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PAPER

Diastereoselective intermolecular ene reactions: synthesis of 4,5,6,7-tetrahydro-1*H*-benzo[*d*]imidazoles†

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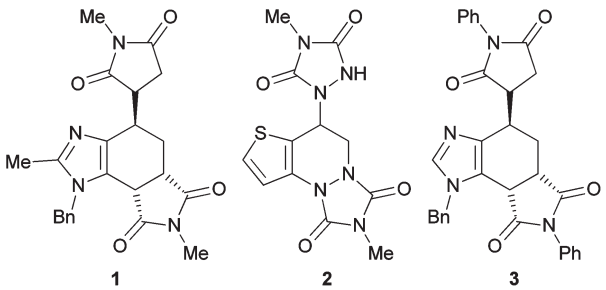
The Diels–Alder cycloadducts of 4-vinylimidazoles and *N*-phenylmaleimide are shown to undergo facile intermolecular ene reactions. Overall the reaction of three simple molecules (a diene, a dienophile and an enophile) in a two-step process gives 4,5,6,7-tetrahydro-1*H*-benzo[*d*]imidazoles with high yields, high atom economy and diastereocontrol of up to 5 new stereocentres.

Introduction

1*H*-Benzo[*d*]imidazoles are a core structure of many biologically active molecules, including drugs such as mebendazole and albendazole. However, despite the success of many aromatic compounds of this type, medicinal chemistry is moving from stereochemistry as "a source of problems" to stereochemistry as a vital tool for improving selectivity and efficacy.[1,2] Thus, there is an increasing interest in unsaturated, chiral 1*H*-benzo[*d*]imidazole analogues as medicinal leads.[3]

Recently we disclosed our investigations into the Diels–Alder (D–A) reactions of *N*-trityl-4-vinylimidazoles and *N*-phenylmaleimide. This resulted in the observation of novel domino reaction processes including D–A, [1,3]-H shift, [1,3]-trityl migrations and D–A, [1,3]-H shift, [1,3]-trityl migration, Michael reactions.[4]

These results prompted us to examine the reactivity of the D–A cycloadducts of 4-vinylimidazoles and maleimides in more detail.[5] During the study of D–A reactions of various vinyl-heteroaromatics with reactive dienophiles, a handful of research groups have reported the observation of an intriguing, if low-yielding, by-product formed from one molecule of vinyl-heteroaromatic and two molecules of the dienophile. It has been postulated that this occurs *via* an intermolecular Diels–Alder/intermolecular ene (IMDA/IME) reaction sequence, the products of which are shown (Scheme 1).[6] There are, however, no examples of this reaction sequence being carried out with the separation of the ene reaction from the other steps, allowing variation of the enophile.



Scheme 1 Observed by-products arising from postulated IMDA/IME reactions of vinyl-heteroaromatics.

Intermolecular pericyclic reactions are powerful tools in synthetic organic chemistry due to their ability to generate multiple covalent bonds and stereocentres in a single step.[7] Thus use of an intermolecular Diels–Alder and an intermolecular ene reaction would allow, in two steps and from three simple starting materials, rapid access to complex unsaturated 1*H*-benzo[*d*]-imidazole analogues with 100% atom economy and high diastereomeric control in the formation of the multiple C–C and C–X bonds.[7,8]

Through the introduction of different enophiles this reaction sequence would provide a hitherto unexplored synthetic approach for the diastereoselective generation of complex unsaturated 1*H*-benzo[*d*]imidazoles. Herein we discuss our investigations into the ability of the D–A cycloadducts of 4-vinyl-imidazoles and *N*-phenylmaleimide to undergo diastereoselective ene reactions with a broad range of enophiles (Scheme 2).[9]

Examination of the X-ray crystal structures of molecules such as **5** shows that the *twix* C–H σ-bond is coplanar with the electron-rich cyclohexenyl C=C π-bond.[10] In addition an ene reaction involving the *twix* C–H results in the rearomatisation of the imidazole ring providing highly favourable thermodynamics.[11] Thus we envisaged that ene reactions with molecules such as **5** would be both regio- and diastereoselective.

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†Electronic supplementary information (ESI) available: ^{1}H and ^{13}C NMR spectra for all compounds, X-ray structures and .cif files for **6b**, **7c**, **7d**, **8a**. CCDC 860567–860571. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2ob26009c

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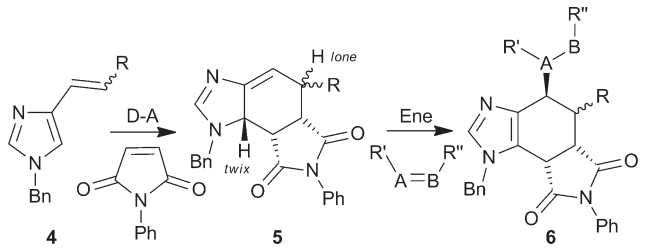


Scheme 2 Planned IMDA/IME reaction sequence of vinylimidazoles.

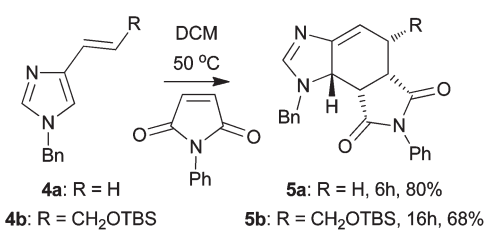
Results and discussion

The desired cycloadducts (**5a–b**) were prepared through the D–A reaction of *N*-phenylmaleimide (NPM) and the requisite vinylimidazole precursors (**4a–b**). 1-Benzyl-4-vinyl-1*H*-imidazole (**4a**) was synthesised *via* a thermal decarboxylation of urocanic acid followed by a benzyl protection of the sterically most accessible nitrogen atom. (*E*)-1-Benzyl-4-(3-((*tert*-butyldimethylsilyl)-oxy)prop-1-en-1-yl)-1*H*-imidazole (**4b**) was also synthesised starting from urocanic acid *via* an esterification, *N*-benzyl protection, DIBAL reduction and finally *O*-TBS protection. Vinylimidazoles (**4a–b**) were then reacted with NPM to give (**5a–b**) respectively (Scheme 3).[4,6b]

Reaction of **5a** was successful with a range of reactive enophiles including arylnitroso compounds (**6a–c**),[12] benzyne (**6d**, generated from trimethylsilylphenyl triflate and TBAF *in situ*),[13] PTAD (**6e**), and diethyl 2-oxomalonate (**6f**). These reactions gave good to excellent yields of the ene products as single diastereomers (Table 1). The ene reactions proved to be remarkably facile, requiring a few hours at moderate to low temperatures without the requirement of a Lewis acid catalyst. Relative stereochemistry of the ene products was determined through comparison with the results of single-crystal X-ray analysis of **6b** (see ESI†).[14]

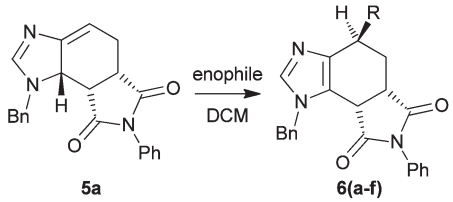
Interestingly, in the case of less reactive enophiles (*N*-phenyl- or *N*-methylmaleimide, maleic anhydride, *etc*.) even extended reaction times resulted in no observed ene products but only rearomatisation of the imidazole, and in some cases concurrent oxidation (potentially air oxidation) of the imidazolyl methylene.

