 (C═N), 129.9 (ArCH), 127.9 (ArCH), 77.6 (TBSOCCH_3), 62.0 (CH_2CH_3), 52.2 (CO_2Me), 25.4 ($Si(CH_3)_2C(CH_3)_3$), 24.1 ($Si(CH_3)_2C(CH_3)_3$), 21.6 (Ar*Me*), 18.0 (CH_2CH_3), 13.7 (TBSOCCH_3), −2.9 ($Si(CH_3)_2C(CH_3)_3$) and −3.3 ($Si(CH_3)_2C(CH_3)_3$); HRMS *m*/*z* (M + H^+), found 487.1944. $C_{21}H_{35}N_2O_7SSi$ requires 487.1934.

Model study for selective ozonolysis

A solution of hydrazone **13** (137 mg, 0.29 mmol), benzylated isoprenol **14**[10] (51 mg, 0.29 mmol) and Sudan red 7B[11] (1 mg) in CH_2Cl_2 (20 mL) was cooled to −78 °C. A stream of O_3 in oxygen was bubbled through the solution. Ozone treatment was terminated when the colour of the reaction turned light pink. The excess O_3 was removed by bubbling N_2 through the reaction mixture. Then Me_2S (0.82 mL, 5.91 mmol) was added and the reaction mixture was warmed to rt. After stirring for 12 h, the solution was concentrated under reduced pressure to give a mixture of **13** and ketone **15**[12] as a colourless oil.[13]

General procedure A for the formation of hydrazones

(i) Mg turnings (50.6 mmol) were flame-dried under vacuum for 15 min and then allowed to cool to rt under argon. A mixture of THF/Et_2O (0.88 mL $mmol^{-1}$, 1 : 1) was added, followed by dropwise addition of bromoalkene (16.9 mmol). The mixture was stirred for 15 min and then transferred dropwise to a solution of diethyl oxalate (11.3 mmol) in THF/Et_2O (0.88 mL $mmol^{-1}$, 1 : 1) at −78 °C. After 2 h at −78 °C, the reaction was quenched with sat. aq NH_4Cl (15 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give α-ketoester as colourless oil, which was used in the next step without further purification. (ii) A mixture of crude α-ketoester (11.2 mmol) and $TsNHNH_2$ (13.4 mmol) in MeOH (1.3 mL $mmol^{-1}$ of α-ketoester) was heated to 45 °C overnight. The mixture was then cooled to rt, concentrated under reduced pressure and purified by column chromatography to give the hydrazone.

General procedure B for ozonolysis/Bamford–Stevens process

A solution of hydrazone (1.48 mmol) in CH_2Cl_2 (115 mL $mmol^{-1}$) was cooled to −78 °C. A stream of O_3 in oxygen was bubbled through the solution. Ozone treatment was terminated when the colour of the reaction mixture changed from colourless to light blue. The excess O_3 was removed by bubbling N_2 through the reaction mixture. After 10 min, Et_3N (5.91 mmol) was added and the reaction mixture was warmed to rt. After stirring for 3 h, the reaction mixture was passed through a pad of silica, evaporated under reduced pressure and purified by column chromatography to give the diazocarbonyl compound.

Ethyl 6-methyl-2-oxohept-6-enoate (20) and ethyl (*Z*)-6-methyl-2-(2-tosylhydrazineylidene)hept-6-enoate (24). Following the general procedure **A(i)** using Mg turnings (206 mg, 8.46 mmol), 5-bromo-2-methylpent-1-ene **16**[30] (600 mg, 3.68 mmol) and diethyl oxalate (0.40 mL, 2.94 mmol) to give ethyl 6-methyl-2-oxohept-6-enoate (**20**) (542 mg, 63%) as colourless oil; R_f 0.79 (20% Et_2O in petrol); IR (film, ν_{max} cm^{-1}) 2930 w, 1726 s, 1447 w, 1254 s, 1084 s, 1045 s; ^1H NMR (500 MHz; $CDCl_3$) δ 4.75 (1H, s, 1H of H_2C═C), 4.69 (1H, s, 1H of H_2C═C), 4.32 (2H, q, *J* 7.0, CH_2CH_3), 2.84 (2H, t, *J* 7.0, CH_2C═O), 2.07 (2H, t, *J* 7.0, CH_2C═CH_2), 1.80 (2H, q, *J* 7.5, $CH_2CH_2CH_2C$═O), 1.71 (3H, s, CH_3C═C), 1.37 (3H, t, *J* 7.0, CH_2CH_3); ^{13}C NMR (125 MHz; $CDCl_3$) δ 194.7 (*C*═OCO_2Et), 161.3 (C═OCO_2Et), 144.7 (CH_3C═C), 111.1 (C═CH_2), 62.5 (CH_2CH_3), 38.6 (CH_2C═O), 36.9 (CH_2C═CH_2), 22.2 (CH_3C═CH_2), 20.8 ($CH_2CH_2CH_2C$═O), 14.1 (CH_2CH_3); HRMS *m*/*z* (M + Na^+), found 185.1174, $C_{10}H_{17}O_3$ requires 185.1172. Following the general procedure **A(ii)** using 6-methyl-2-oxohept-6-enoate (**20**) (38.0 mg, 0.206 mmol) and $TsNHNH_2$

