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Microwave-Assisted Competing Domino Processes in the Octaline Diol Series

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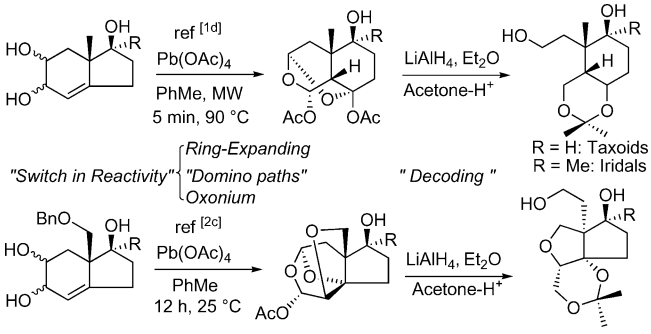
A $Pb(OAc)_4$-mediated, path selective, modular domino transformation using an octaline diol framework as a probe is described. Alteration of the nature of the angular substituent or the length of the tether chain controls the effectiveness of the "ring-expanded" versus "ring-retained" domino path. The solvent can modify the behaviour of the transient intermediates and the reaction time is reduced under microwave heating, whereas water cleanly promotes oxidative/pericyclic transformations leading to half-cascade intermediates when used as the solvent. Irrespective of the nature of the substituents (alkyl, alkenyl, alkoxy, acyloxy) and the solvent, all diol substrates react with $PhI(OAc)_2$ to afford exclusively the interrupted cascade as the only domino product.

Introduction

Unsaturated bicyclic vicinal diols can react with $Pb(OAc)_4$ or $PhI(OAc)_2$, which act as domino promoters in several ways, depending on the reaction conditions.[1] When the angular position bears a functional substituent, such as an alkoxy, an ester or a carbonyl group, more than one domino reaction path could be put into competition.[2] In the hydrindene diol series, the reaction course could be directed towards either of two distinct pathways, simply by the judicious choice of the angular substituent. As illustrated by Scheme 1, examples of this process include competition of two domino processes for diol substrates differing only at the angular substitution. Ether linkage was a prerequisite for the oxonium path, whereas its efficiency was shown to decrease with increasing separation of the oxygen from the angular position and the bulk of the linking chain.[2b] Conversely, any ester or alkyl group at the angular position completely reversed the tendency to undergo ring expansion.[2c] Moreover, a dramatic increase in rate was observed in the reactions conducted under microwave activation at either 60 or 90 °C, which represent an important experimental improvement.

This captivating path selectivity prompted us to scope out the features associated with selective construction of the [6+7] fused ring system, precursor of elaborated cycloheptanes,[3] and to investigate the regiochemical course in the presence of a variety of functional groups. We report in this paper on the feasibility of the microwave-assisted[4] version of this process, as well as the effect of varying the angular substituent, the solvent and the domino[5] promoter.



Scheme 1. Scope with respect to the angular substituent.

Results and Discussion

Access to the requisite octaline diols with varying chain lengths and steric requirements was readily achieved from a known bicyclic diol used in our earlier studies,[2a] through trivial transformations. To probe the path selectivity, competition experiments involving the domino reactions of **1a** and **5a** were conducted as a preliminary screen (Scheme 2). We chose the above octaline diols, as their structures seemed to lend themselves to a useful test of the methodology given the precedents in the lower homologue hydrindene diol series. Thus, investigating the role of tether length to control the orientation for selective access to either ring-expanded **8a** or ring-retained **3a**, we first found that the solvent played a critical role in the product distribution in the octaline diol series.[6] A survey of three solvents, PhMe, H_2O and AcOH, revealed that AcOH was the solvent of

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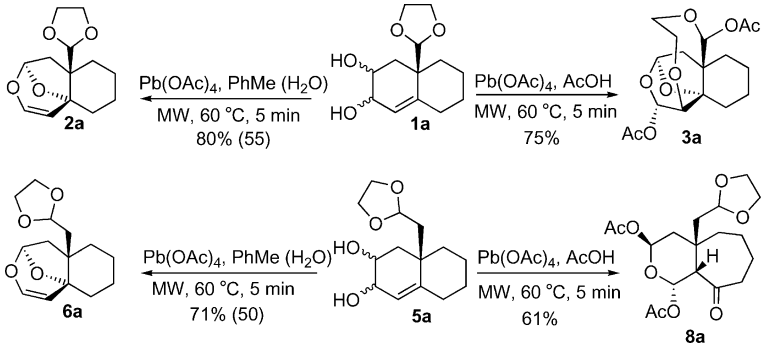


Scheme 2. Scope with respect to the tether length.

choice, increasing the propensity of the diol to undergo oxyplumbation (necessary for either the oxonium or ring-expansion path). A few minutes of microwave irradiation led to the selective formation of the desired domino product in satisfactory yield, by using the appropriate solvent, as outlined in Scheme 2. Accordingly, when operating in PhMe as solvent, only half-cascade domino products **2a** and **6a** were obtained.[7] Carrying out the same sequence in water[8] afforded cleanly 55% of **2a** and 50% of **6a**, along with recovered starting diols.[9] Switching to AcOH changed the product distribution leading to either **3a** or **8a**, depending upon the length of the linking chain. Hence, treatment of unsaturated diol **1a** with $Pb(OAc)_4$ cleanly afforded tetracyclic trisacetal **3a** in 75% yield as a single domino product. Its higher homologue **5a**, under the same reaction conditions gave rise to ring-enlarged domino product **8a** in 61% isolated yield.

The mechanism of these one-pot multistage transformations was investigated in our previous studies and it is established that, following glycol fission (**i**, Figure 1), the reaction proceeds through a hetero-[4π+2π] cycloaddition leading to cyclic ene–acetal **ii** and a subsequent oxyplumbation, which sets the final destination on the basis of the geometry of the transient organolead intermediate (**iii** or **v**) along with the nature of the angular substituent.[1a,1b,2c] As portrayed in Figure 1, the product distribution can be altered through the magnitude of the connecting chain, thus ensuring a regioselective profile for the oxyplumbation–deplumbation sequence. Although the one-pot conversions of **1a** into **3a** and **5a** into **8a** proceed through a similar transient organolead intermediate of type **v** and **iii**, respectively, the product distribution is markedly different for each template differing only in tether length. These outstandingly selective domino reactions associate entropy as a powerful control element in product formation along with orbital alignment considerations.[10]

With a representative range of templates in the octaline diol series, the stage was at hand to explore the factors that govern the path selectivity. The diols were subjected to $Pb(OAc)_4$-mediated oxidative cleavage under five sets of conditions (methods A, B, C, D and E).[11] The reliance on the solvent was examined by using PhMe, AcOH and H_2O. Three of the methods, B, D and E, employ microwave irradiation at 60 °C, whereas methods A and C operate at room

