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MICROWAVE-ASSISTED DIELS−ALDER REACTION OF 2*H*-PYRAN-2-ONES WITH MALEIMIDES TOWARDS FUSED BICYCLO[2.2.2]OCTENES[#]

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Abstract – An efficient, green access to functionalized and highly constrained heteropolycyclic derivatives via a microwave-assisted cycloaddition reaction is reported. The double Diels−Alder reaction of a series of 2*H*-pyran-2-ones with maleimide and its *N*-substituted derivatives takes place in an aqueous mixture (and in some cases as neat reaction) to give a variety of fused bicyclo[2.2.2]oct-7-enes.

INTRODUCTION

Bicyclo[2.2.2]octenes and their fused derivatives[1] as well as their hydrogenated analogues, bicyclo[2.2.2]octanes,[1c,2] have been shown to serve as useful building blocks in organic syntheses. Among them, bicyclo[2.2.2]oct-7-enes (bicyclo[2.2.2]oct-2-enes when unsubstituted) containing a free or protected amino group at the bridgehead carbon atom are very rare compounds,[3a] and can be found in the skeleton of naturally occurring *Kopsia* alkaloids.[3b] During our recent investigation of the transformations of the 2*H*-pyran-2-ones and fused pyran-2-ones we synthesized a series of aminobicyclo[2.2.2]oct-7-enes bearing fused heterocyclic rings in their structure, such as a fused maleic anhydride moiety[4a] or a fused substituted succinimide moiety.[4b–e] The transformation of the bicyclo[2.2.2]oct-7-ene-2*exo*,3*exo*,5*exo*,6*exo*-tetracarboxylic acid 2,3:5,6-dianhydrides with hydrazine derivatives resulted in the preparation of the corresponding fused succinimides.[5]

Over the past few years the developments in the field of green chemistry have been oriented towards adopting methods and processes that use less-toxic chemicals, produce smaller amounts of by-products and consume less energy.[6] Among them, microwave-assisted reactions[7] have attracted considerable attention and many efficient, eco-friendly syntheses of a variety of organic products were developed in water.[5,8] In pursuit of our studies on atom- and energy-economical reactions, we developed a sequential

[#] Dedicated to the memory of the late Professor Ivar Ugi.

microwave-assisted cycloaddition reaction followed by a heterogeneous hydrogenation, representing an expedient route to complex functionalized heteropolycyclic derivatives.[4c,e]

RESULTS AND DISCUSSION

In our previous communication we presented an efficient, green synthesis of sterically constrained prochiral dehydroamino acid derivatives of type **3**, containing a bicyclo[2.2.2]oct-7-ene skeleton and an unsaturated amino ketone or ester functionality.[4c,e] These compounds were shown to be attractive precursors of sterically constrained heterocyclic derivatives. Here we report on a detailed study based on our preliminary research[4c] with the emphasis on showing the scope and limitation of the above synthesis of the compounds of type **3**. The synthesis of **3** was based on the Diels−Alder reaction[9] of 2*H*-pyran-2-ones (**1**)[10] with maleimide and its *N*-substituted derivatives (**2**). Encouraged by our previous results using microwave irradiation and in the transformations of pyran-2-one representatives,[4,11] we decided to employ a green approach to the synthesis of **3**. Our previous results in this field showed that 2*H*-pyran-2-ones serve as useful dienes in reactions with alkenes (maleic anhydride, maleimides)[4a−c] and alkynes.[11c−e] With the cycloaddition between fused pyran-2-ones and maleimides, under severe conditions (in boiling decalin or toluene), we prepared a series of fused isoindoles[4b] that were, in a few cases, accompanied by double cycloadducts of type **3** (fused bicyclo[2.2.2]octene derivatives). Therefore, we decided to extend our previous green methodology[4c] for the preparation of compounds (**3**) (from **1** and **2**) to a variety of examples, also including those with heterocyclic moieties attached to position 6 of the starting 2*H*-pyran-2-ones (**1**). Indeed, microwave irradiation as the source of energy and water as the solvent (or in some cases no solvent at all) proved to be excellent reaction conditions for the synthesis of **3**. Despite the negligible solubility of the substrates (**1**) in water at room temperature, most of the cycloadditions were complete within one hour (with the exception of the synthesis of **3k**,**l**) of the irradiation with microwaves at 150 ºC, affording the bicyclic derivatives (**3**) in very good yields (Scheme 1, Table 1). In certain examples, such as the syntheses of **3a** (Run 1), **3h** (Run 8), **3i** (Run 9), **3k** (Run 11) and **3l** (run 12), the use of water as the solvent was shown not to be advantageous as complex mixtures also containing some of the desired products were obtained (**3a**,**h**,**i**) or relatively long reaction times were required (**3k**,**l**). For example, for the synthesis of **3k** in an aqueous mixture (under microwave irradiation at 150 °C) after 90 min the estimated conversion was still below 70%, as was evident from the ^{1}H NMR spectrum of the crude reaction mixture. On the other hand, the same transformation carried out as a neat reaction, but with the other conditions identical to those described above, was practically finished after 90 min (conversion above 98%). Therefore, to avoid the formation of complex mixtures of products and also to shorten the reaction times the above-mentioned reactions were better carried out without the addition of water, yielding relatively pure products (**3**) (though