(46.0 mg, 0.248 mmol) gave Z^{29}-hydrazone **24** (37.8 mg, 66%) as colourless oil; R_f 0.67 (20% Et_2O in petrol); IR (film, ν_{max} cm^{-1}) 3672 w, 3235 w, 1721 s, 1430 s, 1204 s, 1113 s; ^1H NMR (500 MHz; $CDCl_3$) δ 11.79 (1H, s, NH), 7.83 (2H, d, J 8.0, 2xArCH), 7.30 (2H, d, J 8.0, 2xArCH), 4.70 (1H, s, 1H of $H_2C{=}C$), 4.61 (1H, s, 1H of $H_2C{=}C$), 4.26 (2H, d, J 7.0, CH_2CH_3), 2.42 (5H, m, $ArCH_3$ and $CH_2C{=}CH_2$), 1.92 (2H, t, J 7.0, $CH_2CH_2C{=}N$), 1.66 (3H, s, $CH_3C{=}CH_2$), 1.61 (2H, t, J 7.0, $CH_2CH_2C{=}N$), 1.32 (3H, t, J 7.0, CH_2CH_3); ^{13}C NMR (125 MHz; $CDCl_3$) δ 162.3 (CO_2Et), 145.2 ($C{=}CH_2$), 144.3 (ArCMe), 139.1 (ArC), 135.7 (C=N), 129.7 (ArCH), 128.0 (ArCH), 110.3 ($C{=}CH_2$), 62.0 (CH_2CH_3), 36.9 ($CH_2C{=}CH_2$), 32.7 ($CH_2CH_2C{=}N$), 24.5 ($CH_2C{=}N$), 22.4 ($CH_3C{=}CH_2$), 21.7 ($ArCH_3$), 14.1 (CH_2CH_3); HRMS m/z ($M + Na^+$), found 375.1350, $C_{17}H_{24}N_2NaO_4S$ requires 375.1349.