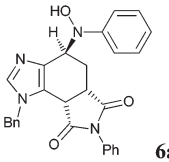
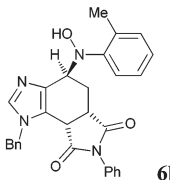
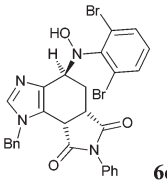
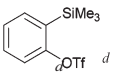
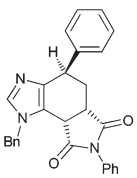
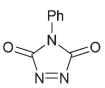
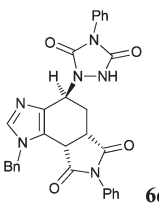
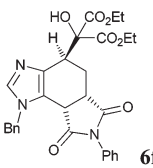
We then subjected **5b** to our previous ene reaction conditions. For **5b** ene reactions with arylnitroso compounds were not successful, but reactions with PTAD and diethyl 2-oxomalonate gave moderate yields of **6(g–h)** as single diastereomers, resulting in the generation, over two steps, of four contiguous stereocentres and three C–C/X bonds *via* the IMDA/IME three-component reaction sequence (Table 2).



Scheme 3 Synthesis of reactive cycloadducts **5a** and **5b**.

Table 1 Ene reactions of **5a**[a]



Enophile	Reaction conditions	Product	Yield[c]
	r.t., 1 h	 **6a**	95%
	r.t., 2 h	 **6b**[b]	68%
	r.t., 1 h	 **6c**	87%
 [d]	TBAF, 40 °C, 2 h	 **6d**	68%
	−78 °C, 1 h	 **6e**	74%
	r.t., 16 h	 **6f**	83%

[a] All compounds shown were isolated as single diastereomers. [b] Structure confirmed by single-crystal X-ray analysis. [c] Isolated yield of the ene reaction. [d] Benzyne precursor.

Both **5a** and **5b** were then reacted with the prochiral enophiles, ethyl 2-oxoacetate and ethyl 3,3,3-trifluoro-2-oxopropanoate, in order to introduce an additional exocyclic stereocentre, generating overall a total of five contiguous stereocentres (Table 3). In all cases reasonable yields were obtained with the *endo*-ene product as the major diastereomer.

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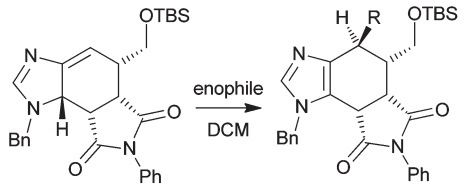
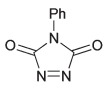
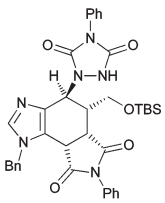
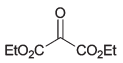
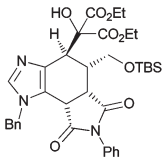
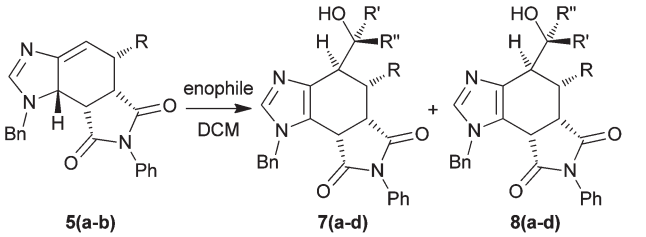
Table 2 Ene reactions of **5b**[a]

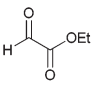
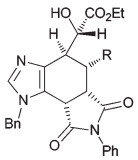
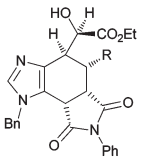
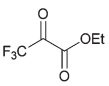
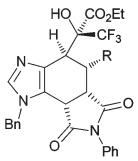
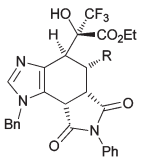


Enophile	Reaction conditions	Product	Yield[b]
	r.t., 1 h	 **6g**	61%
	r.t., 2 h	 **6h**	65%

[a] All compounds shown were isolated as single diastereomers. [b] Isolated yield of the ene reaction.

Table 3 Carbonyl ene reactions of **7(a–b)**[a]



Enophile	Substrate, conditions and yields[b]	Major diastereomer (*endo*-)	Minor diastereomer (*exo*-)
	R = H (**7a**/**8a**); r.t., 30 h, 72% R = CH_2OTBS (**7b**/**8b**); r.t., 16 h, 59%	 **7a**/**8a**[c] = 5:1 **7b**/**8b** ≥ 20:1[d]	
	R = H (**7c**/**8c**); r.t., 16 h, 53% R = CH_2OTBS (**7d**/**8d**); r.t., 72 h, 53%	 **7c**[c] /**8c** ≥ 20:1[e] **7d**[c] /**8d** = 2:1	

[a] All compounds shown were isolated as single diastereomers. [b] Isolated yields. [c] Structures confirmed by single-crystal X-ray analysis. [d] **8b** not observed. [e] **8c** not observed.

Relative stereochemistry of the products was determined through comparison with the results of single-crystal X-ray analysis of **7c**,[15] **7d** and **8a** (see ESI†).[14]

Conclusions

In summary, we have successfully demonstrated that the D–A cycloadducts of 4-vinylimidazoles are viable substrates for high-yielding and highly diastereoselective ene reactions with a wide range of enophiles. Our exemplified 2-step IMDA/IME process allows for the overall combination of three simple components (a vinylimidazole, a dienophile and an enophile) to generate, with 100% atom economy, complex 4,5,6,7-tetrahydro-1*H*-benzo[*d*]imidazoles containing up to 5 new stereocentres through the generation of C–C/X bonds. Current investigations are aimed towards enantioselective variants, extension to other vinyl-aromatic systems, and reaction telescoping.

