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The High Stereoselectivity of the Tandem Sequence Diels–Alder Reaction/ Ireland–Claisen Rearrangement Starting from Substituted *O*-(*E*)-Buta-1,3-dienyl Ketene Acetals and Cyclic Dienophiles

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Dedicated to Professor Paul A. Wender in honor of his 60th birthday

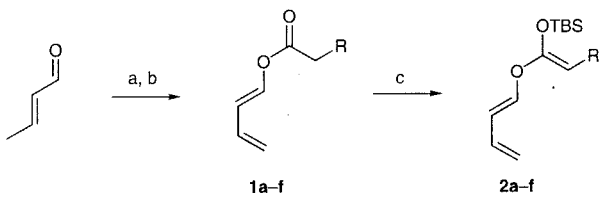
Abstract: A new tandem reaction leads to bicyclic cyclohexene derivatives with complete control of the relative configuration of the four chiral centers formed. The high diastereoselectivity is the consequence of an *endo*-selective Diels–Alder reaction followed by an Ireland–Claisen rearrangement that proceeds via a boat-like transition state.

Key words: cycloaddition, Diels–Alder reaction, rearrangement, stereoselectivity, tandem reaction

One-pot reactions combining several transformations represent effective strategies to increase the efficiency of organic synthesis.[1] Our group has demonstrated the effectiveness of the tandem sequence combining Diels–Alder cycloaddition reactions with [3,3]-sigmatropic rearrangements.[2–4] In this communication we wish to report an improved stereoselective access to substituted *O*-buta-1,3-dienyl-*O*-(trialkylsilyl)-substituted ketene acetals of type **2** and a study of their reactivity and diastereoselectivity in the tandem sequence Diels–Alder reaction/Ireland–Claisen rearrangement.

We have recently shown that buta-1,3-dienyl carboxylates **1** are suitable precursors of the desired ketene acetals **2**.[3d,e] The subsequent synthesis of the ketene acetals **2** proved to be experimentally challenging. To avoid fragmentation[5] lowering the reaction temperature below –110 °C proved to be imperative.[5b] We had to use polar co-solvents such as carcinogenic hexamethylphosphoramide to maintain the reactivity of the lithium enolate against the trapping agent. Applying in situ quench (ISQ) methodology[6] using *tert*-butyldimethylsilyl chloride allowed ketene acetals **2** to be obtained in excellent and reproducible yields (Scheme 1, Table 1).

The substituted ketene acetals **2b–f** were selectively obtained as their *Z*-diastereomers. The structure and relative configuration of product **2f**, isolated by crystallization from pentane, was confirmed by X-ray analysis.[7] The toxic mixture lithium hexamethyldisilazanide/hexamethylphosphoramide (15–25% in THF/2-MeTHF) can be replaced by sodium hexamethyldisilazanide/1,3-dimethyl-3,4,5,6-tetrahydropyrimidin-2(1*H*)-one, (10–15% in THF/2-MeTHF), which maintained the high yield and the excellent diastereoselectivity.[3d] The workup is best achieved by addition of iodomethane at the reaction temperature in order to quench the base before addition of the hexane–water mixture.



Scheme 1 *Reagents and conditions*: (a) *t*-BuOK, THF, –78 °C; (b) RCH_2COCl; (c) LiHMDS or NaHMDS, TBDMSCl, THF, 2-MeTHF, HMPA or DMPU, < –110 °C; MeI, –110 °C; hexane–H_2O, –110 °C to r.t.

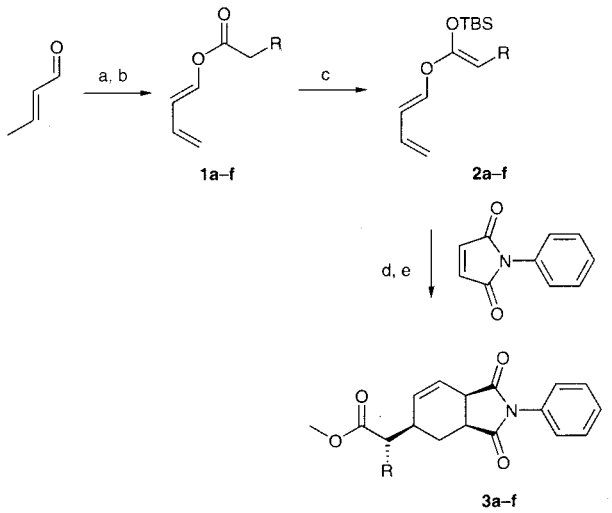
Table 1 Synthesis of *O*-(*E*)-Buta-1,3-dienyl-Substituted (*Z*)-Ketene Acetals

R	(*E*)-Buta-1,3-dienyl ester	Yield (%)	Ketene acetal	Yield (%)
H	**1a**	70	**2a**	81
Me	**1b**	78	**2b**	61
t-Bu	**1c**	53	**2c**	65
OMe	**1d**	58	**2d**	75[a]
OTBDMS	**1e**	40	**2e**	67
NPhth	**1f**	81	**2f**	43[a]

[a] LHMDS in combination with HMPA was used.

The ketene acetals **2a–f** underwent the desired tandem reaction sequence Diels–Alder reaction/Ireland–Claisen rearrangement under mild reaction conditions and in good yields (Scheme 2, Table 2). The reaction of *N*-phenylmaleimide, as an archetypical cyclic dienophile, with a slight excess of ketene acetal was complete after three hours at

60 °C. The rearrangement reaction following the Diels–Alder reaction was rapid; in the ^{1}H NMR spectra no signals were detected that could have been attributed to the intermediate Diels–Alder product. The silyl esters, the products of the tandem process, were deprotected by treatment with 40 mol% hydrogen hexafluorosilicate[8] and the resulting carboxylic acids were directly converted into the methyl ester by treatment with diazo(trimethylsilyl)methane. Purification by chromatography yielded the products **3a–f** in 43–83% overall yield over the four synthetic steps; thus, the average yield of each individual reaction step is 80–95%.



Scheme 2 *Reagents and conditions*: (a) *t*-BuOK, THF, –78 °C; (b) RCH_2COCl; (c) LiHMDS, TBDMSCl, THF, 2-MeTHF, HMPA, < –110 °C; MeI, –110 °C; hexane–H_2O, –110 °C to r.t.; (d) THF, 60 °C, 3 h; (e) H_2SiF_6, DME; (f) $TMSCHN_2$, THF, MeOH.

Table 2 Synthesis of the Tandem products **3a–f**

Ketene acetal	R	Tandem product	Yield (%)
2a	H	**3a**	70
2b	Me	**3b**	77
2c	*t*-Bu	**3c**	70
2d	OMe	**3d**	66
2e	OTBDMS	**3e**[a]	40
2f	NPhth	**3f**	65

[a] R = OH.

The NMR spectra showed the signals for one single diastereomer. The relative configuration of the chiral centers in the cyclohexene ring was confirmed by the observation of two *trans*-diaxial coupling constants for H_{ax} of the methylene group in **3a–f**. All the substituents attached to the cyclohexene ring of the products **3** are *cis*. The relative configuration of the products is compatible with an *endo*-selective Diels–Alder reaction followed by a suprafacial rearrangement. To determine the relative configuration of the exocyclic chiral center, the X-ray structure of the free acid **5** (Figure 1) was determined. A boat-like transition state of the Ireland–Claisen rearrangement is compatible with the observed relative configuration. The relative configuration of the product **3c** was identical to the relative configuration of **5** as confirmed by its X-ray structure. The relative configuration of the products **3b,d,f** was tentatively attributed based on the ^{1}H NMR coupling pattern.

In acyclic [3,3]-sigmatropic shifts the chairlike transition state is preferred.[9] The rearrangements of cyclohexenyl ester enolates are less selective and can involve both boatlike as well as chairlike transition states.[10,11] To obtain an insight into the high stereoselectivity of our tandem process, we determined the X-ray structure of the Diels–Alder product **4** (Figure 1).

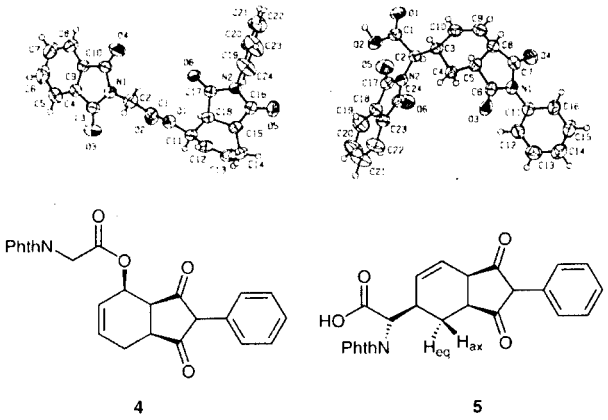


Figure 1 The X-ray structures of the Diels–Alder product **4** and of the product of the sequence Diels–Alder reaction/Ireland–Claisen rearrangement **5**.[5,7]

The annulated *N*-phenylmaleimide ring imposes a boat conformation on the cyclohexene ring. Prior to the rearrangement the ketene acetal substituent located in an equatorial position has to switch to an axial or pseudo-axial position. A chairlike transition state imposes strong steric interactions of the *Z*-enolate with the opposite flagpole position. The boatlike transition state avoids these destabilizing contacts as shown in Figure 2.

In conclusion, we report an improved and more environmentally friendly synthesis of the (*Z*)-ketene acetals **2a–f**. These substituted butadiene derivatives undergo a highly controlled tandem process Diels–Alder reaction/Ireland–

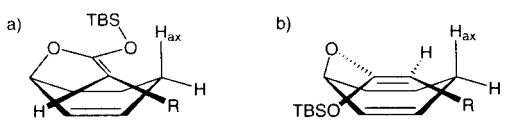


Figure 2 The two diastereomeric transition states for the Ireland–Claisen rearrangement for the sequence leading from **2** to **3**; (a) the chairlike transition state; (b) the boatlike transition state; for clarity the five-membered ring of *N*-phenylmaleimide has not been drawn.

Claisen rearrangement with the cyclic dienophile *N*-phenylmaleimide. Three carbon–carbon bonds are formed in this one-pot reaction. The relative configuration of the four centers of chirality can be unequivocally deduced from the reaction mechanism. The high preference for the boatlike transition state of the Ireland–Claisen rearrangement is especially important for the overall diastereoselectivity of our reaction sequence.

