Regioselective Preparation of 7-Oxanorborna-2,5-diene-2,3-dicarboxylic Acid Derivatives by the Diels–Alder Reaction: A Selective Access to Furans by Retro-Diels–Alder Reaction

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Abstract: Hydrolysis of 1-substituted 7-oxanorborna-2,5-diene-2,3-dicarboxylates occurred regioselectively at the ester group in the 3-position to give monocarboxylic acids from which diesters containing two different alkoxy groups and amido esters were selectively prepared. Hydrogenation of these oxanorbornadiene derivatives followed by a retro-Diels–Alder reaction gave the corresponding furans as single regioisomers.

Key words: Diels–Alder reactions, hydrolyses, esters, amides, regioselectivity, furans, heterocycles

Various 7-oxanorborna-2,5-dienes (ONDs) bearing one or two electron-withdrawing groups on a carbon–carbon double bond are versatile intermediates for the preparation of aromatic, ethylenic, and heterocyclic products. For instance, treatment of ONDs under acidic conditions gives the corresponding phenols,[1] whereas aromatic compounds are obtained by deoxygenation.[2] Ethylenic[3,4] and heterocyclic compounds[5–11] are synthesized by reactions of electron-deficient carbon–carbon double bonds of ONDs with nucleophiles or 1,3-dipolar reactants, followed by a retro-Diels–Alder reaction. Moreover, retro-Diels–Alder reactions performed after selective hydrogenation of electron-rich carbon–carbon double bonds of ONDs give substituted furans regioselectively.[1e,12–14] Furthermore, the presence of a substituent on the bridgehead carbon atom of the dialkyl oxanorbornadiene-2,3-dicarboxylate framework permits regioselective reactions, such as cycloadditions of azomethine ylides[5a,b] or nucleophilic additions of thiols.[3e]

ONDs can be synthesized by Diels–Alder reactions of the corresponding furans with alkynes. The reactions of ONDs generally give the same ethylenic or heterocyclic product as those formed by reactions of the parent alkyne with nucleophiles or 1,3-dipolar reactants. However, the chemoselectivity can differ[3f] and, generally, the three-step sequence via the OND is more selective,[3d,f,5a,b] sometimes faster,[6c,7b] and generally provides better yields[5b,c] than the corresponding sequence starting from alkyne.

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Most ONDs have been prepared by Diels–Alder reactions of furan derivatives with symmetrical dialkyl acetylenedicarboxylates.[2,3c,e,5,13,15] Cycloaddition of nonsymmetrical alkynes with 2-substituted furans might provide increased molecular diversity of the products prepared via ONDs. In a few cases, such as those of 4,4-diethoxybut-2-ynal,[3b,d,f,16] ethyl 4,4,4-trifluorobutynoate,[17] or methyl 3-(phenylsulfonyl)prop-2-ynoate,[18] the cycloaddition delivers one regioisomer exclusively or predominantly, but a mixture of regioisomers is generally obtained. For example, the reaction of 2-methylfuran with ethynyl phenyl sulfone in dichloromethane at room temperature for four days gave a 53:47 mixture of the two regioisomeric products,[19] whereas cycloaddition of the same furan with methyl 4-(cyclohexylamino)-4-oxobut-2-ynoate in refluxing toluene for three hours gave a 3:2 mixture of the corresponding products.[12f] The reactions of 2-ethylfuran with ethynyl 4-tolyl sulfone (CH_2Cl_2, r.t., 9 d), methyl 4-anilino-4-oxobut-2-ynoate (toluene, reflux, 8 h), and methyl 3-(dimethoxyphosphoryl)prop-2-ynoate (toluene, 80 °C, 1 d) gave, respectively, 51:49, 77:23, and 63:37 mixtures of the corresponding cycloadducts.[17]

Here, we describe a selective monohydrolysis of unsymmetrical oxanorbornadienedicarboxylates to give half esters that can be converted into diesters containing two different alkoxy groups or into amido esters. Because selective monohydrolyses of symmetrical dimethyl and diethyl 7-oxanorborna-2,5-diene-2,3-dicarboxylate have been reported to occur under enzymatic or chemical conditions,[20,21] we expected to be able to achieve regioselective syntheses of diesters and amido esters.

The 7-oxanorborna-2,5-diene-2,3-dicarboxylates **7**–**11** were prepared by treatment of furan (**1**), 2-ethylfuran (**2**), or 2-benzylfuran (**3**) with dimethyl acetylenedicarboxylate (**4**), diethyl acetylenedicarboxylate (**5**), or diisobutyl acetylenedicarboxylate (**6**). Reactions were performed in solution in toluene or in the absence of a solvent (Table 1). Under the usual conditions for such reactions, an excess of the acetylenedicarboxylate was used to avoid the formation of products resulting from Diels–Alder reactions between the OND and the furan reagent. After heating at 80 or 110 °C for four hours, solutions of 3:1 mixtures of dimethyl acetylenedicarboxylate (**4**) and the 2-alkylfurans **2** or **3** in toluene gave the expected cycloadducts **8** and **9** in

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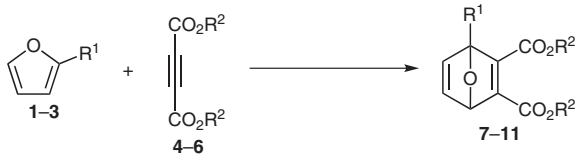
Table 1 Preparation of 7-Oxanorbornadienes **7–11**[a]



Entry	Furan	R^1	Alkyne	R^2	Ratio furan/alkyne	Temp (°C)	Time	Product	Yield[b] (%)
1	**1**	H	**4**	Me	1.5:1[c]	80	14 h	**7**	63[d]
2	**2**	Et	**4**	Me	1:3	80	4 h	**8**	96
3	**2**	Et	**4**	Me	1:1[e]	35	2 d	**8**	98[f]
4	**3**	Bn	**4**	Me	1:3	110	4 h	**9**	88
5	**2**	Et	**5**	Et	1:1[e]	35	7 d	**10**	99[f]
6	**2**	Et	**6**	*i*-Bu	1:1.2	80	1 d	**11**	60

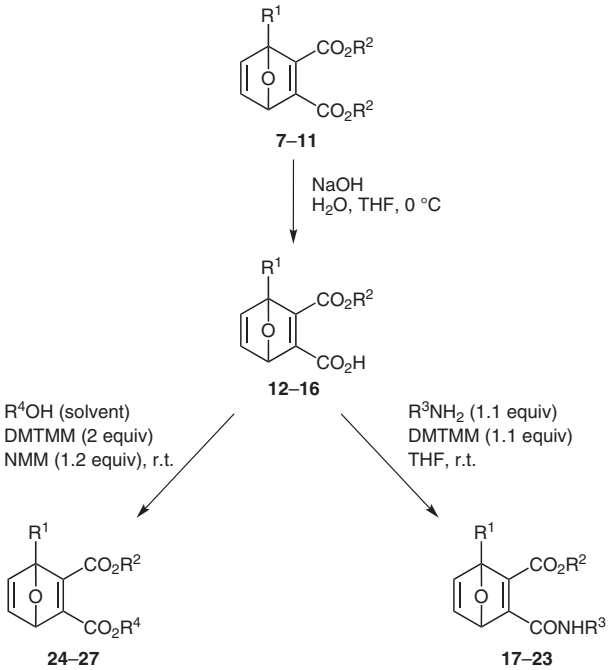
[a] Unless otherwise noted, reactions were performed in toluene solution.
[b] In general, the product was purified by chromatography on silica gel.
[c] Reaction performed in a vacuum-sealed tube after freeze–pump–thaw cycles.
[d] Isolated by distillation.
[e] Reaction performed in the absence of a solvent.
[f] Isolated by evaporation of residual reactants under vacuum.

excellent yields after chromatography on silica gel (entries 2 and 4).

By using a slight excess of the freshly prepared diisobutyl diester **6** (**6**/**2** = 1.2:1), the adduct **11** was obtained in a medium yield after one day at 80 °C (entry 6). The reaction of dimethyl acetylenedicarboxylate (**4**) with furan (**1**) was performed in a vacuum-sealed tube to prevent loss of the volatile **1**. Moreover, furan (**1**) was introduced in excess because, at 80 °C, it exists partially in the gas phase and might be less available. After 14 hours, adduct **7** was isolated by distillation (entry 1). Interestingly, cycloadduct **8** and the corresponding diethyl ester **10** were easily prepared by keeping equimolar mixtures of ethylfuran (**2**) with dimethyl acetylenedicarboxylate (**4**) or diethyl acetylenedicarboxylate (**5**), respectively, with no solvent, at 35 °C for several days (entries 3 and 5). Under these very mild conditions, products of adequate purity were obtained by evaporation of the residual starting materials under low pressure.

Treatment of the diesters **7–11** with a mixture of aqueous sodium hydroxide and tetrahydrofuran at 0 °C gave the corresponding monocarboxylic acids **12–16** selectively (Scheme 1 and Table 2). These reactions were generally carried out with a 0.5 M solution of sodium hydroxide until the starting diester disappeared. The monoacid **12** was obtained from the symmetrical diester **7** by using a 0.25 M solution of sodium hydroxide, because the use of more-concentrated sodium hydroxide solutions resulted in hydrolyses of both ester functions. ^{1}H and ^{13}C NMR spectra of the monoacids **13–16** showed the presence of a single regioisomer in each case.

The resulting carboxylic acids were coupled with amines or alcohols in the presence of 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholin-4-ium chloride (DMTMM),[22] to give the corresponding amido esters or diesters with different alkoxy groups, respectively (Scheme 1, Table 2).