Experimental section

(5a*S**,8a*S**)-1-Benzyl-7-phenyl-1,5,5a,8b-tetrahydroimidazo-[4,5-*e*]isoindole-6,8(7*H*,8a*H*)-dione (5a)

To 1-benzyl-4-vinyl-1*H*-imidazole (200 mg, 1.09 mmol) in dichloromethane (5 mL) was added *N*-phenylmaleimide (470 mg, 6.93 mmol) and the reaction mixture was stirred at 50 °C for 6 h. The solution was concentrated to a low volume then cooled and filtered to give a white solid. The filtrate was concentrated and purified by chromatography with silica gel (diethyl ether–methanol, 98 : 2) to yield the product as a white solid, 313 mg (80%).

R_f 0.13 (UV active, diethyl ether–methanol, 98 : 2); mp: 193–195 °C (lit.[6b] 195–196 °C); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.45–7.28 (9H, m), 7.16–7.13 (2H, m), 5.62 (1H, ddd, J = 7.9, 3.8, 3.8 Hz), 4.90 (1H, d, J = 15.1 Hz), 4.77 (1H, d, J = 15.1 Hz), 4.02 (1H, ddd, J = 7.7, 3.8, 3.8 Hz), 3.64 (1H, dd, J = 8.9, 7.7 Hz), 3.12 (1H, ddd, J = 8.9, 6.7, 1.8 Hz), 3.11 (1H, ddd, J = 15.4, 7.9, 1.8 Hz), 1.95 (1H, dddd, J = 15.4, 6.7, 3.8, 3.8 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 177.8, 173.9, 159.4, 154.6, 135.3, 131.6, 129.1, 129.2, 128.8, 128.3, 128.1, 126.5, 102.4, 56.9, 49.9, 41.1, 36.8, 25.5; IR (neat): ν_{max}/cm^{-1} 3067, 3029, 2964, 2829, 1771, 1699, 1542, 1496, 758, 694; HRMS (ES-ToF): calcd for $C_{22}H_{19}N_3O_2$ (M + H)$^+$: 358.1550, found 358.1554.

1,3-Dibromo-2-nitrosobenzene[12]

To 2,6-dibromoaniline (0.52 g, 2.05 mmol) in trifluoroacetic acid (3.5 mL) was added H_2O_2 (35% solution in water, 0.15 mol, 4.67 mL), and the mixture stirred at r.t. for 16 h. The mixture was then poured into ice-water (20 mL) and the orange/brown precipitate was filtered and recrystallised from *n*-hexane to give the title compound as a beige solid, 339 mg (62%).

R_f 0.60 (UV active, diethyl ether–petroleum ether 40–60, 50 : 50); mp: 112–114 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.77

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(2H, d, J = 7.7 Hz), 7.28 (1H, t, J = 7.7 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 172.5, 138.6, 134.5, 116.7; IR (neat): ν_{max}/cm^{-1} 3069, 1563, 1437, 1279, 777, 733; HRMS (ES-ToF): calcd for $C_6H_3NOBr_2$ $(M + H)^+$: 265.8633, found 265.8625.

(4*S,5a*S**,8a*S**)-1-Benzyl-4-(hydroxy(phenyl)amino)-7-phenyl-5,5a,7,8a-tetrahydroimidazo[4,5-*e*]isoindole-6,8(1*H*,4*H*)-dione (6a)**

To (5a*S**,8a*S**)-1-benzyl-7-phenyl-1,5,5a,8b-tetrahydroimidazo-[4,5-*e*]isoindole-6,8(7*H*,8a*H*)-dione (**5a**) (200 mg, 0.56 mmol) in dichloromethane (15 mL) was added nitrosobenzene (60 mg, 0.56 mmol) and the solution stirred at r.t. for 1 h. The reaction was concentrated and purified by chromatography with silica gel (ethyl acetate–petroleum ether 40–60, 50 : 50) to yield the product as an off-white solid, 248 mg (95%).

R_f 0.33 (UV active, ethyl acetate–petroleum ether 40–60, 50 : 50); mp: 189–190 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.61 (1H, s), 7.47–7.44 (2H, m), 7.40–7.34 (4H, m), 7.28–7.18 (8H, m), 6.96 (1H, t, J = 7.2 Hz, *N*-phenyl C–H), 5.67 (1H, d, J = 15.3 Hz), 5.34 (1H, d, J = 15.3 Hz), 4.75 (1H, dd, J = 7.8, 4.9 Hz), 3.94 (1H, d, J = 8.1 Hz), 3.55 (1H, dd, J = 13.1, 5.5 Hz), 2.38–2.32 (1H, m), 2.25–2.18 (1H, m); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 177.0, 174.7, 150.8, 139.4, 138.7, 135.7, 131.5, 129.3, 129.2, 128.9, 128.8, 128.4, 127.6, 126.4, 122.0, 121.4, 117.2, 57.5, 49.9, 39.4, 38.7, 23.4; IR (neat): ν_{max}/cm^{-1} 2980, 2884, 1773, 1715, 1597, 1496, 1377, 734, 690; HRMS (ES-ToF): calcd for $C_{28}H_{23}N_4O_3$ $(M + H)^+$: 465.1921, found 465.1916.

(4*S,5a*S**,8a*S**)-1-Benzyl-4-(hydroxy(*o*-tolyl)amino)-7-phenyl-5,5a,7,8a-tetrahydroimidazo[4,5-*e*]isoindole-6,8(1*H*,4*H*)-dione (6b)**

To (5a*S**,8a*S**)-1-benzyl-7-phenyl-1,5,5a,8b-tetrahydroimidazo-[4,5-*e*]isoindole-6,8(7*H*,8a*H*)-dione (**5a**) (200 mg, 0.56 mmol) in dichloromethane (5 mL) was added 2-nitrosotoluene (81 mg, 0.67 mmol) and the solution stirred at r.t. for 2 h. The solvent was removed and the crude residue was chromatographed on silica gel (diethyl ether) to yield the title compound as an off-white solid, 181 mg (68%).

