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1,3- and 1,2-Carbo-Migration of 2-Vinylbicyclo[2.2.2]octenols: Facile and Concise Synthesis of Bicyclo[4.2.2]/[3.2.2] Skeleton by Two/One-Carbon Ring Expansion

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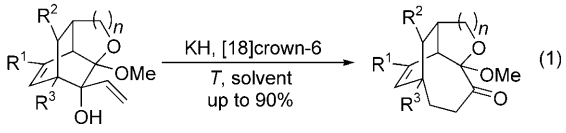
Dedicated to Professor Ryoji Noyori on the occasion of his 70th birthday

Abstract: The synthesis of a series of bicyclo[4.2.2]octenones and bicyclo[3.2.2]heptenones by 1,3- or 1,2-migration reaction from 2-vinylbicyclo[2.2.2]octenols is reported. These ring-expansion reactions were accomplished under basic or neutral conditions. Whether 1,3- or 1,2-migration takes place depends on endo- or exocyclic olefin displacement in the substrates.

Keywords: bicyclic compounds · carbocycles · ene reaction · rearrangement · ring expansion

Introduction

The carbobicyclic structure is one of the most interesting moieties in the skeletons of natural products. Among them, the bicyclo[2.2.2]octane skeleton was considered the most accessible owing to its facile construction by the Diels–Alder reaction of cyclohexadiene derivatives with various dienophiles.[1] The ring-expansion reaction of the bicyclo[2.2.2]octane skeleton could potentially provide a facile route to the formation of counterparts with larger cyclic systems that were considered synthetically challenging.[2,3] Previously, we reported a practical method to synthesize bicyclo[4.2.2]dec-7-en-4-one derivatives through a two-carbon ring-expansion of 2-vinylbicyclo[2.2.2]octenols by anionic [1,3] rearrangement[4] [Eq. (1)]. Although there have been extensive studies on 1,3-migration to generate a two-carbon ring expansion,[5,6] most of them cannot be easily applied to general organic synthesis. In our previous report, the reactions, which were carried out under basic conditions, gave good to excellent yields of the ring-enlarged 1,3-rearranged products.



(1)

This methodology was proven to be synthetically useful when we applied the strategy to synthesize the natural product (±)-pallescensin B. This furanosesquiterpenoid compound, which bears a rare bicyclo[4.2.2]decane system, was constructed by use of anionic 1,3-rearrangement of a 2-vinylbicyclo[2.2.2]octenol derivative as the key step.[7] On the basis of the above result, we explored the scope and limitation of this type of ring-expansion reaction; the effect of substituents on the reaction was investigated. We found that, besides basic conditions, neutral conditions that involve heating the reaction mixture in a sealed tube could also afford the same type of 1,3-rearranged products. Interestingly, we discovered that the endocyclic olefin plays an important role in this ring-expansion reaction; in contrast, substrates with a double bond displaced to the exocyclic position on the bicyclo[2.2.2]octenone derivatives underwent 1,2-rearrangement to give bicyclo[3.2.2]nonenones. We report herein our findings.

Results and Discussion

Ring Expansion by 1,3-Migration

As shown in Table 1, several cases of the ring-expansion reaction of 2-vinylbicyclo[2.2.2]octenols **1** under basic condi-

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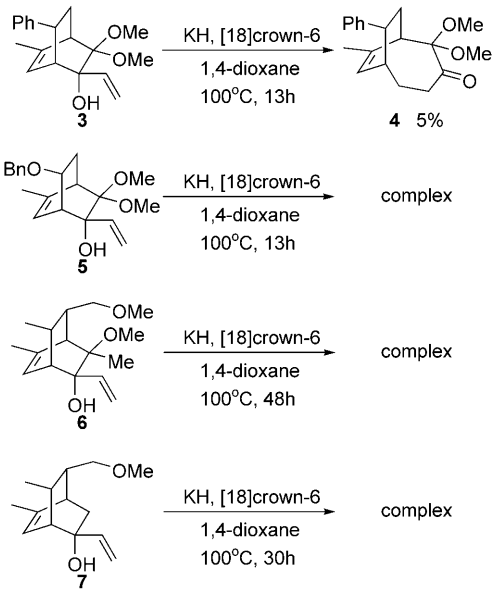
Table 1. Ring-expansion reaction of 2-vinylbicyclo[2.2.2]octenols **1** by anionic 1,3-migration.[a]

1a–k **2a–k**

Entry	R^1	R^2	R^3	R^4	*n*	Solvent	*T* [°C]	*t* [h]	Product	Yield [%]
1	H	H	H	H	1	THF	RT	12	**2a**	76
2	Me	H	H	H	1	THF	RT	12	**2b**	73
3	H	Me	H	H	1	THF	RT	12	**2c**	90
4	H	Ph	H	H	1	THF	RT	12	**2d**	88
5	Me	Me	H	H	1	1,4-dioxane	80	50 min	**2e**	81
6	Me	Ph	H	H	1	1,4-dioxane	80	50 min	**2f**	53
7	Me	H	H	OMe	1	THF	RT	5	**2g**	77
8	Me	Ph	H	OMe	1	THF	RT	30 min	**2h**	90
9	Me	Me	Me	H	1	1,4-dioxane	80	4	**2i**	35
10	Me	H	H	H	2	1,4-dioxane	80	50 min	**2j**	70
11	Me	H	H	OMe	2	1,4-dioxane	55	1	**2k**	65

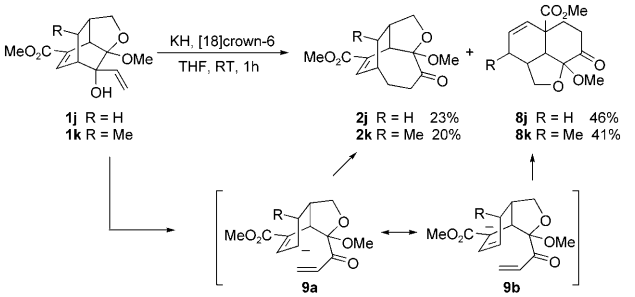
[a] Entries 1–8 and 10 were reported in reference [4]; spectral data for entries 9 and 11 can be found in the Experimental Section and Supporting Information.

tions are listed. Most of these transformations proceeded smoothly at room temperature or upon mild heating to give moderate to excellent yields of products **2**. Notably, more highly substituted substrates required higher reaction temperatures (**1e**, **1f**, and **1h**). In the case of **1i** (Table 1, entry 9), the dramatically decreased yield could be due to the installation of three methyl groups, of which remote steric effect caused the resultant **2i** to be obtained in low yield. Furthermore, compounds with a larger cyclic ketal linkage also needed heating during the reaction (Table 1, entries 10 and 11). To survey the role of the cyclic ketal function in the reaction, we next tried a series of substrates that lack the cyclic ketal linkage (Scheme 1). The results strongly imply the need for the cyclic ketal group, as substrates without this functional group afforded low yields or no desired products.



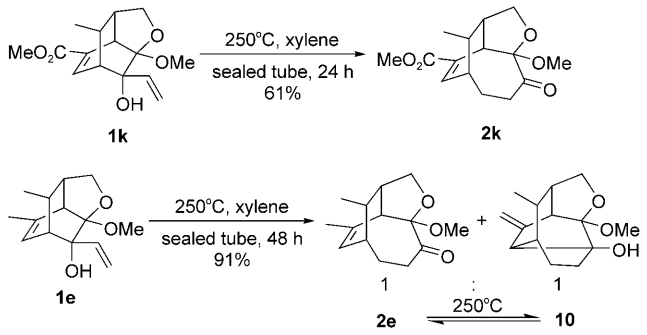
Scheme 1. Attempt at anionic 1,3-migration of substrates with no cyclic ketal group. Bn = benzyl.

Aside from the examples listed in Table 1, an unexpected result was found when substrates with the electron-withdrawing group CO_2Me were treated under the same basic conditions (Scheme 2). In the cases of **1j** and **1k**, 1,3-migration gave the minor products, whereas vinylogous retro-aldol–Michael addition ([3,3] rearrangement) yielded the major products. This result could be explained by the anion-stabilizing effect of the ester group to provide the anionic intermediate **9** with the canonical structures **9a** and **9b**; thus, the reaction proceeds through a stepwise mechanism and produced both ring-expansion and retro-aldol–Michael addition ([3,3] rearrangement) products. This phenomenon implies that the relative stability of the intermediate is the key point; as the two olefinic moieties are in *anti* positions,[13] which forbids the occurrence of the [3,3] sigmatropic process,[8a] the ester group in **1j** and **1k** could stabilize the anionic intermediate **9** by delocalization with longer lifetimes than their alkyl counterparts, thus making it possible for the relaxation of the initial boat geometry in **9** and leading to *cis*-decalin formation. This hypothesis was further proved by heating **1k** in xylene in a sealed tube at 250 °C; the exclusive formation of **2k** suggests that the same starting material could undergo reaction by an alternative pathway, probably through homolytic cleavage, to yield the 1,3-migration compound as the only product[8b] (Scheme 3).