Ethyl 5-methyl-2-oxohex-5-enoate (21) and ethyl (*Z*)-5-methyl-2-(2-tosylhydrazineylidene)hex-5-enoate (25). Following the general procedure **A(i)** using Mg turnings (376 mg, 15.48 mmol), 4-bromo-2-methylbut-1-ene **17** (1.00 g, 6.71 mmol) and diethyl oxalate (0.70 mL, 5.16 mmol) to give α-ketoester **21**[31] (324 mg, 37%) as colourless oil; R_f 0.72 (20% Et_2O in petrol); ^1H NMR (500 MHz; $CDCl_3$) δ 4.77 (1H, s, 1H of $H_3CC{=}CH_2$), 4.70 (1H, s, 1H of $H_3CC{=}CH_2$), 4.33 (2H, q, J 7.0, CH_2CH_3), 3.00 (2H, t, J 7.0, $CH_2C{=}O$), 2.35 (2H, t, J 7.0, $CH_2CH_2{=}O$), 1.75 (3H, s, CH_3), 1.38 (3H, t, J 7.0, CH_2CH_3); ^{13}C NMR (125 MHz; $CDCl_3$) δ 194.1 (C=O), 161.1 (CO_2Et), 143.6 ($C{=}CH_2$), 110.8 ($C{=}CH_2$), 62.5 (CH_2CH_3), 37.6 ($CH_2C{=}CH_2$), 30.8 ($CH_2C{=}O$), 22.7 (CH_3), 14.1 (CH_2CH_3). Following the general procedure **A(ii)** using ethyl 5-methyl-2-oxohex-5-enoate (**21**) (320 mg, 1.88 mmol) and $TsNHNH_2$ (420 mg, 2.26 mmol) gave Z^{29}-hydrazone **25** (537 mg, 84%) as a white solid; R_f 0.43 (20% EtOAc in petrol); m.p. 42–44 °C; IR (film, ν_{max} cm^{-1}) 3210 w, 2930 w, 1693 m, 1371 s, 1296 s, 1186 s, 1170 s, 1084 s; ^1H NMR (500 MHz; $CDCl_3$) δ 11.8 (1H, s, NH), 7.83 (2H, d, J 8.0, 2xArCH), 7.31 (2H, d, J 8.0, 2xArCH), 4.60 (1H, s, 1H of $H_3CC{=}CH_2$), 4.54 (1H, s, 1H of $H_3CC{=}CH_2$), 4.27 (2H, q, J 7.0, CH_2CH_3), 2.58 (2H, t, J 7.0, $CH_2C{=}N$), 2.43 (3H, s, CH_3Ar), 2.18 (2H, t, J 7.0, $CH_2CH_2C{=}N$), 1.65 (3H, s, $CH_3C{=}CH_2$), 1.33 (3H, t, J 7, CH_2CH_3); ^{13}C NMR (125 MHz; $CDCl_3$) δ 162.2 (CO_2Et), 144.5 ($C{=}CH_2$), 144.3 (ArCMe), 138.7 (ArC), 135.8 (C=N), 129.7 (ArCH), 128.0 (ArCH), 110.9 ($C{=}CH_2$), 62.0 (CH_2CH_3), 34.8 ($CH_2C{=}CH_2$), 31.5 ($CH_2C{=}N$), 22.4 ($CH_3C{=}CH_2$), 21.7 ($ArCH_3$), 14.1 (CH_2CH_3); HRMS m/z ($M + Na^+$), found 339.1374, $C_{16}H_{23}O_4N_2S$ requires 339.1373.

Ethyl (*Z*)-2-(2-tosylhydrazineylidene)hept-6-enoate (26). Following the general procedure **A** using Mg turnings (1.23 g, 50.6 mmol), 5-bromopent-1-ene **18** (2.0 mL, 16.9 mmol) and diethyl oxalate (1.53 mL, 11.3 mmol). A mixture of crude α-ketoester **22** (1.90 g, 11.2 mmol) and $TsNHNH_2$ (2.50 g, 13.4 mmol) gave Z^{29}-hydrazone **26** (3.04 g, 80% over 2 steps) as a white solid; R_f 0.44 (20% Et_2O in petrol); m.p. 69–71 °C; IR (film, ν_{max} cm^{-1}) 3213 br, 2980 br, 1715 m, 1641 m, 1166 s, 1065 s; ^1H NMR (500 MHz; $CDCl_3$) δ 11.79 (1H, s, NH), 7.83 (2H, d, J 8.0, 2xArCH), 7.31 (2H, d, J 8.0, 2xArCH), 5.78–5.68 (1H, m, $H_2C{=}CH$), 4.99–4.92 (2H, m, $H_2C{=}CH$), 4.26 (2H, q, J 7.0, CH_2CH_3), 2.48–2.40 (5H, m, CH_3Ar and $CH_2CH{=}CH_2$), 1.96 (2H, q, J 7.0, $CH_2CH_2C{=}N$), 1.58 (2H, q, J 7.5, $CH_2CH_2C{=}N$), 1.32 (3H, t, J 7.0, CH_2CH_3); ^{13}C NMR (125 MHz; $CDCl_3$) δ 162.2 (CO_2Et), 144.3 (ArCMe), 139.1 (ArC), 138.2 ($H_2C{=}CH$), 135.8 (C=N), 129.7 (ArCH), 128.0 (ArCH), 115.0 ($H_2C{=}CH$), 62.0 (CH_2CH_3), 32.9 ($CH_2CH{=}CH_2$), 32.5 ($CH_2CH_2C{=}N$), 25.8 ($CH_2CH_2C{=}N$), 21.7 ($ArCH_3$), 14.1 (CH_2CH_3); HRMS m/z ($M + Na^+$), found 339.1374, $C_{16}H_{23}N_2O_4S$ requires 339.1373.