R_f 0.12 (UV active, diethyl ether); mp: 202–204 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.60 (1H, d, J = 7.3 Hz), 7.49 (1H, s), 7.46–7.42 (2H, m), 7.39–7.33 (4H, m), 7.25–7.14 (5H, m), 7.12–7.10 (1H, m), 7.06–7.03 (1H, m), 6.82 (1H, br s), 5.70 (1H, d, J = 15.6 Hz), 5.30 (1H, d, J = 15.6 Hz), 4.29 (1H, dd, J = 7.3, 5.0 Hz), 3.90 (1H, d, J = 7.8 Hz), 3.64–3.59 (1H, m), 2.39–2.32 (1H, m), 2.26 (3H, s), 2.16–2.10 (1H, m); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 176.9, 174.6, 149.0, 139.2, 135.7, 131.5, 131.3, 130.8, 129.3, 129.2, 128.9, 128.4, 127.6, 126.4, 126.3, 125.2, 121.8, 121.1, 57.9, 49.9, 39.5, 38.7, 24.8, 18.1; IR (neat): ν_{max}/cm^{-1} 3068, 3030, 2879, 1781, 1703, 1597, 1498, 1377, 730, 691; HRMS (ES-ToF): calcd for $C_{29}H_{28}N_4O_3$ $(M + H)^+$: 479.2078, found 479.2065; HRMS (ES-ToF): calcd for $C_{29}H_{26}N_4O_3$ $([M - H_2O] + H)^+$: 461.1972, found 461.1967.

(4*S,5a*S**,8a*S**)-1-Benzyl-4-((2,6-dibromophenyl)(hydroxy)amino)-7-phenyl-5,5a,7,8a-tetrahydroimidazo[4,5-*e*]isoindole-6,8(1*H*,4*H*)-dione (6c)**

To (5a*S**,8a*S**)-1-benzyl-7-phenyl-1,5,5a,8b-tetrahydroimidazo-[4,5-*e*]isoindole-6,8(7*H*,8a*H*)-dione (**5a**) (200 mg, 0.56 mmol) in dichloromethane (5 mL) was added 1,3-dibromo-2-nitrosobenzene (163 mg, 0.62 mmol), and the solution stirred at r.t. for 72 h. The solvent was removed and the crude residue was chromatographed on silica gel (diethyl ether–petrol, 80 : 20) to yield the title compound as an oil, 256 mg (73%).

R_f 0.22 (UV active, diethyl ether–petrol, 80 : 20); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.49–7.23 (11H, m), 6.98 (2H, d, J = 6.3 Hz), 6.90 (1H, t, J = 8.0 Hz), 6.62 (1H, br s, OH), 5.82 (1H, d, J = 15.8 Hz), 5.34 (1H, t, J = 3.2, 2.9 Hz), 5.18 (1H, d, J = 15.8 Hz), 4.03–3.97 (1H, m), 3.78 (1H, d, J = 7.9 Hz), 3.03–2.97 (1H, m), 1.91–1.84 (1H, m); ^{13}C NMR (101 MHz, $CDCl_3$): 178.0, 174.2, 144.3, 139.2, 136.2, 135.8, 131.6, 129.5, 129.4, 129.0, 128.1, 127.3, 126.4, 122.3, 56.2, 50.0, 39.4, 38.4, 30.6; IR (neat): ν_{max}/cm^{-1} 2980, 2907, 2850, 1781, 1713, 1598, 1497, 1377, 748, 717, 691, 615; HRMS (ES-ToF): calcd for $C_{28}H_{22}Br_2N_4O_3$ $(M + H)^+$: 621.0131, found 621.0130; EA: calcd C: 54.04%, H: 3.56%, N: 9.00%, found C: 53.92%, H: 3.45%, N: 8.95%.

(4*R,5a*S**,8a*S**)-1-Benzyl-4,7-diphenyl-5,5a,7,8a-tetrahydroimidazo[4,5-*e*]isoindole-6,8(1*H*,4*H*)-dione (6d)**

To (5a*S**,8a*S**)-1-benzyl-7-phenyl-1,5,5a,8b-tetrahydroimidazo-[4,5-*e*]isoindole-6,8(7*H*,8a*H*)-dione (**5a**) (200 mg, 0.56 mmol) and trimethylsilylphenyl triflate (250 mg, 0.84 mmol, 204 μL) in dichloromethane (10 mL) was added tetra-butylammonium fluoride (1 M in THF, 219 mg, 0.84 mmol, 840 μL) and the solution heated at 40 °C for 2 h. The solvent was removed and the crude residue was chromatographed on silica gel (diethyl ether–petroleum ether 40–60, 50 : 50 → diethyl ether) to yield the title compound as a white solid, 165 mg (68%).

R_f 0.13 (UV active, diethyl ether); mp: 228–229 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.55 (1H, s), 7.47–7.45 (2H, m), 7.40–7.30 (6H, m), 7.29–7.19 (5H, m), 7.14–7.12 (2H, m), 5.77 (1H, d, J = 15.6 Hz), 5.32 (1H, d, J = 15.6 Hz), 4.08 (1H, dd, J = 8.1, 4.9 Hz), 3.94 (1H, d, J = 8.2 Hz), 3.38–3.33 (1H, m), 2.65–2.59 (1H, m), 2.17–2.10 (1H, m); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 177.1, 174.8, 142.1, 141.7, 139.4, 136.2, 131.6, 129.3, 129.2, 128.9, 128.7, 128.4, 128.2, 127.4, 127.0, 126.4, 119.9, 49.8, 39.5, 38.9, 38.8, 32.9; IR (neat): ν_{max}/cm^{-1} 3034, 2916, 2866, 1775, 1703, 1598, 1496, 734, 693; HRMS (ES-ToF): calcd for $C_{28}H_{23}N_3O_2$ $(M + H)^+$: 434.1863, found 434.1862.

(4*S,5a*S**,8a*S**)-1-Benzyl-4-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-7-phenyl-5,5a,7,8a-tetrahydroimidazo[4,5-*e*]isoindole-6,8-(1*H*,4*H*)-dione (6e)**

To (5a*S**,8a*S**)-1-benzyl-7-phenyl-1,5,5a,8b-tetrahydroimidazo-[4,5-*e*]isoindole-6,8(7*H*,8a*H*)-dione (**5a**) (200 mg, 0.56 mmol) in dichloromethane (7 mL) at −78 °C was added 4-phenyl-1,2,4-triazoline-3,5-dione (98 mg, 0.56 mmol) in dichloromethane (3 mL) dropwise, and the solution stirred for 1 h. The solvent was removed and the crude residue was chromatographed on silica gel (ethyl acetate 100%) to yield the title compound as a white solid, 220 mg (74%).