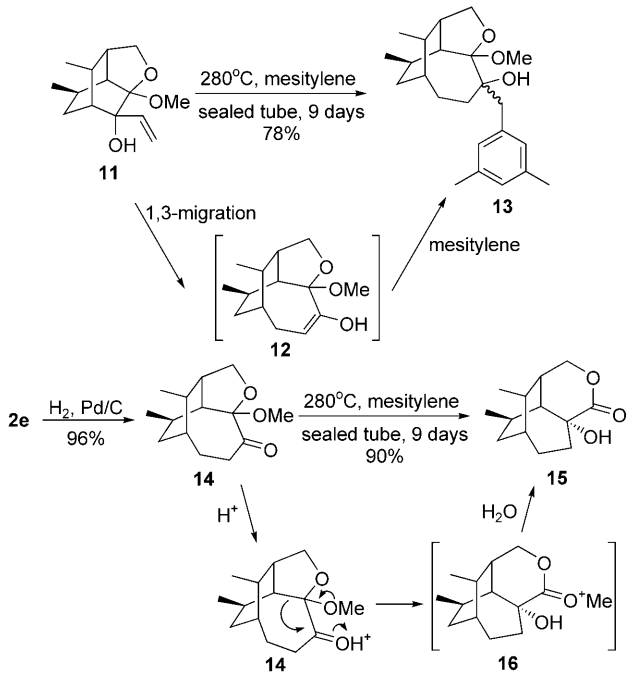
Scheme 2. 1,3-Migration and retro-aldol–Michael reaction of **1j** and **1k** to form products from the two resonance forms.

As neutral conditions were found to be applicable for the substrate with an electron-withdrawing ester group (Scheme 3), we next subjected alkylated substrate **1e** to the same reaction conditions. The reaction was found to give a high yield of a 1:1 mixture of the desired 1,3-migration product **2e** and compound **10**, which is proposed as a secondary product from **2e** through an intramolecular ene reaction.



Scheme 3. 1,3-Migration under neutral conditions.

The ratio of the mixture was shown to be the result of thermodynamic equilibrium at 250 °C by subjecting **2e** or **10** to the exact reaction conditions from which the 1:1 ratio of **2e** to **10** was obtained. To investigate the role of the endocyclic olefin, the reduced compound **11** from **1e** was heated in a sealed tube (Scheme 4). The reaction was found to be slug-



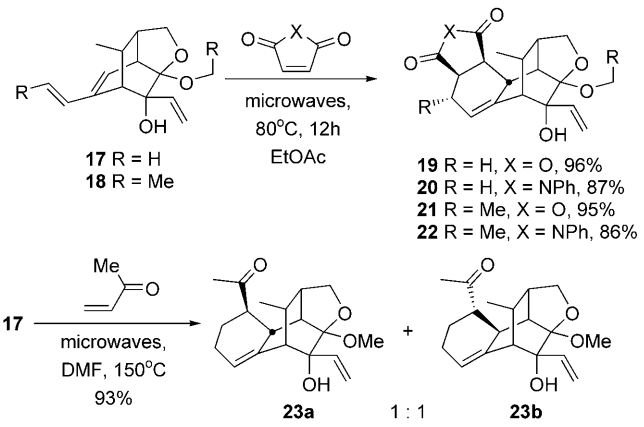
Scheme 4. Attempt at anionic 1,3-migration of substrates without an endocyclic olefin.

gish and required elongated reaction times of up to 9 days at 280 °C in mesitylene. A mixture of stereoisomers of **13** was obtained in a 3:1 ratio. Spectral characterization showed that 1,3-migration occurred with the participation of mesitylene. Although the mechanism is unclear, the structure of **13** suggests that after the ring expansion takes place, the enol form **12** probably undergoes a radical-type reaction with the solvent before returning to the keto form **14**. The possibility of **13** being a secondary product from the 1,3-migration product **14** was ruled out as the experimental result showed **15** as the only product, presumably from a rarely seen acid-catalyzed benzyl–benzylic acid type rearrangement.[9,10]

From the above experimental result, we can summarize the target 1,3-migration ring-expansion reaction as the following: 1) The steric effect of substituents installed on the 2-vinylbicyclo[2.2.2]octenol provides a small to moderate influence on the reaction. 2) The cyclic ketal linkage is crucial for the reaction. Increasing the ring size or removing the cyclic ether moiety would result in low yields or no observable products. An explanation for this observation could be that the extra fused ketal linkage retains the geometry of the intermediate, thus placing both ends of the diradical termini in close proximity, which facilitates the ring-closure process. 3) As the Woodward–Hoffmann rule indicates, a suprafacial [1,3] sigmatropic rearrangement is symmetrically forbidden.[11] The observed [1,3] migration would thus require a stepwise mechanism; therefore, the stability and lifetime of the intermediates would determine the reaction outcome. The endocyclic olefin provides an important electronic effect. The attachment of an ester significantly increases the relative stability of the anionic intermediate; thus, the alternative route of [3,3] rearrangement was instead found to be the major pathway. Saturation of the olefinic moiety would slow the reaction significantly, which suggests that the presence of a double bond would stabilize the reaction intermediate from the initial homolytic cleavage. This is in agreement with previous research stating the need of an activating group in this type of 1,3-migration.[6b] On the basis of these observations, we next investigated substrates with an olefin at the exocyclic position.

Ring Expansion by 1,2-Migration

To establish analogous substrates with an olefin in an exocyclic position to the bicyclo[2.2.2]octanol moiety, we made use of a second Diels–Alder reaction of compounds **17** and **18** with dienophiles (Scheme 5). A long reaction time was needed with conventional heating. However, microwave



Scheme 5. Diels–Alder reaction to generate an exocyclic olefin. DMF = *N*,*N*-dimethylformamide.

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conditions efficiently speeded up the reaction, and high yields of products were obtained stereospecifically for reactions with *N*-phenylmaleimide and maleic anhydride. The series of products **19**–**22** were structurally assigned by IR and NMR spectroscopy and mass spectrometry. X-ray diffraction was employed for **21** to determine its relative stereochemistry (Figure 1). On the other hand, two stereoisomers were obtained in a 1:1 ratio from the reaction of **17** with methyl vinyl ketone. The relative stereochemistry of **23a** and **23b** was assigned by spectral comparison with known analogues.[12]

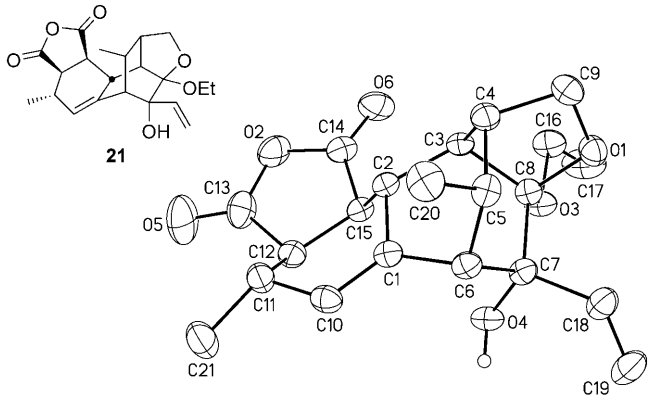


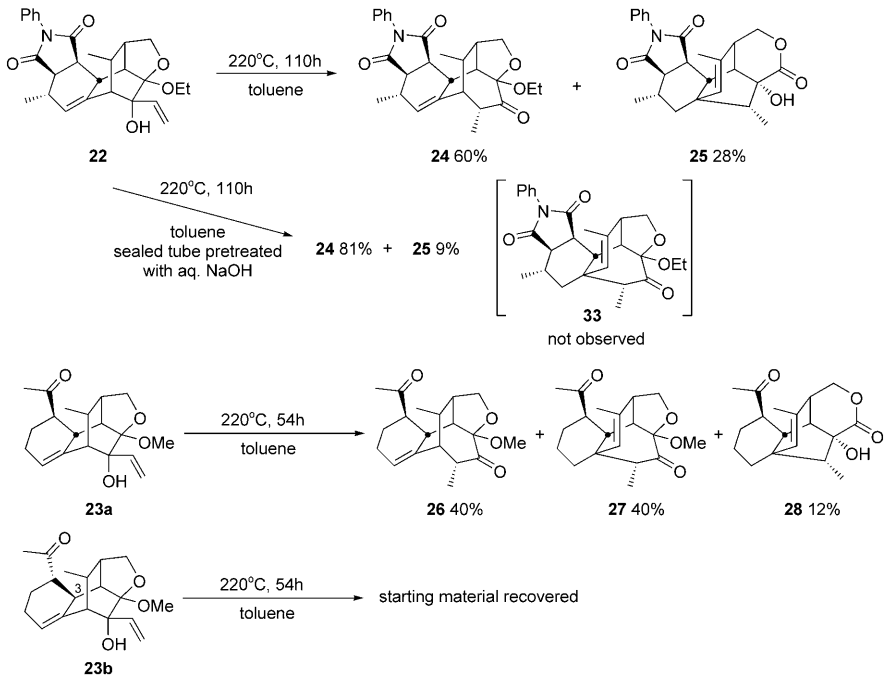
Figure 1. Structure and ORTEP diagram of **21**. Thermal ellipsoids are drawn at the 50% probability level.