Scheme 1 Selective two-step syntheses of OND amido esters **17–23** and diesters **24–27**

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Table 2 Preparation of Monocarboxylic Acids **12**–**16**, Amido Esters **17**–**23**, and Diesters **24**–**27**

			Monocarboxylic acid[a]			Amido ester[b]				Diester[c]		
Substrate	R^1	R^2	Time (min)		Yield (%)	R^3	Time (h)		Yield[d] (%)	R^4		Yield[d] (%)
7	H	Me	30	**12**[e]	76	Ph	4.5	**17**	11			
8	Et	Me	35	**13**	78	Ph	3.5	**18**	67	Et[f]	**24**	69
						Bn	4.5	**19**	33	Bn	**25**	70
						Cy	4	**20**	64	*i*-Bu	**26**	55
9	Bn	Me	25	**14**	87	Ph	3.5	**21**	36			
10	Et	Et	50	**15**	74	Ph	3.5	**22**	51	Me	**27**	70
11	Et	*i*-Bu	120	**16**	89	Ph	6[g]	**23**	75			

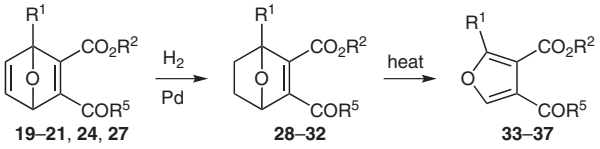
[a] Unless otherwise noted, reactions were performed with 0.5 M aq NaOH.
[b] Generally, reactions were performed with amine (1.1 equiv) and DMTMM.
[c] Unless otherwise noted, the reaction time was 16 h.
[d] Isolated yield after column chromatography (silica gel).
[e] 0.25 M aq NaOH was used.
[f] Reaction time 5 h.
[g] After the indicated time, additional portions of the amine and DMTMM (0.4 equiv each) were added, and the reaction was continued for a further 1 h.

Slight excesses of amine (aniline, benzylamine, or cyclohexylamine) and DMTMM were used to prepare the amido esters **17**–**23**, which were isolated in good to low yields after chromatography on silica gel. By using the appropriate alcohol as the solvent in the presence of DMTMM (2 equiv) and 4-methylmorpholine (1.2 equiv), diesters **24**–**27** were obtained in good yields after chromatography on silica gel. Note that diesters **24** and **27** are the two regioisomers that would be formed by cycloaddition of 2-ethylfuran (**2**) with ethyl methyl acetylenedicarboxylate.

The structure of the amido ester **22** was determined by X-ray diffraction analysis of a single crystal (Figure 1).[23] This confirmed unambiguously that hydrolysis of the diester **10** occurred selectively at the ester group distal to the small ethyl group on the bridgehead carbon atom. We believe that the same regioselectivity occurs in the monohydrolysis reactions of diesters **8**, **9**, and **11**. A similar regioselective hydrolysis has been claimed to occur in the case of a dimethyl oxanorbornadienedicarboxylate bearing a bulky (dansylamino)methyl group in the 1-position.[3e]

The structure of compound **22** contains pyramidalized ethylenic carbons at C2 and C3. The dihedral angle of the bond between the ester carbonyl carbon and carbon C2 with bond C3–C4 is 171.6°, whereas that between the bond between the amide carbonyl carbon and carbon C3 with bond C1–C2 is 169.9°; the dihedral angle between carbons C1, C2, C3, and C4 is only 0.34°. Clearly, ester and amide groups are slightly shifted on the *endo* face, making the *exo* face more accessible. A strong hydrogen bond between the hydrogen of the NH group and the oxygen atom of the ester carbonyl group is another feature of this structure; the H···O distance is 1.97 Å and the angle N–H···O is 154.6°.

Table 3 Preparation of Furan Derivatives **33**–**37** via the Oxanorbornenes **28**–**32**



19–**21**, **24**, **27** **28**–**32** **33**–**37**

Substrate	R^1	R^2	R^5	Oxanorbornene[a]	Yield[c] (%)	Furan[b]	Yield[c] (%)
19	Et	Me	NHBn	**28**	87	**33**	94
20	Et	Me	NHCy	**29**[d]	95	**34**	62
21	Bn	Me	NHPh	**30**[e]	93	**35**	96[f]
24	Et	Me	OEt	**31**[g]	85	**36**	88
27	Et	Et	OMe	**32**[e]	90	**37**	94

[a] Reaction conditions: H_2, 5% Pd/$BaSO_4$, PE, r.t., 40 min (unless otherwise noted).
[b] Reaction conditions: decalin, 190 °C, 75 min.
[c] Isolated yield after column chromatography (silica gel).
[d] Reaction time 90 min.
[e] Solvent PE–THF.
[f] See experimental section.
[g] Reaction time 55 min.

To highlight the importance of the OND products, we prepared various furan derivatives regioselectively by a short sequence involving hydrogenation and a retro-Diels–Alder reaction[12] (Table 3).

Reduction of amido esters **19**, **20**, and **21** and diesters **24** and **27** with dihydrogen in the presence of palladium/barium sulfate occurred at the more electron-rich carbon–

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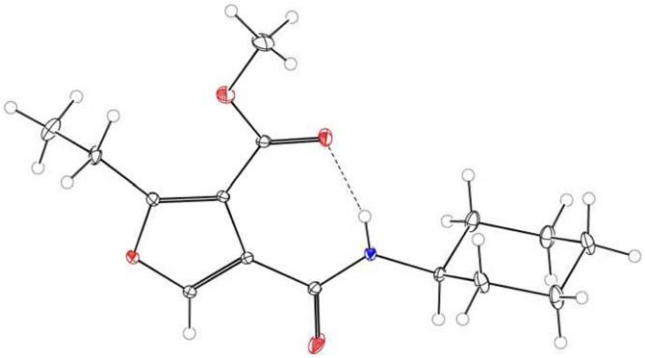

Figure 2 ORTEP structure of furan **34**;[23] ellipsoids are drawn at the 30% probability level

carbon double bond. Note that the reaction time for diesters must be carefully controlled to avoid the formation of oxanorbornanes. The resulting norbornenes **28**–**32** were converted selectively into furans **33**–**37** by heating in decalin. In each case, a single regioisomer was obtained.

The structure of furan **34** was confirmed by X-ray diffraction analysis (Figure 2).[23]

This sequence is significant, because direct reaction of methyl 4-(cyclohexylamino)-4-oxobut-2-ynoate with 2-methylfuran followed by hydrogenation and retro-Diels–Alder reaction gives a mixture of two regioisomeric products that are active against carcinomas and model carcinoma cell lines, but it is necessary to separate the regioisomeric products.[12f] Furan **34**, obtained in a pure form after the retro-Diels–Alder reaction, is an analogue of one of these regioisomers. Moreover, diesters **36** and **37** are the two regioisomers that should be obtained as mixtures from a similar sequence of reactions starting from 2-ethylfuran and ethyl methyl acetylenedicarboxylate.

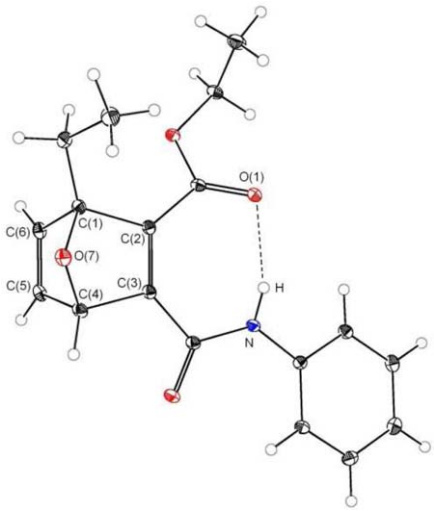

Figure 1 ORTEP structure of compound **22**;[23] ellipsoids are drawn at the 30% probability level

In summary, we have developed a simple three-step sequence that permits regioselective preparation of amido esters and of diesters with different alkoxy groups by coupling amines or alcohols, respectively, with monoesters of 1-substituted 7-oxanorborna-2,5-diene-2,3-dicarboxylic acids. The main feature of this sequence is the selective hydrolysis of the diesters derived from these diacids, which occurs on the ester group in 3-position, even in the presence of a small ethyl group on the bridgehead carbon atom. The starting diesters are easily obtained by Diels–Alder reactions of 2-substituted furans with symmetrical acetylenedicarboxylates. This highly selective synthesis of oxanorbornadiene derivatives permits the selective preparation of furans with various electron-withdrawing groups by hydrogenation followed by a retro-Diels–Alder reaction.

^{1}H and ^{13}C NMR spectra were recorded on Bruker AC250 (250 and 62.9 MHz, respectively), Bruker DRX300 (300 and 75.5 MHz, respectively), and Bruker AM360 (360 and 90.6 MHz, respectively) spectrometers. Chemical shifts (δ) are given in ppm relative to solvent signals as internal standards ($CHCl_3$: δ = 7.27 ppm; $CDCl_3$: δ = 77.00 ppm). Assignments were aided by JMOD pulse sequences and heteronuclear two-dimensional experiments (HSQC). Positive (ES^+) and negative (ES^-) electrospray mass spectra and high-resolution mass spectra were recorded with a Bruker Daltonics MicrOTOF-Q spectrometer or a Waters LCT spectrometer (Gif-sur-Yvette, France). Positive chemical ionization (CI^+) and electron impact (EI) mass spectra were recorded with a Thermo Scientific DSQ spectrometer. IR spectra were recorded by using an FT-IR Perkin-Elmer (Spectrum One) spectrophotometer or an FT-IR Bruker (Vertex 70) spectrophotometer with an ATR accessory.

X-ray diffraction data for **22** and **34** were collected by using a Kappa X8 APPEX II Bruker diffractometer with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). The temperature of the crystal was maintained at 100 K (± 1 K) by means of a 700-series Cryostream cooling device. The data were corrected for Lorentz polarization and absorption effects. The structures were solved by direct methods using SHELXS-97[24] and refined against F2 by full-matrix least-square techniques using SHELXL-97[24] with anisotropic displacement parameters for all nonhydrogen atoms. Hydrogen atoms were located on a difference Fourier map and introduced into calculations as a riding model with isotropic thermal parameters. All calculations were performed by using the crystal structure crystallographic software package WINGX.[25]

Diisobutyl Acetylenedicarboxylate (6)

A soln of DMAD (**4**) (1.00 g, 0.87 mL, 7.04 mmol), *i*-BuOH (2.40 g, 2.99 mL, 39.3 mmol), and a catalytic amount of PTSA (126 mg, 0.66 mmol) in cyclohexane (10 mL) was refluxed for 3 d while the MeOH that formed was removed with a 5 Å MS trap maintained at 16 °C. The mixture was then cooled to r.t. and, after addition of Et_2O (60 mL), the organic layer was washed sequentially with 0.1 M aq $NaHCO_3$ (2 × 20 mL) and H_2O (20 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude residue was purified by column chromatography [silica gel, hexane–Et_2O (98:2)] to give a yellowish oil; yield: 1.53 g (95%); R_f = 0.35 (hexane–Et_2O, 94:6). Spectroscopic data were in agreement with those reported.[26]

^{1}H NMR (360 MHz, $CDCl_3$): δ = 0.97 [d, *J* = 6.8 Hz, 12 H, $OCH_2CH(CH_3)_2$], 2.01 [nonuplet, *J* = 6.8 Hz, 2 H, $OCH_2CH(CH_3)_2$], 4.03 [d, *J* = 6.8 Hz, 4 H, $OCH_2CH(CH_3)_2$].