All moisture-sensitive reactions were carried out under argon or N_2 using oven-dried glassware. All reagents were of commercial quality if not specifically mentioned. Solvents were freshly distilled prior to use. Flash chromatography (FC): SDS silica gel A C.C. Chromagel (35–70 μm); under positive pressure, 0.5–0.9 bar. TLC: precoated silica gel thin-layer sheets 60 F 254 from Merck, detection by UV or/and basic $KMnO_4$ soln. GC: Perkin Elmer SIGMA 3B Dual FID chromatograph with Macherey-Nagel SE 54-DF-0.25 (0.25 μm, 0.32 mm × 25 m) and Perkin Elmer LCI-100 integrator or Agilent 6890 Series with HP-5 crosslinked 5% PhMe siloxane (0.25 μm, 0.32 mm × 30 m) and ChemStation. HPLC: Knauer HPLC programmer 50 with Knauer HPLC pump 64 pumps, Applied Biosystems 757 absorbance detector (254 nm), Shimadzu C-R18 Chromatopak integrator, and Knauer Li Chrosorb 17RP18 column (7 mm, 4 × 250 mm). Melting points: Büchi B 510; uncorrected. Refractive index (n_D): Carl Zeiss. IR Spectra: Perkin Elmer FT-IR 1720 X. NMR Spectra: Bruker Avance-400 (400 and 100 MHz) or Varian Gemini XL-2000 (200 and 50 MHz), at r.t., if not specified; TMs as internal reference. MS: ESI: Finnigan LCQ; EI: Nermag RC 30-10 (70 eV); DCI: NH_4^+; HR-MS: Bruker FTMS 4.7T BioAPEXII. Elemental analyses were performed by the Chemistry department of the Ecole d'ingénieurs et d'architectes, Fribourg (CH) and by the Ciba-Geigy SA at 1723 Marly (CH).

(*E*)-Buta-1,3-dienyl Esters 1; General Procedure

Crotonaldehyde (distilled) (60 mmol) was added dropwise over 10 min to a mechanical stirred soln of *t*-BuOK (70 mmol) in THF (40 mL) at –78 °C under N_2; after 10 min the yellow enolate was formed. A soln of the desired electrophile (acid chloride, anhydride, or activated ester) (70 mmol) in THF (10 mL) was added over 10 min. The mixture became orange-red at the beginning and orange at the end of the addition. The mixture was stirred at –78 °C for 15 min and then the cooling bath was removed and the reaction quenched with H_2O and extracted with Et_2O (3 × 50 mL). The extracts were washed with Na_2CO_3 soln (3 × 10 mL), NH_4Cl soln (3 × 10 mL), and NaCl soln (3 × 10 mL) and dried (Na_2SO_4).

(*E*)-Buta-1,3-dienyl Acetate (1a)

Using crotonaldehyde (4.14 g, 60 mmol) and AcCl (5.5 g, 70 mmol) according to the general procedure, purification by distillation gave pure **1a** as a clear liquid; yield: 3.7 g (55%); bp 32–34 °C/18.7 mbar; R_f (hexane–Et_2O, 2:1) = 0.5.

IR: 3090 (w), 3041 (w), 2979 (w), 1762 (s), 1660 (s), 1420 (m), 1373 (s), 1305 (w), 1289 (w), 1218 (s), 1176 (s), 1109 (s), 1047 (m), 998 (s), 958 (w), 926 (s), 893 (s), 836 (w), 653 cm^{-1} (w).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.39 [dd, $^3J(1.1,1.2)$ = 12.4 Hz, $^4J(1.1,1.3) \approx {}^5J(1.1,1.4a) \approx {}^5J(1.1,1.4b)$ = 0.6 Hz, 1 H, H-C(1.1)], 6.26 [dddd, $^3J(1.3,1.4b)$ = 16.9 Hz, $^3J(1.3,1.2)$ = 11.0 Hz, $^3J(1.3,1.4a)$ = 10.3 Hz, $^4J(1.3,1.1)$ = 0.5 Hz, 1 H, H-C(1.3)], 6.03 [ddt, $^3J(1.2,1.1)$ = 12.4 Hz, $^3J(1.2,1.3)$ = 11.0 Hz, $^4J(1.2,1.4a) \approx {}^4J(1.2,1.4b)$ = 0.7 Hz, 1 H, H-C(1.2)], 5.21 [ddt, $^2J(1.4b,1.4a)$ = 1.6 Hz, $^3J(1.4b,1.3)$ = 16.9 Hz, $^4J(1.4b,1.2) \approx {}^5J(1.4b,1.1)$ = 0.7 Hz, 1 H, Hb-C(1.4)], 5.08 [ddt, $^2J(1.4a,1.4b)$ = 1.6 Hz, $^3J(1.4a,1.3)$ = 10.2 Hz, $^4J(1.4a,1.2) \approx {}^5J(1.4a,1.1)$ = 0.6 Hz, 1 H, Ha-C(1.4)], 2.14 [s, 3 H, H-C(2)].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.8 [C(1)], 138.7 [C(1.1)], 131.7 [C(1.3)], 117.2 [C(1.4)], 116.0 [C(1.2)], 20.6 [C(2)].

MS (EI, 70 eV): *m/z* (%) = 112 (51) $[M]^+$, 70 (34), 69 (23), 43 (100).

(*E*)-Buta-1,3-dienyl Propanoate (1b)

Using crotonaldehyde (4.14 g, 60 mmol) and propanoyl chloride (6.8 g, 73 mmol) according to the general procedure, purification by distillation gave pure **1b** as a clear liquid; yield: 4.98 g (66%); bp 50 °C/18.7 mbar; R_f (hexane–Et_2O, 2:1) = 0.58.

IR: 3090 (w), 2986 (w), 2945 (w), 2886 (vw), 1762 (s), 1658 (m), 1464 (w), 1421 (m), 1360 (m), 1270 (w), 1232 (m), 1153 (s), 1114 (m), 1086 (m), 997 (m), 974 (w), 925 (w), 904 (w), 877 (w), 806 (w), 790 cm^{-1} (w).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.40 [dq, $^3J(1.1,1.2)$ = 12.4 Hz, $^4J(1.1,1.3) \approx {}^5J(1.1,1.4a) \approx {}^5J(1.1,1.4b)$ = 0.7 Hz, 1 H, H-C(1.1)], 6.26 [dddd, $^3J(1.3,1.4b)$ = 16.9 Hz, $^3J(1.3,1.2)$ = 11.0 Hz, $^3J(1.3,1.4a)$ = 10.3 Hz, $^4J(1.3,1.1)$ = 0.6 Hz, 1 H, H-C(1.3)], 6.01 [ddt, $^3J(1.2,1.1)$ = 12.4 Hz, $^3J(1.2,1.3)$ = 11 Hz, $^4J(1.2,1.4a) \approx {}^4J(1.2,1.4b)$ = 0.7 Hz, 1 H, H-C(1.2)]); 5.18 [ddt, $^2J(1.4b,1.4a)$ = 1.6 Hz, $^3J(1.4b,1.3)$ = 16.9 Hz, $^4J(1.4b,1.2) \approx {}^5J(1.4b,1.1)$ = 0.8 Hz, 1 H, Hb-C(1.4)], 5.05 [ddt, $^3J(1.4a,1.3)$ = 10.3 Hz, $^2J(1.4a,1.4b)$ = 1.6 Hz, $^4J(1.4a,1.2) \approx {}^5J(1.4b,1.1)$ = 0.7 Hz, 1 H, Ha-C(1.4)], 2.40 [q, $^3J(2,3)$ = 7.5 Hz, 2 H, H-C(2)], 1.16 [d, $^3J(3,2)$ = 7.5 Hz, 3 H, H-C(3)].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.2 [C(1)], 138.7 [C(1.1)], 131.7 [C(1.3)], 116.9 [C(1.4)], 115.8 [C(1.2)], 27.2 [C(2)], 8.7 [C(3)].

MS (EI, 70 eV): *m/z* (%) = 126 (34) $[M]^+$, 97 (2), 86 (21) 84 (35), 70 (16), 69 (11), 57 (100), 51 (11) 49 (29).

HRMS: *m/z* $[M]^+$ calcd for $C_7H_{10}O_2$: 126.06764; found: 126.06753.

Buta-1,3-dienyl 3,3-Dimethylbutanoate (1c)

Using crotonaldehyde (1.37 g, 20 mmol) and 3,3-dimethylbutanoyl chloride (2.68 g, 20 mmol) according to the general procedure, purification by flash chromatography (hexane–EtOAc, 95:5) gave pure **1c** as a clear liquid; yield: 2.9 g (86%); R_f (hexane–Et_2O, 2:1) = 0.77.

IR: 2960 (m), 2909 (m), 2871 (m), 1752 (s), 1707 (m), 1659 (m), 1477 (m), 1467, 1419 (m), 1397 (m), 1368 (m), 1352 (m), 1322 (m), 1222 (s), 1127 (vs), 1032 (m), 996 (m), 963 (m), 926 (m), 898 (m), 425 cm^{-1} (m).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.40 [dd, $^3J(1.1,1.2)$ = 12.4 Hz, $^4J(1.1,1.3) \approx {}^5J(1.1,1.4a) \approx {}^5J(1.1,1.4b)$ = 0.6 Hz, 1 H, H-C(1.1)], 6.27 [dddd, $^3J(1.3,1.4b)$ = 16.9 Hz, $^3J(1.3,1.4a)$ = 10.3 Hz, $^3J(1.3,1.2)$ = 10.8 Hz, $^4J(1.3,1.1)$ = 0.5 Hz, 1 H, H-C(1.3)], 6.03 [ddt, $^3J(1.2,1.1)$ = 12.3 Hz, $^3J(1.2,1.3)$ = 11.1 Hz, $^4J(1.2,1.4a) \approx {}^4J(1.2,1.4b)$ = 0.7 Hz, 1 H, H-C(1.2)], 5.19 [ddt, $^2J(1.4b,1.4a)$ = 1.6 Hz, $^3J(1.4b,1.3)$ = 16.9 Hz, $^4J(1.4b,1.2) \approx {}^5J(1.4b,1.1)$ = 0.7 Hz, 1 H, H-C(1.4b)], 5.06 [ddt, $^2J(1.4a,1.4b)$ = 1.6 Hz, $^3J(1.4a,1.3)$ = 10.3 Hz, $^4J(1.4a,1.2) \approx {}^5J(1.4a,1.1)$ = 0.7 Hz, 1 H, H-C(1.4a)], 2.27 [s, 2 H, H-C(2)], 1.04 [s, 9 H, $(CH_3)_3C$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.0 [C(1)], 138.5 [C(1.1)], 131.8 [C(1.3)], 117.0 [C(1.4)], 115.8 [C(1.2)], 47.5 [C(2)], 30.9 [C(3)], 29.5 ($[CH_3)_3C(3)$].

MS (CI): *m/z* = 169.12 $[M + H]^+$.

HRMS: *m/z* $[M + H]^+$ calcd for $C_{10}H_{17}O_2$: 169.1223; found: 169.1224.

Buta-1,3-dienyl Methoxyacetate (1d)

Using crotonaldehyde (10 mL, 0.12 mol) and methoxyacetyl chloride (13.6 mL, 0.15 mol) according to the general procedure, the crude product was filtered through Celite and purification by distil-

lation gave pure **1d** as a clear liquid; yield: 9.95 g (58%); bp 41 °C/ 0.05 mbar; R_f (hexane–Et_2O, 2:1) = 0.43.

