Synthesis of New Methano[1,5]dioxocines *via* a Domino Reaction of 4-Hydroxy-2*H*-pyran-2-ones / 4-Hydroxy-2*H*-chromen-2-ones with Acyclic 1,3-Diketones

Heiko Leutbecher, Jürgen Conrad, and Uwe Beifuss

Bioorganische Chemie, Institut für Chemie, Universität Hohenheim, Garbenstraße 30, D-70599 Stuttgart, Germany

Reprint requests to Prof. Dr. U. Beifuss. Fax: (+49)711-459-22951.
E-mail: ubeifuss@uni-hohenheim.de

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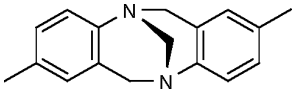
New methano[1,5]dioxocines, *O*-heterocycles with a framework similar to Tröger's base, were prepared by means of a three-component reaction. The scope of this domino reaction was studied.

Key words: Domino Reactions, Tröger's Base, *O*-Heterocycles

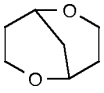
Introduction

Tröger's base, which was first prepared by Julius Tröger more than a century ago [1], is a molecule with a fascinating structure [2], for which some decades later Spielman was able to establish its bridged methano[1,5]diazocine pattern [3]. The chirality of the chiral heterocyclic amine with C_2 symmetry is due to the presence of two stereogenic nitrogen atoms.



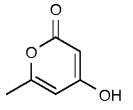
Tröger's base

Since the discovery of Tröger's base numerous structural analogs with a central [1,5]diazocine skeleton were synthesized [3, 4]. Both the chirality and the rigid concave structure of the methano[1,5]diazocine skeleton are the reasons why Tröger's base und derivatives thereof have found interest in the design of receptors for the molecular recognition of neutral molecules [5], as chiral solvating agents [6], and in the field of asymmetric synthesis [7].

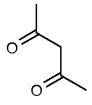


The 2,6-methano[1,5]dioxocine skeleton

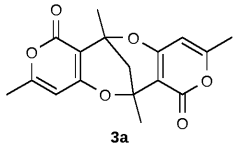
Oxo analogs like the 2,6-methano[1,5]dioxocine belong to the same symmetry group as the [1,5]diazocines. One method for the preparation of this unusual skeleton is based on the acid-catalyzed reaction of salicylaldehydes with either *o*-vinylphenols or