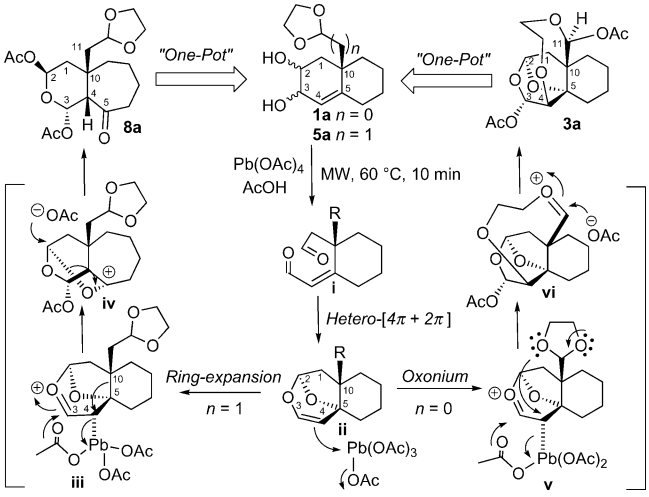
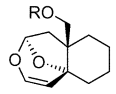
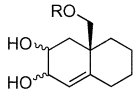
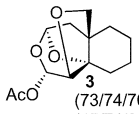
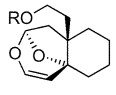
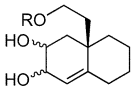
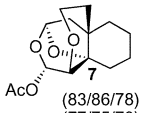
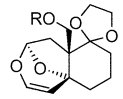
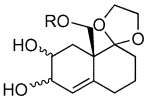
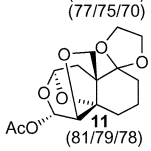
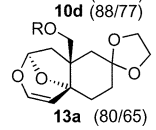
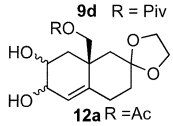
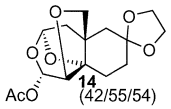
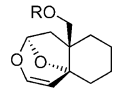
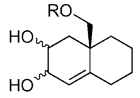
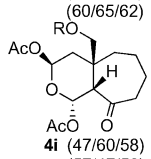
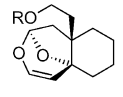
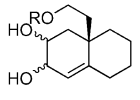
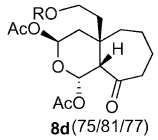
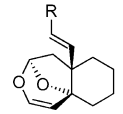
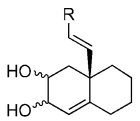
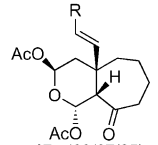


Figure 1. Competing domino processes by tuning the tether length – a mechanistic rationale.

temperature (A) or with conventional heating at 60 °C (C). Methods A, B, and C use AcOH as solvent. Method D, which can be also realized with $PhI(OAc)_2$ as the domino promoter, uses PhMe, and finally method E uses H_2O as solvent. The scope and efficiency of the presented work are illustrated by the results summarized in Tables 1 and 2. With PhMe or H_2O as solvent (domino conditions D and E), only the glycal-type half-cascade products (i.e., **2**, **6**, **10**, **13**, **16**) were obtained, irrespective of the nature of the angular substitution. These compounds, whose synthetic utility was explored,[12] are also cleanly obtained in PhMe by using $PhI(OAc)_2$ as the domino promoter. In AcOH, treatment of unsaturated diols **1b**–**h** with $Pb(OAc)_4$ under all domino conditions (A, B or C) gave no detectable quantities of ring-expanded structures. The only product isolated from this reaction was **3** (Table 1, Entry 1). The same trend was observed with substrates **9** and **12**, where corresponding ring-retained domino products **11** and **14** were obtained exclusively (Table 1, Entries 3 and 4).

In the case involving homologated ether linkage, with OMe and OTMS groups at the angular position (**5b**,**c**; Table 1, Entry 2), the reaction proceeds via an intermediate oxonium with exclusive formation of tetracyclic bis(acetal) **7**. Tuning the length of the connecting chain along with the

Table 1. Variation of the product distribution by alternating the factors controlling the competition.

Entry	Domino product yield [%]	(D/E)[a] ← Substrate → (A/B/C)[b]	Domino product yield [%]
1			
	2b (86/61) **2c** (89/59) **2d** (89/56) **2e** (87/58) **2f** (88/57) **2g** (84/53) **2h** (81/57)	**1b** R = Ac **1c** R = Mac **1d** R = Bn **1e** R = Tr **1f** R = MOM **1g** R = BOM **1h** R = Me	**3** (73/74/70) (45/74/68) (60/74/71) (60/86/78) (81/84/84) (77/73/75) (74/72/70)
2			
	6b (82/61) **6c** n.a.	**5b** R = Me **5c** R = TMS	**7** (83/86/78) (77/75/70)
3			
	10a (88/72) **10b** (84/78) **10c** (90/70) **10d** (88/77)	**9a** R = TBS **9b** R = Ac **9c** R = MOM **9d** R = Piv	**11** (81/79/78) (74/73/72) (81/80/80) n.a.
4			
	13a (80/65) **13b** (82/66)	**12a** R =Ac **12b** R = MOM	**14** (42/55/54) (60/65/62)
5			
	2i (88/62) **2j** (87/54) **2k** (77/58)	**1i** R = Piv **1j** R = Bz **1k** R = ChloroPiv	**4i** (47/60/58) **4j** (57/47/52) **4k** (37/60/55)
6			
	6d (90/67) **6e** (89/61) **6f** (88/60) **6g** (90/62) **6h** (91/58) **6i** (87/67) **6j** (84/63) **6k** (91/65)	**5d** R = Tr **5e** R = Ac **5f** R = Bz **5g** R = Mac **5h** R = Piv **5i** R = Cyclopropanoyl **5j** R = Cyclohexanoyl **5k** R = 2Me-butanoyl	**8d** (75/81/77) **8e** (70/73/65) **8f** (71/71/68) **8g** (75/81/70) **8h** (83/85/80) **8i** (69/73/70) **8j** (72/68/69) **8k** (74/69/67)
7			
	16a (84/63) **16b** (81/60)	**15a** R = H **15b** R = CO_2Et	**17a** (69/67/65) **17b** (59/62/55)

[a] Methods D, E: The substrate (1.0 mmol) and $Pb(OAc)_4$ (1.2 mmol) were heated in a microwave for 5–10 min at 60 °C; in 1 mL of PhMe (D) or in 1 mL of H_2O (E). [b] Methods A, B, C: reactions conducted with $Pb(OAc)_4$ (2.4 mmol) and the diol substrate (1.0 mmol) in AcOH (1 mL). Method A: room temperature for 12–15 h; method B: microwave irradiation, 10 min at 60 °C; method C: conventional heating, 10 min at 60 °C.

steric bulk of the angular alkoxy substituent (OPiv group at the angular position, **5d**; Table 1, Entry 6) allowed the path selectivity to be changed, as the trityl protection was sufficiently bulky to considerably obstruct cyclic trityloxonium formation. When subjected to the action of $Pb(OAc)_4$ in AcOH (Methods A, B, C), a bulky ester group (**1i**–**k**) gave rise to a single domino product of type **4** isolated in high yield (Table 1, Entry 5). Under the same conditions, the less sterically demanding esters (**1b**,**c**), like any ether linkage, delivered ring-retained domino product **3**, unless additional steric bulk and chain lengthening was introduced (Table 1, Entry 6). The absence of the ring-expanded domino product from **1b** and **1c** could be due to the fact that the intermediate of type **v** (Figure 1) did not live long enough to allow for C9–C5 bond migration. The observed divergent behaviour in the octaline diol series shows that fused-ring size is an important regiodeterminant in these reactions.