IR: 3090 (w), 2934 (w), 2832 (w), 1775 (s), 1659 (m), 1452 (w), 1420 (m), 1376 (w), 1291 (w), 1243 (m), 1190 (s), 1167 (s), 1132 (s), 998 (m), 929 (m), 905 (m), 835 (w), 727 (w), 660 (w), 569 cm^{-1} (w).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.42 [dd, $^3J(1.1,1.2)$ = 12.3 Hz, $^4J(1.1,1.3) \approx {}^5J(1.1,1.4_a) \approx {}^5J(1.1,1.4_b)$ = 0.6 Hz, 1 H, H-C(1.1)], 6.25 [dddd, $^3J(1.3,1.4_b)$ = 16.90 Hz, $^3J(1.3,1.4_a)$ = 10.3 Hz, $^3J(1.3,1.2)$ = 11.0 Hz, $^4J(1.3,1.1)$ = 0.5 Hz, 1 H, H-C(1.3)], 6.06 [ddt, $^3J(1.2,1.1)$ = 12.3 Hz, $^3J(1.2,1.3)$ = 11.0 Hz, $^4J(1.2,1.4_a) \approx {}^4J(1.2,1.4_b)$ = 0.7 Hz, 1 H, H-C(1.2)], 5.21 [ddt, $^2J(1.4_b,1.4_a)$ = 1.6 Hz, $^3J(1.4_b,1.3)$ = 16.9 Hz, $^4J(1.4_b,1.2) \approx {}^5J(1.4_b,1.1)$ = 0.7 Hz, 1 H, H_b-C(1.4)], 5.09 [ddt, $^2J(1.4_a,1.4_b)$ = 1.6 Hz, $^3J(1.4_a,1.3)$ = 10.2 Hz, $^4J(1.4_a,1.2) \approx {}^5J(1.4_a,1.1)$ = 0.7 Hz, 1 H, H_a-C(1.4)], 4.10 [s, 2 H, H-C(2)], 3.45 [s, 3 H, H-C(2′)].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.2 [C(1)], 137.8 [C(1.1)], 131.2 [C(1.3)], 117.8 [C(1.4)], 116.8 [C(1.2)], 69.3 [C(2)], 59.4 [C(2′)].

MS (EI, 70 eV): *m/z* (%) = 142 (10) $[M]^+$, 114 (24), 84 (6), 68 (10), 53 (7), 45 (100), 39 (22).

Anal. Calcd for $C_7H_{10}O_3$ (142.15): C, 59.15; H, 7.09. Found: C, 59.04; H, 7.09.

Buta-1,3-dienyl (*tert*-Butyldimethylsiloxy)acetate (1e) Activated Precursor 4-Nitrophenyl (*tert*-Butyldimethylsiloxy)acetate

To a soln of (*tert*-butyldimethylsiloxy)acetic acid (1.295 g, 6.8 mmol) in CH_2Cl_2 (34 mL) were added DCC (1.54 g, 7.48 mmol), 4-nitrophenol (950 mg, 6.83 mmol), and DMAP (74 mg, 0.6 mmol). After 48 h at r.t., the mixture was filtered and poured into H_2O (30 mL). The organic phase was washed with H_2O (3 × 30 mL) and dried (Na_2SO_4). After evaporation, the crude product was purified by flash chromatography (hexane–EtOAc, 95:5) to give a yellow oil that crystallized; yield: 923 mg (43%); mp 44–46 °C; R_f (hexane–EtOAc, 9:1) = 0.44.

IR: 3117 (w), 3087 (w), 3024 (w), 2954 (s), 2930 (vs), 2895 (m), 2857 (s), 2741 (vw), 2119 (w), 1793 (s), 1737 (m), 1700 (m), 1617 (m), 1594 (s), 1527 (vs), 1491 (s), 1472 (m), 1463 (m), 1444 (m), 1388 (m), 1349 (vs), 1325 (m), 1305 (m), 1253 (s), 1210 (vs), 1162 (s), 1020 (vs), 1048 (m), 1014 (m), 1005 (m), 957 (w), 919 (m), 867 (s), 840 (vs), 786 (s), 762 (s), 712 (m), 675 (m), 636 (m), 570 (w), 494 (m), 438 cm^{-1} (w).

^1H NMR (400 MHz, $CDCl_3$): δ = 8.27 and 7.31 [2 d, system AA′BB′, $^2J(A,B)$ = 9.2 Hz, 2 H each, H_{arom}], 4.52 [s, 2 H, H_2-C(2)], 0.94 [s, 9 H, $SiC(CH_3)_3$], 0.15 [s, 6 H, $Si(CH_3)_2$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.42 [C(1)], 154.99 [C(1.4)], 145.33 [C(1.1)], 125.20 and 122.14 [C(1.3) and C(1.3′) or C(1.2) and C(1.2′)], 61.65 [C(2)], 25.62 [$SiC(CH_3)_3$], 18.30 [$SiC(CH_3)_3$], –4.48 [$Si(CH_3)_2$].

MS (ESI): *m/z* = 334.11 $[M + Na]^+$.

HRMS: *m/z* $[M + Na]^+$ calcd for $C_{14}H_{21}NNaO_5Si$: 334.1081; found: 334.1089.

Buta-1,3-dienyl (*tert*-Butyldimethylsiloxy)acetate (1e)

Using crotonaldehyde (205 mg, 3 mmol) and 4-nitrophenyl (*tert*-butyldimethylsiloxy)acetate[12] (900 mg, 3 mmol) according to the general procedure, the crude product was purified by flash chromatography (hexane–EtOAc, 98:2), giving pure **1e** as a yellow oil; yield: 435 mg (60%); R_f (hexane–EtOAc, 2:1) = 0.85.

IR: 3090 (w), 3072 (w), 3040 (w), 2955 (s), 2931 (s), 2897 (m), 2858 (s), 2741 (vw), 1782 (s), 1757 (m), 1731 (m), 1660 (m), 1605 (w), 1593 (w), 1518 (w), 1496 (w), 1473 (m), 1464 (m), 1443 (m), 1419 (w), 1392 (m), 1368 (m), 1344 (w), 1305 (m), 1256 (s), 1187 (s), 1154 (vs), 1096 (m), 1006 (m), 995 (m), 940 (w), 924 (m), 905 (m), 841 (vs), 817 (m), 781 (s), 743 (w), 708 (w), 683 (w), 665 (w), 582 (vw), 498 (vw), 484 cm^{-1} (vw).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.42 [dd, $^3J(1.1,1.2)$ = 12.3 Hz, 1 H, H-C(1.1)], 6.26 [dddd, $^3J(1.3,1.4b)$ = 16.9 Hz, $^3J(1.3,1.4a)$ = 10.3 Hz, $^3J(1.3,1.2)$ = 11.1 Hz, 1 H, H-C(1.3)], 6.04 [dd, $^3J(1.2,1.1) \approx$ 11.9 Hz, $^3J(1.2,1.3)$ = 11.2 Hz, 1 H, H-C(1.2)], 5.20 [ddt, $^2J(1.4b,1.4a)$ = 1.5 Hz, $^3J(1.4b,1.3)$ = 16.9 Hz, $^4J(1.4b,1.2) \approx {}^5J(1.4b,1.1)$ = 0.7 Hz, 1 H, H-C(1.4b)], 5.08 [ddt, $^2J(1.4a,1.4b)$ = 1.5 Hz, $^3J(1.4a,1.3)$ = 10.25 Hz, $^4J(1.4a,1.2) \approx {}^5J(1.4a,1.1)$ = 0.8 Hz, 1 H, H-C(1.4a)], 4.31 [s, 2 H, H-C(2)], 0.92 [s, 9 H, $SiC(CH_3)_3$], 0.1 [s, 6 H, $Si(CH_3)_2$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.5 [C(1)], 138.0 [C(1.1)], 131.3 [C(1.3)], 117.3 [C(1.4)], 116.4 [C(1.2)], 61.2 [C(2)], 25.5 [$SiC(CH_3)_3$], –5.6 [$Si(CH_3)_2$].

MS (ESI): *m/z* = 264.3 $[M - H + Na]^+$.

Buta-1,3-dienyl (1,3-Dioxo-2,3-dihydro-1*H*-isoindol-2-yl)acetate (1f)

Using crotonaldehyde (5 mL, 60 mmol) and (1,3-dioxo-2,3-dihydro-1*H*-isoindol-2-yl)acetyl chloride (13.4 g, 60 mmol) diluted in THF (60 mL) according to the general procedure; extraction with EtOAc gave a crude product that was crystallized (hexane) and finally recrystallized (pentane) to give pure **1f** as a yellow powder; yield: 11.62 g (81%); mp 142–143 °C; R_f (hexane–Et_2O, 2:1) = 0.20.

IR: 3071 (vw), 2975 (vw), 2936 (vw), 1782 (m), 1765 (s), 1723 (s), 1719 (s), 1658 (w), 1615 (vw), 1471 (w), 1418 (s), 1396 (m), 1366 (m), 1343 (vw), 1318 (w), 1192 (s), 1169 (s), 1112 (m), 1092 (w), 1073 (w), 1020 (vw), 998 (w), 955 (m), 932 (m), 915 (w), 747 (m), 715 (m), 631 (w), 530 cm^{-1} (w).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.89–7.87 [m, 2 H, H_{Phth}-C(2.3)], 7.75–7.73 [m, 2 H, H_{Phth}-C(2.4)], 7.35 [dd*, $^3J(1.1,1.2)$ = 12.2 Hz, $^4J(1.1,1.3) \approx {}^5J(1.1,1.4_a) \approx {}^5J(1.1,1.4_b)$ = 0.6 Hz, 1 H, H-C(1.1)], 6.24 [dddd, $^3J(1.3,1.4_b)$ = 16.8 Hz, $^3J(1.3,1.2)$ = 11.0 Hz, $^3J(1.3,1.4_a)$ = 10.2 Hz, $^4J(1.3,1.1)$ = 0.5 Hz, 1 H, H-C(1.3)], 6.08 [ddt, $^3J(1.2,1.1)$ = 12.2 Hz, $^3J(1.2,1.3)$ = 11.1 Hz, $^4J(1.2,1.4_a) \approx {}^4J(1.2,1.4_b)$ = 0.6 Hz, 1 H, H-C(1.2)], 5.23 [ddt, $^2J(1.4_b,1.4_a)$ = 1.6 Hz, $^3J(1.4_b,1.3)$ = 16.8 Hz, $^4J(1.4_b,1.2) \approx {}^5J(1.4_b,1.1)$ = 0.7 Hz, 1 H, H_b-C(1.4)], 5.11 [ddt, $^2J(1.4_a,1.4_b)$ = 1.6 Hz, $^3J(1.4_a,1.3)$ = 10.2 Hz, $^4J(1.4_a,1.2) \approx {}^5J(1.4_a,1.1)$ = 0.6 Hz, 1 H, H_a-C(1.4)], 4.52 [s, 2 H, H-C(2)].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.2 [C_{Phth}(2.1)], 164.4 [C(1)], 138.1 [C(1.1)], 134.3 [C_{Phth}(2.4)], 131.8 [C_{Phth}(2.2)], 131.0 [C(1.3)], 123.7 [C_{Phth}(2.3)], 118.2 [C(1.4)], 117.3 [C(1.2)], 38.5 [C(2)].

MS (EI, 70 eV): *m/z* (%) = 257 (0.2) $[M]^+$, 188 (17), 161 (13), 160 (100), 133 (5), 104 (4), 77 (5), 76 (3).

Anal. Calcd for $C_{14}H_{11}NO_4$ (257.24): C, 65.37; H, 4.31; N, 5.45. Found: C, 65.17; H, 4.63; N, 5.15.