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Diethyl 1-Ethyl-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (10)

A mixture of 2-ethylfuran (**2**; 1.92 g, 2.11 mL, 20.0 mmol) and $EtO_2CC{\equiv}CCO_2Et$ (**5**; 3.40 g, 3.20 mL, 19.9 mmol) was stirred at 35 °C for 7 d. Evaporation of the residual reactants at 40 °C under vacuum (0.1 Torr) for 2 h gave an almost pure orange-yellow oil; yield: 5.27 g (99%); R_f = 0.32 (PE–Et_2O, 2:1).

IR (neat): 2982, 2940, 1725, 1712, 1639, 1559, 1465, 1370, 1310, 1267, 1231, 1197, 1095, 1041, 919, 733 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.04 (t, *J* = 7.5 Hz, 3 H, CH_2CH_3), 1.30 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 1.35 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 2.12–2.29 (m, 2 H, CH_2CH_3), 4.23 (q, *J* = 7.0 Hz, 2 H, OCH_2CH_3), 4.31 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 5.65 (d, *J* = 1.9 Hz, 1 H, H-4), 6.99 (d, *J* = 5.0 Hz, 1 H, H-6), 7.20 (dd, *J* = 5.0, 1.9 Hz, 1 H, H-5).

^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 8.4 (CH_2CH_3), 13.5 (2 OCH_2CH_3), 21.4 (CH_2CH_3), 60.4 (OCH_2CH_3), 60.6 (OCH_2CH_3), 82.6 (C-4), 97.7 (C-1), 144.24 and 144.25 (C-5 and C-6), 150.7 and 155.3 (C-2 and C-3), 161.8 (CO_2), 164.3 (CO_2).

MS (ES^+): *m/z* (%) = 193 (12), 289 (100) $[M + Na]^+$, 290 (15), 305 (21), 555 (0.5) $[2M + Na]^+$.

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{14}H_{18}NaO_5$: 289.1046; found: 289.1039.

Diisobutyl 1-Ethyl-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (11)

A soln of 2-ethylfuran (**2**; 213 mg, 234 μL, 2.22 mmol) and diisobutyl acetylenedicarboxylate (**6**; 600 mg, 2.65 mmol) in toluene (2.4 mL), previously filtered over basic Al_2O_3, was stirred at 80 °C for 1 d. The solvent was evaporated under vacuum and the crude product was purified by column chromatography [silica gel, PE–Et_2O (19:1)] to give a yellow oil; yield: 430 mg (60%); R_f = 0.40 (PE–Et_2O, 9:1).

IR (neat): 2965, 2876, 1721, 1711, 1640, 1468, 1377, 1314, 1277, 1261, 1229, 1197, 1138, 1079, 920 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 0.94 [d, *J* = 6.6 Hz, 6 H, $OCH_2CH(CH_3)_2$], 0.97 [d, *J* = 6.6 Hz, 6 H, $OCH_2CH(CH_3)_2$], 1.05 (t, *J* = 7.5 Hz, 3 H, CH_2CH_3), 2.00 [nonuplet, *J* = 6.6 Hz, 2 H, 2 $OCH_2CH(CH_3)_2$], 2.13–2.28 (m, 2 H, CH_2CH_3), 3.95 [d, *J* = 6.6 Hz, 2 H, $OCH_2CH(CH_3)_2$ on C-3], 3.97 (dd, *J* = 11.1, 6.6 Hz) and 4.08 (dd, *J* = 11.1, 6.6 Hz) [AB part of an ABX system, 2 H, $OCH_2CH(CH_3)_2$ on C-2], 5.66 (d, *J* = 1.9 Hz, 1 H, H-4), 6.99 (d, *J* = 5.2 Hz, 1 H, H-6), 7.20 (dd, *J* = 5.2, 1.9 Hz, 1 H, H-5).

^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 8.9 (CH_2CH_3), 19.00 [2 $OCH_2CH(CH_3)_2$], 19.01 [$OCH_2CH(CH_3)_2$], 19.05 [$OCH_2CH(CH_3)_2$], 22.0 (CH_2CH_2), 27.7 [2 $OCH_2CH(CH_3)_2$], 71.2 [$OCH_2CH(CH_3)_2$], 71.4 [$OCH_2CH(CH_3)_2$], 83.3 (C-4), 98.4 (C-1), 144.76 and 144.77 (C-5 and C-6), 150.9 and 156.1 (C-2 and C-3), 162.4 (CO_2), 165.1 (CO_2).

MS (CI/NH_3): *m/z* (%) = 69 (98), 322 (11), 323 (100) $[M + H]^+$, 324 (19), 340 (77) $[M + NH_4]^+$, 341 (15).

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{18}H_{26}NaO_5$: 345.1672; found: 345.1666.

7-Oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylic Acid Monoesters 12–16; General Procedure

0.5 M or 0.25 M aq NaOH (2.0 equiv) was added to a 0.12 M soln of the starting diester (2 mmol) in THF at 0 °C. When the conversion of the diester was complete (TLC; silica gel) at 0 °C, the mixture was washed with Et_2O (2 × 20 mL) and then acidified to pH ≈ 3 with aq HCl. The monoacid was extracted with $CHCl_3$ (3 × 30 mL) and after each separation the pH was readjusted to ≈ 3. The separated organic soln was immediately concentrated under vacuum, and the residue was taken up with fresh $CHCl_3$ (50 mL). The organic phases were combined, dried (Na_2SO_4), and concentrated under vacuum to give the crude acid that was used without purification in the next step. ***Caution***: Extraction after acidification to pH ≈ 1 resulted in isolation of small amounts of the corresponding diacid.

3-(Methoxycarbonyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene-2-carboxylic Acid (12)

Treatment of dimethyl diester **7** (130 mg, 0.62 mmol) with 0.25 M aq NaOH gave a brown oil; yield: 92 mg (76%); R_f = 0.18 (CH_2Cl_2–MeOH, 8:2).

^1H NMR (360 MHz, $CDCl_3$): δ = 3.99 (s, 3 H, OCH_3), 5.79 (t, *J* = 1.8 Hz, 1 H, H-1, or H-4), 5.83 (t, *J* = 1.9 Hz, 1 H, H-4, or H-1), 7.20 (dd, *J* = 5.3, 1.9 Hz, 1 H, H-5, or H-6), 7.28 (dd, *J* = 5.3, 1.8 Hz, 1 H, H-6, or H-5).

Spectroscopic data were in agreement with those reported.[7b]

4-Ethyl-3-(methoxycarbonyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene-2-carboxylic Acid (13)

Treatment of dimethyl diester **8** (1.19 g, 5.00 mmol) with 0.5 M aq NaOH gave a yellow solid; yield: 876 mg (78%); mp 87 °C; R_f = 0.24 (CH_2Cl_2–MeOH, 8:2).

IR (neat): 3400–2500, 2974, 2941, 2884, 1729, 1713, 1641, 1613, 1559, 1440, 1324, 1277, 1206, 916, 733 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.02 (t, *J* = 7.5 Hz, 3 H, CH_2CH_3), 2.33 (q, *J* = 7.5 Hz, 2 H, CH_2CH_3), 3.97 (s, 3 H, OCH_3), 5.71 (d, *J* = 2.0 Hz, 1 H, H-1), 6.92 (d, *J* = 5.1 Hz, 1 H, H-5), 7.21 (dd, *J* = 5.1, 2.0 Hz, 1 H, H-6), 12.50 (br s, 1 H, CO_2H).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 9.2 (CH_2CH_3), 22.9 (CH_2CH_3), 53.8 (OCH_3), 83.8 (C-1), 98.2 (C-4), 144.5 (C-5), 144.9 (C-6), 152.5 and 161.8 (C-2 and C-3), 163.1 (CO_2Me), 167.3 (CO_2H).

MS (CI/NH_3): *m/z* (%) = 97 (5), 181 (6), 225 (67) $[M + H]^+$, 226 (9), 242 (100) $[M + NH_4]^+$, 243 (13).

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{11}H_{12}NaO_5$: 247.0577; found: 247.0580.

4-Benzyl-3-(methoxycarbonyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene-2-carboxylic Acid (14)

Treatment of dimethyl diester **9** (400 mg, 1.33 mmol) with 0.5 M aq NaOH gave an orange oil; yield: 332 mg (87%); R_f = 0.24 (EtOAc).

IR (neat): 3500–2600, 3031, 2955, 1729, 1714, 1635, 1561, 1497, 1436, 1274, 1079, 984, 703 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 3.59 (d, *J* = 15.4 Hz) and 3.67 (d, *J* = 15.4 Hz) (AB system, 2 H, CH_2Ph), 3.89 (s, 3 H, OCH_3), 5.72 (d, *J* = 1.9 Hz, 1 H, H-1), 7.02 (d, *J* = 5.1 Hz, 1 H, H-5), 7.19 (dd, *J* = 5.1 et 1.9 Hz, 1 H, H-6), 7.21–7.34 (m, 5 H, Ph), 8.65 (br s, 1 H, CO_2H).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 35.6 (CH_2Ph), 53.4 (OCH_3), 83.6 (C-1), 97.2 (C-4), 126.8 (C_{Ar}-*p*), 128.2 and 129.6 (C_{Ar}-*o*, C_{Ar}-*m*), 136.0 ($C_{Ar}CH_2$), 144.5 and 144.6 (C-5, C-6), 153.3 and 160.4 (C-2, C-3), 162.3 (CO_2CH_3), 166.7 (CO_2H).

MS (CI/NH_3): *m/z* (%) = 159 (36), 243 (62), 287 (49) $[M + H]^+$, 288 (11), 304 (100) $[M + NH_4]^+$, 305 (17).

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{16}H_{14}NaO_5$: 309.0733; found: 309.0728.

3-(Ethoxycarbonyl)-4-ethyl-7-oxabicyclo[2.2.1]hepta-2,5-diene-2-carboxylic Acid (15)

Treatment of diethyl diester **10** (1.02 g, 3.83 mmol) with a 0.5 M aq soln of NaOH gave a caramel-colored oil; yield: 803 mg (88%); R_f = 0.34 (CH_2Cl_2–MeOH, 8:2).