At first, we subjected **22** to the thermal reaction at 220°C in a sealed tube; surprisingly, instead of 1,3-migration, the 1,2-migration product **24** was isolated along with by-product **25** (Scheme 6). For the reaction of **23a**, the 1,2-migration product **26** was obtained along with by-products **27** and **28**. Structural determination of the products was performed with IR and NMR spectroscopy, mass spectrometry, and X-ray diffraction see the Supporting Information. Product **28** is assumed to be a secondary product of **27** presumably derived from an acid-catalyzed benzyl–benzylic acid type rearrangement similar to the case of **15** (Scheme 4).

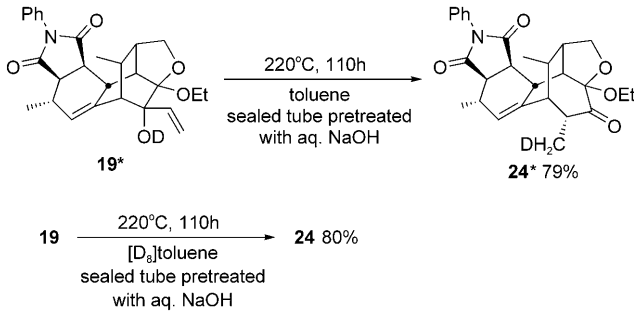
However, in the reaction of **22**, there was no observation of the precursor (**33**) of **25**; when we attempted to suppress the acid-catalyzed formation of **25** by pretreating the tube sequentially with aqueous NaOH and H_2O and then drying it in an oven, the yield of the primary product **24** significantly increased with **25** as a minor product. These contrasting results of obtaining bicyclo[3.2.2]nonenone derivatives from 1,2-migration with ring expansion were unexpected and are clearly related to the displacement of the original endocyclic olefin to the exocyclic position. On the other hand, **23b** was recovered under the same reaction conditions, which shows that the configuration of C3 has an important influence on the nearby geometry and disfavors the initial cleavage.

This intriguing outcome led us to perform a deuterium-labeling experiment (Scheme 7). The deuterium atom was transferred from the tertiary alcohol to the methyl group in the 1,2-migration product **24***. The hydrogen-transfer process was further proven to be intramolecular by heating unlabeled compound **22** in [D_8]toluene; the reaction yielded **24** exclusively without giving any deuterized product. On the basis of these observations, we propose a mechanism for the ring-expanding 1,2-migration (Scheme 8). The intermediate **32** is initially formed by a retro-ene reaction from thermolysis. Next, an intramolecular ene reaction proceeds with hydrogen abstraction from carbon a to the *exo* position of the right-hand olefin to form **24** with insertion of a one-carbon unit; this explains the displacement of deuterium in the labeling experiment. As for the by-product **25**, we imagine that it came from the common intermediate **32**, which also undergoes an intramolecular ene reaction but with hydrogen abstraction from carbon b to the *exo* olefin to yield **33**, which is prone to acid-catalyzed benzyl–benzylic acid type rearrangement to form **25**.

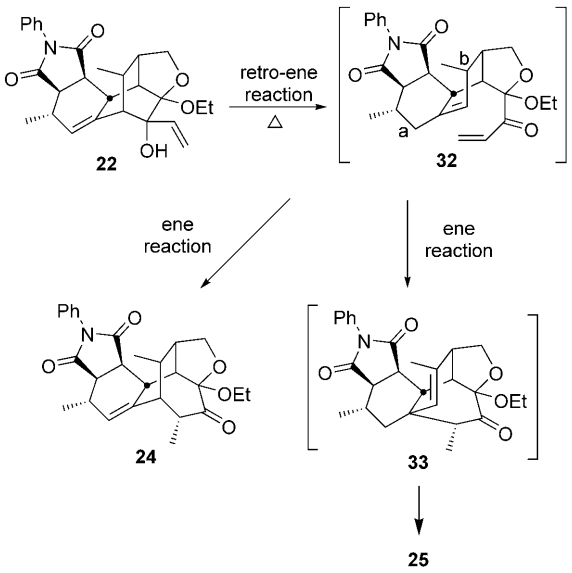
When the structures of the preliminary resultant compounds were determined, we then applied the same reaction conditions to **19**, **20**, and **21** (Table 2). Good yields of 1,2-migration compounds were obtained. This result reaffirms the



Scheme 6. 1,2-Migration of **22** and **23** under sealed-tube conditions.

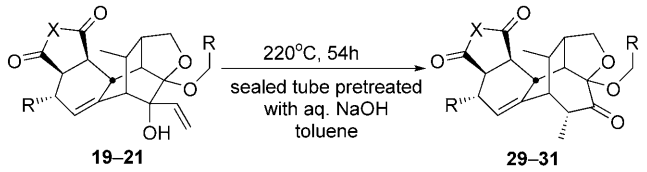


Scheme 7. Deuterium-labeling experiment for 1,2-migration.



Scheme 8. Proposed mechanism for the formation of **24** and **33**.

Table 2. Examples of 1,2-migration.



Starting material	R	X	Product	Yield [%]
19	H	O	**29**	75
20	H	NPh	**30**	82
21	Me	O	**31**	78

effect of the exocyclic olefin on the bicyclo[2.2.2]octanol moiety in this ring-expansion reaction with one-carbon-unit insertion.

Conclusions

In summary, we have reported a novel ring-expansion reaction with a 2-vinylbicyclo[2.2.2]octenol system to yield bicyclo[4.2.2]decenone and bicyclo[3.2.2]nonenone moieties with complete control by manipulating the endo/exocyclic position of the olefin in the 2-vinylbicyclo[2.2.2]octenol system. The reactions gave moderate to excellent yields of products and provide an efficient and effective route to the synthesis of less easily accessible bicyclic systems from bicyclo[2.2.2]octenones, which can be easily obtained from well-developed masked *o*-benzoquinone chemistry.[1d,e,13]

Experimental Section

Details for the preparation of the 2-vinylbicyclo[2.2.2]octenols used as starting materials in this study are reported in our previous publication.[13]

General procedure for anionic 1,3-migration: Anhydrous THF (5 mL), the 2-vinylbicyclo[2.2.2]octenol (0.4 mmol, 1 equiv, in 2 mL THF), and [18]crown-6 (2 mmol, 5 equiv, in 3 mL THF) were added successively to prewashed KH (2 mmol, 5 equiv). The reaction mixture was then stirred at the required temperature and tracked by TLC. Saturated aqueous NH_4Cl was added to quench the reaction, and the aqueous layer was extracted with ethylamine and concentrated to yield the crude product.

General procedure for reaction in a sealed tube: The 2-vinylbicyclo-[2.2.2]octenol (0.28 mmol) was dissolved in toluene (3 mL) in a pyrex glass tube (10 cm × 1.5 cm). The tube was then sealed under vacuum and placed in a high-temperature oven at 220 °C for the appropriate time. The solvent was removed by rotary evaporation to give the crude product.

2i: *rac*-(1*R*,4*R*,8*S*,11*R*,12*R*)-4-Methoxy-1,10,12-trimethyl-3-oxatricyclo[6.3.1.0^{4,11}]didec-9-en-5-one: Yellowish oil. IR (neat): $\tilde{\nu}$ = 2959 (m), 2936 (m), 1718 (s), 1445 (m), 1455 (m), 1381 (w), 1295 (w), 1174 (m), 1125 cm^{-1} (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (s, 3H), 0.98 (d, J = 7.6 Hz, 3H), 1.65–1.73 (m, 1H), 1.70 (d, J = 1.6 Hz, 3H), 1.87–1.92 (m, 1H), 2.01–2.06 (m, 1H), 2.16–2.22 (m, 2H), 2.40 (s, 1H), 3.23 (s, 3H), 3.33–3.41 (m, 1H), 3.87 (ABq, J = 8 Hz, 2H), 5.52 ppm (app d, J = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.4 (CH_3), 20.4 (CH_3), 23.5 (CH_3), 31.0 (CH_2), 34.4 (CH_2), 35.2 (CH), 41.1 (CH), 47.8 (C), 52.1 (CH_3), 62.3 (CH), 82.2 (CH_2), 114.3 (C), 126.3 (CH), 131.5 (C), 209.4 ppm (C); MS (EI): m/z (%) = 250 $[M]^+$ (2), 232 (14), 218 (23), 193 (100), 178 (9), 160 (10), 146 (19), 134 (43), 118 (36); HRMS (EI): m/z calcd for $C_{15}H_{22}O_3$: 250.1569; found: 250.1564.