***O*-[(*E*)-Buta-1,3-dienyl)-*O*-(trialkylsilyl)ketene Acetals 2; General Procedure**

Procedure A: 1 M LHMDS in THF (20 mL, 20 mmol) was added to 2-MeTHF (15 mL) in a 200-mL flask equipped with a mechanical stirrer. The soln was cooled to –60 °C, then HMPA (6.5 mL, distilled over Na) was rapidly added followed by the trapping agent TBDMSCl or TIPSCl (15 mmol) dissolved in THF (10 mL) was added. The yellow soln was cooled to –110 °C (EtOH, N_2). At this temperature the desired (*E*)-buta-1,3-dienyl ester (15 mmol) dissolved in THF/2-MeTHF (2:1, 15 mL) was added over 10 min. The temperature must remain below –110 °C in order to avoid decomposition of the ketene acetal enolate. The mixture was then stirred at ca. –115 °C for 1.5 h. The reaction was quenched at this temper-

ature with NH_4Cl soln (30 mL) or 2 M NaH_2PO_4 (30 mL) and poured into pentane (150 mL). The aqueous phase was extracted with pentane (3 × 150 mL), the extracts were washed with NH_4Cl soln (3 × 30 mL) and NaCl soln (3 × 30 mL), and dried (Na_2SO_4). The crude yellow oil was purified by distillation.

Procedure B: As described in procedure A with 1 M NaHMDS instead of 1 M LHMDS and DMPU (6 mL) instead of HMPA.

[1-(Buta-1,3-dienyloxy)vinyloxy]*tert*-butyldimethylsilane (2a)
Using 1 M LHMDS in THF (50 mL, 50 mmol), HMPA (14 mL)], TBDMSCl (7.5 g, 50 mmol), and **1a** (4.34 g, 38.7 mmol) according to procedure B, purification by distillation gave pure **2a** as a clear colorless liquid; yield: 6.97 g (80%); bp 47 °C/0.08 mbar; R_f (hexane–Et_2O, 2:1) = 0.65.

IR: 3091 (vw), 3049 (vw), 2959 (m), 2932 (m), 2888 (w), 2861 (m), 1662 (s), 1657 (s), 1605 (vw), 1536 (vw), 1473 (w), 1465 (w), 1419 (w), 1392 (w), 1364 (w), 1316 (m), 1291 (m), 1256 (s), 1177 (m), 1153 (s), 1025 (s), 1005 (m), 994 (m), 957 (vw), 922 (m), 894 (w), 843 (s), 827 (s), 813 (m), 788 (s), 762 cm^{-1} (w).

^1H NMR (400 MHz, $CDCl_3$): δ = 6.59 [dd*, $^3J(1.1,1.2)$ = 12.1 Hz, $^4J(1.1,1.3) \approx {}^5J(1.1,1.4a) \approx {}^5J(1.1,1.4b)$ = 0.6 Hz, 1 H, H-C(1.1)], 6.25 [dddd, $^3J(1.3,1.4b)$ = 16.9 Hz, $^3J(1.3,1.2)$ = 11.0 Hz, $^3J(1.3,1.4a)$ = 10.3 Hz, $^4J(1.3,1.1)$ = 0.6 Hz, 1 H, H-C(1.3)], 5.91 [ddt, $^3J(1.2,1.1)$ = 12.1 Hz, $^3J(1.2,1.3)$ = 11.0 Hz, $^4J(1.2,1.4a) \approx {}^4J(1.2,1.4b)$ = 0.7 Hz, 1 H, H-C(1.2)], 5.13 [ddt, $^2J(1.4b,1.4a)$ = 1.7 Hz, $^3J(1.4b,1.3)$ = 16.9 Hz, $^4J(1.4b,1.2) \approx {}^5J(1.4b,1.1)$ = 0.7 Hz, 1 H, Hb-C(1.4)], 4.98 [ddt, $^2J(1.4a,1.4b)$ = 1.7 Hz, $^3J(1.4a,1.3)$ = 10.3 Hz, $^4J(1.4a,1.2) \approx {}^5J(1.4a,1.1)$ = 0.7 Hz, 1 H, Ha-C(1.4)], 3.41, 3.39 [2 d, ^3J = 2.7 Hz, 2 H, H_2-C(2)], 0.95 [s, 9 H, $SiC(CH_3)_3$], 0.20 (s, 6 H, Si-CH_3). * Only two signals of the quartet are resolved.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.0 [C(1)], 143.5 [C(1.1)], 132.0 [C(1.3)], 115.1 [C(1.4)], 114.5 [C(1.2)], 66.0 [C(2)], 25.5 [$SiC(CH_3)_3$], 18.1 [$SiC(CH_3)_3$], –4.8 ($SiCH_3$).

MS (EI, 70 eV): *m/z* (%) = 227 (1.9) $[M + 1]^+$, 211 (1.4, $[M - 15]^+$), 169 (14), 127 (19), 117 (14), 115 (18), 99 (10), 75 (28), 74 (39), 73 (100), 59 (30), 45 (13).

HRMS: *m/z* $[M + H]^+$ calcd for $C_{12}H_{22}O_2Si$: 227.1462; found: 227.1451.

[1-(Buta-1,3-dienyloxy)prop-1-enyloxy]*tert*-butyldimethylsilane (2b)
Using 1 M LHMDS in THF (40 mL, 40 mmol), HMPA (11 mL), TBDMSCl (6.0 g, 40 mmol), and **1b** (3.84 g, 30 mmol) according to procedure A with purification by distillation gave pure **2b**; yield: 5.96 g (83%). Alternatively, using 1 M NaHMDS in THF (20 mL, 20 mmol), DMPU (6 mL), TBDMSCl (3.0 g, 20 mmol), and **1b** (1.89 g, 15 mmol) according to procedure B with purification by distillation gave pure **2b** as a clear colorless liquid; yield: 3.02 g (84%); bp 53 °C/0.06 mbar; R_f (hexane–Et_2O, 2:1) = 0.7.

IR: 3091 (w), 3048 (vw), 2959 (m), 2931 (s), 2887 (w), 2861 (m), 1692 (s), 1657 (s), 1605 (vw), 1473 (w), 1464 (w), 1418 (w), 1389 (m), 1363 (w), 1338 (s), 1290 (w), 1256 (s), 1195 (s), 1174 (s), 1153 (s), 1095 (m), 1055 (s), 993 (m), 919 (m), 906 (m), 842 (s), 824 (m), 810 (s), 787 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 6.49 [dd*, $^3J(1.1,1.2)$ = 12.1 Hz, $^4J(1.1,1.3) \approx {}^5J(1.1,1.4a) \approx {}^5J(1.1,1.4b)$ = 0.6 Hz, 1 H, H-C(1.1)], 6.23 [dddd, $^3J(1.3,1.4b)$ = 16.9 Hz, $^3J(1.3,1.2)$ = 11.0 Hz, $^3J(1.3,1.4a)$ = 10.3 Hz, $^4J(1.3,1.1)$ = 0.6 Hz, 1 H, H-C(1.3)], 5.83 [ddt, $^3J(1.2,1.1)$ = 12.1 Hz, $^3J(1.2,1.3)$ = 11 Hz, $^4J(1.2,1.4a) \approx {}^4J(1.2,1.4b)$ = 0.7 Hz, 1 H, H-C(1.2)], 5.09 [ddt, $^2J(1.4b,1.4a)$ = 1.7 Hz, $^3J(1.4b,1.3)$ = 16.9 Hz, $^4J(1.4b,1.2) \approx {}^5J(1.4b,1.1)$ = 07 Hz, 1 H, Hb-C(1.4)], 4.93 [ddt, $^2J(1.4a,1.4b)$ = 1.7 Hz, $^3J(1.4a,1.3)$ = 10.3 Hz, $^4J(1.4a,1.2) \approx {}^5J(1.4b,1.1)$ = 0.6 Hz, 1 H, Ha-C(1.4)], 3.81 (q, $^3J(2,3)$ = 6.6 Hz, 1 H, H-C(2)], 1.52 [d, $^3J(3,2)$ = 6.6 Hz, 3 H, H-C(3)], 0.95 [s, 9 H, $SiC(CH_3)_3$], 0.17 (s, 6 H, Si-CH_3). * Only two signals of the quartet are resolved.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.0 [C(1)], 145.1 [C(1.1)], 132.2 [C(1.3)], 114.2 [C(1.4)], 113.4 [C(1.2)], 78.0 [C(2)], 25.6 [$SiC(CH_3)_3$], 18.0 [$SiC(CH_3)_3$], 9.6 [C(3)], –4.4 ($SiCH_3$).

MS (EI, 70 eV): *m/z* (%) = 240 (1.4) $[M]^+$, 183 (11), 115 (17), 75 (19), 74 (29), 73 (100) 59 (32), 45 (25).

Anal. Calcd for $C_{13}H_{24}O_2Si$ (240.42): C, 64.95; H, 10.06. Found: C, 64.92; H, 10.09.

[1-(Buta-1,3-dienyloxy)-3,3-dimethylbut-1-enyloxy]*tert*-butyldimethylsilane (2c)
Using 1 M NaHMDS in THF (10 mL, 10 mmol), DMPU (3 mL), TBDMSCl (1.5 g, 10 mmol), and **1c** (1.26 g, 7.5 mmol) according to procedure B, with purification by distillation gave pure **2c** as a clear colorless liquid; yield: 1.39 g (65%); bp 64 °C/0.05 mbar; R_f (hexane–Et_2O, 2:1) = 0.84.

IR: 3090 (vw), 3046 (vw), 2957 (vs), 2931 (s), 2861 (m), 2901 (m), 2861 (m), 1679 (vs), 1655 (s), 1605 (vw), 1472 (m), 1463 (m), 1418 (w), 1393 (m), 1352 (s), 1311 (vw), 1288 (vw), 1256 (s), 1225 (s), 1159 (vs), 1041 (m), 1009 (s), 992 (m), 947 (m), 917 (w), 890 (w), 841 (s), 825 (s), 813 (m), 785 (m), 714 (w), 672 (w), 621 (w), 559 (vw), 493 cm^{-1} (vw).

^1H NMR (400 MHz, $CDCl_3$): δ = 6.44 [dd, $^3J(1.1,1.2)$ = 12.1 Hz, $^4J(1.1,1.3) \approx {}^5J(1.1,1.4a) \approx {}^5J(1.1,1.4b)$ = 0.6 Hz, 1 H, H-C(1.1)], 6.25 [ddd, $^3J(1.3,1.4b)$ = 16.9 Hz, $^3J(1.3,1.4a)$ = 10.4 Hz, $^3J(1.3,1.2)$ = 11.0 Hz, 1 H, H-C(1.3)], 5.81 [ddt, $^3J(1.2,1.1) \approx$ 11.8 Hz, $^3J(1.2,1.3)$ = 11.1 Hz, $^4J(1.2,1.4a) \approx {}^4J(1.2,1.4b) \approx$ 0.6 Hz, 1 H, H-C(1.2)], 5.09 [ddt, $^2J(1.4b,1.4a)$ = 1.7 Hz, $^3J(1.4b,1.3)$ = 16.9 Hz, $^4J(1.4b,1.2) \approx {}^5J(1.4b,1.1) \approx$ 0.7 Hz, 1 H, H-C(1.4b)], 4.94 [ddt*, $^2J(1.4a,1.4b)$ = 1.7 Hz, $^3J(1.4a,1.3)$ = 10.3 Hz, 1 H, H-C(1.4a)], 3.67 [s, 1 H, H-C(2)], 1.09 [s, 9 H, $(CH_3)_3C$], 0.96 [s, 9 H, $(SiC(CH_3)_3$], 0.19 [s, 6 H, $(CH_3)_2Si$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.2 [C(1)], 145.2 [C(1.1)], 132.2 [C(1.3)], 114.3 [C(1.4)], 113.3 [C(1.2)], 92.8.0 [C(2)], 30.8 [C(4)], 29.6 [C(3)], 25.9 [$C(CH_3)_3$], 18.1 [$SiC(CH_3)_3$], –4.0 [$Si(CH_3)_2$].