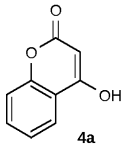
1a



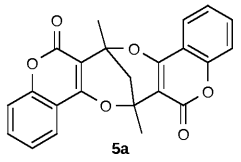
2a



3a



4a

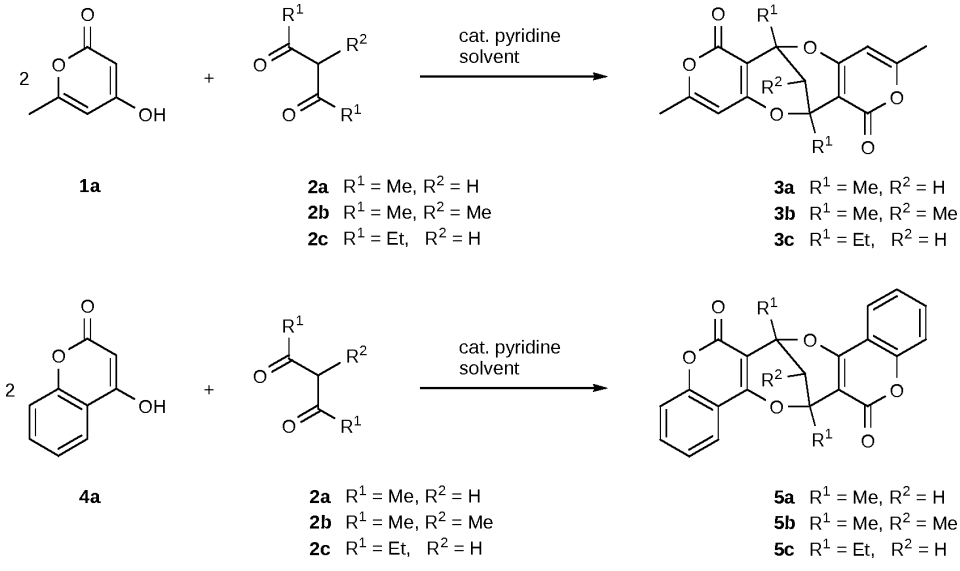


5a

o-coumaric acids [8]. Another approach relies on the conversion of suitably substituted flavylium salts [9]. And finally, using the Moreno-Mañas method, methano[1,5]dioxocines can be made accessible by reacting two equivalents of a cyclic 1,3-dicarbonyl compound with one equivalent of an acyclic 1,3-diketone. The synthesis of 3,6,9,12-tetramethyl-1*H*,6*H*,7*H*,12*H*-6,12-methanodipyrano[4,3-*b*:4,3-*f*]dioxocin-1,7-dione (**3a**) [10] and 7,15-dimethyl-7,15-methano-6*H*,7*H*,14*H*,15*H*-[1,5]dioxocino[3,2-*c*:7,6-*c*′]bis[1]benzopyran-6,14-dione (**5a**) [11] could be achieved by reaction of 4-hydroxy-6-methyl-2*H*-pyran-2-one (**1a**) and 4-hydroxy-2*H*-chromen-2-one (**4a**), respectively, with 2,4-pentanedione (**2a**). A common feature of all the methods published so far is that only little is known concerning their scope and limitations.

Entry	Equiv. of **1a**	Equiv. of **2a**	Solvent	*T* (°C)	Time (h)	Yield of **3a** (%)
1	2	1	1-nitropropane	110	18	20
2	2	1	1,1,2-trichloroethane	110	18	23
3	1	2	1,1,2-trichloroethane	110	22.5	38
4	1	1	1,1,2-trichloroethane	110	15	53
5	1	2	toluene	110	16	77

Table 1. Domino reactions of **1a** with **2a** under different reaction conditions.



Scheme 1.

In the context of our studies on domino reactions of 4-hydroxy-2*H*-pyran-2-ones and related compounds [12] we were encouraged by Moreno-Mañas's elegant approach to methano[1,5]dioxocines to study the scope of this domino reaction and to optimize the reaction conditions. Here we present our studies on the reaction of 4-hydroxy-6-methyl-2*H*-pyran-2-one (**1a**), 4-hydroxy-2*H*-chromen-2-one (**4a**) and related compounds with several 1,3-diketones to give new compounds with a 2,6-methano[1,5]dioxocine skeleton (Scheme 1).

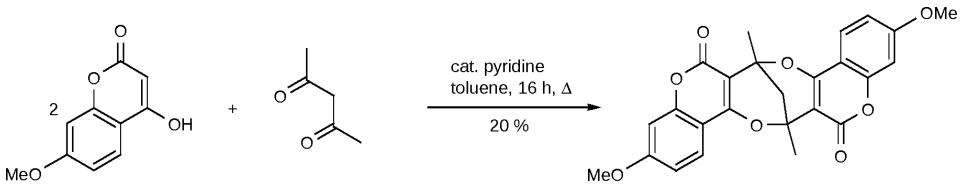
Results and Discussion

Based on our experience with domino reactions of 4-hydroxy-2*H*-pyran-2-ones and related compounds we set out to study the influence of the reaction conditions on the reaction between 4-hydroxy-6-methyl-2*H*-pyran-2-one (**1a**) and 2,4-pentanedione (**2a**) (Table 1). When 2 equivs. of **1a** and 1 equiv. of **2a** were reacted in the presence of catalytic amounts of pyridine in solvents like ethanol, *iso*-propanol and THF at 110 °C in a sealed tube, only the decomposition of **1a** was observed. In 1-nitropropane and 1,1,2-trichloroethane as a solvent, however, the product **3a** was formed with yields of 20 and 23 %, respectively (Table 1, entries 1 and 2). In 1,1,2-trichloroethane, the yield of **3a** could be further enhanced to 38 and 53 %, respectively, by increasing the amount of **2a** (Table 1, entries 3 and 4).

Table 2. Reactions of **1a** and **4a** with the acyclic 1,3-diketones **2a** – **c**.