2k: *rac*-(1*R*,5*R*,9*R*,10*R*)-1,5-Dimethoxy-11-methyl-6-oxatricyclo[7.3.1.0^{5,11}]tridec-11-en-4-one: Colorless liquid. IR (neat): $\tilde{\nu}$ = 2917 (s), 1716 (s), 1453 (s), 1212 (s), 1097(s), 947 (s), 913 (m), 845 (m), 770 cm^{-1} (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15–1.21 (m, 1H), 1.60 (t, J = 13.7 Hz, 1H), 1.77–1.99 (m, 4H), 2.17 (d, J = 1.3 Hz, 3H), 2.16–2.24 (m, 1H), 2.40–2.70 (m, 3H), 3.24 (s, 3H), 3.37 (s, 3H), 3.91–3.96 (m, 1H), 4.17–4.30 (m, 1H), 5.49 ppm (q, J = 1.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.0 (CH_3), 29.4 (CH_3), 31.6 (CH), 34.1 (CH_2), 36.8 (CH_2), 42.1 (CH_2), 49.5 (CH), 50.9 (CH_3), 51.0 (CH_3), 60.7 (CH_2), 76.4 (C), 104.6 (C), 129.2 (CH), 142.8 (C), 207.3 ppm (C); MS (EI): m/z (%) = 266 $[M]^+$ (5), 251 (4), 235 (5), 181 (100), 151 (59), 137 (35), 123 (56); HRMS (EI): m/z calcd for $C_{15}H_{22}O_4$: 266.1518; found: 266.1515.

5: *rac*-(1*S*,2*R*,4*R*,7*R*)-7-Benzyloxy-2-ethenyl-3,3-dimethoxy-5-methylbicyclo[2.2.2]oct-5-en-2-one: Colorless liquid. IR (neat): $\tilde{\nu}$ = 3558 (s), 2946 (s), 1447 (m), 1337 (m), 1174 (m), 1099 (s), 1075 (s), 997 cm^{-1} (m); ^{1}H NMR (400 MHz, [D]acetone): δ = 1.25 (app dt, J = 13.3, 3.3 Hz, 1H), 2.00 (d, J = 1.4 Hz, 3H), 2.32 (ddd, J = 13.3, 8.3, 2.7 Hz, 1H), 2.79–2.81 (m, 1H), 2.83 (dd, J = 6.0, 2.5 Hz, 1H), 3.04 (s, 3H), 3.35 (s, 3H), 3.36 (s, 3H), 4.15–4.17 (m, 1H), 4.54 (ABq, J = 12.0 Hz, 1H), 4.59 (ABq, J = 12.0 Hz, 1H), 5.17 (dd, J = 10.6, 2.7 Hz, 1H), 5.61 (dd, J = 17.2, 10.6 Hz, 1H), 5.85 (app d, J = 6.0 Hz, 1H) 6.42 (dd, J = 17.2, 10.6 Hz, 1H), 7.39–7.48 ppm (m, 5H); ^{13}C NMR (100 MHz, [D]acetone): δ = 21.4 (CH_3), 31.6 (CH_2), 45.1 (CH), 50.3 (CH_3), 52.3 (CH_3), 53.0 (CH), 70.8 (CH_2), 74.7 (CH), 78.5 (C), 106.4 (C), 112.7 (CH_2), 122.9 (CH), 128.4 (CH), 128.6 (2 × CH), 129.3 (2 × CH), 140.6 (C), 141.5 (CH), 142.3 ppm (C); MS (EI):

m/z (%) = 329 $[M-1]^+$ (26), 297 (29), 206 (74), 190 (100), 166 (50), 163 (42), 158 (78); HRMS (EI): *m/z* calcd for $C_{20}H_{26}O_4$: 330.1831; found: 330.1815.

6: *rac*-(1*S*,3*R*,4*R*,7*R*,8*R*)-3-Methoxy-8-methoxymethyl-3,5,7-trimethylbicyclo[2.2.2]oct-5-en-2-one: Colorless liquid. IR (neat): $\tilde{\nu}$ = 3037 (w), 2921 (s), 1729 (s), 1646 (w), 1452 (m), 1371 (m), 1196 (m), 1111 (s), 1053 (m), 846 cm^{-1} (w); ^1H NMR (400 MHz, $CDCl_3$): δ = 0.99 (d, *J* = 6.8 Hz, 3H), 1.23 (s, 3H), 1.38–1.43 (m, 1H), 1.79–1.85 (m, 1H), 1.87 (d, *J* = 1.7 Hz, 3H), 2.77 (d, *J* = 1.7 Hz, 1H), 2.81 (dd, *J* = 6.0, 1.5 Hz, 1H), 3.29 (s, 3H), 3.35 (s, 3H), 3.54 (dd, *J* = 9.0, 6.3 Hz, 1H), 3.71 (dd, *J* = 9.0, 8.7 Hz, 1H), 5.60 ppm (app d, *J* = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.6 (CH_3), 20.6 (CH_3), 21.1 (CH_3), 33.9 (CH), 45.8 (CH), 48.8 (CH), 50.3 (CH_3), 54.4 (CH), 58.6 (CH_3), 75.3 (CH_2), 76.1 (C), 118.1 (CH), 147.8 (C), 208.4 ppm (C); MS (EI): *m/z* (%) = 238 $[M]^+$ (1), 209 (92), 206 (100), 176 (15), 162 (11), 145 (29), 132 (69); HRMS (EI): *m/z* calcd for $C_{14}H_{22}O_3$: 238.1569; found: 238.1670.

10: *rac*-(3*R*,3a*R*,4a*R*,5*S*,7a*R*,7b*S*,8*S*)-7b-Methoxy-8-methyl-4-methyleneoctahydro-3,5-methanopentaleno[1,2-*b*]furan-7a(4*H*)-ol: Yellowish oil. IR (neat): $\tilde{\nu}$ = 3549 (b), 2951 (s), 2873 (m), 1674 (m), 1455 (m), 1361 (m), 1241 (m), 1069 (m), 886 cm^{-1} (m); ^1H NMR (400 MHz, $CDCl_3$): δ = 1.04 (d, *J* = 7.2 Hz, 3H), 1.38–1.47 (m, 2H), 1.69–1.77 (m, 1H), 2.14–2.26 (m, 3H), 2.41–2.50 (m, 2H), 2.65 (dd, *J* = 2.4, 10.0 Hz, 1H), 3.02 (dd, *J* = 2.4, 7.6 Hz, 1H), 3.36 (s, 3H, OMe), 3.88 (d, *J* = 8.4 Hz, 1H), 4.15 (dd, *J* = 4.8, 8.4 Hz, 1H), 5.02 ppm (d, *J* = 5.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.8 (CH_3), 31.9 (CH_2), 34.2 (CH_2), 40.6 (CH), 46.7 (CH), 50.8 (CH_3), 51.1 (CH), 51.3 (CH), 57.1 (CH), 78.2 (C H_2), 89.2 (C), 108.7 (CH_2), 115.9 (C), 147.3 ppm (C); MS (EI): *m/z* (%) = 236 $[M]^+$ (27), 208 (19), 204 (81), 180 (15), 176 (80), 161 (25), 148 (23), 133 (60), 119 (100); HRMS (EI): *m/z* calcd for $C_{14}H_{20}O_3$: 236.1412; found: 236.1412.

14: *rac*-(3*R*,3a*S*,4*R*,6*R*,9a*R*,10*S*)-9a-Methoxy-4,10-dimethyloctahydro-3,6-methanocycloocta[*b*]furan-9(4*H*)-one: Yellowish oil. IR (neat): $\tilde{\nu}$ = 2955 (s), 2930 (s), 2877 (s), 1717 (s), 1456 (m), 1385 (m), 1108 (m), 1057 (m), 1044 (m), 990 (m), 938 cm^{-1} (m); ^1H NMR (400 MHz, $CDCl_3$): δ = 0.93 (d, *J* = 7.2 Hz, 3H), 0.94–0.99 (m, 1H), 1.08 (d, *J* = 7.6 Hz, 3H), 1.64–1.70 (m, 1H), 1.86–2.11 (m, 5H), 2.17–2.20 (m, 1H), 2.45–2.53 (m, 2H), 2.71–2.78 (m, 1H), 3.19 (s, 3H, OMe), 3.95 (d, *J* = 8.8 Hz, 1H), 4.26 ppm (dd, *J* = 6.0, 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.9 (CH_3), 23.2 (CH), 25.9 (CH_3), 26.3 (CH_2), 31.7 (CH_2), 33.8 (CH), 38.9 (CH_2), 40.7 (CH), 45.9 (CH), 51.0 (CH_3), 54.8 (CH), 476.9 (CH_2), 109.4 (C), 211.1 ppm (C); MS (EI): *m/z* (%) = 238 $[M]^+$ (2), 237 (10), 210 (38), 207 (48), 182 (21), 178 (14), 167 (30) , 99 (100), 92 (23); HRMS (EI): *m/z* calcd for $C_{14}H_{22}O_3$: 238.1569; found: 238.1568.