in the cases of **3a**,**h**,**i** the resulting crude adducts had to be crystallized from EtOH to give the pure products).

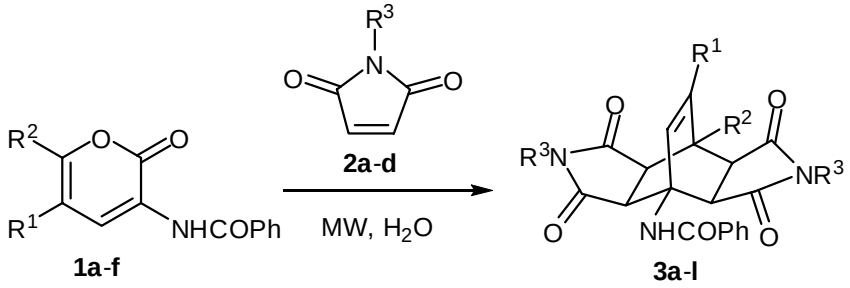


Table 1: Reaction times and yields of products (**3**) under microwave reaction conditions

Run	Starting compounds **1** and **2**					Prod. **3**	MW cond.[a]	
	R^1	R^2	**1**	R^3	**2**		*t* / min	Yield (%)[b]
1	COMe	Me	**1a**	H	**2a**	**3a**	20[c]	82[d]
2	COMe	Me	**1a**	Me	**2b**	**3b**	30	87
3	COMe	Me	**1a**	Et	**2c**	**3c**	30	92
4	COMe	Me	**1a**	Ph	**2d**	**3d**	30	94
5	CO_2Et	Me	**1b**	Me	**2b**	**3e**	45	86
6	CO_2Et	Me	**1b**	Et	**2c**	**3f**	45	87
7	CO_2Et	Me	**1b**	Ph	**2d**	**3g**	60	91
8	CO_2Me	CH_2CO_2Me	**1c**	Et	**2c**	**3h**	30[c]	82[d]
9	CO_2Me	CH_2CO_2Me	**1c**	Ph	**2d**	**3i**	30[c]	81[d]
10	*p*-MeO-C_6H_4	Me	**1d**	Ph	**2d**	**3j**	10	93
11	H	2-furyl	**1e**	Ph	**2d**	**3k**	90[c]	99
12	H	2-thienyl	**1f**	Et	**2c**	**3l**	150[c]	96

[a] Microwave irradiation in aqueous suspension at 150 °C in a pressurized tube. [b] Yield of isolated products. [c] Neat reaction. [d] Yield after crystallization from EtOH.

For comparison, the conventional synthesis of the same cycloadducts, such as **3b** and **3e**, required higher temperatures and longer reaction times: in boiling decalin, bp 189−191 ºC, after 90−120 min of reflux **3b** or **3e** were obtained in 81 and 76% yields, respectively. When refluxing an aqueous mixture of **1a** and **2c**, after 2 h only approximately 60% of the starting 2*H*-pyran-2-one (**1a**) was consumed to give **3c**. The results for the reaction between **1e** and **2d** were similar: after 90 min of reflux in an aqueous mixture, only around 21% of the starting **1e** was transformed to **3k** (the remaining **1e** being unchanged). On the basis of these

experiments it is evident that transformations are much more efficient under the microwave condition. We believe that the acceleration observed (at least in water) is most probably the consequence of the increased reaction temperature, rather than that of any specific microwave effect.