Entry	Pyrone / Coumarin	1,3-Diketone	R^1	R^2	Product	Yield (%)
1	**1a**	**2a**	Me	H	**3a**	77
2	**1a**	**2b**	Me	Me	**3b**	16
3	**1a**	**2c**	Et	H	**3c**	11
4	**4a**	**2a**	Me	H	**5a**	80
5	**4a**	**2b**	Me	Me	**5b**	31
6	**4a**	**2c**	Et	H	**5c**	51

The best results were obtained with toluene as a solvent. So the methano[1,5]dioxocine **3a** was isolated in 77 % yield when 1 equiv. of 4-hydroxy-6-methyl-2*H*-pyran-2-one (**1a**) and 2 equivs. of 2,4-pentanedione (**2a**) were reacted with catalytic amounts of pyridine in toluene as a solvent at 110 °C (Table 1, entry 5 and Table 2, entry 1). Upon the reaction of 4-hydroxy-2*H*-chromen-2-one (**4a**) and **2a** under the reaction conditions developed in our laboratory the benzopyrano annulated methano[1,5]dioxocine **5a** was



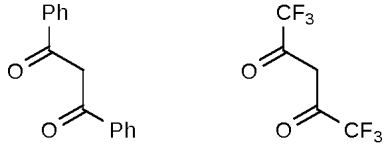
4b **2a** **5d**

Scheme 2.

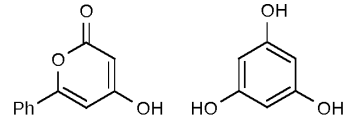
formed with even higher yields (80 %) (Table 2, entry 4). The influence of toluene as a solvent is remarkable as the products are formed with considerably lower yields when the transformations are performed without any solvent [10, 11]. For example, Moreno-Mañas *et al*. achieved the synthesis of **3a** in 62 % yield upon reaction of **1a** with a large excess (> 8 equivs.) of **2a** in the presence of catalytic amounts of pyridine [10]. Under similar conditions Talapatra *et al.* obtained **5a** in 68 % yield [11]. Experiments to run the three-component reaction of **1a** and **2a** under microwave conditions failed as decomposition was observed at temperatures exceeding 130 °C.

This is why we focussed on the scope of the domino reaction. We found that 4-hydroxy-6-methyl-2*H*-pyran-2-one (**1a**) as well as 4-hydroxy-2*H*-chromen-2-one (**4a**) react with 3-methyl-2,4-pentanedione (**2b**) and 3,5-heptanedione (**2c**) to give the expected heterocycles **3b**, **c** and **5b**, **c** (Table 2). The pyran derivatives **3b** and **3c** were isolated with yields of 16 and 11 %, respectively (Table 2, entries 2 and 3), and the corresponding benzopyran derivatives **5b** and **5c** were obtained in 31 and 51 % yield, respectively (Table 2, entries 5 and 6). These results indicate that a) the yields of the transformations with **4a** were higher than those with **1a** and b) the yields of the reactions with **2b** and **2c** were generally lower than those of the transformations of **1a** and **4a** with 2,4-pentanedione (**2a**).

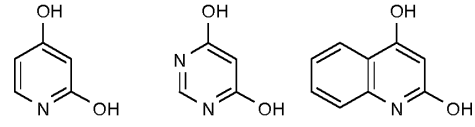
Apart from the lower reactivity of **2b** and **2c**, the yields of **3b**, **c** and **5b**, **c** are considerably diminished through losses upon purification of the products by means of column chromatography. In contrast, **3a** and **5a** crystallized from the corresponding reaction mixture in high purity.



2d **2e**



1b **6**



7 **8** **9**

We then tried to react 4-hydroxy-2*H*-pyran-2-one **1a** with additional 1,3-diketones in terms of the multicomponent reaction presented here. While dibenzoylmethane (**2d**) did not react with **1a** at all, the reaction of **1a** with 1,1,1,5,5,5,-hexafluoro-2,4-pentanedione (**2e**) afforded a product that could not be isolated in pure form.

Finally, our focus was on the variation of the reaction partners of 1,3-diketones. The reaction of 4-hydroxy-7-methoxy-2*H*-chromen-2-one (**4b**) with 2,4-pentanedione (**2a**) was successful, and the expected methano[1,5]dioxocine **5d** was isolated in 20 % yield (Scheme 2). Using our protocol we were not able, though, to react 4-hydroxy-6-phenyl-2*H*-pyran-2-one (**1b**), 1,3,5-trihydroxybenzene (**6**), 2,4-dihydroxypyridine (**7**), 4,6-dihydroxypyrimidine (**8**) or 2,4-dihydroxyquinoline (**9**) with **2a**.