MS (EI, 70 eV): *m/z* (%) = 283 (3.4) $[M]^+$, 189 (24), 173 (75), 169 (17), 157 (13), 143 (11), 127 (19), 117 (40), 115 (31), 99 (21), 84 (10), 83 (30), 75 (44), 74 (12), 73 (100), 57 (35), 55 (16), 47 (16), 45 (31), 44 (13), 43 (54), 42 (21), 41 (97).

MS (DCI): *m/z* (%) = 283 (100) $[M + H]^+$.

[1-(Buta-1,3-dienyloxy)-2-methoxyvinyloxy]*tert*-butyldimethylsilane (2d)
Using 1 M LHMDS in THF (20 mL, 20 mmol), HMPA (6.5 mL), TBDMSCl (3.0 g, 20 mmol), and **1d** (2.14 g, 15 mmol) according to procedure A, with purification by distillation gave pure **2d** as a colorless oil; yield: 2.87 g (75%); bp 63 °C/0.06 mbar; R_f (hexane–Et_2O, 2:1) = 0.63.

IR: 3089 (vw), 2952 (m), 2932 (s), 2898 (m), 2860 (m), 2832 (m), 1719 (m), 1656 (s), 1604 (vw), 1473 (m), 1464 (m), 1446 (w), 1446 (w), 1418 (w), 1392 (w), 1363 (m), 1340 (s), 1290 (vw), 1254 (s), 1202 (s), 1171 (s), 1138 (s), 1001 (s), 940 (w), 915 (w), 889 (w), 842 (s), 826 (s), 813 (m) 788 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 6.50 [dq, $^3J(1.1,1.2)$ = 12.2 Hz, $^4J(1.1,1.3) \approx {}^5J(1.1,1.4_a) \approx {}^5J(1.1,1.4_b)$ = 0.6 Hz, 1 H, H-C(1.1)], 6.20 [dddd, $^3J(1.3,1.4_b)$ = 16.9 Hz, $^3J(1.3,1.2)$ = 11.0 Hz, $^3J(1.3,1.4_a)$ = 10.3 Hz, $^4J(1.3,1.1)$ = 0.6 Hz, 1 H, H-C(1.3)], 5.81 [ddt, $^3J(1.2,1.1)$ = 12.2 Hz, $^3J(1.2,1.3)$ = 11.0 Hz, $^4J(1.2,1.4_a) \approx {}^4J(1.2,1.4_b)$ = 0.8 Hz, 1 H, H-C(1.2)], 5.48 [s, 1 H, H-C(2)], 5.06 [ddt, $^2J(1.4_b,1.4_a)$ = 1.8 Hz, $^3J(1.4_b,1.3)$ = 16.9 Hz, $^4J(1.4_b,1.2) \approx {}^5J(1.4_b,1.1)$ = 0.8 Hz, 1 H, H_b-C(1.4)], 4.91 [ddt, $^2J(1.4_a,1.4_b)$ = 1.7

Hz, $^3J(1.4_a,1.3) = 10.3$ Hz, $^4J(1.4_a,1.2) \approx {}^5J(1.4_a,1.1) = 0.7$ Hz, 1 H, H_a-C(1.4)], 3.49 [s, 3 H, (H-C(3)], 0.94 [s, 9 H, $SiC(CH_3)_3$], 0.18 (s, 6 H, $SiCH_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.8 [C(1.1)], 145.9 [C(1)], 132.2 [C(1.3)], 117.7 [C(2)], 113.9 [C(1.4)], 112.4 [C(1.2)], 60.0 [C(3)], 25.5 [$SiC(CH_3)_3$], 18.2 [$SiC(CH_3)_3$], –4.8 ($SiCH_3$).

MS (EI, 70 eV): *m/z* (%) = 254 (3.3) $[M]^+$, 256 (2.3) $[M]^+$, 197 (7), 127 (5), 115 (8), 89 (16), 75 (11), 73 (100).

Anal. Calcd for $C_{13}H_{24}O_3Si$ (256.42): C, 60.89; H, 9.43. Found: C, 60.93; H, 9.58.

1-[1,2-Bis(*tert*-butyldimethylsiloxy)vinyloxy]buta-1,3-diene (2e)
Using 1 M NaHMDS in THF (6 mL, 6 mmol), DMPU (3.5 mL), TBDMSCl (900 mg, 6 mmol), and **1e** (1.0 g, 4.13 mmol) according to procedure B, with purification by bulb-to-bulb distillation (150 °C/0.1 mbar) gave pure **2e** as a clear colorless liquid; yield: 982 mg (67%); R_f (hexane–Et_2O, 2:1) = 0.83.

IR: 3089 (w), 2956 (s), 2931 (s), 2887 (m), 2859 (s), 1746 (m), 1718 (m), 1656 (m), 1473 (m), 1461 (m), 1418 (m), 1391 (m), 1363 (m), 1255 (s), 1167 (vs), 994 (m), 939 (m), 923 (m), 839 (vs), 813 (m), 784 (s), 674 (w), 494 cm^{-1} (vw).

^1H NMR (400 MHz, $CDCl_3$): δ = 6.51 [dd, $^3J(1.1,1.2) = 12.1$ Hz, $^4J(1.1,1.3) \approx {}^5J(1.1,1.4a) \approx {}^5J(1.1,1.4b) = 0.6$ Hz, 1 H, H-C(1.1)], 6.22 [dddd, $^3J(1.3,1.4b) = 16.9$ Hz, $^3J(1.3,1.2) = 10.9$ Hz, $^3J(1.3,1.4a) = 10.3$ Hz, $^4J(1.3,1.1) = 0.6$ Hz, 1 H, H-C(1.3)], 5.82 [ddt, $^3J(1.2,1.1) = 12.1$ Hz, $^3J(1.2,1.3) = 11.0$ Hz, $^4J(1.2,1.4a) \approx {}^4J(1.2,1.4b) = 0.7$ Hz, 1 H, H-C(1.2)], 5.71 [s, 1 H, H-C(2)], 5.07 [ddt, $^2J(1.4b,1.4a) = 1.8$ Hz, $^3J(1.4b,1.3) = 16.9$ Hz, $^4J(1.4b,1.2) \approx {}^5J(1.4b,1.1) = 0.7$ Hz, 1 H, Hb-C(1.4)], 4.92 [ddt, $^2J(1.4a,1.4b) = 1.8$ Hz, $^3J(1.4a,1.3) = 10.3$ Hz, $^4J(1.4a,1.2) \approx {}^5J(1.4a,1.1) = 0.8$ Hz, 1 H, Ha-C(1.4)], 0.96 [s, 9 H, $SiC(CH_3)_3$], 0.95 [s, 9 H, $SiC(CH_3)_3$], 0.20 [s, 6 H, $Si(CH_3)_2$], 0.14 [s, 6 H, $Si(CH_3)_2$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.6 [C(1.1)], 146.4 [C(1)], 132.3 [C(1.3)], 113.6 [C(1.4)], 111.9 [C(1.2)], 111.1 [C(2)], 25.8 [$SiC(CH_3)_3$], 25.5 [$SiC(CH_3)_3$], 18.3 [$SiC(CH_3)_3$], 18.1 [$SiC(CH_3)_3$], –4.5 [$Si(CH_3)_2$], –5.3 [$Si(CH_3)_2$].

MS (ESI): *m/z* = 413.0 $[M - H + 58]^-$.

2-[2-(Buta-1,3-dienyloxy)-2-(*tert*-butyldimethylsiloxy)vinyl]-1*H*-isoindole-1,3(2*H*)-dione (2f)
Using 1 M LHMDS in THF (20 mL, 20 mmol), HMPA (14 mL), TBDMSCl (3.0 g, 20 mmol), and **1f** (3.9 g, 15 mmol), diluted in 2-MeTHF/THF (1:2, 45 mL) according to procedure A or B. Before quenching, MeI (1.6 mL, 25 mmol) diluted in THF (5 mL) was added, after 0.5 h at –108 °C, pentane (140 mL) was added, and finally the reaction was quenched with H_2O (50 mL). After extraction and evaporation, the crude yellow oil was crystallized (pentane) to give pure **2f** as yellow crystals; yield: 2.44 g (43%); mp 92–93 °C; R_f (hexane–Et_2O, 2:1) = 0.30.

IR: 3104 (w), 3030 (w), 2958 (m), 2932 (m), 2886 (w), 2860 (m), 2715 (vw), 2504v (w), 2258 (vw), 1961 (vw), 1923 (vw), 1782 (m), 1762 (m), 1718 (s), 1680 (s), 1656 (s), 1611 (w), 1469 (m), 1400 (s), 1366 (s), 1340 (m), 1288 (w), 1258 (m), 1217 (s), 1173 (m), 1135 (s), 1114 (s), 1088 (m), 1071 (w), 1037 (m), 1008 (s), 995 (m), 985 (m), 924 (m), 884 (s), 844 (m), 826 (m), 812 (m), 787 (m), 722 (s), 681 (m), 614 (w), 559 (w), 530 cm^{-1} (w).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.85–7.83 [m, 2 H, H_{Phth}-C(2.3)], 7.71–7.69 [m, 2 H, H_{Phth}-C(2.4)], 6.69 [dd, $^3J(1.1,1.2) = 12.0$ Hz, $^4J(1.1,1.3) \approx {}^5J(1.1,1.4_a) \approx {}^5J(1.1,1.4_b) = 0.6$ Hz, 1 H, H-C(1.1)], 6.26 (dddd, $^3J(1.3,1.4_b) = 16.9$ Hz, $^3J(1.3,1.2) = 11.0$ Hz, $^3J(1.3,1.4_a) = 10.3$ Hz, $^4J(1.3,1.1) = 0.6$ Hz, 1 H, H-C(1.3)], 6.02 (ddt, $^3J(1.2,1.1) = 12.0$ Hz, $^3J(1.2,1.3) = 11.0$ Hz, $^4J(1.2,1.4_a) \approx {}^4J(1.2,1.4_b) = 0.7$ Hz, 1 H, H-C(1.2)], 5.19 [ddt, $^2J(1.4_b,1.4_a) = 1.6$ Hz, $^3J(1.4_b,1.3) = 16.9$ Hz, $^4J(1.4_b,1.2) \approx {}^5J(1.4_b,1.1) = 0.7$ Hz, 1 H, H_b-C(1.4)], 5.05 [ddt, $^2J(1.4_a,1.4_b) = 1.6$ Hz, $^3J(1.4_a,1.3) = 10.3$ Hz, $^4J(1.4_a,1.2) \approx {}^5J(1.4_a,1.1) = 0.7$ Hz, 1 H, H_a-C(1.4)], 4.84 [s, 1 H, H-C(2)], 0.76 [s, 9 H, $SiC(CH_3)_3$], 0.17 (s, 6 H, $Si\text{-}CH_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.6 [C_{Phth}(2.1)] 157.0 [C(1)], 142.6 [C(1.1)], 133.9 [C_{Phth}(2.4)], 132.1 [C_{Phth}(2.2)], 131.2 [C(1.3)], 123.2 [C_{Phth}(2.3)], 116.7 [C(1.2)], 116.6 [C(1.4)], 76.8 [C(2)], 25.3 [$SiC(CH_3)_3$], 17.7 [$SiC(CH_3)_3$], –4.4 ($Si\text{-}CH_3$).