15: *rac*-(4*R*,4a*S*,5*R*,7*R*,9a*S*,10*S*)-9a-Hydroxy-5,10-dimethyloctahydro-4,7-methanocyclohepta[*c*]pyran-1(3*H*)-one: Yellowish oil. IR (neat): $\tilde{\nu}$ = 3464 (b), 2948 (m), 2914 (m), 2873 (m), 1709 (s), 1469 (m), 1390 (m), 1257 (m), 1139 (m), 1071 cm^{-1} (m); ^1H NMR (400 MHz, $CDCl_3$): δ = 1.08 (d, *J* = 7.2 Hz, 3H), 1.15–1.19 (m, 1H), 1.22 (d, *J* = 7.2 Hz, 3H), 1.25–1.30 (m, 1H), 1.42–1.46 (m, 1H), 1.75–1.79 (m, 1H), 1.87–1.93 (m, 2H), 1.94–1.97 (m, 2H), 2.02–2.10 (m, 3H), 4.19 (dd, *J* = 1.6, 11.2 Hz, 1H), 4.38 ppm (dd, *J* = 3.2, 11.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0 (CH_3), 23.2 (CH_3), 27.4 (CH_2), 31.5 (CH), 31.8 (CH_2), 35.7 (CH), 35.8 (CH_2), 38.2 (CH), 42.2 (CH), 45.0 (CH), 73.7 (CH_2), 77.6 (C), 178.2 ppm (C); MS (EI): *m/z* (%) = 224 $[M]^+$ (2), 181 (12), 180 (100), 178 (13), 165 (62), 162 (29), 152 (19), 151 (43), 147 (40); HRMS (EI): *m/z* calcd for $C_{13}H_{20}O_3$: 224.1412; found: 224.1413.

19: *rac*-(3a*R*,6*R*,7*S*,7a*S*,10*S*,10a*R*,10b*R*,10c*S*,11*S*)-7-Hydroxy-7a-methoxy-11-methyl-7-vinyl-3a,4,6,7,7a,9,10,10a,10b,10c-decahydro-6,10-methanonaphtho[2,1-*b*:7,8-*c*′]difuran-1,3-dione: White crystals. M.p.: 158.6–159.2 °C; IR (neat): $\tilde{\nu}$ = 3553 (b), 2955 (m) 2928 (m), 1859 (s), 1780 (s), 1220 (m), 1058 (m), 1007 (m), 921 cm^{-1} (m); ^1H NMR (600 MHz, $CDCl_3$): δ = 0.93 (d, *J* = 7.2 Hz, 3H), 1.85 (ddd, *J* = 2.4, 3.0, 3.0 Hz, 1H), 1.96 (ddq, *J* = 2.4, 3.0, 7.2 Hz, 1H), 2.11 (dddd, *J* = 2.4, 3.0, 10.8, 15.6 Hz, 1H), 2.22 (d, *J* = 3.0 Hz, 1H), 2.37 (dddd, *J* = 2.4, 3.0, 3.0, 10.8 Hz, 1H), 2.77 (br, 1H), 2.79 (ddd, *J* = 6.6, 7.8, 15.6 Hz, 1H), 2.95 (dd, *J* = 3.0, 3.0 Hz, 1H), 3.16 (ddd, *J* = 7.8, 10.8, 10.8 Hz, 1H), 3.36 (dd, *J* = 10.8, 10.8 Hz, 1H), 3.46 (s, 3H), 3.59 (d, *J* = 7.8 Hz, 1H), 3.98 (dd, *J* = 3.0, 7.8 Hz, 1H), 5.21 (dd, *J* = 1.8, 10.8 Hz, 1H), 5.43 (dd, *J* = 1.8, 17.4 Hz, 1H), 5.78 (ddd, *J* = 3.0, 3.0, 6.6 Hz, 1H), 6.39 ppm (dd, *J* = 10.8, 17.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2 (CH_3), 23.5 (CH_2), 33.3 (CH), 33.7 (CH), 36.0 (CH), 40.4 (CH), 42.3 (CH), 44.8 (CH), 49.6 (CH_3), 51.7 (CH), 72.5 (CH_2), 77.3 (C), 106.4 (C), 113.9 (CH_2), 121.0 (CH), 138.0 (CH), 138.2 (C), 173.1 (C), 173.4 ppm (C); MS (EI): *m/z* (%) = 346 $[M]^+$ (57), 314 (27), 274 (14), 256 (15), 253 (12), 165 (100), 164 (20), 155 (56); HRMS (EI): *m/z* calcd for $C_{19}H_{22}O_6$: 346.1416; found: 346.1413; elemental analysis: calcd for $C_{19}H_{22}O_6$: C 65.88, H 6.40; found: C 65.78, H 6.44.

20: *rac*-(3a*R*,6*R*,7*S*,7a*S*,10*S*,10a*R*,10b*R*,10c*S*,11*S*)-7-Hydroxy-7a-methoxy-11-methyl-2-phenyl-7-vinyl-3a,4,6,7,7a,9,10,10a,10b,10c-decahydro-1*H*-6,10-methano[1]benzofuro[4,5-*e*]isoindole-1,3(2*H*)-dione: White crystals. M.p.: 162.7–163.4 °C; IR (neat): $\tilde{\nu}$ = 3549 (b), 2954 (w), 1774 (w), 1708 (s), 1500 (m), 1378 (m), 1183 (m), 1005 (m), 925 (w), 734 cm^{-1} (w); ^1H NMR (600 MHz, $CDCl_3$): δ = 0.95 (d, *J* = 7.2 Hz, 3H), 1.84 (ddd, *J* = 2.4, 3.0, 3.6 Hz, 1H), 1.97 (ddq, *J* = 2.4, 3.0, 7.2 Hz, 1H), 2.06 (dddd, *J* = 2.4, 3.0, 10.8, 15.0 Hz, 1H), 2.23 (d, *J* = 3.0 Hz, 1H), 2.36 (dddd, *J* = 2.4, 3.0, 3.0, 11.4 Hz, 1H), 2.85 (br, 1H), 2.87 (ddd, *J* = 6.6, 7.2, 15.0 Hz, 1H), 3.05 (ddd, *J* = 7.2, 10.2, 10.8 Hz, 1H), 3.13 (dd, *J* = 3.0, 3.0 Hz, 1H), 3.23 (dd, *J* = 10.2, 11.4 Hz, 1H), 3.49 (s, 3H), 3.58 (d, *J* = 7.2 Hz, 1H), 3.96 (dd, *J* = 3.6, 7.2 Hz, 1H), 5.21 (dd, *J* = 1.8, 10.8 Hz, 1H), 5.46 (dd, *J* = 1.8, 17.4 Hz, 1H), 5.83 (ddd, *J* = 3.0, 3.0, 6.6 Hz, 1H), 6.42 (dd, *J* = 10.8, 17.4 Hz, 1H), 7.29–7.48 ppm (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2 (CH_3), 24.2 (CH_2), 33.8 (CH), 33.9 (CH), 36.2 (CH), 40.2 (CH), 41.7 (CH), 45.0 (CH), 49.6 (CH_3), 51.8 (CH), 72.5 (CH_2), 77.2 (C), 106.6 (C), 113.8 (CH_2), 122.1 (CH), 126.3 (2×CH), 128.3 (CH), 128.9 (2×CH), 131.5 (C), 138.1 (CH), 138.5 (C), 177.9 (C), 178.9 ppm (C); MS (EI): *m/z* (%) = 421 $[M]^+$ (100), 389 (24), 335 (19), 307 (10), 291 (27), 174 (24), 159 (17), 157 (18); HRMS (EI): *m/z* calcd for $C_{25}H_{27}NO_5$: 421.1889; found: 421.1889; elemental analysis: calcd for $C_{25}H_{27}NO_5$: C 71.24, H 6.46, N 3.32; found: C 71.15, H 6.22, N 3.17.

21: *rac*-(3a*R*,4*S*,6*S*,7*R*,7a*R*,10*R*,10a*S*,10b*S*,10c*S*,11*R*)-7a-Ethoxy-7-hydroxy-4,11-dimethyl-7-vinyl-3a,4,6,7,7a,9,10,10a,10b,10c-decahydro-6,10-methanonaphtho[2,1-*b*:7,8-*c*′]difuran-1,3-dione: White crystals. M.p.: 167.6–168.3 °C; IR (neat): $\tilde{\nu}$ = 3541 (b), 2958 (m), 2929 (m), 1857 (s), 1776 (s), 1213 (m), 1055 (m), 1099 (m), 975 cm^{-1} (m); ^1H NMR (400 MHz, $CDCl_3$): δ = 0.92 (d, *J* = 7.2 Hz, 3H), 1.16 (t, *J* = 7.2 Hz, 3H), 1.45 (d, *J* = 6.8 Hz, 3H), 1.80–1.84 (m, 1H), 1.92–1.98 (m, 1H), 2.18 (d, *J* = 2.8 Hz, 1H), 2.35–2.38 (m, 2H), 2.72 (dd, *J* = 10.4, 10.4 Hz, 1H), 2.86 (br, 1H), 2.92 (dd, *J* = 2.8, 3.6 Hz, 1H), 3.38 (dd, *J* = 10.8, 10.8 Hz, 1H), 3.56 (d, *J* = 7.6 Hz, 1H), 3.76 (q, *J* = 7.2 Hz, 2H), 3.95 (dd, *J* = 3.2, 7.6 Hz, 1H), 5.18 (dd, *J* = 1.2, 10.8 Hz, 1H), 5.51 (dd, *J* = 1.2, 17.2 Hz, 1H), 5.46–5.50 (m, 1H), 6.37 ppm (dd, *J* = 10.8, 17.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.0 (CH_3), 19.0 (CH_3), 21.2 (CH_3), 30.7 (CH), 33.4 (CH), 33.6 (CH), 36.6 (CH), 42.9 (CH), 44.6 (CH), 47.7 (CH), 51.1 (CH), 57.6 (CH_2), 72.3 (CH_2), 76.5 (CH_2), 106.0 (C), 113.7 (CH_2), 128.5 (CH), 137.2 (C), 137.9 (CH), 172.3 (C), 173.2 ppm (C); MS (EI): *m/z* (%) = 374 $[M]^+$ (71), 328 (32), 302 (13), 273 (24), 245 (19), 227 (10), 217 (21), 202 (27), 185 (10), 173 (19), 55.0 (100); HRMS (EI): *m/z* calcd for $C_{21}H_{26}O_6$: 374.1729; found: 374.1730; elemental analysis: calcd for $C_{21}H_{26}O_6$: C 67.36, H 7.00; found: C 67.45, H 6.82.