IR (neat): 3400–2500, 2981, 2940, 2880, 2670, 1729 (br), 1639, 1613, 1560, 1425, 1373, 1320, 1276, 1203, 1036, 919, 698 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.00 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3), 1.40 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 2.20–2.42 (m, 2 H, CCH_2CH_3), 4.26–4.53 (m, 2 H, OCH_2CH_3), 5.68 (br s, 1 H, H-1), 6.91 (d, *J* = 5.1 Hz, 1 H, H-5), 7.19 (br d, *J* = 5.1 Hz, 1 H, H-6), 10.63 (br s, 1 H, CO_2H).

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^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 9.1 (CH_2CH_3); 13.7 (OCH_2CH_3), 22.8 (CCH_2CH_3), 63.4 (OCH_2CH_3), 83.6 (C-1), 98.1 (C-4), 144.5 and 144.7 (C-5, C-6), 152.9 and 162.2 (C-2, C-3), 162.0 (CO_2CH_3), 166.7 (CO_2H).

MS (CI/NH_3): *m/z* (%) = 239 (100) $[M + H]^+$, 240 (14), 256 (73) $[M + NH_4]^+$, 257 (10).

HRMS (ES^-): *m/z* $[M - H]^-$ calcd for $C_{12}H_{13}O_5$: 237.0768; found: 237.0774.

4-Ethyl-3-(isobutoxycarbonyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene-2-carboxylic Acid (16)

Treatment of diisobutyl diester **11** (380 mg, 1.18 mmol) with 0.5 M aq NaOH gave a yellow oil; yield: 280 mg (89%); R_f = 0.15 (PE–EtOAc, 2:1).

IR (neat): 3500–2600, 2969, 2941, 2876, 1727 (br), 1636, 1559, 1381, 1316, 1276, 1201, 1142, 994, 918, 879, 699 cm^{-1}.

^{1}H NMR (360 MHz, $CDCl_3$): δ = 1.03 [d, *J* = 6.5 Hz, 6 H, $CH(CH_3)_2$], 1.05 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3), 2.10 [nonuplet, *J* = 6.7 Hz, 1 H, $OCH_2CH(CH_3)_2$], 2.29–2.45 (m, 2 H, CH_2CH_3), 4.10 (dd, *J* = 10.8, 6.5 Hz) and 4.21 (dd, *J* = 10.8, 6.8 Hz) [AB part of an ABX system, 2 H, $OCH_2CH(CH_3)_2$], 5.73 (d, *J* = 2.0 Hz, 1 H, H-1), 6.92 (d, *J* = 5.2 Hz, 1 H, H-5), 7.24 (dd, *J* = 5.1, 2.0 Hz, 1 H, H-6), 12.53 (br s, 1 H, CO_2H).

^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 9.1 (CH_2CH_3), 18.92 [$OCH_2CH(CH_3)_2$], 18.96 [$OCH_2CH(CH_3)_2$], 23.0 (CH_2CH_3), 27.5 [$OCH_2CH(CH_3)_2$], 73.4 [$OCH_2CH(CH_3)_2$], 83.7 (C-1), 98.2 (C-4), 144.5 and 144.9 (C-5, C-6), 152.8 and 161.9 (C-2, C-3), 162.6 [$CO_2CH_2CH(CH_3)_2$], 167.0 (CO_2H).

MS (CI/NH_3): *m/z* (%) = 97 (8), 223 (7), 267 (100) $[M + H]^+$, 268 (16), 284 (36) $[M + NH_4]^+$, 285 (5).

HRMS (ES^-): *m/z* $[M - H]^-$ calcd for $C_{14}H_{17}O_5$: 265.1081; found: 265.1086.

Amido Esters 17–23; General Procedure

The freshly distilled amine (1.1 equiv) was added to a stirred 0.2 M soln of the diacid monoester (1 mmol) in THF, followed, after 5 min, by anhyd solid DMTMM (1.1 equiv). The mixture was stirred for the appropriate time (Table 2) under argon at r.t., then H_2O (20 mL) was added and the product was extracted with Et_2O (3 × 30 mL). Each separated organic phase was washed successively with sat. aq Na_2CO_3 (2 × 10 mL), H_2O (10 mL), 1 M aq HCl (10 mL), and H_2O (10 mL). The organic phases were combined, dried (Na_2SO_4), and concentrated under vacuum to give a crude product that was purified by column chromatography [silica gel, PE–EtOAc (4:1 to 2:1)].

Methyl 3-(Phenylcarbamoyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene-2-carboxylate (17)

From monoacid **12** (177 mg, 0.90 mmol). Flash chromatography [PE–EtOAc (2:1)] gave a yellow oil; yield: 26 mg (11%); R_f = 0.55 (PE–EtOAc, 2:1).

IR (neat): 3294, 3095, 2953, 1692, 1662, 1620, 1599, 1559, 1496, 1446, 1330, 1304, 1268, 1243, 1211, 881, 754, 701 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.92 (s, 3 H, OCH_3), 5.81 (t, *J* = 1.9 Hz, 1 H, H-1, or H-4), 5.96 (t, *J* = 1.9 Hz, 1 H, H-4, or H-1), 7.13 (br t, *J* = 7.6 Hz, 1 H, H_{Ar}-*p*), 7.20 (dd, *J* = 5.2, 1.9 Hz, 1 H, H-5, or H-6), 7.30 (dd, *J* = 5.2, 1.9 Hz, 1 H, H-6, or H-5), 7.35 (br t, *J* = 7.6 Hz, 2 H, H_{Ar}-*m*), 7.69 (br d, *J* = 7.6 Hz, 2 H, H_{Ar}-*o*), 11.07 (br s, 1 H CONH).

^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 53.0 (OCH_3), 85.1 and 85.7 (C-1, C-4), 119.9 (C_{Ar}-*o*), 124.6 (C_{Ar}-*p*), 129.0 (C_{Ar}-*m*), 137.9 (C_{Ar}NH), 142.8 and 143.4 (C-5, C-6), 146.6 (C-3), 159.3 (C-2), 163.4 and 165.3 (CONH, CO_2).

MS (CI/NH_3): *m/z* (%) = 272 (100) $[M + H]^+$, 273 (16).

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{15}H_{13}NNaO_4$: 294.0737; found: 294.0745.

Methyl 1-Ethyl-3-(phenylcarbamoyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene-2-carboxylate (18)

From monoacid **13** (115 mg, 0.51 mmol). Flash chromatography [PE–EtOAc (4:1)] gave a yellow-green oil; yield: 103 mg (67%); R_f = 0.33 (PE–EtOAc, 4:1).

IR (neat): 3301, 3087, 2973, 2881, 1693, 1661, 1621, 1601, 1557, 1497, 1446, 1328, 1303, 1252, 1201, 994, 931, 757 cm^{-1}.

^{1}H NMR (360 MHz, $CDCl_3$): δ = 1.05 (t, *J* = 7.5 Hz, 3 H, CH_2CH_3), 2.28–2.40 (m, 2 H, CH_2CH_3), 3.91 (s, 3 H, OCH_3), 5.79 (d, *J* = 1.8 Hz, 1 H, H-4), 6.93 (d, *J* = 5.0 Hz, 1 H, H-6), 7.13 (br t, *J* = 7.6 Hz, 1 H, H_{Ar}-*p*), 7.28 (dd, *J* = 5.0, 1.8 Hz, 1 H, H-5), 7.35 (br t, *J* = 7.6 Hz, 2 H, H_{Ar}-*m*), 7.66 (br d, *J* = 7.6 Hz, 2 H, H_{Ar}-*o*), 10.48 (br s, 1 H CONH).

^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 9.2 (CH_2CH_3), 22.9 (CH_2CH_3), 52.6 (OCH_3), 84.1 (C-4), 98.4 (C-1), 119.7 (C_{Ar}-*o*), 124.4 (C_{Ar}-*p*), 128.9 (C_{Ar}-*m*), 137.8 (C_{Ar}NH), 144.1 (C-6), 144.6 (C-5), 147.7 (C-3), 159.9 (C-2), 163.4 and 166.4 (CONH, CO_2).

MS (CI/NH_3): *m/z* (%) = 300 (100) $[M + H]^+$, 301 (18).

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{17}H_{17}NNaO_4$: 322.1050; found: 322.1049.

Methyl 3-[(Benzylcarbamoyl)carbonyl]-1-ethyl-7-oxabicyclo[2.2.1]hepta-2,5-diene-2-carboxylate (19)

From monoacid **13** (351 mg, 1.57 mmol). Flash chromatography [PE–EtOAc (4:1)] gave a yellow oil; yield: 160 mg (33%); R_f = 0.37 (PE–EtOAc, 2:1).

IR (neat): 3313, 3032, 2971, 2881, 1713, 1694, 1650, 1622, 1539, 1454, 1438, 1362, 1318, 1272, 1252, 1207, 1081, 928, 701 cm^{-1}.

^{1}H NMR (360 MHz, $CDCl_3$): δ = 1.01 (t, *J* = 7.6 Hz, 3 H, CH_2CH_3), 2.22–2.36 (m, 2 H, CH_2CH_3), 3.78 (s, 3 H, OCH_3), 4.47 (dd, *J* = 15.1, 6.0 Hz) and 4.57 (dd, *J* = 15.1, 6.0 Hz) (AB part of an ABX system, 2 H, $NHCH_2$), 5.72 (d, *J* = 2.1 Hz, 1 H, H-4), 6.90 (d, *J* = 5.0 Hz, 1 H, H-6), 7.25 (dd, *J* = 5.0, 2.1 Hz, 1 H, H-5), 7.27–7.34 (m, 5 H, Ph), 8.59 (br s, 1 H CONH).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 9.2 (CH_2CH_3), 22.7 (CH_2CH_3), 43.6 (NCH_2Ph), 52.4 (OCH_3), 84.1 (C-4), 98.2 (C-1), 127.4 (C_{Ar}-*p*), 127.6 and 128.6 (C_{Ar}-*o*, C_{Ar}-*m*), 137.6 ($C_{Ar}CH_2$), 144.0 and 144.6 (C-5, C-6), 147.6 (C-3), 161.9 and 162.1 and 165.8 (C-2, CONH, CO_2).

MS (ES^+): *m/z* (%) = 91 (100), 173 (28), 218 (63), 240 (31), 314 (14) $[M + H]^+$, 336 (26) $[M + Na]^+$, 352 (63) $[M + K]^+$.