MS (DCI, NH_3): *m/z* (%) = 374 (25, $[M + 3]^+$), 373 (98, $[M + 2]^+$), 372 (12, $[M + 1]^+$), 275 (12), 270 (19), 262 (14), 258 (17), 252 (14), 196 (13), 160 (20), 133 (15), 132 (100), 130 (17), 104 (16), 91 (17), 90 (95), 73 (17).

HRMS (CI, isobutane): *m/z* $[M + H]^+$ calcd for $C_{20}H_{26}NO_4Si$: 372.1626; found: 372.1658.

Anal. Calcd for $C_{20}H_{25}NO_4Si$: C, 64.66; H, 6.78; N, 3.77. Found: C, 64.20; H, 6.68; N, 3.66.

Methyl (1,3-Dioxo-2-phenyl-2,3,3a,4,5,7a-hexahydro-1*H*-isoindol-5-yl)acetates 3; General Procedure
N-Phenylmaleimide (250 mg, 1.44 mmol) in THF (2 mL) was heated at 60 °C under argon. The desired ketene acetal **2** (0.35 mmol) was added in one portion and the mixture was heated 70 °C for 4 h to 16 h. The oil bath was removed and the mixture cooled to r.t. The mixture diluted with DME (3 mL) and 25% H_2SiF_6 in H_2O (0.3 mL, 0.45 mmol) was added to cleave the silyl ester. The mixture was stirred at r.t. for 0.5–1 h. The solvents were evaporated, the crude mixture dissolved in Et_2O (10 mL), washed with sat. $NaHCO_3$ (3 × 20 mL). The aqueous phase was carefully acidified at 0 °C to pH ~2 with concd HCl and extracted with Et_2O (3 × 50 mL). The organic phase was dried (Na_2SO_4) and evaporated. The crude carboxylic acid residue was dissolved in THF–MeOH (5:2, 10 mL) and treated with ~0.3 M CH_2N_2 in Et_2O soln or with commercial 2 M $TMSCHN_2$ in hexane soln (0.5 mL, 1 mmol). After 1 h at r.t., excess diazomethane compound was destroyed by the addition of a few drops of glacial AcOH and the solvents were evaporated. The crude methyl ester was purified by flash chromatography.

Methyl (1,3-Dioxo-2-phenyl-2,3,3a,4,5,7a-hexahydro-1*H*-isoindol-5-yl)acetate (3a)
Using *N*-phenylmaleimide (100.0 mg, 0.577 mmol) diluted in THF (2 mL) and **2a** (262.6 mg, 1.16 mmol) according to the general procedure, with purification by flash chromatography (CH_2Cl_2–Et_2O–hexane, 7:1:2) gave a colorless oil that crystallized (CH_2Cl_2–hexane) to give pure **3a** as a white powder; yield: 121.5 mg (70%); mp 109–109.5 °C; R_f (CH_2Cl_2–Et_2O–hexane, 7:1:2) = 0.26.

IR: 3064 (vw), 3032 (w), 3003 (vw), 2952 (w), 2907 (w), 2875 (w), 2854 (w), 1728 (s), 1713 (s), 1597 (w), 1502 (w), 1493 (w), 1454 (w), 1435 (w), 1401 (m), 1384 (m), 1359 (w), 1325 (w), 1278 (w), 1261 (m), 1247 (w), 1227 (w), 1202 (s), 1186 (m), 1166 (s), 1129 (w), 1079 (w), 1062 (w), 1029 (w), 996 (w), 823 (w), 754 (m), 712 (w), 696 (m), 576 cm^{-1} (w).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.44 [m, 2 H, H_{Ph}-C(2.2^{III})], 7.41–7.36 [m, 1 H, H_{Ph}-C(2.2^{IV})], 7.28–7.25 [m, 2 H, H_{Ph}-C(2.2^{II})], 6.06 [ddd, $^3J(2.7,2.6) = 10.0$ Hz, $^3J(2.7,2.7_a) = 3.6$ Hz, $^4J(2.7,2.5) = 2.6$ Hz, 1 H, H-C(2.7)], 5.93 [dt, $^3J(2.6,2.7) = 10.0$ Hz, $^3J(2.6,2.5) \approx {}^4J(2.6,2.7_a) = 2.2$ Hz, 1 H, H-C(2.6)], 3.70 [s, 3 H, H-C(1′)], 3.52 [dq, $^3J(2.7_a,2.3_a) = 8.8$ Hz, $^3J(2.7_a,2.7) \approx {}^4J(2.7_a,2.6) \approx {}^5J(2.7_a,2.5) = 3.0$ Hz, 1 H, H-C(2.7$_a$)], 3.21 [ddd, $^3J(2.3_a,H_a\text{-}2.4) = 11.2$ Hz, $^3J(2.3_a,2.7_a) = 8.6$ Hz, $^3J(2.3_a,H_b\text{-}2.4) = 6.1$ Hz, 1 H, H-C(2.3$_a$)], 2.75–2.67 [m, 1 H, H-C(2.5)], 2.44–2.32 [m, 3 H, $H_{a,b}$-C(2), H_b-C(2.4)], 1.39 [ddd, $^2J(H_a\text{-}2.4,H_b\text{-}2.4) = 12.9$ Hz, $^3J(H_a\text{-}2.4,2.3_a) = 11.2$ Hz, $^3J(H_a\text{-}2.4,2.5) = 9.7$ Hz, 1 H, H_a-C(2.4)].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.8 [C(2.3)], 175.5 [C(2.1)], 172.1 [C(1)], 134.2 [C(2.6)], 131.7 [C_{Ph}(2.2^I)], 129.1 [C_{Ph}(2.2^{III})], 128.6 [C_{Ph}(2.2^{IV})], 126.3 [C_{Ph}(2.2^{II})], 121.3 [C(2.7)], 51.8 [C(1′)],

40.7 [C(2.7$_a$)], 39.6 [C(2)], 38.9 [C(2.3$_a$)], 30.7 [C(2.5)], 19.8 [C(2.4)].

MS (DCI): *m/z* (%) = 299 (9) $[M]^+$, 239 (9), 92 (38), 91 (35), 79 (17), 77 (24), 74 (100), 44 (13).

Anal. Calcd for $C_{17}H_{17}NO_4$ (299.32): C, 68.22; H, 5.72; N, 4.68. Found: C, 68.21; H, 5.89; N, 4.45.

Methyl 2-(1,3-Dioxo-2-phenyl-2,3,3a,4,5,7a-hexahydro-1*H*-isoindol-5-yl)propanoate (3b)

Using *N*-phenylmaleimide (349.6 mg, 2.02 mmol) and **2b** (766.5 mg, 3.19 mmol) according to the general procedure, with purification by flash chromatography (CH_2Cl_2–Et_2O–hexane, 7:1:2) gave a colorless oil that crystallized (CH_2Cl_2–hexane) to give pure **3b** as a white powder; yield: 486.9 mg (77%); mp 102–102.5 °C; R_f (CH_2Cl_2–Et_2O–hexane, 7:1:2) = 0.29.

IR: 3055 (vw), 3023 (vw), 2986 (vw), 2960 (vw), 2907 (vw), 2875 (vw), 1775 (vw), 1708 (s), 1644 (vw), 1600 (vw), 1503 (w), 1458 (vw), 1437 (vw), 1384 (m), 1355 (w), 1302 (vw), 1284 (vw), 1274 (vw), 1253 (vw), 1228 (w), 1197 (m), 1180 (m), 1170 (w), 1149 (w), 1138 (w), 1123 (vw), 1069 (vw), 1055 (vw), 1033 (vw), 991 (vw), 824 (vw), 753 (w), 709 (w), 700 (w), 692 (vw), 586 cm^{-1} (vw).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.45 [m, 2 H, H_{Ph}-C(2.2^{III})], 7.41–7.37 [m, 1 H, H_{Ph}-C(2.2^{IV})], 7.29–7.26 [m, 2 H, $H_{Ph.}$-C(2.2^{II})], 6.07 [ddd, ^3J(2.7,2.6) = 10.1 Hz, ^3J(2.7,2.7a) = 3.6 Hz, ^4J(2.7,2.5) = 2.5 Hz, 1 H, H-C(2.7)], 5.89 [dt, ^3J(2.6,2.7) = 10.1 Hz, ^3J(2.6,2.5) ≈ ^4J(2.6,2.7a) = 2.1 Hz, 1 H, H-C(2.6)], 3.70 [s, 3 H, H-C(1′)], 3.52 [dq, ^3J(2.7a,2.3a) = 8.3 Hz, ^3J(2.7a,2.7) ≈ ^4J(2.7a,2.6) ≈ ^5J(2.7a,2.5) = 3.2 Hz, 1 H, H-C(2.7a)], 3.19 [ddd, ^3J(2.3a,Ha-2.4) = 11.5 Hz, ^3J(2.3a,2.7a) = 8.6 Hz, ^3J(2.3a,Hb-2.4) = 6.0 Hz, 1 H, H-C(2.3a)], 2.60–2.53 [m, 1 H, H-C(2.5)], 2.48 [quint, ^3J(2,3) = ^3J(2,2.5) = 7.1 Hz, 1 H, H-C(2)], 2.27 [ddd, ^2J(Hb-2.4,Ha-2.4) = 12.8 Hz, ^3J(Hb-2.4,2.3a) = 5.5 Hz, ^3J(Hb-2.4,2.5) = 4.5 Hz, 1 H, Hb-C(2.4)], 1.41 [ddd, ^2J(Ha-2.4,Hb-2.4) = 12.7 Hz, ^3J(Ha-2.4,2.3a) = 11.5 Hz, ^3J(Ha-2.4,2.5) = 10.1 Hz, 1 H, Ha-C(2.4)], 1.18 [d, ^3J(3,2) = 7.0 Hz, 3 H, H-C(3)].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.0 [C(2.1)], 175.5 [C(2.3)], 175.3 C((1)], 133.7 [C(2.6)], 131.7 [C_{Ph}(2.2^I)], 129.1 [C_{Ph}(2.2^{III})], 128.6 [C_{Ph}(2.2^{IV})], 126.4 [C_{Ph}(2.2^{II})], 121.5 [C(2.7)], 51.8 [C(1′)], 43.4 [C(2)], 40.8 [C(2.7a)], 39.0 [C(2.3a)], 36.6 [C(2.5)], 26.7 [C(2.4)],13.7 [C(3)].