R_f 0.31 (UV active, ethyl acetate, 100%); mp: 173–174 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.44–7.26 (12H, m), 7.16 (2H, d,

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J = 7.4 Hz), 7.07–7.05 (2H, m), 5.46 (1H, d, J = 15.4 Hz), 5.28 (1H, dd, J = 8.1, 5.4 Hz), 5.17 (1H, d, J = 15.4 Hz), 3.92 (1H, d, J = 8.2 Hz), 3.51–3.46 (1H, m), 2.63–2.57 (1H, m), 2.18–2.11 (1H, m); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 176.1, 174.1, 154.7, 153.6, 139.8, 135.4, 135.1, 131.4, 129.3, 129.3, 129.2, 129.0, 128.6, 128.3, 127.7, 126.5, 126.0, 122.2, 49.9, 49.6, 38.8, 38.3, 26.0; IR (neat): ν_{max}/cm^{-1} 3067, 1770, 1705, 1598, 1499, 862, 739, 692; HRMS (ES-ToF): calcd for $C_{30}H_{24}N_6O_4$ $(M + H)^+$: 533.1932, found 533.1923; EA: calcd C: 67.66%, H: 4.54%, N: 15.78%, found C: 67.73%, H: 4.58%, N: 15.59%.

Diethyl 2-((4*S,5a*S**,8a*S**)-1-benzyl-6,8-dioxo-7-phenyl-1,4,5,5a,6,7,8,8a-octahydroimidazo[4,5-*e*]isoindol-4-yl)-2-hydroxymalonate (6f)**

To (5a*S**,8a*S**)-1-benzyl-7-phenyl-1,5,5a,8b-tetrahydroimidazo-[4,5-*e*]isoindole-6,8(7*H*,8a*H*)-dione (**5a**) (230 mg, 0.64 mmol) in dichloromethane (6 mL) was added diethyl ketomalonate (134 mg, 0.77 mmol, 118 μL) and the solution stirred at r.t. for 16 h. The solvent was removed and the crude residue was chromatographed on silica gel (diethyl ether) to yield the title compound as a white solid, 283 mg (83%).

R_f 0.16 (UV active, diethyl ether); mp: 147–149 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.47–7.28 (7H, m), 7.24–7.23 (2H, m), 7.15–7.13 (2H, m), 5.61 (1H, d, J = 15.5 Hz), 5.28 (1H, d, J = 15.5 Hz), 4.46–4.22 (4H, m), 4.13 (1H, s, OH), 3.92 (1H, dd, J = 8.4, 1.3 Hz), 3.85 (1H, dd, J = 9.9, 4.5 Hz), 3.56–3.52 (1H, m), 2.39 (1H, dt, J = 13.4, 4.6 Hz), 2.08–2.00 (1H, m), 1.34–1.31 (6H, m); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 177.1, 175.1, 170.3, 169.6, 138.9, 137.9, 136.0, 131.8, 129.5, 129.4, 129.1, 128.5, 127.8, 126.6, 120.8, 80.8, 63.2, 63.1, 49.9, 40.1, 38.7, 37.4, 24.3, 14.4, 14.3; IR (neat): ν_{max}/cm^{-1} 3481, 2982, 2967, 1783, 1711, 1734, 1597, 1499, 1380, 1249, 1029, 1185, 737, 690; HRMS (ES-ToF): calcd for $C_{29}H_{29}N_3O_7$ $(M + H)^+$: 532.2078, found 532.2071.

(5*S,5a*S**,8a*S**)-1-Benzyl-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-7-phenyl-1,5,5a,8b-tetrahydroimidazo[4,5-*e*]isoindole-6,8(7*H*,8a*H*)-dione (5b)**

To (*E*)-1-benzyl-4-(3-(*tert*-butyldimethylsilyloxy)prop-1-enyl)-1*H*-imidazole (772 mg, 2.35 mmol) in dichloromethane (23.5 mL) was added *N*-phenylmaleimide (1.02 g, 5.87 mmol) and the solution stirred at 50 °C for 16 h. The solvent was removed and the crude residue was chromatographed on silica gel (petroleum ether 40–60–ethyl acetate, 25 : 75) to yield the title compound as a white solid, 802 mg (68%).

R_f 0.32 (UV active, petroleum ether 40–60–ethyl acetate, 25 : 75); mp: 199–201 °C (lit.[6b] mp: 203–204 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.46–7.33 (7H, m), 7.31–7.29 (2H, m), 7.12–7.10 (2H, m), 5.44 (1H, dd, J = 4.1, 4.1 Hz), 4.91 (1H, d, J = 15.2 Hz), 4.80 (1H, d, J = 15.2 Hz), 4.35 (1H, dd, J = 9.6, 8.9 Hz), 4.06–4.01 (2H, m), 3.62 (1H, t, J = 8.4 Hz), 3.35 (1H, dd, J = 8.5, 4.9 Hz), 2.24–2.15 (1H, m), 0.89 (9H, s), 0.09 (6H, s); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 175.8, 173.9, 159.9, 154.4, 135.5, 134.4, 131.8, 129.4, 129.0, 128.6, 128.3, 126.9, 105.1, 63.1, 57.8, 50.3, 41.9, 41.8, 38.2, 26.2, 18.6, −5.0, −5.1; IR (neat): ν_{max}/cm^{-1} 2951, 2927, 2855, 1772, 1703, 1541, 1498, 837, 777, 692; HRMS (ES-ToF): calcd for $C_{29}H_{35}N_3O_3Si$ $(M + H)^+$: 502.2520, found 502.2517.

(4*S,5*R**,5a*S**,8a*S**)-1-Benzyl-5-(((*tert*-butyldimethylsilyl)oxy)-methyl)-4-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-7-phenyl-5,5a,7,8a-tetrahydroimidazo[4,5-*e*]isoindole-6,8(1*H*,4*H*)-dione (6g)**

To (5*S**,5a*S**,8a*S**)-1-benzyl-5-(((*tert*-butyldimethylsilyl)oxy)-methyl)-7-phenyl-1,5,5a,8b-tetrahydroimidazo[4,5-*e*]isoindole-6,8-(7*H*,8a*H*)-dione (**5b**) (250 mg, 0.50 mmol) in dichloromethane (5 mL) at −78 °C was added dropwise 1,2,4-phenyltriazoline-3,5-dione (87 mg, 0.50 mmol) in dichloromethane (5 mL), and the solution stirred for 1 h. The solvent was removed and the crude residue was chromatographed on silica gel (eluting with diethyl ether–methanol, 98 : 2) to yield the major diastereoisomer as an orange solid, 206 mg (61%).