A highly efficient environmentally benign microwave-assisted synthesis of bicyclo[2.2.2]oct-7-enes (**3**) in water was demonstrated. In some cases this transformation took place with higher yields when carried out as a neat reaction. Moreover, the work-up required only the filtration of the product from a cooled reaction mixture. Alternatively, the products of the neat reactions were isolated as pure compounds after the crystallization or by the addition of a small amount of water followed by the filtration. Some of the compounds thus prepared were used for further studies towards the corresponding bicyclo[2.2.2]octanes.[4c,e] It is also important to mention that the transformation described brings an additional insight into the chemistry of heterocyclic α,β-didehydro-α-amino acid derivatives.[12]

EXPERIMENTAL

Melting points were determined on a Kofler micro hot stage and are uncorrected. ^{1}H NMR spectra were recorded with a Bruker Avance DPX 300 spectrometer at 29 °C (unless otherwise stated) and 300 MHz using TMS as an internal standard. ^{13}C NMR spectra were recorded on the same instrument at 75.5 MHz and are referenced against the central line of the solvent signal (DMSO-d_6 septet at δ = 39.5 ppm). The coupling constants (*J*) are given in Hz. IR spectra were obtained with a Bio-Rad FTS 3000MX (KBr pellets for all products). MS spectra were recorded with a VG-Analytical AutoSpec Q instrument. Elemental analyses (C, H, N) were performed with a Perkin Elmer 2400 Series II CHNS/O Analyzer. TLC was carried out on Fluka silica-gel TLC-cards. The starting compounds (**1**) were prepared according to the published procedures;[10] all other reagents and solvents were used as received from commercial suppliers. MW reactions were conducted in air using a focused MW unit (Discover by CEM Corporation, Matthews, NC). The machine consists of a continuous, focused-microwave power-delivery system with an operator-selectable power output from 0 to 300 W. Reactions were performed in glass vessels (capacity 10 mL) sealed with a septum. The pressure was controlled by a load cell connected to the vessel *via* the septum. The temperature of the contents of the vessel was monitored using a calibrated infrared temperature controller mounted under the reaction vessel. All the mixtures were stirred with a Teflon-coated magnetic stir bar in the vessel. Temperature, pressure and power profiles were recorded using commercially available software provided by the manufacturer of the MW unit.

General procedure for the preparation of 3a–l.

A mixture of 2*H*-pyran-2-one (**1**) (1 mmol) and maleimide (**2**) (2.1 mmol) in 3 mL of distilled water was irradiated in the focused-microwave equipment for the time specified (the final temperature was set to 150

ºC, the power to 100 W, and the ramp time 3 min). For typical temperature, pressure and power profiles, see Figure 1. Thereafter, the reaction mixture was cooled to room temperature; the precipitated solid was filtered off and washed with water (0.5−1 mL). The procedure under neat conditions was identical, except that no solvent was used. Isolation for **3a**,**h**,**i**: crude solid obtained after microwave irradiation was crystallized from EtOH; for **3k**,**l**: crude solid was homogenized in 1 mL of water, the precipitated solid was filtered off and washed with water (0.5−1 mL).

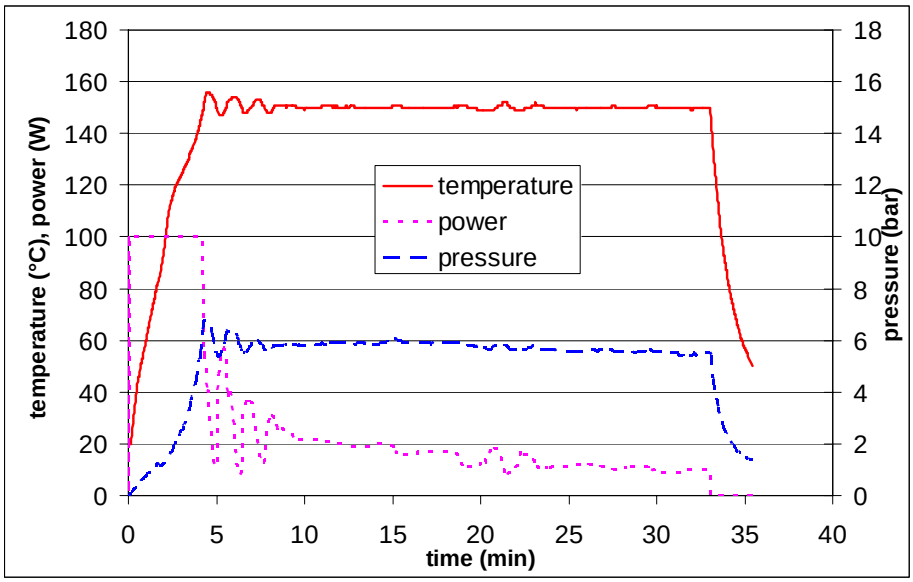
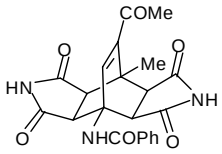
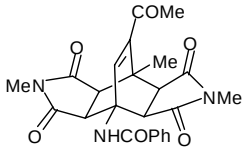