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{18}H_{19}NNaO_4$: 336.1206; found: 336.1191.

Methyl 3-(Cyclohexylcarbamoyl)-1-ethyl-7-oxabicyclo[2.2.1]hepta-2,5-diene-2-carboxylate (20)

From monoacid **13** (576 mg, 2.57 mmol). Chromatography [PE–THF (4:1)] gave a yellow oil; yield: 504 mg (64%); R_f = 0.23 (PE–Et_2O, 1:1).

IR (neat): 3315, 3073, 2933, 2855, 1719, 1699, 1650, 1619, 1544, 1451, 1437, 1372, 1327, 1300, 1274, 1251, 1205, 1154, 1081, 1031, 993, 930, 893, 801, 733, 710 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.01 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3), 1.17–1.50 (m, 5 H, H_{Cy}), 1.53–1.80 (m, 3 H, H_{Cy}), 1.80–2.00 (m, 2 H, H_{Cy}), 2.29 (dq, *J* = 14.8, 7.4 Hz) and 2.32 (dq, *J* = 14.8, 7.4 Hz) (AB part of an ABM_3 system, 2 H, CH_2CH_3), 3.80–3.88 (m, CHN) and 3.85 (s, OCH_3) (4 H), 5.68 (d, *J* = 2.0 Hz, 1 H, H-4), 6.89 (d, *J* = 5.2 Hz, 1 H, H-6), 7.24 (dd, *J* = 5.2, 2.0 Hz, 1 H, H-5), 8.20 (br d, *J* = 6.7 Hz, 1 H, CONH).

^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 9.3 (CH_2CH_3), 22.8 (C_{Cy}), 24.4 (C_{Cy}), 25.5 (CH_2CH_3), 32.5 and 32.7 (C_{Cy}), 48.1 (NCH), 52.3

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(OCH_3), 84.2 (C-4), 98.1 (C-1), 144.0 and 144.7(C-5, C-6), 146.8 (C-3), 161.2 (C-2), 162.6 and 165.9 (CON, CO_2).

MS (EI): 55 (38), 57 (34), 81 (80), 91 (27), 96 (100), 98 (68), 119 (49), 128 (22), 135 (52), 148 (24), 149 (27), 150 (79), 151 (38), 165 (29), 166 (58), 179 (43), 180 (92), 181 (56), 191 (25), 192 (28), 207 (32), 210 (32), 216 (23), 217 (38), 246 (54), 247 (20), 248 (53), 249 (28), 305 (35) $[M]^+$.

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{17}H_{23}NNaO_4$: 328.1519; found: 328.1508.

Methyl 1-Benzyl-3-(phenylcarbamoyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene-2-carboxylate (21)

From monoacid **14** (210 mg, 0.73 mmol). Flash chromatography [PE–EtOAc (2:1)] gave a yellow solid; yield: 96 mg (36%); mp 118 °C [$CHCl_3$–Et_2O (1:1), at –20 °C]; R_f = 0.40 (PE–EtOAc, 2:1).

IR (neat): 3300, 3147, 3086, 3065, 3035, 2954, 2927, 1729, 1695, 1601, 1558, 1496, 1446, 1303, 1260, 1201, 988, 756, 704 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 3.65 (s, 2 H, CH_2Ph), 3.88 (s, 3 H, OCH_3), 5.80 (d, *J* = 2.0 Hz, 1 H, H-4), 7.02 (d, *J* = 5.0 Hz, 1 H, H-6), 7.14 (br t, *J* = 7.2 Hz, 1 H, H_{Ar}-*p* of NHPh), 7.20–7.40 (m, 8 H, H-5, H_{Ar} of CH_2Ph, H_{Ar}-*m* of NHPh), 7.62 (br d, *J* = 8.7 Hz, 2 H, H_{Ar}-*o* of NHPh), 10.30 (br s, 1 H, CONH).

^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 35.9 (*C*H_2Ph), 52.5 (OCH_3), 84.2 (C-4), 97.4 (C-1), 119.7 (C_{Ar}-*o* of NHPh), 124.4 (C_{Ar}-*p* of NHPh), 126.7 (C_{Ar}-*p* of CH_2Ph), 128.2 and 128.8 and 129.6 (C_{Ar}-*o* and C_{Ar}-*m* of CH_2Ph, and C_{Ar}-*m* of NHPh), 136.5 (*C*$_{Ar}CH_2$), 137.6 (*C*$_{Ar}NH$), 144.3 (C-6), 144.6 (C-5), 147.7 (C-3), 159.7 (C-2), 162.4 and 166.0 (CONH, CO_2).

MS (CI/NH_3): *m/z* (%) = 176 (37), 275 (100), 276 (15), 362 (71) $[M + H]^+$, 363 (18), 379 (10) $[M + NH_4]^+$.

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{22}H_{19}NNaO_4$: 384.1206; found: 384.1202.

Ethyl 1-Ethyl-3-(phenylcarbamoyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene-2-carboxylate (22)

From monoacid **15** (457 mg, 1.92 mmol). Chromatography [PE–Et_2O (3:1)] gave yellow crystals; yield: 305 mg (51%); mp: 101 °C; R_f = 0.45 (PE–Et_2O, 1:1).

IR (KBr): 3254, 3139, 3040, 2977, 2933, 1682, 1657, 1615, 1597, 1560, 1497, 1446, 1329, 1298, 1252, 1234, 1196, 1008, 901, 770, 714 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.05 (t, *J* = 7.4 Hz, 3 H, CCH_2CH_3), 1.40 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 2.31 (dq, *J* = 14.8, 7.4 Hz) and 2.40 (dq, *J* = 14.8, 7.4 Hz) (AB part of an ABM_3 system, 2 H, CCH_2CH_3), 4.29 (dq, *J* = 10.9, 7.1 Hz) and 4.46 (dq, *J* = 10.9, 7.1 Hz) (AB part of an ABX_3 system, 2 H, OCH_2CH_3), 5.79 (d, *J* = 2.0 Hz, 1 H, H-4), 6.93 (d, *J* = 5.1 Hz, 1 H, H-6), 7.13 (br t, *J* = 7.6 Hz, 1 H, H_{Ar}-*p*), 7.30 (dd, *J* = 5.1, 2.0 Hz, 1 H, H-5), 7.34 (br t, *J* = 7.6 Hz, 2 H, H_{Ar}-*m*), 7.66 (br d, *J* = 7.6 Hz, 2 H, H_{Ar}-*o*), 10.56 (br s, 1 H, CONH).

^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 9.3 (CCH_2CH_3), 14.0 (OCH_2CH_3), 23.0 (CCH_2CH_3), 62.1 (OCH_2CH_3), 84.1 (C-4), 98.4 (C-1), 119.8 (C_{Ar}-*o*), 124.5 (C_{Ar}-*p*), 128.9 (C_{Ar}-*m*), 137.8 (*C*$_{Ar}NH$), 144.2 and 144.7 (C-5, C-6), 148.0 (C-3), 160.0 (C-2), 163.1 and 166.0 (CONH, CO_2).

MS (ES^+): *m/z* (%) = 218 (24), 240 (15), 336 (100) $[M + Na]^+$, 337 (17).

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{18}H_{19}NNaO_4$: 336.1206; found: 336.1191.

X-ray Crystal Data:[23] $C_{18}H_{19}NO_4$, M = 313.34, monoclinic, space group $P2_1/c$, Z = 4, *a* = 8.3840(6) Å, *b* = 16.4306(11) Å, *c* = 11.4385(8) Å, *V* = 1524.79(18) $Å^3$, *d* = 1.365 g/cm^3, *R*1 = 0.0376, *wR*2 = 0.1025, 4463 independent reflections were collected (R_{int}=0.0226).

Isobutyl 1-Ethyl-3-(phenylcarbamoyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene-2-carboxylate (23)

From monoacid **16** (260 mg, 0.98 mmol) treated under the general conditions for 6 h, then stirred for 1 h after introduction of additional aniline (0.4 equiv) and DMTMM (0.4 equiv). Chromatography [PE–EtOAc (4:1)] gave a yellow oil; yield: 250 mg (75%); R_f = 0.52 (PE–EtOAc, 4:1).

IR (neat): 3302, 3091, 2969, 2876, 1684, 1660, 1599, 1559, 1498, 1446, 1326, 1302, 1249, 1197, 992, 921, 756 cm^{-1}.

^1H NMR (360 MHz, $CDCl_3$): δ = 1.01 [d, *J* = 6.8 Hz, 6 H, $CH(CH_3)_2$], 1.07 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3), 2.06 [nonuplet, *J* = 6.7 Hz, 1 H, $OCH_2CH(CH_3)_2$], 2.31 (dq, *J* = 14.8, 7.4 Hz) and 2.40 (dq, *J* = 14.8, 7.4 Hz) (AB part of an ABM_3 system, 2 H, CH_2CH_3), 4.04 (dd, *J* = 10.6, 6.5 Hz) and 4.14 [dd, *J* = 10.6, 6.3 Hz) (AB part of an ABX system, 2 H, $OCH_2CH(CH_3)_2$], 5.79 (d, *J* = 1.8 Hz, 1 H, H-4), 6.91 (d, *J* = 5.1 Hz, 1 H, H-6), 7.13 (br t, *J* = 7.2 Hz, 1 H, H_{Ar}-*p*), 7.28 (dd, *J* = 5.1, 1.8 Hz, 1 H, H-5), 7.34 (br t, *J* = 7.5 Hz, 2 H, H_{Ar}-*m*), 7.66 (br d, *J* = 7.5 Hz, 2 H, H_{Ar}-*o*), 10.58 (br s, 1 H, CONH).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 9.2 (CH_2CH_3), 18.88 ($CH(CH_3)_2$], 18.94 [$CH(CH_3)_2$], 22.9 (CH_2CH_3), 27.4 [$OCH_2CH(CH_3)_2$], 72.0 [$OCH_2CH(CH_3)_2$], 84.0 (C-4), 98.2 (C-1), 119.6 (C_{Ar}-*o*), 124.2 (C_{Ar}-*p*), 128.7 (C_{Ar}-*m*), 137.7 (*C*$_{Ar}NH$), 144.0 and 144.6 (C-5, C-6), 147.9 (C-3), 159.8 (C-2), 163.2 and 166.0 (CONH, CO_2).

MS (CI/NH_3): *m/z* (%) = 341 (7), 342 (100) $[M + H]^+$, 343 (22).