R_f 0.37 (UV active, diethyl ether–methanol, 95 : 5); mp: 147–148 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.57–7.37 (12H, m), 7.22–7.18 (3H, m), 5.63 (1H, d, J = 15.4 Hz), 5.35–5.32 (1H, m), 5.29 (1H, d, J = 15.4 Hz), 4.37 (1H, dd, J = 10.5, 6.2 Hz), 4.12 (1H, dd, J = 10.5, 6.2 Hz), 3.99 (1H, d, J = 8.1 Hz), 3.83 (1H, dd, J = 8.1, 4.5 Hz), 2.52–2.45 (1H, m); ^{13}C NMR (101 MHz, $CDCl_3$): 175.1, 174.0, 154.8, 154.0, 140.2, 136.0, 135.5, 131.6, 131.5, 129.4, 129.4 129.3, 129.1, 128.7, 128.5, 127.8, 126.5, 126.2, 122.5, 62.7, 52.9, 50.1, 42.4, 40.7, 39.5, 26.2, 18.6, −5.2, −5.3; IR: ν_{max}/cm^{-1} 3067, 2930, 2857, 1771, 1712, 1600, 1500, 1380, 836, 778, 705, 690; HRMS (ES-ToF): calcd for $C_{37}H_{40}N_6O_5Si$ $(M + H)^+$: 677.2902, found 677.2899.

(4*S,5*R**,5a*S**,8a*S**)-Diethyl 2-(1-benzyl-5-(((*tert*-butyldimethylsilyl)-oxy)methyl)-6,8-dioxo-7-phenyl-1,4,5,5a,6,7,8,8a-octahydroimidazo-[4,5-*e*]isoindol-4-yl)-2-hydroxymalonate (6h)**

To (5*S**,5a*S**,8a*S**)-1-benzyl-5-(((*tert*-butyldimethylsilyl)oxy)-methyl)-7-phenyl-1,5,5a,8b-tetrahydroimidazo[4,5-*e*]isoindole-6,8-(7*H*,8a*H*)-dione (**7b**) (250 mg, 0.50 mmol) in dichloromethane (18 mL) was added diethyl ketomalonate (87 mg, 76 μL, 0.50 mmol) and the solution stirred at r.t. for 16 h. The solvent was removed and the crude residue was chromatographed on silica gel (diethyl ether–petroleum ether 40–60, 60 : 40) to yield the title compound as a white solid, 175 mg (65%).

R_f 0.22 (UV active, diethyl ether–petroleum ether, 25 : 75); mp: 112–114 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.45–7.25 (9H, m), 7.06–7.04 (2H, m), 5.70 (1H, d, J = 15.6 Hz), 5.32 (1H, d, J = 15.6 Hz), 4.43–4.36 (2H, m), 4.29 (2H, q, J = 7.2 Hz), 4.03 (1H, s), 3.97 (1H, dd, J = 8.6, 6.5 Hz), 3.84 (1H, br s), 3.77–3.71 (3H, m), 2.75–2.71 (1H, m), 1.36 (3H, t, J = 7.2 Hz), 1.31 (3H, t, J = 7.2 Hz), 0.72 (9H, s), −0.10 (3H, s), −0.18 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$): 176.9, 174.9, 170.6, 169.5, 138.6, 136.4, 135.7, 132.2, 129.4, 129.3, 128.9, 128.4, 127.5, 126.7, 122.2, 82.6, 66.2, 64.9, 63.6, 62.8, 50.1, 41.9, 41.7, 39.9, 38.6, 26.1, 18.6, 15.6, 14.4, 14.3, −5.4; IR (neat): ν_{max}/cm^{-1} 3474, 2988, 2941, 1711, 1597, 1498, 1381, 1284, 1225, 1248, 1029, 1185, 740, 691; HRMS (ES-ToF): calcd for $C_{36}H_{45}N_3O_8Si$ $(M + H)^+$: 676.3049, found 676.3042; EA: calcd C: 63.98%, H: 6.71%, N: 6.22%, found C: 63.99%, H: 6.65%, N: 6.12%.

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(*R)-Ethyl 2-((4*S**,5a*S**,8a*S**)-1-benzyl-6,8-dioxo-7-phenyl-1,4,5,5a,6,7,8,8a-octahydroimidazo[4,5-*e*]isoindol-4-yl)-2-hydroxyacetate (7a) and (*S**)-ethyl 2-((4*S**,5a*S**,8a*S**)-1-benzyl-6,8-dioxo-7-phenyl-1,4,5,5a,6,7,8,8a-octahydroimidazo[4,5-*e*]isoindol-4-yl)-2-hydroxyacetate (8a)**

To (5a*S**,8a*S**)-1-benzyl-7-phenyl-1,5,5a,8b-tetrahydroimidazo-[4,5-*e*]isoindole-6,8(7*H*,8a*H*)-dione (**5a**) (200 mg, 0.56 mmol) in dichloromethane (5 mL) was added ethyl glyoxalate (50% in toluene, 0.14 mmol, 0.67 mL) and the solution stirred at r.t. for 30 h. The solvent was removed and the crude residue was chromatographed on silica gel (ethyl acetate–methanol, 95 : 5) to yield the major diastereomer **7a** as a white solid, 154 mg (60%), and the minor diastereomer **8a** as a white solid, 32 mg (12%).

Major diastereomer

(*S)-Ethyl 2-((4*S**,5a*S**,8a*S**)-1-benzyl-6,8-dioxo-7-phenyl-1,4,5,5a,6,7,8,8a-octahydroimidazo[4,5-*e*]isoindol-4-yl)-2-hydroxyacetate (7a).** R_f 0.18 (UV active, ethyl acetate–methanol, 95 : 5); mp: 80–82 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.47–7.43 (3H, m), 7.40–7.32 (4H, m), 7.25–7.21 (2H, m), 7.16–7.14 (2H, m), 5.64 (1H, d, J = 15.5 Hz), 5.28 (1H, d, J = 15.5 Hz), 4.38 (1H, dq, J = 10.7, 7.1 Hz), 4.33–4.24 (2H, m), 4.08 (1H, br s), 3.92 (1H, dd, J = 8.4, 1.0 Hz), 3.56–3.52 (1H, m), 3.29–3.24 (1H, m), 2.53 (1H, dt, J = 13.6, 4.6 Hz), 1.97 (1H, ddd, J = 13.7, 10.4, 5.6 Hz), 1.32 (3H, t, J = 7.2 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 177.1, 175.1, 173.3, 139.1, 139.0, 136.0, 131.8, 129.5, 129.5, 129.2, 128.7, 127.8, 126.7, 120.6, 73.6, 62.1, 50.0, 40.2, 38.8, 35.6, 26.3, 14.6; IR: ν_{max}/cm^{-1} 2935, 1709, 1597, 1497, 1383, 1187, 724, 693; HRMS (ES-ToF): calcd for $C_{26}H_{24}N_3O_5$ $(M + H)^+$: 460.1867, found 460.1862.