The oxonium path could be also completely suppressed by carrying out the domino reactions on substrates having longer connecting chains (ethylene tethered esters **5e**–**k**; Table 1, Entry 6). With diol substrates bearing an alkyl[1a] or an alkenyl substituent at the bridgehead position, exemplified by compounds **15a** and **15b**, the cascade culminating in a ring-expanding rearrangement proceeded selectively to give domino products **17a** and **17b**, respectively (Table 1, Entry 7). A comparison of the products from Entries 1 vs. 6 and 2 vs. 7 reveals the subtle effect of the angular substituent; it has a controlling influence on the course of the domino reaction, the products of which are either type **4**, **8** or **17** ring-expanded *cis*-fused [6+7] bicyclic systems or ring-retained *cis*-fused tetrahydrofurans (i.e., **3**, **11**, **14**) and *cis*-fused tetrahydropyrans (i.e., **7**). The structure of crystalline domino product **8e** first ascertained by the measurement of spatial proximity effects by using 2D NOESY experiments was confirmed by a single-crystal X-ray diffraction study (Figure 2) and served to corroborate the relative configurations of all ring-expanded domino products (i.e., **4**, **8**, **17**). The structures of **3**, **3a** and **7** were assigned by analogy to their lower homologues.[2b,2c] The half-cascade domino products were obtained exclusively, in either PhMe or AcOH, when $PhI(OAc)_2$ was used as the domino promoter.

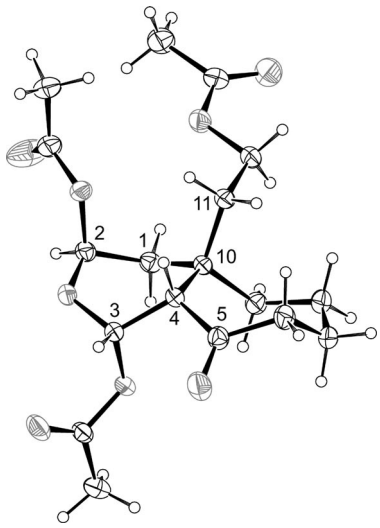


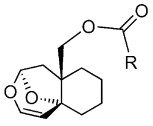
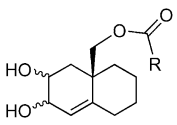
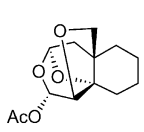
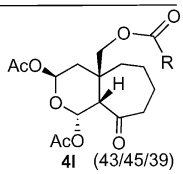
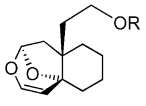
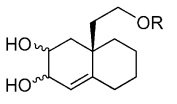
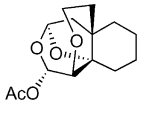
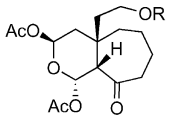
Figure 2. ORTEP view of the molecular structure of **8e**.

Examining the results depicted in Table 1, one can figure out that diols of type **1**, **5**, **9**, **12** or **15** can lead to either the half-cascade (i.e., **2**, **6**, **10**, **13**, **16**), the ring-expanded domino (i.e., **4**, **8**, **17**) or the ring-retained domino products (i.e., **3**, **7**, **11**, **14**) through the appropriate choices of solvent, oxidant and angular substituent. A partial explanation for the dominant reaction pathway and product distribution may be found in the relative rates of cyclic oxonium formation vs. C5–C10 ring-expanding bond migration.

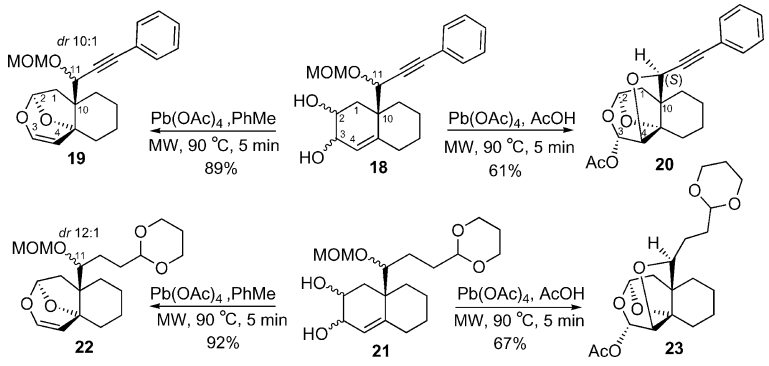
To further investigate the effect of angular substitution on the ability to orient a domino path, we performed additional experiments on a range of substrates portrayed in Table 2 and Scheme 3. The experiments listed in Table 2, like those in Table 1, were all performed competitively, with the same amount of reagent in three different solvents, at room temperature or at 60 °C (conventional or microwave heating). The ester-tethered substrates, which in the hydrindene diol series proceed in a totally selective manner to yield a ring-expanded domino product, displayed dual behaviour in the octaline diol series. The drop in path selectivity could be attributed to the fused ring size effect in orbital alignment.

The domino reaction of **1l–o** gave a mixture of three compounds, half-cascade **2l–o** (a common intermediate for both domino paths), ring-retained **3** and ring-expanded **4l–o** in varying yields and ratios (Table 2, Entries 1–4). In the ether-tethered substrates, the isolation of ring-retained in addition to ring-expanded products was also observed upon homologation (Table 2, Entries 5–8). Thus, exploring diols **5l–o** we found that two domino products, **7** and **8l–o**, were formed in each case investigated along with their precursor, tricyclic ene–acetal **6l–o** (half-cascade). Even though the oxonium pathway (heteroatom promoted anchimerically assisted deplumbation) leading to **7** was expected to be severely compromised as the tether length increases, rather mixed results were obtained. Again, the interrupted cascade sequence in water (domino conditions D) under microwave irradiation occurs rapidly to afford cleanly **2l–o**

Table 2. Orienting experiments for modular construction of oxygen heterocycles.

Entry	Domino product yield [%] (D/E)[a]	Substrate	(A/B/C)[b] Domino product yield [%]	
				
1	**2l** (91/63)	**1l** R = $CH(Et)_2$	**3** (9/9/16)	**4l** (43/45/39)
2	**2m** (89/57)	**1m** R = CH(Me)Pr	**3** (25/15/20)	**4m** (35/33/31)
3	**2n** (89/60)	**1n** R = Cyclohexyl	**3** (16/7/18)	**4n** (35/41/37)
4	**2o** (73/59)	**1o** R = Cyclopropyl	**3** (22/32/28)	**4o** (43/38/36)
				
5	**6l** (86/73)	**5l** R = Bn	**7** (42/41/39)	**8l** (45/37/39)
6	**6m** (82/70)	**5m** R = MOM	**7** (60/58/55)	**8m** (22/28/24)
7	**6n** (88/48)	**5n** R = BOM	**7** (27/25/26)	**8n** (56/44/42)
8	**6o** (89/63)	**5o** R = Allyl	**7** (53/47/45)	**8o** (26/25/24)

[a] Methods D, E: The substrate (1.0 mmol) and $Pb(OAc)_4$ (1.2 mmol) were heated in a microwave for 5–10 min at 60 °C; in 1 mL of PhMe (D) or in 1 mL of H_2O (E). [b] Methods, A, B, C: reactions conducted with $Pb(OAc)_4$ (2.4 mmol) and the diol substrate (1.0 mmol) in AcOH (1 mL). Method A: room temperature for 12–15 h; method B: microwave irradiation, 10 min at 60 °C; method C: conventional heating, 10 min at 60 °C.



Scheme 3.

and **6l**–**o** in good yields (see the Supporting Information for the ^{1}H NMR spectrum of the crude reaction mixture for **2l**).