Figure 1. Typical temperature (red; ——), power (violet; ·····) and pressure (blue; – – –) profiles for the microwave irradiated synthesis of **3b**.

Analytical and spectroscopic data of products:

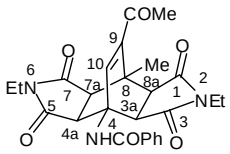


***N*-[9-Acetyl-2,3,3a,4a,5,6,7,7a,8,8a-decahydro-8-methyl-1,3,5,7-tetraoxo-4,8-ethenobenzo[1,2-*c*:4,5-c']dipyrrol-4(1*H*)-yl]benzamide (3a):** mp > 358 °C (EtOH) (lit.,[4c] mp > 358 °C).



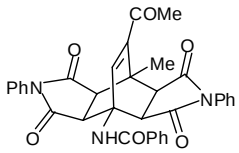
***N*-[9-Acetyl-2,3,3a,4a,5,6,7,7a,8,8a-decahydro-2,6,8-trimethyl-1,3,5,7-tetraoxo-4,8-ethenobenzo[1,2-*c*:4,5-*c*']dipyrrol-4(1*H*)-yl]benzamide (3b):** mp 294─296 °C (EtOH) (lit.,[4c] mp 294─296 °C).

***N*-[9-Acetyl-2,6-diethyl-2,3,3a,4a,5,6,7,7a,8,8a-decahydro-8-methyl-1,3,5,7-tetraoxo-4,8-ethenobenzo[1,2-*c*:4,5-*c*']dipyrrol-4(1*H*)-yl]benzamide (3c):**[4c,e] mp 274–276 °C (EtOH); IR (KBr) ν_{max}/cm^{-1}: 1768, 1703 br, 1645, 1548; ^{1}H NMR (300 MHz, DMSO-d_6): δ 0.89 (t, J = 7.2 Hz, 6H, 2 × NCH_2CH_3), 1.92 (s, 3H, Me), 2.09 (s, 3H, COMe), 3.08 (d,



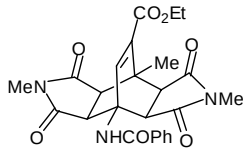
J = 8.1 Hz, 2H, 7a-H, 8a-H), 3.27 (q, *J* = 7.2 Hz, 4H, 2 × NCH_2CH_3), 4.30 (d, *J* = 8.1 Hz, 2H, 3a-H, 4a-H), 7.25 (s, 1H, 10-H), 7.56 (m, 3H, Ph), 7.90 (m, 2H, Ph), 8.75 (s, 1H, NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 12.7, 18.1, 27.3, 32.6 (four signals for 2 × Me and 2 × Et), 41.2, 42.8, 48.8, 57.8 (four signals for 3a-C, 4-C, 4a-C, 7a-C, 8-C, 8a-C), 127.5, 128.1, 131.2, 135.4, 138.4, 142.4 (6 signals for Ph and C=C), 167.7, 173.9, 175.1, 195.9 (four signals for 6 × C=O); MS (*m/z*, %) 477 (M^+, 17), 105 (100). *Anal.* Calcd for $C_{26}H_{27}N_3O_6$ + ¼ H_2O: C, 64.79; H, 5.75; N, 8.72. Found: C, 64.86; H, 5.80; N, 9.04.