Ethyl (*E*)-2-(2-tosylhydrazineylidene)hex-5-enoate (27). Following the general procedure **A** using Mg turnings (1.23 g, 50.6 mmol), 4-bromobut-1-ene **19** (1.0 mL, 5.88 mmol) and diethyl oxalate (0.53 mL, 3.92 mmol). A mixture of crude α-ketoester **23** (612 mg, 3.92 mmol) and $TsNHNH_2$ (876 mg, 4.70 mmol) gave *E*-hydrazone **27** (903 mg, ~71%, over 2 steps, containing unknown trace impurity by NMR) as a white solid; R_f 0.35 (30% EtOAc in petrol); m.p. 80–82 °C; IR (film, ν_{max} cm^{-1}) 3211 w, 3076 w, 1715 m, 1641 m, 1372 w, 1187 s, 1056 s; ^1H NMR (500 MHz; $CDCl_3$) δ 8.79 (1H, s, NH), 7.86 (2H, d, J 8.0, 2xArCH), 7.32 (2H, d, J 8.0, 2xArCH), 5.71–5.59 (1H, m, $H_2C{=}CH$), 4.93 (1H, d, J 17.0, 1 H of $H_2C{=}CH$), 4.86 (1H, d, J 10.0, 1H of $H_2C{=}CH$), 4.23 (2H, q, J 7.0, CH_2CH_3), 2.54 (2H, t, J 7.5, $CH_2C{=}N$), 2.43 (3H, s, CH_3Ar), 2.16 (2H, q, J 7.5, $CH_2CH_2C{=}N$), 1.31 (3H, t, J 7.0, CH_2CH_3); ^{13}C NMR (125 MHz; $CDCl_3$) δ 163.7 (CO_2Et), 146.8 (ArCMe), 144.7 (ArC), 136.0 ($H_2C{=}CH$), 134.9 (C=N), 129.7 (ArCH), 128.1 (ArCH), 116.7 ($H_2C{=}CH$), 61.8 (CH_2CH_3), 29.4 ($CH_2CH_2C{=}N$), 25.5 ($CH_2CH_2C{=}N$), 21.7 ($ArCH_3$), 14.2 (CH_2CH_3); HRMS m/z ($M + H^+$) found 325.1216, $C_{15}H_{21}N_2O_4S$ requires 325.1217.

Ethyl 2-diazo-6-oxoheptanoate (28). Following the general procedure **B** using hydrazone **24** (25 mg, 0.071 mmol), CH_2Cl_2 (5 mL) and Et_3N (40 μL, 0.30 mmol) gave diazocarbonyl **28**[17] (8 mg, 57%) as a yellow oil; R_f 0.43 (30% Et_2O in petrol); IR (film, ν_{max} cm^{-1}) 2081 s, 1686 s, 1371 m, 1158 m; ^1H NMR (500 MHz; $CDCl_3$) δ 4.22 (2H, q, J 7.0, CH_2CH_3), 2.51 (2H, t, J 7.0, $CH_2C{=}O$), 2.33 (2H, t, J 7.5, CH_2CN_2), 2.16 (3H, s, $CH_3C{=}O$), 1.80 (2H, quint, J 7.0, J 7.0, $CH_2CH_2CN_2$), 1.28 (3H, t, J 7.0, CH_2CH_3); ^{13}C NMR (125 MHz; $CDCl_3$) δ 208.1 ($CH_3C{=}O$), 167.7 (CO_2Et), 61.0 (CH_2CH_3), 42.3 ($CH_2C{=}O$), 30.2 ($CH_3C{=}O$), 22.8 (CH_2CN_2), 21.9 ($CH_2CH_2CN_2$), 14.7 (CH_2CH_3) [CN_2 not observed]; HRMS [$M + Na]^+$ found 221.0896, $C_9H_{14}N_2NaO_3$ requires 221.0897.

Ethyl (*Z*)-5-oxo-2-(2-tosylhydrazineylidene)hexanoate (29). Following the general procedure **B** using hydrazone **25** (180 mg, 0.53 mmol), CH_2Cl_2 (65 mL) and Et_3N (0.30 mL, 2.13 mmol) gave keto hydrazone **29** (36 mg, 20%) as a yellow oil; R_f 0.46 (40% EtOAc in petrol); IR (film, ν_{max} cm^{-1}) 2924 w, 1714 s, 1693 m, 1370 s, 1277 s, 1167 s, 1085 s; ^1H NMR (500 MHz; $CDCl_3$) δ 7.75 (2H, d, J 8.0, 2xArCH), 7.31 (2H, d, J 8.0, 2xArCH), 4.25 (2H, q, J 7.0, CH_2CH_3), 2.72 (2H, t, J 7.0, $CH_2C{=}O$), 2.65 (2H, q, J 7.5, $CH_2C{=}N$), 2.42 (3H, s, CH_3Ar), 2.14 ($CH_3C{=}O$), 1.31 (3H, t, J 7.0, CH_2CH_3); ^{13}C NMR (125 MHz; $CDCl_3$) δ 207.3 (C=O), 162.0 (CO_2Et), 144.4 (ArCMe), 137.1 (ArC), 135.8 (C=N), 129.8 (ArCH), 127.8 (ArCH), 62.2 (CH_2CH_3), 38.7 ($CH_2C{=}O$), 30.3 ($CH_3C{=}O$), 26.7