MS (DCI): *m/z* (%) = 314 (32) $[M + 1]^+$, 313 (39) $[M]^+$, 282 (32), 254 (37), 253 (100), 119 (14), 107 (18), 106 (51), 105 (22), 91 (43), 88 (80), 79 (58), 78 (13), 77 (40), 57 (12).

Anal. Calcd for $C_{18}H_{19}NO_4$ (313.35): C, 69.00; H 6.11; N 4.47. Found: C, 69.26; H, 6.18; N, 4.38.

Methyl 2-(1,3-Dioxo-2-phenyl-2,3,3a,4,5,7a-hexahydro-1*H*-isoindol-5-yl)-3,3-dimethylbutanoate (3c)

Using *N*-phenylmaleimide (250 mg, 1.44 mmol) and **2c** (100 mg, 0.35 mmol) according to the general procedure, with purification by flash chromatography (CH_2Cl_2) gave a colorless oil that was crystallized (CH_2Cl_2–hexane) to give pure **3c** as a white powder; yield: 66 mg (53%); mp 164–166 °C; R_f (hexane–EtOAc, 98:2) = 0.83. Monocrystals were obtained by recrystallization (CH_2Cl_2–hexane).

IR: 3100 (vw), 3070 (vw), 3049 (w), 2989 (m), 2962 (s), 2921 (m), 2907 (m), 2866 (m), 2554 (vw), 2336 (vw), 1974 (vw), 1899 (vw), 1778 (m), 1708 (vs), 1593 (m), 1491 (s), 1468 (m), 1452 (m), 1468 (m), 1440 (m), 1434 (m), 1397 (s), 1376 (vs), 1271 (s), 1249 (m), 1230 (m), 1215 (s), 1179 (vs), 1168 (s), 1148 (vs), 1137 (s), 1090 (m), 1077 (m), 1065 (m), 1023 (w), 992 (m), 978 (m), 942 (m), 922 (vw), 903 (w), 849 (w), 819 (m), 810 (m), 780 (w), 757 (s), 732 (vw), 719 (w), 678 (w), 631 (w), 621 (m), 581 (m), 567 (m), 534 (m), 511 (w), 456 (vw), 437 cm^{-1} (vw).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.52–7.47 [m, 2 H, H_{Ph}-C(2.2^{III})], 7.43–7.38 [m, 1 H, H_{Ph}-C(2.2^{IV})], 7.33–7.30 [m, 2 H, H_{Ph}-C(2.2^{II})], 6.25 [dt, ^3J(2.7,2.6) = 10.3 Hz, ^3J(2.7,2.7a) ≈ ^4J(2.7,2.5) ≈ 2.0 Hz, 1 H, H-C(2.7)], 6.02 [dt, ^3J(2.6,2.7) = 10.3 Hz, ^3J(2.6,2.5) ≈ ^4J(2.6,2.7a) ≈ 3.1 Hz, 1 H, H-C(2.6)], 3.62 [s, 3 H, H_3-C(1′)], 3.50 [dq, ^3J(2.7a,2.3a) = 8.8 Hz, ^3J(2.7a,2.7) ≈ ^4J(2.7a,2.6) ≈ ^5J(2.7a,2.5) ≈ 3.1 Hz, 1 H, H-C(2.7a)], 3.26 [ddd, ^3J(2.3a,Ha-2.4) = 12.0 Hz, ^3J(2.3a,2.7a) = 8.8 Hz, ^3J(2.3a,Hb-2.4) = 6.1 Hz, 1 H, H-C(2.3a)], 2.64–2.58 [m, 1 H, H-C(2.5)], 2.34–2.28 [m, 1 H, Hb-C(2.4)], 2.29 [d, ^3J(2,2.5) = 3.4 Hz, 1 H, H-C(2)], 1.53 [dt*, ^2J(Ha-2.4,Hb-2.4) ≈ 12.2 Hz, ^3J(Ha-2.4,2.3a) ≈ ^3J(Ha-2.4,2.5) ≈ 11.2 Hz, 1 H, Ha-C(2.4)], 1.08 [s, 9 H, $C(CH_3)_3$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.87 [C(2.1)], 175.52 [C(2.3)], 173.38 [C(1)], 133.80 [C(2.6)], 131.68 [C_{Ph}(2.2^I)], 129.10 [C_{Ph}(2.2^{III})], 128.54 [C_{Ph}(2.2^{IV})], 126.32 [C_{Ph}(2.2^{II})], 120.51 [C(2.7)], 58.95 [C(2)], 51.00 C(1′)], 40.38 [C(2.7a)], 39.47 [C(2.3a)], 33.64 [C(3)], 32.89 [C(2.5)], 31.66 [C(2.4)], 28.18 [C(3′)].

MS (ESI): *m/z* = 378.3 $[M + Na]^+$.

HRMS: *m/z* $[M + Na]^+$ calcd for $C_{21}H_{25}NNaO_4$: 378.16758; found: 378.16763.

Methyl (1,3-Dioxo-2-phenyl-2,3,3a,4,5,7a-hexahydro-1*H*-isoindol-5-yl)(methoxy)acetate (3d)

Using *N*-phenylmaleimide (350.6 mg, 2.02 mmol) and **2d** (758.6 mg, 2.96 mmol) according to the general procedure, with purification by flash chromatography (CH_2Cl_2–Et_2O–hexane, 7:1:2) gave an colorless oil that crystallized (CH_2Cl_2–hexane) to give pure **3d** as a white powder; yield: 441.6 mg (66%); mp 124.5 °C; R_f (CH_2Cl_2–Et_2O–hexane, 7:1:2) = 0.20.

IR: 3067 (vw), 3044 (vw), 3009 (vw), 2963 (vw), 2936 (vw), 2882 (vw), 2860 (vw), 2830 (vw), 1733 (s), 1709 (s), 1597 (vw), 1501 (w), 1454 (w), 1444 (vw), 1391 (m), 1341 (vw), 1325 (w), 1302 (w), 1289 (w), 1274 (m), 1243 (w), 1230 (w), 1202 (m), 1186 (m), 1165 (w), 1117 (m), 1082 (w), 1031 (vw), 1055 (vw), 1014 (w), 988 (vw), 976 (w), 824 (w), 756 (w), 694 (m), 581 (w), 493 cm^{-1} (vw).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.42 [m, 2 H, H_{Ph}-C(2.2^{III})], 7.39–7.35 [m, 1 H, H_{Ph}-C(2.2^{IV})], 7.27–7.25 [m, 2 H, H_{Ph}-C(2.2^{II})], 6.12 [ddd, ^3J(2.7,2.6) = 10.0 Hz, ^3J(2.7,2.7$_a$) = 3.7 Hz, ^4J(2.7,2.5) = 2.7 Hz, 1 H, H-C(2.7)], 5.92 [dt, ^3J(2.6,2.7) = 10.1 Hz, ^3J(2.6,2.5) ≈ ^4J(2.6,2.7$_a$) = 2.3 Hz, 1 H, H-C(2.6)], 3.78 [s, 3 H, H-C(2′)], 3.75 [d, ^3J(2,2.5) = 5.3 Hz, 1 H, H-C(2)], 3.50 [dq, ^3J(2.7$_a$,2.3$_a$) = 8.7 Hz, ^3J(2.7$_a$,2.7) ≈ ^4J(2.7$_a$,2.6) ≈ ^5J(2.7$_a$,2.5) = 2.9 Hz, 1 H, H-C(2.7$_a$)], 3.38 [s, 3 H, H-C(1′)], 3.15 [ddd, ^3J(2.3$_a$,H$_a$-2.4) = 11.2 Hz, ^3J(2.3$_a$,2.7$_a$) = 8.6 Hz, ^3J(2.3$_a$,H$_b$-2.4) = 6.3 Hz, 1 H, H-C(2.3$_a$)], 2.70–2.64 [m, 1 H, H-C(2.5)], 2.20 [ddd, ^2J(H$_b$-2.4,H$_a$-2.4) = 13.2 Hz, ^3J(H$_b$-2.4,2.3$_a$) = 6.3 Hz, ^3J(H$_b$-2.4,2.5) = 4.4 Hz, 1 H, H$_b$-C(2.4)], 1.67 [ddd, ^2J(H$_a$-2.4,H$_b$-2.4) = 13.2 Hz, ^3J(H$_a$-2.4,2.3$_a$) = 11.1 Hz, ^3J(H$_a$-2.4,2.5) = 9.9 Hz, 1 H, H$_a$-C(2.4)].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.7 [C(2.3)], 175.3 [C(2.1)], 171.5 [C(1)], 131.7 [$C_{Ph.}$(2.2^I)], 131.2 [C(2.6)], 129.1 [C_{Ph}(2.2^{III})], 128.5 [C_{Ph}(2.2^{IV})], 126.3 [C_{Ph}(2.2^{II})], 122.5 [C(2.7)], 82.6 [C(2)], 58.8 [C(2′)], 52.1 [C(1′)], 40.6 [C(2.7$_a$)], 38.6 [C(2.3$_a$)], 37.3 [C(2.5)], 24.9 [C(2.4)].

MS (DCI): *m/z* (%) = 329 (8) $[M]^+$, 297 (31), 270 (29), 265 (21), 226 (35), 120 (11), 119 (15), 118 (10), 105 (11), 104 (58), 103 (60), 92 (14), 91 (100), 89 (34), 79 (89), 78 (15), 77 (59), 75 (45), 65 (12), 45 (11).

Anal. Calcd for $C_{18}H_{19}NO_5$ (329.35): C, 65.64; H, 5.81; N, 4.25. Found: C, 65.39; H, 5.95; N, 4.27.

Methyl (1,3-Dioxo-2-phenyl-2,3,3a,4,5,7a-hexahydro-1*H*-isoindol-5-yl)(hydroxy)acetate (3e)

Using *N*-phenylmaleimide (291 mg, 1.68 mmol) and **2e** (200 mg, 0.56 mmol) according to the general procedure. In this case after cleavage of the silyl ester with H_2SiF_6, the carboxylic acid was extracted with sat. $NaHCO_3$–Et_2O. The aqueous phase was carefully acidified to pH ~2 with concd HCl and extracted with Et_2O. After evaporation, the crude carboxylic acid was diluted in THF (4 mL) and MeOH (2 mL) and treated with 1 M TBAF in THF (0.6 mL, 0.6 mmol) to cleave the silyl ether. After 2 h at r.t., the reaction was diluted with Et_2O (10 mL) and poured into aq 1 M HCl and extracted with Et_2O (2 × 10 mL). The combined organic phases were dried (Na_2SO_4) and evaporated. The crude carboxylic acid residue was dissolved in THF–MeOH (5:2, 10 mL) and treated with ~0.3 M CH_2N_2 in Et_2O or with commercial 2 M $TMSCHN_2$ in hexane (0.5 mL, 1 mmol). After 1 h at r.t., the excess diazomethane reagent was destroyed by addition of a few drops of glacial AcOH and the solvents were evaporated. Purification by flash chromatography (CH_2Cl_2–EtOAc, 82: 18) gave pure **3e** as a yellow viscous oil; yield: 71 mg (40%); R_f (CH_2Cl_2–EtOAc, 8:2) = 0.35.