22: *rac*-(3a*R*,4*S*,6*S*,7*R*,7a*R*,10*R*,10a*S*,10b*S*,10c*S*,11*R*)-7a-Ethoxy-7-hydroxy-4,11-dimethyl-2-phenyl-7-vinyl-3a,4,6,7,7a,9,10,10a,10b,10c-decahydro-1*H*-6,10-methano[1]benzofuro[4,5-*e*]isoindole-1,3(2*H*)-dione: White crystals. M.p.: 190.6–191.0 °C; IR (neat): $\tilde{\nu}$ = 3553 (b), 2956 (m), 29296, (m), 1772 (m), 1710 (s), 1500 (m), 1459 (m), 1379 (m), 1181 (m), 1061 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 0.94 (d, *J* = 7.2 Hz, 3H), 1.16 (t, *J* = 7.2 Hz, 3H), 1.52 (d, *J* = 7.2 Hz, 3H), 1.81 (ddd, *J* = 1.8, 3.0, 3.6 Hz, 1H), 1.97 (ddq, *J* = 1.8, 3.0, 7.2 Hz, 1H), 2.21 (d, *J* = 3.0 Hz, 1H), 2.34–2.38 (m, 2H), 2.63 (dd, *J* = 9.6, 9.6 Hz, 1H), 3.00 (br, 1H), 3.10 (dd, *J* = 3.0, 3.0 Hz, 1H), 3.24 (dd, *J* = 9.6, 10.8 Hz, 1H), 3.55 (d, *J* = 7.8 Hz, 1H), 3.76 (dq, *J* = 7.2, 9.0 Hz, 1H), 3.89 (dq, *J* = 7.2, 9.6 Hz, 1H), 3.93 (dd, *J* = 3.6, 7.8 Hz, 1H), 5.20 (dd, *J* = 1.8, 10.8 Hz, 1H), 5.45 (dd, *J* = 1.8, 17.4 Hz, 1H), 5.51 (dd, *J* = 2.4, 2.4 Hz, 1H), 6.39 (dd, *J* = 10.8, 17.4 Hz, 1H), 7.29–7.47 ppm (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.2 (CH_3), 19.7 (CH_3), 21.4 (CH_3), 31.5 (CH), 33.9 (CH), 34.4 (CH), 37.1 (CH), 42.6 (CH), 45.1 (CH), 47.5 (CH), 51.3 (CH), 57.7 (CH_2), 72.4 (CH_2), 77.1 (CH), 106.4 (C), 113.7 (CH_2), 126.4 (2×CH), 128.4 (CH), 129.0 (2×CH), 129.1 (CH), 131.7 (C), 137.2 (C), 138.3 (CH), 177.6 (C), 178.2 ppm (C);

MS (EI): *m/z* (%) = 449 $[M]^+$ (100), 403 (28), 348 (18), 320 (11), 305 (25), 266 (9), 183 (13), 174 (20), 171 (14); HRMS (EI): *m/z* calcd for $C_{27}H_{31}NO_5$: 449.2202; found: 449.2203; elemental analysis: calcd for $C_{27}H_{31}NO_5$: C 72.14, H 6.95, N 3.12; found: C 71.97, H 7.28, N 2.84.

23a: *rac*-1-[(1*R*,3a*R*,4*R*,5*S*,9*S*,9a*R*,9b*S*,10*R*)-10-Hydroxy-1-methoxy-4-methyl-10-vinyl-1,3,3a,4,5,7,8,9,9a,9b-decahydro-1,5-methanonaphtho[1,2-*c*]furan-9-yl]ethanone: White crystals. M.p.: 120.3–120.7 °C; IR (neat): $\tilde{\nu}$ = 3538 (b), 2933 (m), 2876 (m), 1705 (s), 1458 (m), 1348 (m), 1184 (m), 998 (m), 729 cm^{-1} (m); ^1H NMR (400 MHz, $CDCl_3$): δ = 1.02 (d, *J* = 7.2 Hz, 3H), 1.50–1.60 (m, 1H), 1.91–2.03 (m, 4H), 2.18–2.20 (m, 4H), 2.27–2.31 (m, 2H), 2.62–2.76 (m, 2H), 3.28 (s, 3H), 3.48 (d, *J* = 7.6 Hz, 1H), 3.92 (dd, *J* = 4.0, 7.6 Hz, 1H), 5.14 (dd, *J* = 2.0, 10.8 Hz, 1H), 5.45–5.50 (m, 2H), 6.33 ppm (dd, *J* = 10.8, 17.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 21.6 (CH_3), 24.7 (CH_2), 27.1 (CH_2), 29.9 (CH_3), 33.9 (CH), 34.5 (CH), 39.4 (CH), 45.4 (CH), 49.7 (CH), 50.8 (CH_3), 54.0 (CH), 72.4 (CH_2), 77.2 (C), 107.0 (C), 113.3 (CH_2), 123.5 (CH), 134.2 (C), 138.8 (CH), 213.1 ppm (C); MS (EI): *m/z* (%) = 318 $[M]^+$ (5), 300 (8), 286 (13), 276 (25), 257 (34), 244 (19), 231 (11), 215 (79), 205 (22), 197 (71), 55.0 (100); HRMS (EI): *m/z* calcd for $C_{19}H_{26}O_4$: 318.1831; found: 318.1834; elemental analysis: calcd for $C_{19}H_{26}O_4$: C 71.67, H 8.23; found: C 71.60, H 8.25.

23b: *rac*-1-[(1*R*,3a*R*,4*R*,5*S*,9*R*,9a*S*,9b*S*,10*R*)-10-Hydroxy-1-methoxy-4-methyl-10-vinyl-1,3,3a,4,5,7,8,9,9a,9b-decahydro-1,5-methanonaphtho[1,2-*c*]furan-9-yl]ethanone: Clear oil. IR (neat): $\tilde{\nu}$ = 3553 (b), 2928 (m) 2871 (m), 1707 (s), 1354 (m), 1253 (m), 1197 (m), 1008 (m), 929 (m), 736 cm^{-1} (m); ^1H NMR (400 MHz, $CDCl_3$): δ = 0.94 (d, *J* = 7.2 Hz, 3H), 1.64–1.75 (m, 2H), 1.83–1.88 (m, 1H), 2.00–2.06 (m, 2H), 2.11–2.12 (m, 1H), 2.17 (s, 3H), 2.20–2.42 (m, 3H), 2.86–2.90 (m, 1H), 3.12 (br, 1H), 3.35 (s, 3H), 3.51 (d, *J* = 6.8 Hz, 1H), 3.74 (dd, *J* = 2.4, 6.8 Hz, 1H), 5.19 (dd, *J* = 2.0, 11.2 Hz, 1H), 5.26–5.28 (m, 1H), 5.47 (dd, *J* = 2.0, 17.2 Hz, 1H), 6.40 ppm (dd, *J* = 11.2, 17.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.7 (CH_3), 24.9 (CH_2), 26.8 (CH_2), 28.4 (CH_3), 32.7 (CH), 35.2 (CH), 38.5 (CH), 40.9 (CH), 49.8 (CH_3), 51.1 (CH), 53.2 (CH), 73.7 (CH_2), 77.9 (C), 108.1 (C), 114.2 (CH_2), 120.3 (CH), 133.6 (C), 138.0 (CH), 211.9 ppm (C); MS (EI): *m/z* (%) = 318 $[M]^+$ (5), 300 (8), 286 (13), 276 (25), 257 (34), 244 (19), 231 (11), 215 (79), 205 (22), 197 (71), 188.2 (100); HRMS (EI): *m/z* calcd for $C_{19}H_{26}O_4$: 318.1831; found: 318.1834.