***N*-[9-Acetyl-2,3,3a,4a,5,6,7,7a,8,8a-decahydro-8-methyl-1,3,5,7-tetraoxo-2,6-diphenyl-4,8-etheno-benzo[1,2-*c*:4,5-*c*']dipyrrol-4(1*H*)-yl]benzamide (3d):**[4c,e] mp 297–299 °C (EtOH);



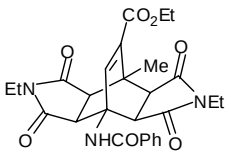
IR (KBr) ν_{max}/cm^{-1}: 1773, 1715, 1646, 1549, 1497; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.96 (s, 3H, Me), 2.25 (s, 3H, COMe), 3.39 (d, *J* = 8.3 Hz, 2H, 7a-H, 8a-H), 4.57 (d, *J* = 8.3 Hz, 2H, 3a-H, 4a-H), 7.11 (m, 4H), 7.48 (m, 10H), 7.87 (m, 2H) (3 × Ph, 10-H), 8.83 (s, 1H, NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 17.8 (Me), 28.1 (Me), 41.5, 43.4, 49.0, 57.9 (four signals for 3a-C, 4-C, 4a-C, 7a-C, 8-C, 8a-C), 126.8, 127.4, 128.1, 128.4, 128.9, 131.2, 132.0, 135.3, 137.7, 143.5 (10 signals for 3 × Ph and C=C), 167.9, 173.4, 174.6, 197.0 (four signals for 6 × C=O); MS-FAB (*m/z*, %) 574 (MH^+). *Anal.* Calcd for $C_{34}H_{27}N_3O_6$: C, 71.19; H, 4.74; N, 7.33. Found: C, 71.30; H, 4.65; N, 7.60.

***N*-[9-Ethoxycarbonyl-2,3,3a,4a,5,6,7,7a,8,8a-decahydro-2,6,8-trimethyl-1,3,5,7-tetraoxo-4,8-etheno-benzo[1,2-*c*:4,5-c']dipyrrol-4(1*H*)-yl]benzamide (3e):** mp 249–252 °C (EtOH); IR



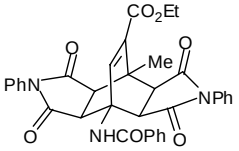
(KBr) ν_{max}/cm^{-1}: 1768, 1721, 1700 br, 1674, 1539; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.14 (t, *J* = 7.0 Hz, 3H, CH_2CH_3), 1.93 (s, 3H, Me), 2.68 (s, 6H, 2 × Me), 3.15 (d, *J* = 8.2 Hz, 2H, 7a-H, 8a-H), 4.06 (q, *J* = 7.0 Hz, 2H, CH_2CH_3), 4.33 (d, *J* = 8.2 Hz, 2H, 3a-H, 4a-H), 7.20 (s, 1H, 10-H), 7.54 (m, 3H, Ph), 7.92 (m, 2H, Ph), 8.83 (s, 1H, NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 13.9, 18.0, 24.3, 40.8 (four signals for 3 × Me and Et), 43.1, 48.9, 57.9, 60.5 (four signals for 3a-C, 4-C, 4a-C, 7a-C, 8-C, 8a-C), 127.5, 128.0, 131.1, 135.3, 138.4 (5 signals for Ph and C=C), 163.0, 167.7, 174.4, 175.3 (four signals for 6 × C=O) (1 signal hidden); MS (*m/z*, %) 479 (M^+, 6), 105 (100). *Anal.* Calcd for $C_{25}H_{25}N_3O_7$: C, 62.62; H, 5.26; N, 8.76. Found: C, 62.59; H, 5.11; N, 8.77.

***N*-[2,6-Diethyl-9-ethoxycarbonyl-2,3,3a,4a,5,6,7,7a,8,8a-decahydro-8-methyl-1,3,5,7-tetraoxo-4,8-ethenobenzo[1,2-*c*:4,5-*c*']dipyrrol-4(1*H*)-yl]benzamide (3f):** mp 305–306 °C (EtOH); IR (KBr) ν_{max}/cm^{-1}: 1767, 1731, 1703, 1643, 1555; ^{1}H NMR (300 MHz, DMSO-d_6): δ 0.88 (t, *J* = 7.1 Hz, 6H, 2 × NCH_2CH_3), 1.12 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.93 (s, 3H, Me), 3.11 (d, *J* = 8.1 Hz, 2H, 7a-H, 8a-H), 3.26 (q, *J* = 7.1 Hz, 4H, 2 × NCH_2CH_3), 4.05 (q, *J* = 7.1 Hz, 2H, $CO_2CH_2CH_3$), 4.31 (d, *J* = 8.1 Hz, 2H, 3a-H, 4a-H), 7.21 (s, 1H, 10-H),