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{20}H_{23}NNaO_4$: 364.1519; found: 364.1505.

Diesters 24–27; General Procedure

Distilled 4-methylmorpholine (1.2 equiv) was added to a stirred 0.2 M soln of the acid (0.5 mmol) in the appropriate alcohol, followed after 5 min by anhyd solid DMTMM (2.0 equiv). After stirring for the indicated time (Table 2) under argon at r.t., the alcohol was evaporated under vacuum and the residue was taken up in Et_2O (20 mL). The organic phase was washed successively with sat. aq Na_2CO_3 (10 mL), H_2O (10 mL), and sat. aq NaCl (5 mL). The aqueous phases were extracted with Et_2O (2 × 10 mL) and the organic phases were combined, dried (Na_2SO_4), and concentrated under vacuum. The crude product was purified by column chromatography [silica gel, PE– Et_2O (1:1)].

3-Ethyl 2-Methyl 1-Ethyl-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (24)

From monoacid **13** (56 mg, 0.25 mmol). Colorless oil; yield: 43 mg (69%); R_f = 0.40 (PE–Et_2O, 1:1).

IR (neat): 2980, 2954, 1712 (broad), 1639, 1562, 1436, 1368, 1316, 1272, 1231, 1139, 919, 734 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.02 (t, *J* = 7.5 Hz, 3 H, CCH_2CH_3), 1.29 (t, *J* = 7.3 Hz, 3 H, OCH_2CH_3), 2.10–2.26 (m, 2 H, CCH_2CH_3), 3.83 (s, 3 H, OCH_3), 4.22 (q, *J* = 7.3 Hz, 2 H, OCH_2CH_3), 5.64 (d, *J* = 1.8 Hz, 1 H, H-4), 6.99 (d, *J* = 5.3 Hz, 1 H, H-6), 7.18 (dd, *J* = 5.3, 1.8 Hz, 1 H, H-5).

^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 8.9 (CCH_2CH_3), 14.0 (OCH_2CH_3), 21.9 (CCH_2CH_3), 52.0 (OCH_3), 61.1 (OCH_2CH_3), 83.2 (C-4), 98.3 (C-1), 144.6 and 144.7 (C-5, C-6), 151.7 and 155.6 (C-2, C-3), 162.3 (CO_2), 165.3 (CO_2).

MS (CI/NH_3): *m/z* (%) = 253 (100) $[M + H]^+$, 254 (12), 270 (34) $[M + NH_4]^+$.

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{13}H_{16}NaO_5$: 275.0890; found: 275.0880.

3-Benzyl 2-Methyl 1-Ethyl-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (25)

From monoacid **13** (51 mg, 0.23 mmol). Colorless oil; yield: 50 mg (70%), R_f = 0.60 (PE–Et_2O, 1:1).

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IR (neat): 3033, 2972, 2952, 1710 (broad), 1638, 1559, 1456, 1436, 1381, 1314, 1271, 1228, 1137, 1079, 928, 699 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.02 (t, *J* = 7.5 Hz, 3 H, CH_2CH_3), 2.18 (q, *J* = 7.5 Hz) and 2.20 (q, *J* = 7.5 Hz) (2 H, CH_2CH_3), 3.63 (s, 3 H, OCH_3), 5.19 (s, 2 H, OCH_2Ph), 5.68 (d, *J* = 1.8 Hz, 1 H, H-4), 6.99 (d, *J* = 5.2 Hz, 1 H, H-6), 7.20 (dd, *J* = 5.2, 1.8 Hz, 1 H, H-5), 7.30–7.41 (m, 5 H, Ph).

^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 8.9 (CH_2CH_3), 21.9 (CH_2CH_3), 51.9 (OCH_3), 66.9 (CH_2Ph), 83.2 (C-4), 98.4 (C-1), 128.2 and 128.5 (C_{Ar}-*o*, C_{Ar}-*m*), 128.3 (C_{Ar}-*p*), 135.1 (C_{Ar}-CH_2), 144.6 (C-5, C-6), 151.0 and 156.3 (C-2, C-3), 162.1 (CO_2), 165.3 (CO_2).

MS (CI/NH_3): *m/z* (%) = 69 (5), 315 (57) $[M + H]^+$, 332 (100) $[M + NH_4]^+$, 333 (20).

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{18}H_{18}NaO_5$: 337.1046; found: 337.1040.

3-Isobutyl 2-Methyl 1-Ethyl-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (26)

From monoacid **13** (55 mg, 0.25 mmol). Colorless oil; yield: 38 mg (55%); R_f = 0.58 (PE–Et_2O, 1:1).

IR (neat): 2967, 2878, 1710 (broad), 1640, 1559, 1465, 1436, 1380, 1317, 1270, 1231, 1200, 1138, 1079, 919, 791 cm^{-1}.

^1H NMR (360 MHz, $CDCl_3$): δ = 0.94 [d, *J* = 6.8 Hz, 6 H, $CH(CH_3)_2$], 1.03 (t, *J* = 7.5 Hz, 3 H, CH_2CH_3), 1.89–2.01 [m, 1 H, $CH_2CH(CH_3)_2$], 2.13–2.26 (m, 2 H, CH_2CH_3), 3.83 (s, 3 H, OCH_3), 3.95 [d, *J* = 6.5 Hz, 2 H, $OCH_2CH(CH_3)_2$], 5.65 (d, *J* = 2.0 Hz, 1 H, H-4), 6.99 (d, *J* = 5.2 Hz, 1 H, H-6), 7.18 (dd, *J* = 5.2, 2.0 Hz, 1 H, H-5).

^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 8.9 (CH_2CH_3), 18.9 [$CH(CH_3)_2$], 22.0 (CH_2CH_3), 27.7 [$CH_2CH(CH_3)_2$], 52.2 (OCH_3), 71.3 [$OCH_2CH(CH_3)_2$], 83.3 (C-4), 98.5 (C-1), 144.74 and 144.77 (C-5, C-6), 151.3 and 155.7 (C-2, C-3), 162.4 (CO_2), 165.5 (CO_2).

MS (CI/NH_3): *m/z* (%) = 69 (100), 281 (64) $[M + H]^+$, 298 (45) $[M + NH_4]^+$, 299 (6).

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{15}H_{20}NaO_5$: 303.1208; found: 303.1198.

2-Ethyl 3-Methyl 1-Ethyl-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (27)

From monoacid **15** (145 mg, 0.61 mmol). Colorless oil; yield: 107 mg (70%); R_f = 0.40 (PE–Et_2O, 1:1).

IR (neat): 2978, 1731, 1713, 1644, 1560, 1436, 1369, 1312, 1264, 1231, 1197, 1138, 1095, 1080, 1041, 900, 709 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.03 (t, *J* = 7.5 Hz, 3 H, CCH_2CH_3), 1.34 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 2.09–2.31 (m, 2 H, CCH_2CH_3), 3.77 (s, 3 H, OCH_3), 4.30 (dq, *J* = 10.9, 7.1 Hz) and 4.33 (dq, *J* = 10.9, 7.1 Hz) (AB part of an ABX_3 system, 2 H, OCH_2CH_3), 5.65 (d, *J* = 2.0 Hz, 1 H, H-4), 6.99 (d, *J* = 5.2 Hz, 1 H, H-6), 7.19 (dd, *J* = 5.2, 2.0 Hz, 1 H, H-5).

^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 9.0 (CCH_2CH_3), 14.1 (OCH_2CH_3), 22.0 (CCH_2CH_3), 52.0 (OCH_3), 61.4 (OCH_2CH_3), 83.3 (C-4), 98.4 (C-1), 144.7 and 144.8 (C-5 and C-6), 151.0 and 156.4 (C-2, C-3), 162.9 (CO_2), 164.9 (CO_2).

MS (ES^+): *m/z* (%) = 179 (22), 275 (100) $[M + Na]^+$, 276 (13).

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{13}H_{16}NaO_5$: 275.0890; found: 275.0892.

Oxanorbornenes 28–32; General Procedure

A preparation of 5% Pd on $BaSO_4$ (8 mg for 1 mmol) was added to a 0.1 M soln of the oxanorbornadiene in PE or a PE–THF mixture, and the mixture was stirred under H_2. The solids were separated by filtration over Clarcel Flo-M and the filtrate was concentrated to give the crude oxanorbornene, which was purified column chromatography (silica gel).

Methyl 3-(Benzylcarbamoyl)-1-ethyl-7-oxabicyclo[2.2.1]hept-2-ene-2-carboxylate (28)

From amido ester **19** (159 mg, 0.51 mmol), hydrogenated for 40 min in PE. Isolated by chromatography [PE–Et_2O (65:35)] as a colorless oil; yield: 138 mg (87%); R_f = 0.25 (PE–Et_2O, 1:1).

IR (neat): 3319, 3064, 3030, 2955, 2879, 1721, 1699, 1657, 1614, 1546, 1455, 1436, 1364, 1330, 1273, 1255, 1176, 1081, 1014, 988, 936, 752, 699 cm^{-1}.

^1H NMR (360 MHz, $CDCl_3$): δ = 0.97 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3), 1.51 (ddd, *J* = 10.8, 8.6, 3.4 Hz, 1 H, H-6_{endo}), 1.59 (ddd, *J* = 11.1, 8.5, 3.4 Hz, 1 H, H-5_{endo}), 1.69 (ddd, *J* = 10.8, 8.7, 3.3 Hz, 1 H, H-6_{exo}), 1.92 (dq, *J* = 14.8, 7.4 Hz, 1 H, A part of an ABM_3 system, CH_2CH_3), 2.13 (dddd, *J* = 11.1, 9.4, 5.0, 3.5 Hz, 1 H, H-5_{exo}), 2.31 (dq, *J* = 14.8, 7.4 Hz, 1 H, B part of an ABM_3 system, CH_2CH_3), 3.79 (s, 3 H, OCH_3), 4.45 (dd, *J* = 14.9, 5.4 Hz) and 4.59 (dd, *J* = 14.9, 6.0 Hz, 2 H,) (AB part of an ABX system, $NHCH_2$), 5.33 (d, *J* = 5.0 Hz, 1 H, H-4), 7.28–7.37 (m, 5 H, Ph), 8.62 (br s, 1 H, CONH).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 9.2 (CH_2CH_3), 24.7 (CH_2CH_3), 27.8 (C-5), 29.5 (C-6), 43.5 (NCH_2Ph), 52.3 (OCH_3), 80.0 (C-4), 93.4 (C-1), 127.4 (C_{Ar}-*p*), 127.7 and 128.6 (C_{Ar}-*o*, C_{Ar}-*m*), 137.8 and 138.2 ($C_{Ar}CH_2$, C-3), 152.0 (C-2), 161.9 and 166.3 (CONH, CO_2).