($CH_2C{=}N$), 21.7 ($ArCH_3$), 14.1 (CH_2CH_3); HRMS *m*/*z* (M + Na^+), found 341.1162, $C_{15}H_{21}O_5N_2S$ requires 341.1165.

Ethyl 3-acetyl-4,5-dihydro-1*H*-pyrazole-5-carboxylate (33). Following the general procedure **B** using hydrazone **25** (100 mg, 0.30 mmol), CH_2Cl_2 (36 mL) and DBU (0.18 mL, 1.18 mmol) gave 2-pyrazoline **33** (22.4 mg, 41%) as a clear oil; R_f 0.54 (40% EtOAc in petrol); IR (film, ν_{max} cm^{-1}) 3338 br, 2983 w, 1735 s, 1662 s, 1346 m, 1207 s, 1095 s; ^1H NMR (500 MHz; $CDCl_3$) δ 6.75 (1H, s, NH), 4.44 (1H, dd, *J* 5.0, *J* 12.5, $CHCO_2Et$), 4.22 (2H, q, *J* 7.0, CH_2CH_3), 3.26 (1H, dd, *J* 5.0, *J* 17.5, 1 H of CH_2), 3.10 (1H, dd, *J* 12.5, *J* 17.5, 1H of CH_2), 2.42 (3H, s, $CH_3C{=}O$), 1.30 (3H, t, *J* 7.0, CH_2CH_3); ^{13}C NMR (125 MHz; $CDCl_3$) δ 194.3 ($C{=}O$), 171.9 (CO_2Et), 150.7 ($C{=}N$), 62.2 (CH_2CH_3), 61.7 ($CHCO_2Et$), 33.4 (CH_2), 25.7 ($CH_3C{=}O$), 14.2 (CH_2CH_3); HRMS *m*/*z* (M + H^+), found 185.0922, $C_8H_{13}O_3N_2$ requires 185.0921.

Ethyl 2-oxocyclopentane-1-carboxylate (34). Following the general procedure **2** using hydrazone **26** (500 mg, 1.48 mmol), CH_2Cl_2 (170 mL) and Et_3N (0.82 mL, 5.91 mmol) gave β-ketoester **34**[32] (37 mg, 16%) as a colourless oil; R_f 0.54 (30% EtOAc in petrol); ^1H NMR (500 MHz; $CDCl_3$) δ 4.19 (2H, q, *J* 7.0, CH_2CH_3), 3.14 (1H, t, *J* 9.5, $CHCO_2Et$) 2.33–2.27 (4H, m, $CHCH_2$ and $CHCH_2CH_2$), 2.17–2.10 (1H, m, CH_2CO), 1.89–1.83 (1H, m, CH_2CO), 1.28 (3H, t, *J* 7.0, CH_2CH_3); ^{13}C NMR (125 MHz; $CDCl_3$) δ 212.6 ($C{=}O$), 169.5 (CO_2Et), 61.5 (CH_2CH_3), 54.9 ($CHCO_2Et$), 38.2 ($CHCH_2$), 27.5 ($CHCH_2CH_2$), 21.1 ($CH_2C{=}O$), 14.3 (CH_2CH_3).