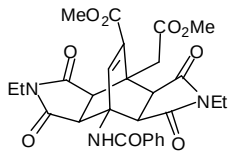


7.54 (m, 3H, Ph), 7.91 (m, 2H, Ph), 8.87 (s, 1H, NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 12.5, 13.9, 17.9, 32.6, 40.9 (five signals for Me and 3 × Et), 42.8, 48.7, 57.9, 60.4 (four signals for 3a-C, 4-C, 4a-C, 7a-C, 8-C, 8a-C), 127.6, 128.0, 131.1, 135.0, 135.4, 138.4 (six signals for Ph and C=C), 163.0, 167.7, 174.0, 174.9 (four signals for 6 × C=O); MS (*m/z*, %) 507 (M^+, 6), 105 (100). *Anal.* Calcd for $C_{27}H_{29}N_3O_7$: C, 63.90; H, 5.76; N, 8.28. Found: C, 64.08; H, 5.91; N, 8.18.

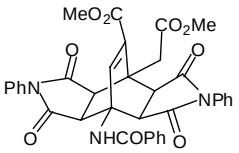
***N*-[9-Ethoxycarbonyl-2,3,3a,4a,5,6,7,7a,8,8a-decahydro-8-methyl-1,3,5,7-tetraoxo-2,6-diphenyl-4,8-ethenobenzo[1,2-*c*:4,5-*c*']dipyrrol-4(1*H*)-yl]benzamide (3g):** mp 326–329 °C (EtOH); IR (KBr) ν_{max}/cm^{-1}: 1771, 1717, 1643, 1544, 1493; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.22 (t, J = 7.1 Hz, 3H, CH_2CH_3), 1.97 (s, 3H, Me), 3.40 (d, J = 8.3 Hz, 2H, 7a-H, 8a-H), 4.19 (q, J = 7.1 Hz, 2H, CH_2CH_3), 4.57 (d, J = 8.3 Hz, 2H, 3a-H, 4a-H), 7.10 (m, 4H), 7.32 (s, 1H, 10-H), 7.46 (m, 9H), 7.87 (m, 2H) (3 × Ph), 8.91 (s, 1H, NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 14.0, 17.6, 41.2 (three signals for Me and Et), 43.3, 48.8, 58.0, 60.9 (four signals for 3a-C, 4-C, 4a-C, 7a-C, 8-C, 8a-C), 126.8, 127.5, 128.0, 128.5, 128.9, 131.1, 132.0, 135.3, 136.2, 137.4 (ten signals for 3 × Ph and C=C), 163.8, 167.8, 173.4, 174.4 (four signals for 6 × C=O); MS (*m/z*, %) 603 (M^+, 6), 105 (100). *Anal.* Calcd for $C_{35}H_{29}N_3O_7$: C, 69.64; H, 4.84; N, 6.96. Found: C, 69.94; H, 4.78; N, 7.10.



***N*-[2,6-Diethyl-2,3,3a,4a,5,6,7,7a,8,8a-decahydro-9-methoxycarbonyl-8-methoxycarbonylmethyl-1,3,5,7-tetraoxo-4,8-ethenobenzo[1,2-*c*:4,5-*c*']dipyrrol-4(1*H*)-yl]benzamide (3h):** mp 259–261 °C (EtOH); IR (KBr) ν_{max}/cm^{-1}: 1767, 1732, 1703, 1638, 1552; ^{1}H NMR (300 MHz, DMSO-d_6): δ 0.88 (t, J = 7.0 Hz, 6H, 2 × NCH_2CH_3), 3.24 (q, J = 7.0 Hz, 4H, 2 × NCH_2CH_3), 3.62 (s, 3H, Me), 3.70 (s, 3H, Me), 3.72 (s, 2H, CH_2), 3.81 (d, J = 8.3 Hz, 2H, 7a-H, 8a-H), 4.38 (d, J = 8.3 Hz, 2H, 3a-H, 4a-H), 7.31 (s, 1H, 10-H), 7.55 (m, 3H, Ph), 7.91 (m, 2H, Ph), 8.88 (s, 1H, NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 12.4, 31.9, 32.7, 40.9, 42.6, 44.1, 51.4, 52.2, 57.7 (nine signals for 2 × Me, 2 × Et, CH_2, 3a-C, 4-C, 4a-C, 7a-C, 8-C, 8a-C), 127.6, 128.1, 131.2, 133.5, 135.2, 139.7 (six signals for Ph and C=C), 163.4, 167.7, 171.5, 174.0, 175.3 (five signals for 7 × C=O); MS (*m/z*, %) 551 (M^+, 10), 105 (100). *Anal.* Calcd for $C_{28}H_{29}N_3O_9$: C, 60.97; H, 5.30; N, 7.62. Found: C, 60.98; H, 5.28; N, 7.74.