24: *rac*-(3a*R*,4*R*,6*S*,7*S*,8a*S*,11*S*,11a*R*,11b*R*,11c*S*,12*R*)-8a-Ethoxy-4,7,12-trimethyl-3a,4,6,7,8a,10,11,11a,11b,11c-decahydro-1*H*-6,11-methanofuro[2′,3′:6,7]cyclohepta[1,2-*e*][2]benzofuran-1,3,8-trione: White crystals. M.p.: 144.2–144.6 °C; IR (neat): $\tilde{\nu}$ = 2971 (m), 2930 (m), 1774 (m), 1712 (s), 1499 (w), 1379 (m), 1182 (m), 1110 (m), 996 (m), 732 cm^{-1} (m); ^1H NMR (600 MHz, $CDCl_3$): δ = 0.99 (d, *J* = 6.6 Hz, 3H), 1.00 (d, *J* = 7.2 Hz, 3H), 1.17 (t, *J* = 7.2 Hz, 3H), 1.40 (d, *J* = 7.2 Hz, 3H), 2.01 (d, *J* = 1.8 Hz, 1H), 2.07–2.14 (m, 2H), 2.18–2.20 (m, 1H), 2.32 (dd, *J* = 10.2, 10.8 Hz, 1H), 2.55–2.58 (m, 1H), 3.13–3.20 (m, 2H), 3.38 (dd, *J* = 4.8, 4.8 Hz, 1H), 3.62 (dq, *J* = 6.6, 7.2 Hz, 2H), 3.93 (d, *J* = 8.4 Hz, 1H), 4.30 (dd, *J* = 4.2, 8.4 Hz, 1H), 5.46 (dd, *J* = 3.0, 3.0 Hz, 1H), 7.26–7.45 ppm (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 13.9 (CH_3), 15.9 (CH_3), 19.3 (CH_3), 23.9 (CH_3), 31.8 (CH), 32.6 (CH), 40.2 (CH), 41.5 (CH), 44.7 (CH), 46.9 (CH), 46.9 (CH), 47.5 (CH), 49.7 (CH), 59.7 (CH_2), 76.2 (CH_2), 109.4 (C), 126.3 (2×CH), 128.2 (CH), 128.8 (2×CH), 131.6 (C), 132.3 (CH), 134.3 (C), 176.8 (C), 178.0 (C), 208.0 ppm (C); MS (EI): *m/z* (%) = 449 $[M]^+$ (2), 421 $[M-28]^+$ (100), 375 (32), 351 (9), 347 (13), 320 (39), 277 (20), 248 (9); HRMS (EI): *m/z* calcd for $C_{27}H_{31}NO_5$: 449.2202, found: 449.2206; elemental analysis: calcd for $C_{27}H_{31}NO_5$: C 72.14, H 6.95, N 3.12; found: C 71.79, H 6.73, N 3.13.

25: *rac*-(3a*R*,4*R*,5a*R*,7a*R*,11*S*,11a*R*,11b*R*,11c*S*,12*S*)-11-Hydroxy-4,7,12-trimethyl-2-phenyl-4,5,7a,8,11,11a,11b,11c-octahydro-1*H*-5a,11-methanoisochromeno[5,6-*e*]isoindole-1,3,10(2*H*,3a*H*)-trione: Yellowish oil. IR (neat): $\tilde{\nu}$ = 3463 (m), 2958 (m), 2927 (m), 1770 (s), 1708 (s), 1598 (w), 1498 (m), 1380 (m), 1243 (m), 1187 (m), 1073 cm^{-1} (m); ^1H NMR (400 MHz, $CDCl_3$): δ = 0.99 (d, *J* = 6.8 Hz, 3H), 1.21–1.25 (m, 2H), 1.30 (d, *J* = 6.4 Hz, 3H), 1.68–1.75 (m, 4H), 1.87–1.96 (m, 1H), 2.15 (d, *J* = 12.4 Hz, 1H), 2.22 (q, *J* = 7.2 Hz, 1H), 2.58–2.63 (m, 2H), 3.30 (d, *J* = 4.8 Hz, 1H), 3.66 (dd, *J* = 9.2, 13.2 Hz, 1H), 4.29 (dd, *J* = 2.4, 11.6 Hz, 1H), 4.49 (dd, *J* = 2.0, 11.6 Hz, 1H), 5.58 (s, 1H), 7.26–7.47 ppm (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 10.8 (CH_3), 18.8 (CH_3), 20.1 (CH_3), 28.8 (CH), 39.3 (CH), 41.6 (CH_2), 41.8 (CH), 45.5 (C), 46.3 (CH), 46.7 (CH), 48.4 (CH), 63.9 (CH), 68.1 (CH_2), 81.5 (C), 126.2 (2×CH), 127.9 (CH), 128.5 (2×CH), 130.5 (C), 131.6 (C), 138.6 (CH), 173.9 (C), 177.6 (C), 178.6 ppm (C); MS (EI): *m/z* (%) = 421 $[M]^+$ (53), 377 (100), 362 (17), 330 (8), 316 (50), 306 (26), 291 (8), 270 (10); HRMS (EI): *m/z* calcd for $C_{25}H_{27}NO_5$: 421.1889; found: 421.1890.

26: *rac*-(1*R*,3a*R*,5*R*,6*R*,10*S*,10a*R*,10b*S*,11*S*)-10-Acetyl-3a-methoxy-5,11-dimethyl-1,2,3a,5,6,8,9,10,10a,10b-decahydro-4*H*-1,6-methanobenzo-[3,4]cyclohepta[1,2-*b*]furan-4-one: White crystals. M.p.: 131.3–131.8 °C; IR (neat): $\tilde{\nu}$ = 2932 (m), 2871 (m), 1725 (s), 1711 (s), 1455 (m), 1376 (m) 1350 (m), 1185 (m), 1152 (m), 1003 cm^{-1} (m); ^1H NMR (400 MHz, $CDCl_3$): δ = 1.1 (d, *J* = 6.4 Hz, 3H), 1.05 (d, *J* = 7.6 Hz, 3H), 1.37–1.48 (m, 1H), 1.84–2.00 (m, 3H), 2.11–2.17 (m, 2H), 2.18–2.22 (m, 4H), 2.49–2.53 (m, 2H), 2.71–2.77 (m, 1H), 2.99 (q, *J* = 6.8 Hz, 1H), 3.30 (s, 3H), 3.86 (d, *J* = 7.6 Hz, 1H), 4.24 (dd, *J* = 4.8, 7.6 Hz, 1H), 5.39–5.42 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (CH_3), 24.0 (CH_3), 25.0 (CH_2), 27.2 (CH_2), 30.2 (CH_3), 34.0 (CH), 40.6 (CH), 45.2 (CH), 46.6 (CH), 47.9 (CH), 48.8 (CH), 49.9 (CH), 51.7 (CH_3), 76.7 (CH_2), 108.7 (C), 123.8 (CH), 131.6 (CH), 207.2 (C), 213.7 ppm (C); MS (EI): *m/z* (%) = 318 $[M]^+$ (54), 290 $[M-28]^+$ (58), 257 (37), 247 (61), 215 (39), 204 (100), 187 (43), 159 (78); HRMS (EI): *m/z* calcd for $C_{19}H_{26}O_4$: 318.1831; found: 318.1833; elemental analysis: calcd for $C_{19}H_{26}O_4$: C 71.67, H 8.23; found: C 71.57, H 8.30.

27: *rac*-(1*R*,3a*S*,5a*R*,9*S*,9a*R*,9b*S*,10*R*)-9-Acetyl-1-methoxy-4,10-dimethyl-3,3a,6,7,8,9, 9a,9b-octahydro-1*H*-1,5a-ethanonaphtho[1,2-*c*]furan-11-one: White crystals. M.p.: 152.4–152.9 °C; IR (neat): $\tilde{\nu}$ = 2930 (m), 2870 (m), 1713 (s), 1446 (m), 1380 (m), 1349 (m) 1271 (m), 1178 (m), 1104 (m), 988 cm^{-1} (m); ^1H NMR (400 MHz, $CDCl_3$): δ = 0.96 (d, *J* = 6.8 Hz, 3H), 1.14–1.32 (m, 2H), 1.41–1.50 (m, 1H), 1.55 (s, 3H), 1.67–1.77 (m, 2H), 1.98–2.02 (m, 1H), 2.12 (dd, *J* = 6.8 Hz the other *J* = 1.6 Hz, 1H), 2.25 (s, 3H), 2.46 (dd, *J* = 2.0, 7.2 Hz, 1H), 2.92 (q, *J* = 6.8 Hz, 1H), 3.26 (s, 3H), 3.30–3.35 (m, 1H), 3.69 (dd, *J* = 2.0, 8.4 Hz, 1H), 4.11 (dd, *J* = 8.8, 8.8 Hz, 1H), 5.25 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.0 (CH_3), 20.4 (CH_3), 20.9 (CH_2), 30.0 (CH_2), 30.9 (CH_3), 34.1 (CH_2), 40.5 (C), 40.9 (CH), 42.7 (CH), 44.5 (CH), 46.6 (CH), 47.8 (CH), 52.1 (CH_3), 68.7 (CH_2), 103.8 (C), 130.7 (CH), 134.8 (CH), 206.8 (C), 212.6 ppm (C); MS (EI): *m/z* (%) = 318 $[M]^+$ (71), 290 $[M-28]^+$ (100), 275 (30), 247 (94), 215 (19), 187 (39), 173 (48), 159 (32); HRMS (EI): *m/z* calcd for $C_{19}H_{26}O_4$: 318.1831; found: 318.1831; elemental analysis: calcd for $C_{19}H_{26}O_4$: C 71.67, H 8.23; found: C 71.60, H 8.02.