We finally examined the path-discriminating ability of the C11 configuration on diols **18** and **21** (epimeric mixture at C11).[13] As in the lower homologue series,[2b] the oxonium path was disadvantaged in one of the two epimers where the stereocentre at the angular position is of the (*R*) configuration. Thus, diols **18** and **21** reacted by an oxonium path for their (C11*S*)-counterparts to furnish **20** and **23** (61 and 67%, respectively), whereas the contribution of their (C11*R*)-counterparts could not be elucidated (Scheme 3).[14] The (C11*S*/C11*R*) ratio was safely measured for half-cascade intermediates **19** and **22** (10:1 and 12:1, respectively) running the domino reaction in PhMe.

In summary, in the octaline diol series, in addition to the importance of the nature of the angular substituent (steric and entropic factors), solvent plays an important role on the balance between the competing pathways, whereas microwave acceleration allows cleaner transformations for the domino reactions than does conventional heating.

Conclusions

At the outset of this investigation, our goal was to develop a modular domino reaction in the octaline diol series, which could provide tuneable access to all the possible domino products (the half-cascade, ring-expanded and ring-retained domino products). The examples presented in this article indicate the wide range of substitution that is compatible with the process. The reaction course can be directed towards either of two distinct pathways or interrupted halfway through by the appropriate choice of the angular substituent, the length of the linking chain, the solvent or the domino promoter. In all cases investigated, microwave heating was found to be more desirable, occurring with a tenfold increase in rate relative to that observed with conventional heating (and a spectacular increase relative to room-temperature runs).

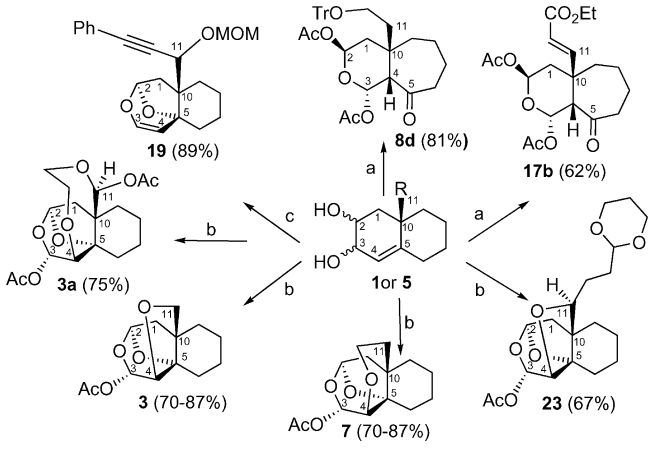


Figure 3. Competing domino paths: (a) "ring-expansion"; (b) "oxonium"; (c) hetero[4π+2π]. Reaction conditions: $Pb(OAc)_4$, MW 60 °C, 10 min in AcOH (for a, b), in PhMe or H_2O (for c).

Of special note is the possibility to use water as solvent under microwave irradiation;[15] up to 78% isolated yields of half-cascade products **2**, **6**, **10**, **13** and **16** were obtained (Table 1, Entries 1–7; Table 2, Entries 1–8). Taking into account the high level of molecular complexity attained in a one-pot transformation, the yields are remarkably high. As summarized in Figure 3, the process may be used for path-determined domino reactions starting from the same bicyclic diol framework **1** or **5** and by switching the reactivity pattern by varying the nature or the length of the linking R chain,[16] the solvent and the domino promoter.

Experimental Section

General: See ref.[2a,2b,2c]

Representative Examples for Microwave-Assisted Domino Transformations

Method B: A microwave tube was charged with a solution of a bicyclic unsaturated diol (1 mmol) in dry toluene (1 mL) and $Pb(OAc)_4$ (2.4 mmol), sealed with a septum and inserted inside a microwave cavity. The reaction mixture was magnetically stirred for 10 min (60 °C at 100 W). The tube was cooled to room temperature, and the mixture was diluted with Et_2O. Brine was added followed by $NaHCO_3$, and the organic layer was dried with $MgSO_4$, filtered, concentrated and purified by flash chromatography.

Method E: A microwave tube was charged with a solution of a bicyclic unsaturated diol (0.1 mmol) in water (0.1 mL) and $Pb(OAc)_4$ (1.2 mmol), sealed with a septum and inserted inside a microwave cavity. The reaction mixture was magnetically stirred for 5 min (60 °C, at 100 W). The tube was cooled to room temperature, and the mixture was diluted with Et_2O. The above procedure was then followed.

Microwave-Assisted Domino Transformations in AcOH following the Oxonium Path

Domino Product 3: Oxidative cleavage of diols **1e** (60 mg, 0.13 mmol) by using method B afforded **3** (30 mg, 86%). White solid. M.p. 81–82 °C (heptane). IR (film): $\tilde{\nu}$ = 2934, 2863, 1738, 1448, 1371, 1236, 1185, 1145, 1057, 945, 936, 845, 748 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.26 (m, 1 H), 1.34 (ddd, J = 5.0, 13.9, 17.8 Hz, 1 H), 1.48 (m, 1 H), 1.59 (m, 3 H), 1.90 (d, J = 12.9 Hz, 1 H), 2.09 (s, 3 H), 2.11 (d, J = 3.8 Hz, 2 H), 2.34 (dd, J = 6.7, 9.2 Hz, 1 H), 3.77 (d, J = 1.3 Hz, 1 H), 3.84 and 3.89 (AB_q, J = 8.7 Hz, 2 H), 5.53 (dd, J = 1.7, 3.7 Hz, 1 H), 6.96 (d, J = 1.3 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.6, 21.3, 21.8, 30.7, 32.0, 47.0, 50.8, 74.9, 82.8, 86.7, 90.8, 98.6, 170.0 ppm. MS (ESI, MeOH): m/z (%) = 277.1 (100) $[M + Na]^+$. HRMS (ESI): calcd. for $C_{13}H_{18}NaO_5$ 277.1052; found 277.1056. $C_{13}H_{18}O_5$ (254.12): calcd. C 61.40, H 7.14; found C 61.01, H 7.47.

Domino Product 3a: Oxidative cleavage of **1a** (60 mg, 0.25 mmol) by using method B afforded ring-retained domino product **3a** (66.8 mg, 75%) after flash chromatography (SiO_2; heptane/EtOAc, 4:1). Colourless oil. IR (film): $\tilde{\nu}$ = 2944, 2912, 1739, 1449, 1371, 1277, 1233, 1172, 1110, 1049, 1012, 938, 795, 735, 667 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.28 (m, 2 H), 1.48 (m, 1 H), 1.66 (m, 2 H), 1.94 (m, 1 H), 1.96 (dd, J = 1.9, 12.1 Hz, 1 H), 1.98 (m, 1 H), 2.00 (s, 3 H), 2.02 (s, 3 H), 2.30 (m, 2 H), 3.58 (d, J = 3.4 Hz, 1 H), 3.72 (dd, J = 2.9, 14.9 Hz, 1 H), 3.76 (dd, J = 3.2, 12.8 Hz, 1 H), 3.88 (dd, J = 3.6, 12.8 Hz, 1 H), 4.14 (dt, J = 3.4, 11.6 Hz, 1 H), 5.40 (d, J = 5.4 Hz, 1 H), 5.89 (d, J = 3.4 Hz, 1 H), 6.34 (s, 1

H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.9, 22.6, 28.9, 31.6, 31.8, 34.5, 46.1, 48.7, 69.3, 70.2, 85.3, 86.2, 92.6, 97.5, 100.5, 169.8, 170.4 ppm. MS (ESI, MeOH + CH_2Cl_2): *m*/*z* (%) = 379.1 (100) [M + Na]$^+$. HRMS (ESI, MeOH + CH_2Cl_2): calcd. for $C_{17}H_{24}NaO_8$ 379.1369; found 379.1354. $C_{17}H_{24}O_8$ (356.14): calcd. C 57.30, H 6.79; found C 56.61, H 6.89.