Conclusion

In summary, the reactions of 4-hydroxy-6-methyl-2*H*-pyran-2-one (**1a**), 4-hydroxy-2*H*-chromen-2-one (**4a**) as well as several other cyclic 1,3-dicarbonyls with a number of acyclic 1,3-diketones **2** under basic conditions have been found to yield a number of new methano[1,5]dioxocines. Although a number of methano[1,5]dioxocines could be made accessible in good yields by developing suitable reaction conditions, the scope of this unusual domino reaction seems to be rather narrow.

Experimental Section

General

Commercial reagents were used without further purification. All solvents were distilled prior to use. Flash chromatography was performed on silica gel 60 (0.040 – 0.063 mm) (Baker). Melting points (Büchi B-545) are uncorrected. TLC: silica gel SIL G/UV_{254} (Macherey-Nagel). UV/Vis: Carey 4 E (Varian). FT-IR: Spectrum One (Perkin Elmer) (ATR). NMR: Varian ^{Unity}INOVA (300/75 MHz and 500/125 MHz, respectively). EIMS: 70 eV, MAT 8200 (Finnigan MAT). Elemental analyses: Microanalytical labaratory of the University of Göttingen.

*Typical procedure for the synthesis of the methano[1,5]dioxocines **3a – c** and **5a – d***

A mixture of 0.368 g (2.27 mmol) 4-hydroxy-2*H*-chromen-2-one (**4a**) and 0.587 mg (4.58 mmol) of 3,5-heptanedione (**2c**) in 5 mL of toluene was treated with 5 drops of pyridine and refluxed for 16 h. The solvent was removed *in vacuo* and the resulting residue purified *via* flash chromatography on silica gel (Et_2O) to give 0.243 g (51 %) 7,15-diethyl-7,15-methano-6*H*,7*H*,14*H*,15*H*-[1,5]dioxocino[3,2-*c*:7,6-*c*']bis[1]benzopyran-6,14-dione (**5c**) in analytically pure form.

Compounds **3a** and **5a** crystallized from the reaction mixture in high purity when **1a** and **4a**, respectively, were reacted with **2a**. The crystals were filtered, washed with Et_2O and dried.

*(6RS,12RS)-3,6,9,12-Tetramethyl-1H,6H,7H,12H-6,12-methanodipyrano[4,3-b:4,3-f][1,5]dioxocin-1,7-dione (**3a**)*

M. p. 246 – 248 °C (methanol; dec.; lit. [10]: 235 – 237 °C). – R_f = 0.33 (SiO_2; Et_2O). – ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.00 (s, 6 H, 6-CH_3, 12-CH_3), 2.06 (s, 2 H, 13-H_2), 2.15 (s, 6 H, 3-CH_3, 9-CH_3), 5.80 (s, 2 H, 4-H, 10-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.14 (3-CH_3, 9-CH_3), 23.07 (6-CH_3, 12-CH_3), 43.98 (C-13), 73.63 (C-6, C-12), 99.47 (C-6a, C-12a), 100.28 (C-4, C-10), 162.02 (C-1, C-7), 163.35 (C-3, C-9), 167.47 (C-4a, C-10a). – MS (EI, 70 eV): *m/z* (%) = 316 (100) $[M]^+$, 301 (71) $[M–CH_3]^+$, 217 (26), 204 (18), 191 (24), 164 (71), 153 (14), 85 (15), 43 (40).

*(6RS,12RS)-3,6,9,12,13-Pentamethyl-1H,6H,7H,12H-6,12-methanodipyrano[4,3-b:4,3-f][1,5]dioxocin-1,7-dione (**3b**)*