28, *rac*-(1*R*,4a*S*,6a*R*,10*S*,10a*S*,10b*S*,11*R*)-10-Acetyl-1-hydroxy-5,11-dimethyl-4,4a,7,8,9,10,10a,10b-octahydro-1,6a-methanobenzo[*f*]isochromen-2(1*H*)-one: White crystals. M.p.: 197.8–198.2 °C; IR (neat): $\tilde{\nu}$ = 3461 (b), 2932 (m), 2868 (m), 1734 (s), 1717 (s), 1685 (m) 1455 (m), 1363 (m), 1174 (m), 1045 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 0.85 (d, *J* = 7.6 Hz, 3H), 1.08–1.18 (m, 1H), 1.22–1.30 (m, 1H), 1.42–1.54 (m, 1H), 1.60–1.68 (m, 5H), 1.94–1.98 (m, 1H), 2.11 (d, *J* = 11.2 Hz, 1H), 2.19 (s, 3H), 2.34 (d, *J* = 5.2 Hz, 1H), 2.45 (q, *J* = 7.6 Hz, 1H), 2.58–2.61 (m, 1H), 3.12–3.20 (m, 2H), 4.19 (dd, *J* = 2.4, 11.6 Hz, 1H), 4.46 (dd, *J* = 2.4, 11.6 Hz, 1H), 5.39–5.42 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.7 (CH_3), 19.0 (CH_3), 20.9 (CH_2), 29.0 (CH_2), 29.5 (CH_2), 30.0 (CH_3), 42.1 (CH), 45.0 (C), 48.8 (CH), 49.0 (CH), 49.3 (CH), 55.6 (CH), 68.9 (CH_2), 82.6 (C), 128.8 (C), 138.1 (CH), 174.9 (C), 212.5 ppm (C); MS (EI): *m/z* (%) = 304 $[M]^+$ (89), 291 (6), 260 (21), 241 (16), 215 (19), 201 (10), 185 (15), 171 (11), 159 (100); HRMS (EI): *m/z* calcd for $C_{18}H_{24}O_4$: 304.1675; found: 304.1665; elemental analysis: calcd for $C_{18}H_{24}O_4$: C 71.03, H 7.95; found: C 70.97, H 7.97.

29: *rac*-(3a*R*,6*S*,7*S*,8a*S*,11*S*,11a*R*,11b*R*,11c*S*,12*R*)-8a-Methoxy-7,12-dimethyl-3a,4,6,7,8a,10,11,11a,11b,11c-decahydro-1*H*-6,11-methanofuro[2′,3′:6,7]cyclohepta[1,2-*e*][2]benzofuran-1,3,8-trione: Clear oil. IR (neat): $\tilde{\nu}$ = 2952 (m), 2371 (m), 1865 (m), 1778 (s), 1717 (s), 1451 (w) 1223 (m), 1040 (m), 914 cm^{-1} (m); ^1H NMR (400 MHz, $CDCl_3$): δ = 0.96 (d, *J* = 6.8 Hz, 3H), 0.98 (d, *J* = 7.2 Hz, 3H), 1.89–1.98 (m, 1H), 2.02–2.06 (m, 1H), 2.08–2.14 (m, 1H), 2.19–2.22 (m, 1H), 2.50–2.55 (m, 1H), 2.64–2.71 (m, 1H), 2.81–2.88 (m, 1H), 3.16–3.20 (m, 2H), 3.27 (dd, *J* = 10.0, 10.0 Hz, 1H), 3.35 (s, 3H), 3.97 (d, *J* = 8.8 Hz, 1H), 4.32 (dd, *J* = 4.0, 8.4 Hz, 1H), 5.75–5.78 ppm (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 13.9 (CH_3), 24.0 (CH_2), 24.5 (CH_2), 32.1 (CH), 40.1 (CH), 40.2 (CH_3),

41.7 (CH), 44.7 (CH), 47.2 (CH), 47.3 (CH), 50.2 (CH), 51.9 (CH_3), 76.6 (CH_2), 109.3 (C), 124.4 (CH), 135.6 (CH), 172.1 (C), 173.4 (C), 208.2 ppm(C); MS (EI): m/z (%) = 346 $[M]^+$ (8), 336 (14), 318 (100), 302 (17), 291 (17), 281 (48), 265 (20), 258 (25); HRMS (EI): m/z calcd for $C_{19}H_{22}O_6$: 346.1416; found: 346.1426.

30: *rac*-(3a*R*,6*S*,7*S*,8a*S*,11*S*,11a*R*,11b*R*,11c*S*,12*R*)-8a-Methoxy-7,12-dimethyl-2-phenyl-3a,4,6,7,8a,10,11,11a,11b,11c-decahydro-6,11-methanofuro[2′,3′:6,7]cyclohepta[1,2-*e*]isoindole-1,3,8(2*H*)-trione: White crystals. M.p.: 208.8–209.4 °C; IR (neat): $\tilde{\nu}$ = 2963 (m), 2858 (m), 1706 (s), 1497 (m), 1451 (w), 1379 (m), 1185 (m), 995 (m), 751 cm^{-1} (w); ^1H NMR (400 MHz, $CDCl_3$): δ = 0.99 (d, J = 7.2 Hz, 3H), 1.00 (d, J = 6.8 Hz, 3H), 1.84–1.92 (m, 1H), 2.05–2.07 (m, 1H), 2.08–2.14 (m, 1H), 2.19–2.21 (m, 1H), 2.52–2.57 (m, 1H), 2.70–2.78 (m, 2H), 3.10–3.20 (m, 2H), 3.34 (s, 3H), 3.40–3.43 (m, 1H), 3.97 (d, J = 8.4 Hz, 1H), 4.32 (dd, J = 4.0, 8.4 Hz, 1H), 5.80–5.82 (m, 1H), 7.25–7.45 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 19.9 (CH_3), 23.9 (CH_3), 25.3 (CH_2), 32.5 (CH), 40.0 (CH), 40.3 (CH), 41.0 (CH), 44.8 (CH), 46.7 (CH), 47.1 (CH), 50.1 (CH), 51.4 (CH_3), 76.5 (CH_2), 109.3 (CH), 124.6 (CH), 126.3 (2×CH), 128.3 (CH), 128.9 (2×CH), 131.6 (C), 135.7 (C), 177.6 (C), 178.2 (C), 207.9 ppm (C); MS (EI): m/z (%) = 421 $[M]^+$ (43), 389 (34), 371 (19), 361 (21), 334 (19), 305 (21), 292 (23), 269 (14), 219.0 (100); HRMS (EI): m/z calcd for $C_{25}H_{27}NO_5$: 421.1889; found: 421.1888; elemental analysis: calcd for $C_{25}H_{27}NO_5$: C 71.24, H 6.46, N 3.32; found: C 71.11, H 6.45, N 3.28.

31: *rac*-(3a*R*,4*R*,6*S*,7*S*,8a*S*,11*S*,11a*R*,11b*R*,11c*S*,12*R*)-8a-Ethoxy-4,7,12-trimethyl-3a,4,6,7,8a,10,11,11a,11b,11c-decahydro-1*H*-6,11-methanofuro[2′,3′:6,7]cyclohepta[1,2-*e*][2]benzofuran-1,3,8-trione: White crystals. M.p.: 163.0–163.5 °C; IR (neat): $\tilde{\nu}$ = 2971 (m), 1853 (m), 1781 (s), 1721 (s), 1458 (w), 1211 (m), 1048 (m), 945 (m), 919 cm^{-1} (m); ^1H NMR (600 MHz, $CDCl_3$): δ = 0.95 (d, J = 6.6 Hz, 3H), 0.98 (d, J = 7.2 Hz, 3H), 1.16 (t, J = 7.2 Hz, 3H), 1.35 (d, J = 6.6 Hz, 3H), 2.00 (s, 1H), 2.08–2.19 (m, 3H), 2.38 (dd, J = 10.8, 10.8 Hz, 1H), 2.52–2.57 (m, 1H), 3.13–3.18 (m, 2H), 3.34 (dd, J = 10.2, 10.2 Hz, 1H), 3.55–3.60 (m, 2H), 3.95 (d, J = 8.4 Hz, 1H), 4.31 (dd, J = 4.2, 8.4 Hz, 1H), 5.45 ppm (dd, J = 3.0, 3.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 13.8 (CH_3), 15.9 (CH_3), 18.8 (CH_3), 24.0 (CH_3), 31.2 (CH), 32.0 (CH), 40.1 (CH), 42.2 (CH), 44.6 (CH), 47.0 (CH), 47.3 (CH), 48.0 (CH), 49.8 (CH), 60.3 (CH_2), 76.3 (CH_2), 109.3 (C), 131.9 (CH), 134.6 (C), 171.5 (C), 173.5 (C), 208.4 ppm (C); MS (EI): m/z (%) = 374 $[M]^+$ (1), 346 $[M-28]^+$ (100), 277 (91), 272 (9), 248 (27), 218 (38), 175 (52), 157 (27); HRMS (EI): m/z calcd for $C_{21}H_{26}O_6$: 374.1729; found: 374.1746; elemental analysis: calcd for $C_{21}H_{26}O_6$: C 67.36, H 7.00; found: C 67.02, H 7.01.

CCDC-681322 (**21**), -681323 (**27**), -681324 (**28**), and -681325 (**31**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre at www.ccdc.cam.ac.uk/data_request/cif.

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