Ethyl 6-hydroxy-1-tosyl-1,4,5,6-tetrahydropyridazine-3-carboxylate (35). Following the general procedure **B** using hydrazone **27** (500 mg, 1.54 mmol), CH_2Cl_2 (170 mL) and Et_3N (0.86 mL, 6.17 mmol) gave tetrahydropyridazinol **35** (322 mg, 64%) as a yellow solid; R_f 0.58 (50% EtOAc in petrol); m.p. 122–125 °C; IR (film, ν_{max} cm^{-1}) 3478 br, 2981 w, 1713 w, 1298 w, 1167 s, 1064 s, 726 s, 666 s; ^1H NMR (500 MHz; $CDCl_3$) δ 7.88 (2H, d, *J* 8.0, ArCH), 7.30 (2H, d, *J* 8.0, ArCH), 5.87 (1H, s, CHOH), 4.26 (2H, q, *J* 8.0, CH_2CH_3), 3.81 (1H, s, OH), 2.68 (1H, dd, *J* 5.0, *J* 18.5, 1H of $CH_2C{=}N$), 2.41 (3H, s, $ArCH_3$), 2.38–2.29 (1H, m, 1H of $CH_2C{=}N$), 2.14 (1H, m, 1H of $CH_2CH_2C{=}N$), 1.57 (1H, m, 1H of $CH_2CH_2C{=}N$), 1.34 (3H, t, *J* 7.0, CH_2CH_3); ^{13}C NMR (125 MHz; $CDCl_3$) δ 163.4 (CO_2Et), 144.6 (ArCMe), 142.7 (ArC), 135.2 ($C{=}N$), 129.6 (ArCH), 128.2 (ArCH), 73.4 (CHOH), 61.6 (CH_2CH_3), 24.0 ($CH_2CH_2C{=}N$), 21.7 ($ArCH_3$), 16.3 ($CH_2C{=}N$), 14.2 (CH_2CH_3); HRMS *m*/*z* (M + H^+), found 327.1009, $C_{14}H_{19}N_2O_5S$ requires 327.1009.

4-Methyl-*N*′-(3-methylcyclopent-2-en-1-ylidene)benzenesulfonohydrazide (38). Following the general procedure **A(ii)** using 3-methylcyclopent-2-en-1-one (**36**) (2.0 mL, 20.4 mmol) and $TsNHNH_2$ (4.94 g, 26.5 mmol) gave an *E*-/*Z*- mixture of hydrazone **38** (4.20 g, 78%, 14 : 86 *E* : *Z* as determined by ^1H NMR NH signals) as a white solid; R_f 0.51 (30% EtOAc in petrol); m.p. 149–151 °C; IR (film, ν_{max} cm^{-1}) 3212 w, 2914 w, 1625 w, 1330 s, 1163 s, 1092 s; ^1H NMR (500 MHz; $CDCl_3$) δ 7.86 (2H, d, *J* 8.0, 2xArCH), 7.53 (1H, s, NH), 7.30 (2H, d, *J* 8.0, 2xArCH), 5.91 (1H, s, $CH_3C{=}CH$), 2.43 (7H, d, *J* 16.0, $ArCH_3$ and $CH_2CH_2C{=}N$), 1.91 (3H, s, $CHCCH_3$); ^{13}C NMR (125 MHz; $CDCl_3$) δ 169.0 ($HC{=}CCH_3$), 160.8 ($C{=}N$), 144.0 (ArC), 135.7 (ArC), 129.7 (ArCH), 128.1 (ArCH), 126.7 ($HC{=}CCH_3$), 34.9 (CH_2CCH_3), 26.6 (CH_2CN), 21.7 ($ArCCH_3$), 18.1 ($HCCCH_3$); HRMS *m*/*z* (M + H^+) found 265.1004, $C_{13}H_{17}N_2O_2S$ requires 265.1005; discernible data for *E*-isomer: ^1H NMR (500 MHz; $CDCl_3$) δ 6.22 (1H, s, $CH_3C{=}CH$), 2.59 (2H, m, $CH_2C{=}N$), 1.96 (3H, s, $CHCCH_3$); ^{13}C NMR (125 MHz; $CDCl_3$) δ 169.8 ($HC{=}CCH_3$), 166.5 ($C{=}N$), 143.9 (ArC), 129.6 (ArCH), 128.1 (ArCH), 119.7 ($HC{=}CCH_3$), 34.1 (CH_2CCH_3), 30.3 (CH_2CN), 21.8 ($ArCCH_3$), 18.8 ($HCCCH_3$).