Minor diastereomer

(*R)-Ethyl 2-((4*S**,5a*S**,8a*S**)-1-benzyl-6,8-dioxo-7-phenyl-1,4,5,5a,6,7,8,8a-octahydroimidazo[4,5-*e*]isoindol-4-yl)-2-hydroxyacetate (8a).** R_f 0.10 (UV active, ethyl acetate–methanol, 95 : 5); mp: 198–199 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.52 (1H, s), 7.47–7.43 (2H, m), 7.40–7.32 (4H, m), 7.21–7.16 (4H, m), 5.62 (1H, d, J = 15.4 Hz), 5.31 (1H, d, J = 15.4 Hz), 5.02 (1H, br s), 4.33 (1H, dq, J = 10.6, 7.1 Hz), 4.22 (1H, dq, J = 10.6, 7.1 Hz), 3.95 (1H, d, J = 8.4 Hz), 3.68 (1H, br s), 3.54–3.49 (1H, m), 3.28–3.25 (1H, m), 2.28 (1H, dt, J = 13.5, 4.2 Hz), 1.98 (1H, ddd, J = 13.5, 10.6, 5.5 Hz), 1.30 (3H, t, J = 7.1 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 177.1, 175.1, 174.0, 139.4, 139.2, 136.0, 131.8, 129.6, 129.4, 129.2, 128.6, 127.9, 126.7, 120.5, 70.9, 62.1, 50.0, 40.2, 38.9, 35.8, 22.6, 14.6; IR (neat): ν_{max}/cm^{-1} 2933, 1743, 1712, 1597, 1495, 1383, 1190, 726, 691; HRMS (ES-ToF): calcd for $C_{26}H_{26}N_3O_5$ $(M + H)^+$: 460.1867, found 460.1865.

Ethyl 2-((5*S,5a*S**,8a*S**)-1-benzyl-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-6,8-dioxo-7-phenyl-1,4,5,5a,6,7,8,8a-octahydroimidazo-[4,5-*e*]isoindol-4-yl)-2-hydroxyacetate (7b).** To (5*S**,5a*S**,8a*S**)-1-benzyl-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-7-phenyl-1,5,5a,8b-tetrahydroimidazo[4,5-*e*]isoindole-6,8(7*H*,8a*H*)-dione (**5b**) (200 mg, 0.40 mmol) in dichloromethane (6 mL) was added ethyl glyoxalate (50% in toluene, 0.48 mmol, 98 μL) and the solution stirred at r.t. for 16 h. The solvent was removed and the crude residue was chromatographed on silica gel (diethyl ether) to yield the title compound as a white solid, 142 mg (59%). *NB: only one diastereomer was observed*.

R_f 0.23 (UV active, diethyl ether); mp: 76–78 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.48–7.44 (3H, m), 7.40–7.29 (4H, m), 7.24–7.22 (2H, m), 7.13–7.11 (2H, m), 5.64 (1H, d, J = 15.5 Hz), 5.27 (1H, d, J = 15.5 Hz), 4.45 (1H, dd, J = 6.4, 2.5 Hz), 4.40 (1H, dq, J = 10.7, 7.1 Hz), 4.33 (1H, dq, J = 10.7, 7.1 Hz), 4.13 (1H, dd, J = 9.8, 7.3 Hz), 3.96–3.91 (2H, m), 3.85 (1H, d, J = 8.2 Hz), 3.51–3.49 (1H, m), 2.98 (1H, d, J = 6.4 Hz), 2.58–2.52 (1H, m), 1.34 (3H, t, J = 7.1 Hz), 0.84 (9H, s), 0.02 (3H, s), 0.00 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 176.2, 174.9, 174.1, 139.3, 136.3, 134.0, 131.9, 129.6, 129.4, 129.1, 128.5, 127.3, 126.6, 122.5, 64.6, 62.6, 50.3, 41.5, 39.0, 38.9, 38.1, 26.0, 18.5, 14.2, −5.3, −5.4; IR (neat): ν_{max}/cm^{-1} 2953, 2929, 2857, 1782, 1714, 1498, 1377, 1252, 1191, 1099, 836, 778, 691; HRMS (ES-ToF): calcd for $C_{33}H_{41}N_3O_6Si$ $(M + H)^+$: 604.2837, found 604.2822.

(*S)-Ethyl 2-((4*S**,5a*S**,8a*S**)-1-benzyl-6,8-dioxo-7-phenyl-1,4,5,5a,6,7,8,8a-octahydroimidazo[4,5-*e*]isoindol-4-yl)-3,3,3-trifluoro-2-hydroxypropanoate (7c).** To (5a*S**,8a*S**)-1-benzyl-7-phenyl-1,5,5a,8b-tetrahydroimidazo[4,5-*e*]isoindole-6,8(7*H*,8a*H*)-dione (**5a**) (90 mg, 0.25 mmol) in dichloromethane (2 mL) was added ethyl trifluoropyruvate (64 mg, 0.38 mmol, 50 μL) and the solution stirred at r.t. for 16 h. The solvent was removed and the crude residue was chromatographed on silica gel (diethyl ether–petroleum ether 40–60, 60 : 40) to yield the title compound as a white solid, 70 mg (53%). *NB: only one diastereomer was observed*.