Domino Product 7: Oxidative cleavage of diols **5b** (37 mg, 0.16 mmol) by using method B afforded **7** (37.6 mg, 86%) after flash chromatography (SiO_2; heptane/EtOAc, 4:1). White solid. M.p. 132–133 °C (heptane). IR (film): $\tilde{\nu}$ = 2932, 2864, 1740, 1452, 1368, 1229, 1175, 1056, 994, 967, 932, 905, 751 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.41 (td, *J* = 1.2, 13.0 Hz, 1 H), 1.50 (m, 3 H, 2H6), 1.62 (m, 3 H), 1.96 (dd, *J* = 3.9, 10.2 Hz, 2 H), 2.02 (dd, *J* = 5.5, 14.3 Hz, 1 H), 2.08 (dd, *J* = 6.3, 13.0 Hz, 1 H), 2.12 (s, 3 H), 2.25 (d, *J* = 14.3 Hz, 1 H), 3.62 (d, *J* = 2.6 Hz, 1 H), 3.78 (ddd, *J* = 2.7, 5.5, 12.5 Hz, 1 H), 3.90 (dt, *J* = 2.7, 12.5 Hz, 1 H), 5.51 (d, *J* = 5.5 Hz, 1 H), 6.20 (d, *J* = 2.6 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.8, 21.3 (2 C), 29.1, 31.1, 38.4, 38.6, 46.8, 58.9, 78.3, 79.0, 90.6, 97.9, 170.1 ppm. MS (ESI, MeOH): *m*/*z* (%) = 291.1 (100) [M + Na]$^+$. HRMS (ESI): calcd. for $C_{14}H_{20}NaO_5$ 291.1208; found 291.1187.

Domino Product 11: Oxidative cleavage of diols **9a** (45 mg, 0.12 mmol) by using method B afforded **11** (30 mg, 79%) after flash chromatography (SiO_2; heptane/EtOAc, 4:1). Colourless oil. IR (film): $\tilde{\nu}$ = 2955, 2882, 1741, 1481, 1372, 1286, 1240, 1157, 1144, 1069, 1020, 973, 958, 937, 771, 729 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.50 (ddd, *J* = 4.8, 5.3, 10.1 Hz, 1 H), 1.62 (m, 2 H), 1.70 (m, 2 H), 1.81 (d, *J* = 13.6 Hz, 1 H), 2.02 (s, 3 H), 2.19 (td, *J* = 3.8, 14.4 Hz, 1 H), 2.66 (dd, *J* = 4.8, 13.6 Hz, 1 H), 3.78 (s, 1 H), 3.88 (m, 4 H), 3.95 and 4.05 (AB_q, *J* = 9.2 Hz, 2 H), 5.50 (d, *J* = 4.8 Hz, 1 H), 5.88 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.3, 21.3, 29.9, 30.6, 42.4, 55.9, 64.4, 64.9, 74.8, 83.3, 90.4, 91.0, 98.9, 109.1, 170.0 ppm. MS (ESI, MeOH + CH_2Cl_2): *m*/*z* (%) = 335.1 (100) [M + Na]$^+$. HRMS (ESI): calcd. for $C_{15}H_{20}NaO_7$ 335.1107; found 335.1082. $C_{15}H_{20}O_7$ (312.12): calcd. C 57.69, H 6.45; found C 56.79, H 6.61.

Domino Product 14: Oxidative cleavage of diols **12a** (38 mg, 0.13 mmol) by using method B afforded **14** (24 mg, 55%) and **13a** (10.3 mg, 27%). Data for **14**: Colourless oil. IR (film): $\tilde{\nu}$ = 2948, 2928, 2888, 1740, 1439, 1370, 1289, 1240, 1150, 1083, 1060, 1042, 1012, 966, 950, 853, 753, 722, 667 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.55 (d, *J* = 14.7 Hz, 1 H), 1.62 (m, 1 H, H1), 1.82 (dt, *J* = 3.8, 13.7 Hz, 1 H), 2.00 (m, 2 H), 2.09 (s, 3 H), 2.16 (d, *J* = 2.7 Hz, 2 H), 2.36 (td, *J* = 3.5, 14.7 Hz, 1 H), 3.80 (m, 1 H), 3.92 (m, 4 H), 3.82 and 4.10 (AB_q, *J* = 8.6 Hz, 2 H), 5.55 (t, *J* = 2.7 Hz, 1 H), 5.98 (d, *J* = 1.1 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.4, 29.1, 29.5, 39.0, 49.4, 51.6, 64.1, 64.5, 75.0, 81.9, 86.2, 90.7, 98.5, 108.0, 169.9 ppm. MS (ESI, MeOH + CH_2Cl_2): *m*/*z* (%) = 335.1 (100) [M + Na]$^+$. HRMS (ESI): calcd. for $C_{15}H_{20}NaO_7$ 335.1107; found 335.1133. $C_{15}H_{20}O_7$ (312.12): calcd. C 57.69, H 6.45; found C 56.14, H 6.33.

Microwave-Assisted Domino Transformations in AcOH following the Ring-Expansion Path

Domino Product 4k: Oxidative cleavage of diols **1k** (50 mg, 0.16 mmol) by using method B afforded **4k** (41 mg, 60%) and **2k** (9 mg, 18%; the intermediate half-cascade product). Data for **4k**: Colourless oil. IR (film): $\tilde{\nu}$ = 2955, 2932, 1750, 1723, 1370, 1226, 1146, 1051, 918, 742 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.22 (s, 6 H), 1.65 (m, 3 H), 1.82 (dd, *J* = 3.5, 14.5 Hz, 2 H), 1.95 (m, 3 H), 2.05 (s, 3 H), 2.07 (s, 3 H), 2.57 (dd, *J* = 4.8, 10.0 Hz, 2 H), 2.88 (d, *J* = 3.6 Hz, 1 H), 3.92 (s, 2 H), 4.23 and 4.36 (AB_q, *J* = 11.2 Hz, 2 H), 6.22 (t, *J* = 3.9 Hz, 1 H), 6.38 (d, *J* = 3.6 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.8, 21.5, 22.6, 24.6, 27.1 (2 C), 34.1, 35.6, 36.2, 38.2, 45.6, 52.6, 56.8, 67.0, 89.2, 91.1, 168.5, 169.0, 176.2, 210.4 ppm. MS (ESI, MeOH): *m*/*z* (%) = 455.1 (100) [M + Na]$^+$. HRMS (ESI): calcd. for $C_{20}H_{39}ClNaO_8$ 455.1449; found 455.1445.