4-Methyl-*N*′-(3-methylcyclohex-2-en-1-ylidene)benzenesulfonohydrazide (39). Following the general procedure **A(ii)** using 3-methylcyclohex-2-en-1-one (**37**) (2.0 mL, 17.6 mmol) and $TsNHNH_2$ (4.27 g, 22.9 mmol) in MeOH (15 mL) gave a mixture of *E*-/*Z*- hydrazone **39** (4.38 g, 89%, 60 : 40 *E* : *Z* as determined by ^1H NMR NH signals) as a white solid; R_f 0.35 (30% EtOAc in petrol); data as lit.[33]

2-Diazo-5-oxohexanal (40). Following the general procedure **B** using hydrazone **38** (1.00 g, 3.78 mmol) in CH_2Cl_2 (420 mL) and Et_3N (2.1 mL, 15.2 mmol) to give s-*E*/s-*Z*-diazoaldehyde **40** (338 mg, 64%, 86 : 14 *E* : *Z*, as determined by ^1H NMR CHO signal and NOE studies) as a yellow oil; R_f 0.38 (50% EtOAc in petrol); IR (film, ν_{max} cm^{-1}) 2927 w, 2087 s, 1712 s, 1615 s, 1280 w, 1146 s; ^1H NMR (500 MHz; $CDCl_3$) δ 9.47 (1H, s, CHO), 2.75 (2H, t, *J* 6.0, $CH_2C{=}O$), 2.54 (2H, t, *J* 6.0, CH_2CN_2), 2.16 (3H, s, CH_3); ^{13}C NMR (125 MHz; $CDCl_3$) δ 207.7 ($C{=}OCH_3$), 182.9 (CHO), 71.2 (CN_2), 41.0 ($CH_2C{=}O$), 29.9 (CH_3), 16.4 (CH_2CN_2); HRMS *m*/*z* (M − H^+), found 139.0510, $C_6H_7N_2O_2$ requires 139.0513; discernible data for *Z*-diazoaldehyde: ^1H NMR (500 MHz; $CDCl_3$) δ 9.23 (1H, s, CHO), 2.67 (2H, t, *J* 6.0, $CH_2C{=}O$), 2.19 (3H, s, CH_3); ^{13}C NMR (125 MHz; $CDCl_3$) δ 206.6 ($C{=}OCH_3$), 185.5 (CHO), 42.9 ($CH_2C{=}O$), 30.1 (CH_3), 17.2 (CH_2CHN_2).

2-Diazo-6-oxoheptanal (41). Following the general procedure **B** using hydrazone **39** (500 mg, 1.80 mmol) in CH_2Cl_2 (200 mL) and Et_3N (1.00 mL, 7.2 mmol) to give s-*E*/s-*Z*-diazoaldehyde **41** (172 mg, 63%, 84 : 16 s-*E* : s-*Z*, as determined by ^1H NMR CHO signal and NOE studies) as a yellow oil; R_f 0.39 (50% EtOAc in petrol); IR (film, ν_{max} cm^{-1}) 2936 w, 2084 s, 1712 s, 1629 s, 1167 s; ^1H NMR (500 MHz; $CDCl_3$) δ 9.56 (1H, s, CHO), 2.50 (2H, t, *J* 7.0, $CH_2C{=}O$), 2.35 (2H, t, *J* 7.5, CH_2CN_2), 2.14 (3H, s, CH_3), 1.79 (2H, p, *J* 7.0, *J* 7.0, $CH_2CH_2CN_2$); ^{13}C NMR (125 MHz; $CDCl_3$) δ 207.9 ($C{=}OCH_3$), 182.8 (CHO), 70.7 (CN_2), 42.2 ($CH_2C{=}O$), 30.2 (CH_3), 21.3 ($CH_2CH_2CN_2$), 20.6 (CH_2CN_2); HRMS *m*/*z* (M + H^+), found 155.0814, $C_7H_{11}N_2O_2$ requires 155.0815; discernible data for *Z*-diazoaldehyde: ^1H NMR (500 MHz; $CDCl_3$) δ 9.19 (1H, s, CHO), 2.54 (2H, t, *J* 7.0, $CH_2C{=}O$), 2.46 (2H, t, *J* 7.5, CH_2CHN_2), 2.17 (3H, s, CH_3), 1.84 (2H, t, *J* 7.0, $CH_2CH_2CHN_2$); ^{13}C NMR (125 MHz; $CDCl_3$) δ 207.4 ($C{=}OCH_3$), 185.4 (CHO), 41.7 ($CH_2C{=}O$), 30.2 (CH_3), 22.8 ($CH_2CH_2CHN_2$), 22.3 (CH_2CHN_2).