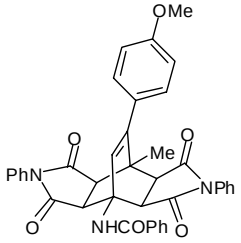


***N*-[2,3,3a,4a,5,6,7,7a,8,8a-Decahydro-9-methoxycarbonyl-8-methoxycarbonyl-methyl-1,3,5,7-tetra-oxo-2,6-diphenyl-4,8-ethenobenzo[1,2-*c*:4,5-*c*']dipyrrol-4-(1*H*)-yl]benzamide (3i):** mp 339–340 °C (AcOEt); IR (KBr) ν_{max}/cm^{-1}: 1772, 1716 br, 1628, 1536, 1493; ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.70 (s, 3H, Me), 3.74 (s, 2H, CH_2), 3.76 (s, 3H, Me), 4.04 (d, J = 8.4 Hz, 2H, 7a-H, 8a-H), 4.65 (d, J = 8.4 Hz, 2H, 3a-H, 4a-H), 7.06 (m,

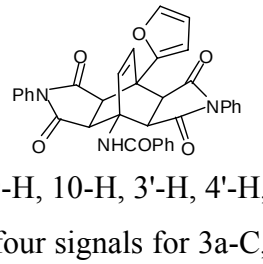


4H), 7.47 (m, 10H), 7.87 (m, 2H) (3 × Ph, 10-H), 8.95 (s, 1H, NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 31.9, 41.2, 43.1, 44.6, 51.5, 52.6, 57.8 (seven signals for 2 × Me, CH_2, 3a-C, 4-C, 4a-C, 7a-C, 8-C, 8a-C), 126.7, 127.5, 128.1, 128.6, 129.0, 131.2, 131.8, 134.5, 135.1, 139.0 (ten signals for 3 × Ph and C=C), 164.0, 167.9, 171.5, 173.4, 174.7 (five signals for 7 × C=O); MS (*m/z*, %) 647 (M^+, 14), 309 (100), 105 (60). *Anal.* Calcd for $C_{36}H_{29}N_3O_9$: C, 66.76; H, 4.51; N, 6.49. Found: C, 66.70; H, 4.42; N, 6.49.

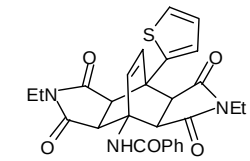
***N*-[2,3,3a,4a,5,6,7,7a,8,8a-Decahydro-8-methyl-9-(4-methoxyphenyl)-1,3,5,7-tetraoxo-2,6-diphenyl-4,8-ethenobenzo[1,2-*c*:4,5-*c*']dipyrrol-4(1*H*)-yl]benzamide (3j):** mp 328–330 °C (EtOH); IR (KBr) ν_{max}/cm^{-1}: 1770, 1715, 1626, 1603, 1535, 1511, 1493; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.83 (s, 3H, Me), 3.46 (d, J = 8.3 Hz, 2H, 7a-H, 8a-H), 3.75 (s, 3H, OMe), 4.56 (d, J = 8.3 Hz, 2H, 3a-H, 4a-H), 6.47 (s, 1H, 10-H), 6.94 (m, 4H, *p*-MeO-C_6H_4), 7.12 (m, 4H), 7.46 (m, 9H), 7.86 (m, 2H) (3 × Ph), 8.76 (s, 1H, NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 18.8 (Me), 42.7, 43.9, 49.2, 55.1, 58.3 (five signals for MeO and 3a-C, 4-C, 4a-C, 7a-C, 8-C, 8a-C), 113.9, 126.7, 127.3, 127.5, 128.0, 128.4, 128.7, 128.9, 129.6, 131.0, 132.1, 135.7, 145.3, 158.9 (14 signals for 3 × Ph, C_6H_4OMe and C=C), 168.1, 173.9, 175.5 (three signals for 5 × C=O); MS (*m/z*, %) 637 (M^+, 9), 105 (100). *Anal.* Calcd for $C_{39}H_{31}N_3O_6$: C, 73.46; H, 4.90; N, 6.59. Found: C, 73.66; H, 4.67; N, 6.50.