Domino Product 8a: Oxidative cleavage of **5a** (50 mg, 0.19 mmol) by using method B afforded ring-expanded domino product **8a** (44.2 mg, 61%) after flash chromatography (SiO_2; heptane/EtOAc, 4:1). Colourless oil. IR (film): $\tilde{\nu}$ = 2931, 2887, 1753, 1715, 1683, 1429, 1368, 1217, 1140, 1098, 1056, 1008, 946, 913, 873, 747, 666 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.74 (m, 4 H), 1.76 (dd, *J* = 3.1, 14.1 Hz, 1 H), 1.85 (m, 3 H), 1.96 (dd, *J* = 4.4, 14.6 Hz, 1 H), 2.02 (s, 6 H), 2.08 (dd, *J* = 5.2, 14.6 Hz, 1 H), 2.50 (dd, *J* = 4.8, 9.4 Hz, 2 H), 2.92 (d, *J* = 3.9 Hz, 1 H), 3.74 (m, 2 H), 3.88 (m, 2 H), 4.85 (t, *J* = 4.7 Hz, 1 H), 6.21 (dd, *J* = 3.1, 6.4 Hz, 1 H), 6.35 (d, *J* = 3.8 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.0, 21.1, 23.4, 23.8, 34.6, 37.2, 38.2, 41.9, 45.6, 56.7, 64.6, 64.8, 90.1, 91.0, 101.5, 168.7, 169.2, 208.8 ppm. MS (ESI, MeOH): *m*/*z* (%) = 393.1 (100) [M + Na]$^+$. HRMS (ESI): calcd. for $C_{18}H_{26}NaO_8$ 393.1525; found 393.1518. $C_{18}H_{26}O_8$ (370.16): calcd. C 58.37, H 7.08; found C 54.42, H 6.41.

Domino Product 8b: Oxidative cleavage of diols **5d** (70 mg, 0.15 mmol) by using method B afforded **8d** (71.2 mg, 81%). Colourless oil. IR (film): $\tilde{\nu}$ = 3057, 3022, 2930, 2864, 1754, 1685, 1596, 1489, 1448, 1368, 1219, 1144, 1102, 1059, 954, 923, 748, 706, 632 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.29 (m, 4 H), 1.55 (dd, *J* = 6.1, 14.2 Hz, 2 H), 1.66 (d, *J* = 4.1 Hz, 1 H), 1.71 (m, 4 H), 2.00 (s, 3 H), 2.06 (m, 2 H), 2.08 (s, 3 H), 2.58 (t, *J* = 4.9 Hz, 2 H), 2.89 (d, *J* = 3.5 Hz, 1 H), 3.25 (d, *J* = 6.8 Hz, 1 H), 6.21 (d, *J* = 3.2, 5.9 Hz, 1 H), 6.41 (d, *J* = 4.1 Hz, 1 H), 7.30 (m, 9 H), 7.45 (m, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.1 (2 C), 23.2, 23.8, 35.2, 36.8, 37.7, 38.1, 45.6, 57.4, 59.2, 87.2, 89.9, 90.8, 127.1 (3 C), 127.8 (6 C), 128.5 (6 C), 143.9 (3 C), 168.7, 169.0, 208.9 ppm. MS (ESI; MeOH + CH_2Cl_2): *m*/*z* (%) = 593.2 (100) [M + Na]$^+$. HRMS (ESI, MeOH + CH_2Cl_2): calcd. for $C_{35}H_{38}NaO_7$ 593.2515; found 593.2503. $C_{35}H_{38}O_7$ (570.26): calcd. C 73.66, H 6.71; found C 70.14, H 6.52.

Domino Product 8f: Oxidative cleavage of diols **5f** (45 mg, 0.14 mmol) by using method B afforded **8f** (43.6 mg, 71%). Colourless oil. IR (film): $\tilde{\nu}$ = 2978, 2936, 1732, 1630, 1367, 1303, 1243, 1214, 1177, 1122, 1141, 1003, 940, 728 cm^{-1}. ^{1}H NMR (300 MHz): δ = 1.63 (m, 2 H), 1.80 (dd, *J* = 6.0, 14.3 Hz, 1 H), 1.88 (m, 3 H), 1.92 (m, 2 H), 2.07 (s, 2 H), 2.08 (s, 3 H), 2.22 (q, *J* = 6.5 Hz, 2 H), 2.59 (m, 2 H), 2.91 (d, *J* = 3.7 Hz, 1 H), 4.43 (m, 2 H), 6.31 (dd, *J* = 3.4, 5.7 Hz, 1 H), 6.43 (d, *J* = 4.2 Hz, 1 H), 7.45 (td, *J* = 1.2, 7.4 Hz, 2 H), 7.57 (m, 1 H), 8.0 (m, 2 H) ppm. ^{13}C NMR (125 MHz): δ = 21.1 (2 C), 23.2, 23.9, 35.2, 36.6, 36.8, 37.4, 45.5, 57.5, 60.4, 89.8, 90.6, 128.5 (2 C), 129.5 (2 C), 129.9, 133.2, 166.4, 168.7, 169.1, 208.4 ppm. MS (ESI, MeOH): *m*/*z* (%) = 455.1 (100) [M + Na]$^+$. HRMS (ESI): calcd. for $C_{23}H_{28}NaO_8$ 455.1682; found 455.1679. $C_{23}H_{28}O_8$ (432.17): calcd. C 63.88, H 6.53; found C 55.67, H 5.51.

Domino Product 8g: Oxidative cleavage of diols **5g** (26 mg, 0.09 mmol) by using method B afforded **8g** (29.7 mg, 81%). Colourless oil. IR (film): $\tilde{\nu}$ = 2931, 2864, 2828, 1749, 1683, 1450, 1370, 1219, 1190, 1126, 1056, 1008, 956, 923 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.59 (ddd, *J* = 3.7, 10.7 Hz, 1 H), 1.70 (dd, *J* = 6.1, 14.2 Hz, 2 H), 1.80 (d, *J* = 3.4 Hz, 1 H,), 1.85 (m, 4 H), 2.07 (s, 3 H), 2.08 (s, 3 H), 2.11 (m, 2 H), 2.55 (m, 2 H), 2.84 (d, *J* = 3.8 Hz, 1 H), 3.43 (s, 3 H), 4.00 (AB_q, 2 H), 4.26 (dt, *J* = 2.4, 7.3 Hz, 2 H), 6.27 (dd, *J* = 3.2, 6.0 Hz, 1 H), 6.38 (d, *J* = 3.8 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.1 (2 C), 23.2, 23.8,

35.1, 36.6 (2 C), 37.5, 45.6, 57.3, 59.4, 60.3, 69.8, 89.7, 90.6, 168.7, 169.1, 170.1, 208.4 ppm. MS (ESI, MeOH): *m/z* (%) = 423.1 (100) $[M + Na]^+$. HRMS (ESI): calcd. for $C_{19}H_{28}NaO_9$ 423.1631; found 423.1633. $C_{19}H_{28}O_9$ (400.17): calcd. C 56.99, H 7.05; found C 60.13, H 7.66.

Domino Product 8i: Oxidative cleavage of diols **5i** (40 mg, 0.14 mmol) by using method B afforded **8i** (41.3 mg, 73%) after flash chromatography (SiO_2; heptane/EtOAc, 4:1). Colourless oil. IR (film): $\tilde{\nu}$ = 2928, 2862, 1758, 1725, 1671, 1579, 1446, 1400, 1370, 1262, 1210, 1194, 1172, 1045, 1017, 990, 884, 870, 834, 772, 745 cm^{-1}. ^1H NMR (500 MHz): δ = 0.78 (m, 3 H), 0.90 (m, 3 H), 1.51 (dq, *J* = 4.3, 7.8 Hz, 2 H), 1.69 (d, *J* = 6.0 Hz, 2 H), 1.73 (d, *J* = 3.4 Hz, 2 H), 1.77 (m, 3 H), 2.00 (s, 3 H), 2.01 (s, 3 H), 2.50 (m, 2 H), 2.80 (d, *J* = 3.9 Hz, 1 H), 4.10 (m, 2 H), 6.21 (dd, *J* = 3.4, 6.0 Hz, 1 H), 6.33 (d, *J* = 3.8 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 8.5 (2 C), 12.7, 21.1 (2 C), 23.2, 23.8, 35.1, 36.6, 36.8, 37.5, 45.5, 57.4, 59.9, 89.8, 90.7, 168.7, 169.1, 174.7, 208.5 ppm. MS (ESI, MeOH): *m/z* (%) = 419.2 (100) $[M + Na]^+$. HRMS (ESI): calcd. for $C_{20}H_{28}NaO_8$ 419.1682; found 419.1702. $C_{20}H_{28}O_8$ (396.18): calcd. C 60.59, H 7.12; found C 60.19, H 7.03.