M. p. 228 °C (methanol/H_2O; dec.). – R_f = 0.41 (SiO_2; Et_2O). – UV/Vis (CH_3CN): λ_{max} ($\lg \varepsilon_{max}$) = 206 (4.60), 285 nm (4.05). – IR (ATR): ν = 2935 (CH_3), 1703 (C=O), 1641 (C=C), 1447 and 1386 (CH_3), 1227 and 1052 (C–O), 829 cm^{-1} (=C–H). – ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.98 (d, $^3J_{13-CH_3,13-H}$ = 7.0 Hz, 3 H, 13-CH_3), 1.85 (q, $^3J_{13-H,13-CH_3}$ = 7.0 Hz, 1 H, 13-H), 1.936 (s, 3 H, 6-CH_3 or 12-CH_3), 1.941 (s, 3 H, 6-CH_3 or 12-CH_3), 2.14 (s, 6 H, 3-CH_3, 9-CH_3), 5.77 (s, 1 H, 4-H or 10-H), 5.78 (s, 1 H, 4-H or 10-H). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 9.11 (13-CH_3), 19.36 (6-CH_3 or 12-CH_3), 20.08 (3-CH_3 or 9-CH_3), 20.10 (3-CH_3 or 9-CH_3), 22.22 (6-CH_3 or 12-CH_3), 43.07 (C-13), 75.73 (C-6, C-12), 97.46 (C-6a, C-12a), 100.08 (C-4 or C-10), 100.23 (C-4 or C-10), 162.09, 162.43 (C-1, C-7, C-4a or C-10a), 163.28 (C-3 or C-9), 163.33 (C-3 or C-9), 166.87, 167.31 (C-1, C-7, C-4a or C-10a). – MS (EI, 70 eV): *m/z* (%) = 330 (72) $[M]^+$, 315 (54) $[M–CH_3]^+$, 287 (6), 246 (30), 231 (26), 218 (53), 205 (53), 178 (32), 134 (17), 119 (7), 85 (26), 67 (28), 43 (100). – $C_{18}H_{18}O_6$ (330.36): calcd. C 65.45, H 5.49; found C 65.22, H 5.20.

*(6RS,12RS)-6,12-Diethyl-3,9-dimethyl-1H,6H,7H,12H-6,12-methanodipyrano[4,3-b:4,3-f][1,5]dioxocin-1,7-dione (**3c**)*

M. p. 197 °C. – R_f = 0.42 (SiO_2; Et_2O). – UV/Vis (CH_3CN): λ_{max} ($\lg \varepsilon_{max}$) = 206 (4.62), 286 nm (4.05). – IR (ATR): ν = 2967 (CH_2, CH_3), 1706 (C=O), 1644 (C=C), 1448 (CH_2, CH_3), 1385 (CH_3), 1219 and 1070 (C–O), 840 cm^{-1} (=C–H). – ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.91 (t, $^3J_{2'-H_3,1'-H_2}$ = $^3J_{2''-H_3,1''-H_2}$ = 7.6 Hz, 6 H, 2′-H_3, 2″-H_3), 2.00 (s, 2 H, 13-H_2), 2.16 (s, 6 H, 3-CH_3, 9-CH_3), 2.31 (dq, $^2J_{1'-H_A,1'-H_B}$ = $^2J_{1''-H_A,1''-H_B}$ = 13.9 Hz, $^3J_{1'-H_A,2'-H_3}$ = $^3J_{1''-H_A,2''-H_3}$ = 7.6 Hz, 2 H, 1′-H_A, 1″-H_A), 2.80 (dq, $^2J_{1'-H_B,1'-H_A}$ = $^2J_{1''-H_B,1''-H_A}$ = 13.7 Hz, $^3J_{1'-H_B,2'-H_3}$ = $^3J_{1''-H_B,2''-H_3}$ = 7.6 Hz, 2 H, 1′-H_B, 1″-H_B), 5.81 (s, 2 H, 4-H, 10-H). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 8.64 (C-2′, C-2″), 20.11 (3-CH_3, 9-CH_3), 27.92 (C-1′, C-1″), 36.45 (C-13), 76.96 (C-6, C-12), 98.30 (C-6a, C-12a), 100.46 (C-4, C-10), 161.87 (C-1, C-7), 163.35 (C-3, C-9), 168.65 (C-4a, C-10a). – MS (EI, 70 eV): *m/z* (%) = 344 (28) $[M]^+$, 315 (100) $[M–C_2H_5]^+$, 301 (4), 273 (1), 259 (2), 231 (21), 203 (4), 178 (30), 85 (10), 69 (6). – $C_{19}H_{20}O_6$ (344.36): calcd. C 66.27, H 5.85; found C 66.03, H 5.80.