R_f 0.77 (UV active, ethyl acetate–petroleum ether 40–60, 2 : 1); mp: 174–175 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.47–7.43 (2H, m), 7.40–7.31 (5H, m), 7.25–7.23 (2H, m), 7.12–7.11 (2H, m), 5.65 (1H, d, J = 15.5 Hz), 5.28 (1H, d, J = 15.5 Hz), 4.52 (1H, dqd, J = 10.6, 7.1, 1.4 Hz), 4.37 (1H, dqd, J = 10.6, 7.1, 1.4 Hz), 4.02 (1H, d, J = 1.0 Hz), 3.90 (1H, d, J = 8.2 Hz), 3.67 (1H, dd, J = 9.2, 5.0 Hz), 3.62–3.57 (1H, m), 2.61–2.55 (1H, m), 2.23–2.16 (1H, m), 1.36 (3H, dt, J = 7.1, 1.4 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 176.9, 174.9, 169.9, 138.9, 136.6, 136.0, 131.8, 129.5, 129.5, 129.1, 128.6, 127.8, 126.6, 125.0 (q, J = 287.8 Hz), 121.5, 78.7 (q, J = 28.1 Hz), 64.3, 50.0, 39.9, 38.7, 35.4, 23.9, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$): δ_F −73.37; IR (neat): ν_{max}/cm^{-1} 3651, 2982, 1705, 1596, 1497, 1375, 1172, 739, 694; HRMS (ES-ToF): calcd for $C_{27}H_{24}F_3N_3O_5$ $(M + H)^+$: 528.1741, found 528.1731; EA: calcd C: 61.48%, H: 4.59%, N: 7.97%, found C: 61.59%, H: 4.52%, N: 7.90%.

(*S)-Ethyl 2-((4*S**,5*S**,5a*S**,8a*S**)-1-benzyl-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-6,8-dioxo-7-phenyl-1,4,5,5a,6,7,8,8a-octahydroimidazo[4,5-*e*]isoindol-4-yl)-3,3,3-trifluoro-2-hydroxypropanoate (7d) and (2*R**)-ethyl 2-((5a*S**,8a*S**)-1-benzyl-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-6,8-dioxo-7-phenyl-1,4,5,5a,6,7,8,8a-octahydroimidazo[4,5-*e*]isoindol-4-yl)-3,3,3-trifluoro-2-hydroxypropanoate (8d).** To (5*S**,5a*S**,8a*S**)-1-benzyl-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-7-phenyl-1,5,5a,8b-tetrahydroimidazo[4,5-*e*]isoindole-6,8(7*H*,8a*H*)-dione (**5b**) (400 mg,

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0.80 mmol) in dichloromethane (6 mL) was added ethyl trifluoropyruvate (162 mg, 0.12 mL, 0.96 mmol) and the solution stirred at r.t. for 72 h. The solvent was removed and the crude residue was chromatographed on silica gel (diethyl ether–petrol, 40 : 60) to yield the major diastereoisomer **7d** as pale yellow crystals, 196 mg (36%), and the minor diastereoisomer **8d** as a white solid, 92 mg (17%).

Major diastereomer

(*S)-Ethyl 2-((4*S**,5*S**,5a*S**,8a*S**)-1-benzyl-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-6,8-dioxo-7-phenyl-1,4,5,5a,6,7,8,8a-octahydroimidazo[4,5-*e*]isoindol-4-yl)-3,3,3-trifluoro-2-hydroxypropanoate (7d).** R_f 0.30 (UV active, diethyl ether–petrol, 50 : 50); mp: 176–178 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.49–7.31 (7H, m), 7.25–7.23 (2H, m), 7.03–7.01 (2H, m), 5.80 (1H, d, J = 15.7 Hz), 5.33 (1H, d, J = 15.7 Hz), 4.55–4.43 (2H, m), 4.04 (1H, s), 3.96 (1H, dd, J = 8.6, 6.1 Hz), 3.78 (1H, br s), 3.71 (1H, d, J = 8.6 Hz), 3.61 (1H, dd, J = 10.1, 4.5 Hz), 3.44 (1H, dd, J = 10.1, 8.4 Hz), 3.10–3.06 (1H, m), 1.45 (3H, t, J = 7.2 Hz), 0.80 (9H, s), −0.09 (3H, s), −0.10 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 176.2, 174.9, 169.9, 139.3, 136.3, 134.0, 131.9, 129.6, 129.4, 129.1, 128.5, 127.3, 126.6, 122.5, 64.6, 62.6, 50.3, 41.5, 39.0, 38.9, 38.1, 26.0, 18.5, 14.2, −5.3, −5.4; ^{19}F NMR (376 MHz, $CDCl_3$): δ_F −72.62; IR (neat): ν_{max}/cm^{-1} 3435, 2949, 2935, 2865, 1749, 1781, 1712, 1598, 1498, 1374, 1244, 1027, 1158, 1149, 1098, 836, 775, 689; HRMS (ES-ToF): calcd for $C_{34}H_{40}F_3N_3O_6Si$ $(M + H)^+$: 672.2711, found 672.2705.

Minor diastereomer

(*R)-Ethyl 2-((4*S**,5*S**,5a*S**,8a*S**)-1-benzyl-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-6,8-dioxo-7-phenyl-1,4,5,5a,6,7,8,8a-octahydroimidazo[4,5-*e*]isoindol-4-yl)-3,3,3-trifluoro-2-hydroxypropanoate (8d).** R_f 0.15 (UV active, diethyl ether–petrol, 50 : 50); mp: 113–114 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.57 (1H, s), 7.48–7.30 (6H, m), 7.23–7.21 (2H, m), 7.05–7.04 (2H, m), 5.85 (1H, d, J = 15.8 Hz), 5.36 (1H, d, J = 15.8 Hz), 4.69 (1H, s), 4.37 (1H, dq, J = 10.7, 7.2 Hz), 4.29 (dq, J = 10.7, 7.2 Hz), 3.92 (1H, s), 3.88 (1H, dd, J = 8.7, 6.4 Hz), 3.75 (1H, d, J = 8.7 Hz), 3.58 (1H, dd, J = 10.2, 4.2 Hz), 3.48 (1H, dd, J = 10.2, 7.5 Hz), 2.63–2.58 (1H, m), 1.32 (3H, t, J = 7.2 Hz), 0.76 (9H, s), −0.10 (3H, s), −0.14 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 176.0, 174.5, 169.7, 139.3, 136.3, 133.8, 131.8, 129.5, 129.4, 129.1, 128.4, 127.2, 126.5, 123.1 (q, J = 287.4 Hz), 121.7, 80.9 (q, J = 28.7 Hz), 64.1, 63.1, 50.4, 41.5, 39.9, 38.4, 38.2, 26.0, 18.5, 14.2, −5.4, −5.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ_F −73.26; IR (neat): ν_{max}/cm^{-1} 3476, 3067, 2954, 2858, 1378, 1250, 1027, 1161, 1143, 836, 745, 692.

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15 Crystallographic data for **7c** are of low quality due to weak scattering and suspected but unresolved twinning; however, they are sufficient for the determination of the relative stereochemistry of the compound.

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