Domino Product 17a: Oxidative cleavage of diols **15a** (25 mg, 0.13 mmol) by using method B afforded **17a** (26 mg, 67%). Colourless oil. IR (film): $\tilde{\nu}$ = 2932, 2860, 2360, 1755, 1690, 1371, 1222, 1050, 956, 925 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.46–1.54 (m, 2 H), 1.71–1.83 (m, 4 H), 1.92 (dd, *J* = 13.9, 2.7 Hz, 1 H), 2.04 (s, 3 H), 2.08 (s, 3 H), 2.12–2.15 (m, 1 H), 2.50 (ddd, *J* = 3.2, 6.4, 13.8 Hz, 1 H), 2.63 (ddd, *J* = 3.6, 12.2, 13.5 Hz, 1 H), 3.23 (d, *J* = 3.8 Hz, 1 H), 5.08 (d, *J* = 17.7 Hz, 1 H), 5.25 (d, *J* = 11.1 Hz, 1 H), 5.84 (dd, *J* = 11.0, 17.7 Hz, 1 H), 6.23 (dd, *J* = 2.6, 6.7 Hz, 1 H), 6.55 (d, *J* = 3.8 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.0, 21.1, 23.9, 24.2, 38.3, 38.6, 41.7, 45.2, 53.5, 89.9, 91.4, 113.2, 145.3, 168.7, 169.2, 209.0 ppm. MS (ESI, MeOH): *m/z* (%) = 333.1 (100) $[M + Na]^+$. HRMS (ESI, MeOH + CH_2Cl_2): calcd. for $C_{16}H_{22}NaO_6$ 333.1314; found 333.1315.

Domino Product 17b: Oxidative cleavage of diols **15b** (27 mg, 0.10 mmol) by using method B afforded **17b** (24 mg, 62%). Colourless oil. IR (film): $\tilde{\nu}$ = 1754, 1713, 1445, 1368, 1224, 1196, 1098, 992, 923 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.31 (t, *J* = 7.2 Hz, 3 H), 1.49 (m, 1 H), 1.67 (m, 1 H), 1.76–1.86 (m, 2 H), 1.86–1.99 (m, 2 H), 1.99–2.14 (m, 2 H), 2.02 (s, 3 H), 2.09 (s, 3 H), 2.54 (t, *J* = 5.0 Hz, 2 H), 3.29 (d, *J* = 3.4 Hz, 1 H), 4.23 (q, *J* = 7.25 Hz, 2 H), 5.89 (d, *J* = 16.4 Hz, 1 H), 6.25 (q, *J* = 2.5 Hz, 1 H), 6.50 (d, *J* = 3.4 Hz, 1 H), 7.00 (d, *J* = 16.4 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2, 20.9, 21.0, 23.7, 24.3, 38.3, 38.6, 40.3, 45.0, 53.3, 60.8, 90.0, 90.1, 119.4, 154.4, 166.1, 168.7, 169.0, 207.7 ppm. MS (ESI, MeOH + CH_2Cl_2): *m/z* (%) = 405.1 (100) $[M + Na]^+$. HRMS (ESI): calcd. for $C_{19}H_{26}NaO_8$ 405.1525; found 405.1515.

Microwave-Assisted Domino Transformations in Water following the Hetero[4π+2π] Path

Domino Product 2g: Oxidative cleavage of diols **1g** (35 mg, 0.11 mmol) by using method E afforded **2g** (18.5 mg, 53%) after flash chromatography (SiO_2; heptane/EtOAc, 4:1). Colourless oil. IR (film): $\tilde{\nu}$ = 2930, 2860, 1622, 1454, 1378, 1202, 1108, 1021, 981, 799, 780, 730, 695 cm^{-1}. ^1H NMR (300 MHz): δ = 1.32 (m, 2 H), 1.40 (m, 2 H), 1.44 (m, 2 H), 1.82 (ddd, *J* = 5.5, 8.4, 12.8 Hz, 1 H), 1.92 (m, 1 H), 1.97 (m, 1 H), 2.15 (m, 1 H), 3.55 (m, 1 H), 3.66 (m, 1 H), 4.60 (s, 2 H), 4.76 (m, 2 H), 5.62 (d, *J* = 5.7 Hz, 1 H), 6.20 (d, *J* = 6.3 Hz, 1 H), 7.30 (m, 5 H) ppm. ^{13}C NMR (125 MHz): δ = 20.2, 21.2, 29.3, 29.6, 48.3, 51.0, 65.8, 69.8, 82.1, 94.2, 99.2, 110.4, 127.1, 127.3 (2 C), 128.4 (2 C), 137.9, 139.8 ppm. MS (ESI, MeOH): *m/z* (%) = 339.2 (100) $[M + Na]^+$. HRMS (ESI): calcd. for $C_{19}H_{24}NaO_4$ 339.1572; found 339.1578.

Domino Product 2n: Oxidative cleavage of **1n** (31 mg, 0.10 mmol) by using method E afforded **2n** (18.5 mg, 60%) after flash chromatography (SiO_2; heptane/EtOAc, 4:1). Colourless oil. IR (film): $\tilde{\nu}$ = 2932, 2856, 1731, 1628, 1449, 1215, 1178, 1057, 939 cm^{-1}. ^1H NMR (300 MHz): δ = 1.32 (m, 3 H), 1.36 (m, 3 H), 1.53 (m, 3 H), 1.70 (m, 3 H), 1.84 (m, 2 H), 1.97 (m, 2 H), 2.15 (d, *J* = 14.0 Hz, 1 H), 2.27 (tt, *J* = 3.5, 11.0 Hz, 1 H), 4.18 (q, *J* = 11.2 Hz, 2 H), 4.72 (d, *J* = 6.2 Hz, 1 H), 5.64 (d, *J* = 5.5 Hz, 1 H), 6.17 (d, *J* = 6.2 Hz, 1 H) ppm. ^{13}C NMR (75 MHz): δ = 20.7, 21.2, 29.3, 29.7, 31.7, 48.7, 51.7, 68.3, 73.8, 82.3, 99.4, 110.0, 127.5, 128.4, 138.4, 139.4 ppm. MS (ESI, MeOH): *m/z* (%) = 329.1 (100) $[M + Na]^+$. HRMS (ESI): calcd. for $C_{18}H_{26}NaO_3$ 329.1729; found 329.1720.