MS (ES^+): 91 (21), 256 (18) $[MH - CH_2{=}CH_2 - MeOH]^+$, 288 (100) $[MH - CH_2{=}CH_2]^+$, 289 (14), 310 (17), 316 (7) $[M + H]^+$, 338 (85) $[M + Na]^+$, 339 (13).

HRMS (ES^+): *m/z* $[M + H]^+$ calcd for $C_{18}H_{22}NO_4$: 316.1543; found: 316.1530.

Methyl 3-(Cyclohexylcarbamoyl)-1-ethyl-7-oxabicyclo[2.2.1]hept-2-ene-2-carboxylate (29)

From amido ester **20** (197 mg, 0.65 mmol), hydrogenated for 1.5 h in PE. Isolated by chromatography [PE–Et_2O (4:1)] as a yellow oil; yield: 188 mg (95%); R_f = 0.23 (PE–Et_2O, 1:1).

IR (neat): 3317, 3073, 2934, 2856, 1721, 1699, 1651, 1613, 1547, 1462, 1452, 1437, 1373, 1363, 1340, 1315, 1272, 1254, 1195, 1176, 1087, 1011, 988, 891, 806, 755 cm^{-1}.

^1H NMR (360 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3), 1.12–1.40 (m, 5 H, H_{Cy}), 1.40–1.72 (m, 6 H, H-5, H-6, H-6′ and 3 H_{Cy}), 1.77–1.92 (m, 3 H, A part of an ABM_3 system of CH_2CH_3 and 2 H_{Cy}), 2.00–2.09 (m, 1 H, H-5′), 2.25 (dq, *J* = 15.0, 7.4 Hz, 1 H, B part of an ABM_3 system, CH_2CH_3), 3.71–3.82 (m, CHN) and 3.78 (s, OCH_3) (4 H), 5.21 (d, *J* = 5.0 Hz, 1 H, H-4), 8.15 (br d, *J* = 7.5 Hz, 1 H, CONH).

^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 9.1 (CH_2CH_3), 24.28 and 24.30 (CH_{2Cy}), 24.6 (CH_{2Cy}), 25.4 (CH_2CH_3), 27.7 (C-5), 29.4 (C-6), 32.3 and 32.6 (CH_{2Cy}), 47.8 (NCH), 52.2 (OCH_3), 79.8 (C-4), 93.2 (C-1), 137.4 (C-3), 152.5 (C-2), 160.8 and 166.2 (CON, CO_2).

MS (ES^+): 248 (3), 280 (12), 302 (17), 303 (3), 308 (5) $[M + H]^+$, 330 (100) $[M + Na]^+$, 331 (33), 637 (7) $[2M + Na]^+$.

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{17}H_{25}NNaO_4$: 330.1676; found: 330.1690.

Methyl 1-Benzyl-3-(phenylcarbamoyl)-7-oxabicyclo[2.2.1]hept-2-ene-2-carboxylate (30)

From amido ester **21** (327 mg, 0.91 mmol), hydrogenated for 40 min in 7:3 PE–THF. Isolated by chromatography [PE–Et_2O (3:1)] as a yellow solid; yield: 307 mg (93%); mp: 108 °C; R_f = 0.42 (PE–Et_2O, 1:1).

IR (ATR): 3298, 3199, 3142, 3089, 3034, 2988, 2955, 2940, 2917, 2878, 1695, 1661, 1598, 1552, 1495, 1446, 1346, 1272, 1247, 1079, 982, 757, 706 cm^{-1}.

^1H NMR (360 MHz, $CDCl_3$): δ = 1.61 (ddd, *J* = 11.4, 8.7, 3.7 Hz, 1 H, H-6_{endo}), 1.70 (ddd, *J* = 11.2, 8.7, 3.5 Hz, 1 H, H-5_{endo}), 1.84 (ddd, *J* = 11.4, 9.4, 3.7 Hz, 1 H, H-6_{exo}), 2.19 (dddd, *J* = 11.2, 9.4, 5.0, 3.6 Hz, 1 H, H-5_{exo}), 3.34 (d, *J* = 15.2 Hz) and 3.56 (d, *J* = 15.2 Hz) (2

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H, AB system, CH_2Ph), 3.86 (s, 3 H, OCH_3), 5.44 (d, J = 5.0 Hz, 1 H, H-4), 7.10 (br t, J = 7.6 Hz, 1 H, H_{Ar}-*p* of NHPh), 7.23–7.34 (m, 7 H, H_{Ar} of CH_2Ph, H_{Ar}-*m* of NHPh), 7.60 (br d, J = 7.6 Hz, 2 H, H_{Ar}-*o* of NHPh), 10.28 (br s, 1 H, CONH).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 27.7 (C-5), 30.3 (C-6), 37.9 (*C*H_2Ph), 52.5 (OCH_3), 80.1 (C-4), 92.9 (C-1), 119.7 (C_{Ar}-*o* of NHPh), 124.3 (C_{Ar}-*p* of NHPh), 126.6 (C_{Ar}-*p* of CH_2Ph), 128.2 and 128.9 and 129.7 (C_{Ar}-*o* and C_{Ar}-*m* of CH_2Ph, C_{Ar}-*m* of NHPh), 136.9 (*C*$_{Ar}CH_2$), 137.7 ($C_{Ar}NH$), 138.2 (C-3), 152.3 (C-2), 159.5 and 166.4 (CONH, CO_2).

MS (ES^+): 304 (6), 336 (13) [MH – CH_2=CH_2]$^+$, 358 (17) [MNa – CH_2=CH_2]$^+$, 386 (100) [M + Na]$^+$, 387 (24).

HRMS (ES^+): *m/z* [M + Na]$^+$ calcd for $C_{22}H_{21}NNaO_4$: 386.1363; found: 386.1352.

3-Ethyl 2-Methyl 1-Ethyl-7-oxabicyclo[2.2.1]hept-2-ene-2,3-dicarboxylate (31)

From diester **24** (239 mg, 0.95 mmol) hydrogenated for 55 min in PE. Isolated by chromatography [toluene–PE–THF (48:49:3)] as a colorless oil; yield: 206 mg (85%); R_f = 0.18 (toluene–PE–THF, 47:47:6).

IR (neat): 2981, 2954, 2883, 1716 (broad), 1635, 1464, 1436, 1372, 1331, 1304, 1272 (broad), 1176, 1123, 1092, 1075, 1034, 1005, 936, 879, 792 cm^{-1}.

^{1}H NMR (360 MHz, $CDCl_3$): δ = 1.02 (t, J = 7.5 Hz, 3 H, CCH_2CH_3), 1.30 (t, J = 7.2 Hz, 3 H, OCH_2CH_3), 1.50 (ddd, J = 11.5, 8.6, 3.6 Hz, 1 H, H-6$_{endo}$), 1.60 (ddd, J = 11.3, 8.6, 3.7 Hz, 1 H, H-5$_{endo}$), 1.72 (ddd, J = 11.5, 9.1, 3.6 Hz, 1 H, H-6$_{exo}$), 1.94 (dq, J = 14.8, 7.5 Hz, 1 H, A part of an ABM_3 system, CCH_2CH_3), 2.08 (dddd, J = 11.3, 8.8, 4.8, 3.8 Hz, 1 H, H-5$_{exo}$), 2.18 (dq, J = 14.8, 7.5 Hz, 1 H, B part of an ABM_3 system, CCH_2CH_3), 3.83 (s, 3 H, OCH_3), 4.23 (q, J = 7.2 Hz, 2 H, OCH_2CH_3), 5.21 (d, J = 4.7 Hz, 1 H, H-4).

^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 8.8 (CCH_2CH_3), 13.9 (OCH_2CH_3), 24.0 (CCH_2CH_3), 27.0 (C-5), 29.0 (C-6), 51.9 (OCH_3), 60.9 (OCH_2CH_3), 78.5 (C-4), 93.1 (C-1), 141.2 and 146.4 (C-2, C-3), 161.8 (CO_2), 165.0 (CO_2).

MS (ES^+): *m/z* (%) = 249 (19) [MNa – CH_2=CH_2]$^+$, 277 (100), 270 (34) [M + Na]$^+$.

HRMS (ES^+): *m/z* [M + Na]$^+$ calcd for $C_{13}H_{18}NaO_5$: 277.1046; found: 277.1035.

2-Ethyl 3-Methyl 1-Ethyl-7-oxabicyclo[2.2.1]hept-2-ene-2,3-dicarboxylate (32)

From diester **27** (145 mg, 0.57 mmol) hydrogenated for 40 min in 85:15 PE–THF. Isolated by chromatography [toluene–PE–THF (48:49:3)] as a colorless oil; yield: 131 mg (90%), R_f = 0.37 (toluene–PE–THF, 46:46:8).

IR (neat): 2981, 2955, 2883, 1716 (broad), 1635, 1463, 1437, 1369, 1327, 1304, 1273, 1259, 1235, 1176, 1126, 1092, 1074, 1018, 984, 891 cm^{-1}.

^{1}H NMR (360 MHz, $CDCl_3$): δ = 1.03 (t, J = 7.5 Hz, 3 H, CCH_2CH_3), 1.34 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 1.51 (ddd, J = 11.5, 8.6, 3.5 Hz, 1 H, H-6$_{endo}$), 1.60 (ddd, J = 11.1, 8.6, 3.7 Hz, 1 H, H-5$_{endo}$), 1.71 (ddd, J = 11.5, 9.4, 3.6 Hz, 1 H, H-6$_{exo}$), 1.94 (dq, J = 14.6, 7.5 Hz, 1 H, A part of an ABM_3 system, CCH_2CH_3), 2.08 (dddd, J = 11.1, 9.4, 4.8, 3.5 Hz, 1 H, H-5$_{exo}$), 2.19 (dq, J = 14.6, 7.5 Hz, 1 H, B part of an ABM_3 system, CCH_2CH_3), 3.78 (s, 3 H, OCH_3), 4.29 (dq, J = 10.8, 7.1 Hz) and 4.34 (dq, J = 10.8, 7.1 Hz) (2 H, AB part of an ABM_3 system, OCH_2CH_3), 5.20 (d, J = 4.8 Hz, 1 H, H-4).