2-Ethoxy-3-methylcyclohex-2-en-1-one (42). To a solution of H_2O_2 (9.86 mL, 116 mmol, 30%) in MeOH (35 mL) at 0 °C was added 3-methylcyclohex-2-en-1-one (**37**) (4.0 mL, 35.3 mmol) followed by dropwise aq NaOH (2.9 mL, 17.6 mmol, 6 M) maintaining the temperature below 5 °C. After 45 min, the

mixture was poured onto ice (5 g) and extracted with CH_2Cl_2 (3 × 15 mL), dried ($MgSO_4$), concentrated under reduced pressure to give the corresponding epoxide[22] (5.80 g) which was used directly in the next step. The crude epoxide (5.80 g, 46.0 mmol) in EtOH (5 mL) was added to a refluxing solution of Na (1.50 g, 69.0 mmol) in EtOH (20 mL). After 5 min, the mixture was cooled to 0 °C and poured onto ice (5 g), extracted with CH_2Cl_2 (3 × 15 mL), washed with brine (15 mL), dried ($MgSO_4$), concentrated under reduced pressure and purified by column chromatography (20% EtOAc in petrol) to give α-ethoxyenone **42** (1.38 g, 25% from **37**) as colourless oil; R_f 0.4 (20% EtOAc in petrol); IR (film, ν_{max} cm^{-1}) 3441 br, 2930 m, 1673 s, 1432 w, 1196 w, 730 w; ^1H NMR (500 MHz; $CDCl_3$) δ 3.78 (2H, q, J 7.0, CH_2CH_3), 2.38 (2H, t, J 7.0, $CH_2C{=}O$), 2.33 (2H, t, J 7.0, CH_2CCH_3), 1.87 (5H, m, $CH_2CH_2CCH_3$ and CCH_3), 1.22 (3H, t, J 7.0, CH_2CH_3); ^{13}C NMR (125 MHz; $CDCl_3$) δ 194.9 (C=O), 148.1 ($C{=}CCH_3$), 146.1 ($C{=}CCH_3$), 67.6 (CH_2CH_3), 38.7 ($CH_2C{=}O$), 31.4 (CH_2CCH_3), 22.2 ($CH_2CH_2CCH_3$), 17.8 (CCH_3), 15.5 (CH_2CH_3); HRMS m/z (M^+) found 155.10667, $C_9H_{14}O_2$ requires 155.10666.

(*E*)-*N*′-(2-Ethoxy-3-methylcyclohex-2-en-1-ylidene)-4-methylbenzenesulfonohydrazide (43). Following the general procedure **A(ii)** using 2-ethoxy-3-methylcyclohex-2-en-1-one (**42**) (1.32 g, 8.51 mmol) and $TsNHNH_2$ (1.90 g, 10.2 mmol) gave *E*-hydrazone **43** (2.57 g, 94%) as a white solid; R_f 0.48 (40% EtOAc in petrol); m.p. 115–117 °C IR (film, ν_{max} cm^{-1}) 3211 w, 2929 w, 1639 w, 1402 m, 1162 s; ^1H NMR (500 MHz; $CDCl_3$) δ 7.95 (1H, s, NH), 7.87 (2H, d, J 8.0, 2xArCH), 7.28 (2H, d, J 8.0, 2xArCH), 3.68 (2H, q, J 7.0, CH_2CH_3), 2.39 (3H, s, $C{=}CCH_3$), 2.33 (2H, t, J 7.5, CH_2CN), 2.11 (2H, t, J 7.0, CH_2CCH_3), 1.77 (3H, s, $ArCH_3$), 1.68 (2H, pent. J 7.0, J 7.0, CH_2CH_2CN), 1.23 (3H, t, J 7.0, CH_2CH_3); ^{13}C NMR (125 MHz; $CDCl_3$) δ 150.7 (C=N), 145.1 (C=COEt) 143.9 (ArC), 135.6 (ArC), 133.4 ($C{=}CCH_3$), 129.5 (ArCH), 128.3 (ArCH), 67.4 (CH_2CH_3), 30.1 (CH_2CCH_3), 25.1 (CH_2CN), 21.7 ($ArCCH_3$), 20.8 (CH_2CH_2CN), 17.5 ($C{=}CCH_3$), 15.6 (CH_2CH_3); HRMS m/z (M + H^+) found 323.14236, $C_{16}H_{23}N_2O_3S$ requires 323.14239.

Ethyl 2-diazo-6-oxoheptanoate (28). Following the general procedure **B** using hydrazone **43** (1.0 g, 3.10 mmol), CH_2Cl_2 (350 mL) and Et_3N (1.73 mL, 12.4 mmol) gave diazoester **28** (348 mg, 57%) as yellow oil; R_f 0.43 (30% Et_2O in petrol); data identical to that reported above.

Conflicts of interest

There are no conflicts of interest to declare.

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