IR: 3472 (s), 3036 (m), 2953 (m), 2332 (vw), 2251 (vw), 1710 (vs), 1598 (m), 1542 (w), 1500 (s), 1456 (m), 1443 (m), 1380 (s), 1317 (m), 1182 (s), 1141 (m), 1117 (m), 1027 (w), 1003 (w), 981 (m), 904 (w), 843 (vw), 819 (m), 799 (w), 755 (m), 722 (m), 693 (s), 621 (w), 581 (w), 525 (vw), 504 (w), 489 (vw), 408 cm^{-1} (vw).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.68–7.44 [m, 2 H, H_{Ph}-C(2.2^{III})], 7.43–7.38 [m, 1 H, H_{Ph}-C(2.2^{IV})], 7.30–7.20 [m, 2 H, H_{Ph}-C(2.2^{II})], 6.18 [ddd, ^3J(2.7,2.6) = 10.1 Hz, ^3J(2.7,2.7a) = 3.7 Hz, ^4J(2.7,2.5) = 2.6 Hz, 1 H, H-C(2.7)], 6.06 [dt, ^3J(2.6,2.7) = 10.2 Hz, ^3J(2.6,2.5) ≈ ^4J(2.6,2.7a) ≈ 2.5 Hz, 1 H, H-C(2.6)], 4.33 [d, ^3J(2,2.5) = 3.5 Hz, 1 H, H-C(2)], 3.86 [s, 3 H, H_3-C(1′)], 3.55 [dq, ^3J(2.7a,2.3a) = 8.7 Hz, ^3J(2.7a,2.7) ≈ ^4J(2.7a,2.6) ≈ ^5J(2.7a,2.5) ≈ 3.0 Hz, 1 H, H-C(2.7a)], 3.21 [ddd, ^3J(2.3a,Ha-2.4) = 10.4 Hz, ^3J(2.3a,2.7a) = 8.7 Hz, ^3J(2.3a,Hb-2.4) = 6.5 Hz, 1 H, H-C(2.3a)], 2.78–2.71 [m, 1 H, H-C(2.5)], 2.11–2.05 [m, 1 H, Hb-C(2.4)], 1.73 [ddd, ^2J(Ha-2.4,Hb-2.4) = 13.3 Hz, ^3J(Ha-2.4,2.3a) = 10.4 Hz, ^3J(Ha-2.4,2.5) = 9.2 Hz, 1 H, Ha-C(2.4)].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.1 [C(2.1)], 175.4 [C(2.3)], 173.7 [C(1)], 131.7 [C_{Ph}(2.2^{I})], 131.3 [C(2.6)], 129.2 [C_{Ph}(2.2^{III})],128.6 [C_{Ph}(2.2^{IV})], 126.4 [C_{Ph}(2.2^{II})], 122.7 [C(2.7)], 72.5 [C(2)], 53.4 [C(1′)], 40.5 [C(2.7a)], 38.4 [C(2.3a)], 37.6 [C(2.5)], 23.6 [C(2.4)].

MS (ESI): *m/z* = 316.0 $[M + H]^+$.

HRMS: *m/z* $[M + Na]^+$ calcd for $C_{17}H_{17}NNaO_5$: 338.09999; found: 338.10002.

Methyl (1,3-Dioxo-2,3-dihydro-1*H*-isoindol-2-yl)(1,3-dioxo-2-phenyl-2,3,3a,4,5,7a-hexahydro-1*H*-isoindol-5-yl)acetate (3f)

Using *N*-phenylmaleimide (257.1 mg, 1.48 mmol) and **2f** (371.6 mg, 1 mmol) according to the general procedure, with purification by flash chromatography (CH_2Cl_2–Et_2O–hexane, 7:1:2) gave pure **3f** as a white powder; yield: 289.1 mg (65%); mp 229.5–230 °C; R_f (CH_2Cl_2–Et_2O–hexane, 7:1:2) = 0.24.

IR: 3066 (vw), 3050 (vw), 2955 (vw), 2909 (vw), 2859 (vw), 1777 (w), 1746 (s), 1708 (s), 1611 (vw), 1599 (vw), 1503 (w), 1469 (vw), 1455 (vw), 1439 (vw), 1391 (s), 1383 (s), 1340 (w), 1281 (w), 1252 (w), 1237 (w), 1194 (m), 1181 (m), 1148 (w), 1134 (vw), 1112 (w), 1094 (w), 1073 (vw), 1020 (vw), 1010 (vw), 964 (w), 926 (vw), 902 (vw), 753 (w), 720 (m), 695 (w), 583 (vw), 560 (vw), 531 cm^{-1} (vw).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.85 [m, 2 H, H_{Phth}-C(2^{III})], 7.78–7.74 [m, 2 H, H_{Phth}-C(2^{IV})], 7.46–7.41 [m, 2 H, H_{Ph}-C(2.2^{III})], 7.38–7.33 [m, 1 H, H_{Ph}-C(2.2^{IV})], 7.26–7.22 [m, 2 H, H_{Ph}-C(2.2^{II})], 6.24 [dt, ^3J(2.6,2.7) = 10.1 Hz, ^3J(2.6,H_b-2.4) ≈ ^4J(2.6,2.7$_a$) = 1.4 Hz, 1 H, H-C(2.6)], 6.14 [dt, ^3J(2.7,2.6) = 10.2 Hz, ^3J(2.7,2.7$_a$) ≈ ^4J(2.7,2.5) = 3.1 Hz, 1 H, H-C(2.7)], 4.77 [d, ^3J(2,2.5) = 8.9 Hz, 1 H, H-C(2)], 3.74 [s, 3 H, H-C(1′)], 3.53 [dq, ^3J(2.7$_a$,2.3$_a$) = 8.6 Hz, ^3J(2.7$_a$,2.7) ≈ ^4J(2.7$_a$,2.6) ≈ ^5J(2.7$_a$,2.5) = 3.1 Hz, 1 H, H-C(2.7$_a$)], 3.38–3.30 [m, 1 H, H-C(2.5)], 3.18 [ddd, ^3J(2.3$_a$,H_a-2.4) = 12.8 Hz, ^3J(2.3$_a$,2.7$_a$) = 8.6 Hz, ^3J(2.3$_a$,H_b-2.4) = 5.8 Hz, 1 H, H-C(2.3$_a$)], 2.27 [dddd, ^2J(H_b-2.4,H_a-2.4) = 12.6 Hz, ^3J(H_b-2.4,2.3$_a$) = 5.8 Hz, ^3J(H_b-2.4,2.5) = 3.8 Hz, ^4J(H_b-2.4,2.6) = 1.2 Hz, 1 H, H_b-C(2.4)], 1.24 [q, ^2J(H_a-2.4,H_b-2.4) ≈ ^3J(H_a-2.4,2.3$_a$) ≈ ^3J(H_a-2.4,2.5) = 12.3 Hz, 1 H, H_a-C(2.4)].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.5 [C(2.3)], 175.2 [C(2.1)], 168.4 [C(1)], 167.5 [$C_{Phth.}$(2^{I})], 134.5 [C_{Phth}(2^{IV})], 132.4 [C(2.6)], 131.5, 131.4 [C_{Phth}(2^{II}), C_{Ph}(2.2^{I})], 129.1 [C_{Ph}(2.2^{III}), 128.6 [C_{Ph}(2.2^{IV})], 126.4 [C_{Ph}(2.2^{II})], 123.8 [C_{Phth}(2^{III})], 122.0 [C(2.7)], 54.2 [C(2)], 52.9 [C(1′)], 40.8 [C(2.7$_a$)], 38.9 [C(2.3$_a$)], 34.7 [C(2.5)], 27.5 [C(2.4)].

MS (DCI): *m/z* (%) = 444 (11) $[M]^+$, 297 (14), 266 (18), 265 (100), 237 (19), 219 (27), 218 (38), 190 (30), 187 (43), 160 (39), 150 (83), 132 (31), 130 (39), 119 (25), 118 (49), 105 (22), 104 (55), 92 (14), 91 (81), 90 (11), 79 (39), 78 (18), 77 (71), 76 (44), 65 (12), 44 (14).

Anal. Calcd for $C_{25}H_{20}N_2O_6$ (444.44): C, 67.56; H 4.54; N, 6.30. Found: C, 67.28; H, 4.70; N, 6.02.

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(7) *Crystal structure analysis of* ***2f***: $C_{20}H_{25}NO_4Si$, $M_r = 371.50$, monoclinic, space group $P2_1$, $a = 8.191(1)$, $b = 23.442(2)$, $c = 11.342(1)$ Å, $\beta = 105.12(1)°$, $V = 2102.4(3)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.174$ g cm^{-3}, $T = 223(2)$ K, $\mu = 1.34$ cm^{-1}, $\lambda = 0.71073$ Å, $1.65 \le c \le 26.05°$, Stoe IPDS diffractometer, crystal dimensions $0.65 \times 0.40 \times 0.15$ mm; 7956 independent reflections, 3934 observed reflections with [I > 2σ(I)]; *R*-values [I > 2σ(I)]: $R_1 = 0.0658$, $wR_2 = 0.1409$.
Crystal structure analysis of ***4***: $C_{24}H_{18}N_2O_6$, $M_r = 430.40$, triclinic, space group *P*, $a = 7.894(2)$, $b = 11.426(3)$, $c = 12.057(4)$Å, $\alpha = 101.78(4)$, $\beta = 97.43(4)$, $\chi = 98.91(3)°$, $V = 1037.2(5)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.378$ g cm^{-3}, $T = 293(2)$ K, $\mu = 1.01$ cm^{-1}, $\lambda = 0.71073$ Å, $1.65 \le c \le 26.05°$, Stoe IPDS diffractometer, crystal dimensions $0.70 \times 0.50 \times 0.40$ mm; 3738 independent reflections, 2453 observed reflections with [I > 2σ(I)]; *R*-values [I > 2σ(I)]: $R_1 = 0.0328$, $wR_2 = 0.0816$.
Crystal structure analysis of ***5***: $C_{24}H_{18}N_2O_6{\cdot}CHCl_3$, $M_r = 549.77$, triclinic, space group *P*, $a = 10.261(3)$, $b = 11.610(3)$, $c = 11.818(4)$Å, $\alpha = 76.81(3)$, $\beta = 67.38(3)$, $\chi = 87.40(2)°$, $V = 1263.9(7)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.445$ g cm^{-3}, $\mu = 1.34$ cm^{-1}, $\lambda = 0.71073$ Å, $2.00 \le c \le 25.50°$, Stoe AED2 diffractometer, crystal dimensions $0.65 \times 0.49 \times 0.23$ mm; 4709 independent reflections, 3504 observed reflections with [I > 2σ(I)]; *R*-values [I > 2σ(I)]: $R_1 = 0.0701$, $wR_2 = 0.1669$. All three structures were refined with full-matrix block least squares on F^2; all non-hydrogen atoms were anisotropically refined. Crystallographic data (excluding structure factors)for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-118778 for **1f**, CCDC-629878 for **2f**, CCDC-629879 for **3c**, CCDC-629880 for **4** and CCDC-629881 for **5**. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(1223)336033; e-mail: deposit@ccdc.cam.ac.uk.

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