Domino Product 6a: Oxidative cleavage of **5a** (30 mg, 0.12 mmol) by using method E afforded **6a** (14.8 mg, 50%) after flash chromatography (SiO_2; heptane/EtOAc, 4:1). Colourless oil. IR (film): $\tilde{\nu}$ = 2934, 1629, 1212, 1058, 1024, 928, 792, 782, 722 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.20 (m, 1 H), 1.40 (m, 3 H), 1.48, (m, 2 H), 1.63 (td, *J* = 3.1, 13.5 Hz, 1 H), 1.82 (dd, *J* = 4.6, 14.2 Hz, 1 H), 1.91 (dd, *J* = 5.6, 13.9 Hz, 3 H), 2.19 (d, *J* = 14.1 Hz, 1 H), 3.76 (m, 2 H), 3.90 (m, 2 H), 4.68 (d, *J* = 6.1 Hz, 1 H), 4.79 (t, *J* = 5.0 Hz, 1 H), 5.60 (d, *J* = 5.7 Hz, 1 H), 6.11 (d, *J* = 6.1 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.6, 21.1, 29.3, 32.1, 34.1, 48.1, 50.0, 64.5, 64.6, 82.1, 90.5, 100.0, 109.8, 139.6 ppm. $C_{14}H_{20}O_4$ (252.13): calcd. C 66.65, H 7.99; found C 66.19, H 7.65.

Domino Product 6j: Oxidative cleavage of **5j** (45 mg, 0.14 mmol) by using method E afforded **6j** (28.2 mg, 63%) after flash chromatography (SiO_2; heptane/EtOAc, 4:1). Colourless oil. IR (film): $\tilde{\nu}$ = 2932, 2857, 1729, 1630, 1451, 1246, 1212, 1172, 1058, 943, 793, 722 cm^{-1}. ^1H NMR (300 MHz): δ = 1.24 (m, 3 H), 1.38 (m, 3 H), 1.53 (m, 3 H), 1.766 (m, 3 H), 1.76 (m, 3 H), 1.90 (m, 3 H), 1.96 (m, 3 H), 2.13 (dd, *J* = 1.0, 13.8 Hz, 1 H), 2.26 (tt, *J* = 3.6, 11.2 Hz, 1 H), 4.02 (dt, *J* = 7.4, 11.0 Hz, 1 H), 4.14 (ddd, *J* = 5.8, 7.9, 11.0 Hz, 1 H), 4.74 (d, *J* = 6.0 Hz, 1 H), 5.66 (d, *J* = 5.5 Hz, 1 H), 6.17 (d, *J* = 6.0 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.7, 21.1, 25.4, 25.7, 28.7, 29.0, 29.2, 31.6, 43.2, 48.6, 51.6, 62.1, 82.2, 99.4, 109.8, 139.6, 176.1 ppm. MS (ESI, MeOH): *m/z* (%) = 343.2 (100) $[M + Na]^+$. HRMS (ESI): calcd. for $C_{19}H_{28}NaO_4$ 343.1885; found 343.1869.

Domino Product 10c: Oxidative cleavage of **9c** (30 mg, 0.10 mmol) by using method E afforded **10c** (20.9 mg, 70%) after flash chromatography (SiO_2; heptane/EtOAc, 4:1). Colourless oil. IR (film): $\tilde{\nu}$ = 2928, 2883, 1627, 1465, 1440, 1388, 1346, 1311, 1291, 1255, 1241, 1197, 1148, 1106, 1088, 1037, 945, 925, 881, 817, 774 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.59 (d, *J* = 13.8 Hz, 1 H, H1), 1.70 (m, 3 H), 1.82 (m, 2 H), 2.01 (dd, *J* = 3.5, 12.4 Hz, 1 H), 2.40 (dd, *J* = 5.8, 13.8 Hz, 1 H), 3.36 (s, 3 H), 3.83 and 4.02 (AB_q, *J* = 9.4 Hz, 2 H), 3.90 (m, 4 H), 4.58 (q, *J* = 6.1 Hz, 2 H), 4.92 (d, *J* = 6.1 Hz, 1 H), 5.60 (d, *J* = 5.7 Hz, 1 H), 6.23 (d, *J* = 6.1 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.2, 30.4, 31.3, 41.6, 55.5, 60.6, 63.6, 65.1, 70.5, 84.2, 96.7, 99.7, 109.5, 110.4, 140.6 ppm. MS (ESI, MeOH + CH_2Cl_2): *m/z* (%) = 321.1 (100) $[M + Na]^+$. HRMS (ESI): calcd. for $C_{15}H_{22}NaO_6$ 321.1314; found 321.1332. $C_{15}H_{22}O_6$ (298.14): calcd. C 60.39, H 7.43; found C 60.92, H 7.44.

Domino Product 10d: Oxidative cleavage of diols **9d** (30 mg, 0.09 mmol) by using method E afforded **10d** (23 mg, 77%) after flash chromatography (SiO_2; heptane/EtOAc, 4:1). Colourless oil. IR (film): $\tilde{\nu}$ = 2959, 2930, 2873, 1725, 1626, 1479, 1460, 1396, 1363, 1280, 1197, 1142, 1114, 1089, 1032, 966, 945, 928, 879, 803, 752,

725 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.22 (s, 9 H), 1.68 (dt, J = 4.0, 13.4 Hz, 2 H), 1.73 (d, J = 13.9 Hz, 2 H), 1.84 (m, 2 H), 2.05 (m, 1 H), 2.48 (dd, J = 5.8, 13.9 Hz, 1 H), 3.90 (m, 2 H), 4.00 (m, 2 H), 4.36 and 4.56 (AB_q, J = 11.3 Hz, 2 H), 4.79 (d, J = 6.1 Hz, 1 H), 5.64 (d, J = 5.7 Hz, 1 H), 6.23 (d, J = 6.1 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.0, 27.3 (3 C), 30.1, 31.0, 38.6, 41.8, 59.9, 63.6, 65.1, 67.2, 83.6, 99.6, 108.8, 109.7, 141.0, 177.8 ppm. MS (ESI, MeOH + CH_2Cl_2): m/z (%) = 361.2 (100) $[M + Na]^+$. HRMS (ESI): calcd. $C_{18}H_{26}NaO_6Si$ 361.1227; found 361.1612.

Domino Product 13a: Oxidative cleavage of **12a** (50 mg, 0.17 mmol) by using method E afforded **13a** (42 mg, 65%) after flash chromatography (SiO_2; heptane/EtOAc, 4:1). Colourless oil. IR (film): $\tilde{\nu}$ = 2957, 2928, 2884, 1737, 1630, 1439, 1367, 1237, 1092, 1047, 996, 978, 944, 851, 771 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.56 (m, 2 H), 1.74 (dd, J = 4.2, 14.2 Hz, 1 H), 1.92 (dd, J = 3.2, 13.7 Hz, 2 H), 2.03 (m, 2 H), 2.07 (s, 3 H), 2.22 (d, J = 14.2 Hz, 1 H), 3.92 (m, 4 H), 4.30 and 4.41 (AB_q, J = 10.6 Hz, 2 H), 4.78 (d, J = 6.1 Hz, 1 H), 5.72 (d, J = 5.5 Hz, 1 H), 6.23 (d, J = 6.1 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.9, 27.9, 29.0, 37.7, 48.6, 55.1, 63.8, 64.5, 66.1, 79.8, 99.3, 107.7, 107.8, 140.5, 171.0 ppm. MS (ESI, MeOH + CH_2Cl_2): m/z (%) = 319.1 (100) $[M + Na]^+$. HRMS (ESI): calcd. for $C_{15}H_{20}NaO_6$ 319.1158; found 335.1147. $C_{15}H_{20}O_6$ (296.12): calcd. C 60.80, H 6.80; found C 58.87, H 6.61.

CCDC-708533 (for **8e**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): Procedures for the synthesis and characterization; 1D and 2D ^1H and ^{13}C NMR spectra for all new compounds.

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