^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 8.9 (CCH_2CH_3), 14.0 (OCH_2CH_3), 24.0 (CCH_2CH_3), 27.1 (C-5), 29.0 (C-6), 51.8 (OCH_3), 61.1 (OCH_2CH_3), 78.5 (C-4), 93.1 (C-1), 140.6 and 147.1 (C-2, C-3), 162.3 (CO_2), 164.6 (CO_2).

MS (ES^+): *m/z* (%) = 181 (20) [MH – CH_2=CH_2 – EtOH]$^+$, 227 (6) [MH – CH_2=CH_2]$^+$, 249 (15) [MNa – CH_2=CH_2]$^+$, 255 (10) [M + H]$^+$, 277 (100) [M + Na]$^+$.

HRMS (ES^+): *m/z* [M + Na]$^+$ calcd for $C_{13}H_{18}NaO_5$: 277.1046; found: 277.1039.

Furans 33–37; General Procedure

A 0.1 M soln of the oxanorbornene in a mixture of *cis*- and *trans*-decalin (previously filtered over basic Al_2O_3) was heated for 75 min at 190 °C under argon then cooled. The furan was generally isolated by column chromatography (silica gel).

Methyl 4-(Benzylcarbamoyl)-2-ethyl-3-furoate (33)

From amido ester **28** (93 mg, 0.30 mmol). Isolated by chromatography [PE then PE–Et_2O (1:1)] as a yellowish solid; yield: 80 mg (94%); mp: 67–68 °C; R_f = 0.24 (PE–Et_2O, 1:1).

IR (ATR): 3282, 3225, 3132, 3087, 2951, 2921, 1688, 1646, 1578, 1556, 1445, 1398, 1298, 1220, 1197, 1135, 1108, 1051, 927, 728, 694 cm^{-1}.

^{1}H NMR (360 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.4 Hz, 3 H, CH_2CH_3), 2.99 (q, J = 7.4 Hz, 2 H, CH_2CH_3), 3.86 (s, 3 H, OCH_3), 4.61 (d, J = 5.4 Hz, 2 H, NCH_2Ph), 7.24–7.38 (m, 5 H, Ph), 8.07 (s, 1 H, H-5), 9.81 (br s, 1 H, CONH).

^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 12.0 (CH_2CH_3), 22.5 (CH_2CH_3), 43.2 (NCH_2Ph), 52.1 (OCH_3), 109.3 (C-3), 122.4 (C-4), 127.0 and 127.5 (C_{Ar}-*o*, C_{Ar}-*m*), 128.4 (C_{Ar}-*p*), 138.5 (*C*$_{Ar}CH_2$), 147.9 (C-5), 161.5 and 166.1 and 166.7 (C-2, CONH, CO_2).

MS (ES^+): *m/z* (%) = 310 (100) [M + Na]$^+$, 311 (16).

HRMS (ES^+): *m/z* [M + Na]$^+$ calcd for $C_{16}H_{17}NNaO_4$: 310.1050; found: 310.1039.

Methyl 4-(Cyclohexylcarbamoyl)-2-ethyl-3-furoate (34)

From amido ester **29** (93 mg, 0.30 mmol). Isolated by chromatography [PE then PE–Et_2O (4:1)] as a white solid; yield: 53 mg (62%); mp 83–84 °C (Et_2O); R_f = 0.20 (PE–Et_2O, 1:1).

IR (neat): 3296, 3165, 3093, 2932, 2855, 1720, 1701, 1650, 1640, 1583, 1559, 1447, 1400, 1319, 1295, 1262, 1220, 1197, 1172, 1140, 1110, 1050, 992, 940, 890, 840, 784, 753 cm^{-1}.

^{1}H NMR (360 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.5 Hz, 3 H, CH_2CH_3), 1.26–1.49 (m, 5 H, H_{Cy}), 1.57–1.67 (m, 1 H, H_{Cy}), 1.71–1.80 (m, 2 H, H_{Cy}), 1.93–2.02 (m, 2 H, H_{Cy}), 2.98 (q, J = 7.5 Hz, 2 H, CH_2CH_3), 3.90–3.99 (m, CHN) and 3.91 (s, OCH_3) (4 H), 8.02 (s, 1 H, H-5), 9.31 (br d, J = 6.0 Hz, 1 H, CONH).

^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 12.0 (CH_2CH_3), 22.6 (CH_{2Cy}), 24.5 (CH_{2Cy}), 25.6 (CH_2CH_3), 32.6 (CH_{2Cy}), 47.8 (NCH), 52.1 (OCH_3), 109.3 (C-3), 122.8 (C-4), 147.7 (C-5), 160.5 and 166.2 and 166.6 (C-2, CONH, CO_2).

MS (EI): 98 (20), 165 (11), 166 (37), 180 (10), 181 (100), 182 (11), 247 (27), 279 (18) [M]$^+$.

HRMS (ES^+): *m/z* [M + Na]$^+$ calcd for $C_{15}H_{21}NNaO_4$: 302.1363; found: 302.1366.

X-ray crystal data:[23] $C_{15}H_{21}NO_4$, M = 279.33, triclinic, space group $P\bar{1}$, Z = 4, a = 9.2922(7) Å, b = 10.0908(8) Å, c = 16.3214(13) Å, V = 1437.57(19) Å^3, d = 1.291 g/cm^3, $R1$ = 0.0897, $wR2$ = 0.2049, 14922 independent reflections were collected (R_{int} = 0.0291).

Methyl 2-Benzyl-4-(phenylcarbamoyl)-3-furoate (35)

From amido ester **30** (221 mg, 0.61 mmol). When the reaction mixture was allowed to stand overnight at –20 °C, the product crystallized and was separated and washed with PE; yield: 162 mg (79%). Column chromatography [silica gel, PE then PE–Et_2O (7:3)] of the residual liquid gave a second crop of the product as a white solid; yield: 35 mg (17%); total yield: 197 mg (96%); mp 124–125 °C; R_f = 0.39 (PE–Et_2O, 1:1).

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IR (ATR): 3253, 3195, 3134, 3087, 2950, 1697, 1661, 1621, 1561, 1491, 1442, 1395, 1332, 1283, 1250, 1181, 1133, 1070, 943, 877, 761, 745, 725, 695 cm^{-1}.

^1H NMR (360 MHz, $CDCl_3$): δ = 3.96 (s, 3 H, OCH_3), 4.34 (s, 2 H, CH_2Ph), 7.13 (br t, *J* = 7.4 Hz, 1 H, H_{Ar}-*p* of NHPh), 7.21–7.40 (m, 7 H, H_{Ar} of CH_2Ph, H_{Ar}-*m* of NHPh), 7.77 (br d, *J* = 7.8 Hz, 2 H, H_{Ar}-*o* of NHPh), 8.18 (s, 1 H, H-5), 11.55 (br s, 1 H, CONH).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 35.0 (CH_2Ph), 52.5 (OCH_3), 110.3 (C-3), 120.0 (C_{Ar}-*o* of NHPh), 123.4 (C-4), 123.9 (C_{Ar}-*p* of NHPh), 126.9 (C_{Ar}-*p* of CH_2Ph), 128.4 and 128.6 and 128.8 (C_{Ar}-*o* and C_{Ar}-*m* of CH_2Ph, C_{Ar}-*m* of NHPh), 136.4 ($C_{Ar}CH_2$), 138.5 ($C_{Ar}NH$), 149.2 (C-5), 159.2 and 163.5 and 166.4 (C-2, CONH, CO_2).

MS (ES^+): *m/z* (%) = 304 (2) $[MH - MeOH]^+$, 336 (7) $[M + H]^+$, 358 (100) $[M + Na]^+$, 359 (24).

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{20}H_{17}NNaO_4$: 358.1050; found: 358.1040.

4-Ethyl 3-Methyl 2-Ethylfuran-3,4-dicarboxylate (36)

From diester **31** (96 mg, 0.38 mmol). Isolated by chromatography [PE then PE–Et_2O (7:3)] as a colorless oil; yield: 76 mg (88%); R_f = 0.41 (PE–Et_2O, 3:2).

IR (neat): 3148, 2983, 2949, 1724 (broad), 1597, 1557, 1443, 1367, 1310, 1294, 1257, 1200, 1139, 1097, 1046, 1019, 764 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.6 Hz, 3 H, CCH_2CH_3), 1.34 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 2.91 (q, *J* = 7.6 Hz, 2 H, CCH_2CH_3), 3.86 (s, 3 H, OCH_3), 4.30 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 7.77 (s, 1 H, H-5).

^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 12.0 (CCH_2CH_3), 14.1 (OCH_2CH_3), 20.8 (CCH_2CH_3), 51.6 (OCH_3), 60.6 (OCH_2CH_3), 111.9 (C-3), 118.9 (C-4), 145.2 (C-5), 162.1 and 163.49 and 163.54 (C-2, CO_2, CO_2).

MS (ES^+): *m/z* (%) = 249 (100) $[M + Na]^+$, 250 (11).

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{11}H_{14}NaO_5$: 249.0733; found: 249.0729.

3-Ethyl 4-Methyl 2-Ethylfuran-3,4-dicarboxylate (37)

From diester **32** (106 mg, 0.42 mmol). Isolated by chromatography [PE then PE–Et_2O (7:3)] as a colorless oil; yield: 90 mg (94%); R_f = 0.42 (PE–Et_2O, 3:2).

IR (ATR): 2982, 2938, 1716 (broad), 1552, 1463, 1439, 1415, 1287, 1258, 1195, 1177, 1137, 1095, 1075, 1048, 988, 803, 758 cm^{-1}.

^1H NMR (360 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.6 Hz, 3 H, CCH_2CH_3), 1.35 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 2.90 (q, *J* = 7.6 Hz, 2 H, CCH_2CH_3), 3.83 (s, 3 H, OCH_3), 4.32 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 7.75 (s, 1 H, H-5).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 11.9 (CCH_2CH_3), 13.9 (OCH_2CH_3), 20.8 (CCH_2CH_3), 51.6 (OCH_3), 60.6 (OCH_2CH_3), 112.2 (C-3), 118.6 (C-4), 145.1 (C-5), 162.5 and 162.9 and 163.3 (C-2, CO_2, CO_2).

MS (ES^+): *m/z* (%) = 249 (100) $[M + Na]^+$, 250 (11).

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{11}H_{14}NaO_5$: 249.0733; found: 249.0727.

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Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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