***N*-[8-(2-Furyl)-2,3,3a,4a,5,6,7,7a,8,8a-decahydro-1,3,5,7-tetraoxo-2,6-diphenyl-4,8-ethenobenzo-[1,2-*c*:4,5-*c*']dipyrrol-4(1*H*)-yl]benzamide (3k):** mp 297–299 °C (EtOH); IR (KBr) ν_{max}/cm^{-1}: 1775, 1719, 1497; ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.86 (d, J = 8.5 Hz, 2H, 7a-H, 8a-H), 4.66 (d, J = 8.5 Hz, 2H, 3a-H, 4a-H), 6.40 (m, 1H), 6.52 (m, 1H), 6.78 (m, 2H), 7.09 (m, 4H), 7.44 (m, 9H), 7.67 (m, 1H), 7.87 (m, 2H) (3 × Ph, 9-H, 10-H, 3'-H, 4'-H, 5'-H), 8.88 (s, 1H, NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 43.0, 43.4, 47.9, 58.3 (four signals for 3a-C, 4-C, 4a-C, 7a-C, 8-C, 8a-C), 108.1, 110.4, 126.8, 127.6, 128.0, 128.3, 128.8, 129.5, 131.0, 132.0, 132.3, 135.6, 142.1, 151.6 (14 signals for 3 × Ph, furyl and C=C), 168.1, 173.2, 173.6 (three signals for 5 × C=O); MS (*m/z*, %) 583 (M^+, 5), 105 (100). *Anal.* Calcd for $C_{35}H_{25}N_3O_6$: C, 72.03; H, 4.32; N, 7.20. Found: C, 72.14; H, 4.18; N, 7.00.



***N*-[2,6-Diethyl-2,3,3a,4a,5,6,7,7a,8,8a-decahydro-1,3,5,7-tetraoxo-8-(2-thienyl)-4,8-ethenobenzo-[1,2-*c*:4,5-*c*']dipyrrol-4(1*H*)-yl]benzamide (3l):** mp 268–271 °C (EtOH); IR (KBr) ν_{max}/cm^{-1}: 1770, 1703, 1665, 1536; ^{1}H NMR (300 MHz, DMSO-d_6): δ 0.94 (t, J = 7.2 Hz, 6H, 2 × NCH_2CH_3), 3.24 (q, J = 7.2 Hz, 4H, 2 × NCH_2CH_3), 3.62 (d, J = 8.2 Hz, 2H, 7a-H, 8a-H), 4.44 (d, J = 8.2 Hz, 2H, 3a-H, 4a-H), 6.56 (m, 2H), 7.04 (m, 1H), 7.19 (m, 1H), 7.47 (m,



1H), 7.53 (m, 3H), 7.93 (m, 2H) (Ph, 9-H, 10-H, 3'-H, 4'-H, 5'-H), 8.67 (s, 1H, NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 12.2, 32.3 (two signals for 2 × Et), 43.3, 44.0, 50.4, 57.7 (four signals for 3a-C, 4-C, 4a-C, 7a-C, 8-C, 8a-C), 123.9, 124.9, 126.1, 127.3, 127.6, 130.1, 130.5, 131.5, 135.6, 143.7 (ten signals for Ph, furyl and C=C), 167.7, 173.2, 173.5 (three signals for 5 × C=O); MS (*m/z*, %) 503 (M^+, 5), 105 (100). *Anal.* Calcd for $C_{27}H_{25}N_3O_5S$ × EtOH: C, 63.37; H, 5.68; N, 7.64. Found: C, 63.40; H, 5.79; N, 7.55.

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