*(7RS,15RS)-7,15-Dimethyl-7,15-methano-6H,7H,14H,15H-[1,5]dioxocino[3,2-c:7,6-c′]bis[1]benzopyran-6,14-dione (**5a**)*

M. p. 259 – 261 °C (CH_2Cl_2/PE; dec.; lit. [11]: 255 °C). – R_f = 0.35 (SiO_2; *tert*-butyl methyl ether/PE = 1 : 1). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.22 (s, 6 H, 7-CH_3, 15-CH_3), 2.31 (s, 2 H, 17-H_2), 7.20 – 7.29 (m, 4 H, 2-H, 10-H, 4-H, 12-H), 7.53 (td, $^3J_{3\text{-H},2\text{-H}}$ = $^3J_{3\text{-H},4\text{-H}}$ = $^3J_{11\text{-H},10\text{-H}}$ = $^3J_{11\text{-H},12\text{-H}}$ = 7.8 Hz, $^4J_{3\text{-H},1\text{-H}}$ = $^4J_{11\text{-H},9\text{-H}}$ = 1.5 Hz, 2 H, 3-H, 11-H), 7.94 (dd, $^3J_{1\text{-H},2\text{-H}}$ = $^3J_{9\text{-H},10\text{-H}}$ = 8.0 Hz, $^4J_{1\text{-H},3\text{-H}}$ = $^4J_{9\text{-H},11\text{-H}}$ = 1.4 Hz, 2 H, 1-H, 9-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.45 (7-CH_3, 15-CH_3), 44.33 (C-17), 74.45 (C-7, C-15) 102.03 (C-6a, C-14a), 114.95 (C-8b, C-16b), 116.56 (C-4, C-12), 124.34 (C-2,

C-10), 124.46 (C-1, C-9), 133.42 (C-3, C-11), 153.32 (C-4a, C-12a), 160.15 (C-6, C-14), 162.99 (C-8a, C-16a). – MS (EI, 70 eV): *m/z* (%) = 388 (59) $[M]^+$, 373 (41) $[M–CH_3]^+$, 253 (19), 226 (20), 200 (100), 121 (33), 92 (7).

*(7RS,15RS)-7,15,17-Trimethyl-7,15-methano-6H,7H,14H,15H-[1,5]dioxocino[3,2-c:7,6-c′]bis[1]benzopyran-6,14-dione (**5b**)*

M. p. 208 °C (dec.). – R_f = 0.61 (SiO_2; Et_2O). – UV/Vis (CH_3CN): λ_{max} ($\lg\varepsilon_{max}$) = 212 (4.66), 267 (4.22), 281 (4.09), 308 nm (4.12). – IR (ATR): ν = 3068 (=C–H), 2932 (CH_3), 1716 (C=O), 1614, 1565 and 1492 (C=C), 1454, 1387 (CH_3), 1235 and 1067 (C–O), 760 cm^{-1} (=C–H, 1,2-disub. ar.). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.16 (d, $^3J_{17-CH_3,17-H}$ = 7.0 Hz, 3 H, 17-CH_3), 2.14 (q, $^3J_{17-H,17-CH_3}$ = 7.0 Hz, 1 H, 17-H), 2.20 (s, 3 H, 7-CH_3 or 15-CH_3), 2.21 (s, 3 H, 7-CH_3 or 15-CH_3), 7.22 – 7.32 (m, 4 H, 2-H, 10-H, 4-H, 12-H), 7.52 – 7.60 (m, 2 H, 3-H, 11-H), 7.92 – 8.00 (m, 2 H, 1-H, 9-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.31 (17-CH_3), 19.76 (7-CH_3 or 15-CH_3), 22.66 (7-CH_3 or 15-CH_3), 43.46 (C-17), 76.62 (C-7 or C-15), 78.20 (C-7 or C-15), 100.09 (C-6a or C-14a), 102.97 (C-6a or C-14a), 114.95 (C-8b or C-16b), 114.94 (C-8b or C-16b), 116.50 (C-4 or C-12), 116.55 (C-4 or C-12), 124.28, 124.34, 124.48 (C-1, C-9, C-2 or C-10), 133.42 (C-3, C-11), 153.37 (C-4a, C-12a), 160.18 (C-6 or C-14), 160.50 (C-6 or C-14), 162.34 (C-8a or C-16a), 162.84 (C-8a or C-16a). – MS (EI, 70 eV): *m/z* (%) = 402 (41) $[M]^+$, 387 (20) $[M–CH_3]^+$, 282 (16), 241 (20), 214 (31), 121 (100), 92 (52), 67 (31), 65 (30). – HRMS (EI, 70 eV): *m/z* = 402.11195 (calcd. 402.11035 for $C_{15}H_{24}O_3$, $[M]^+$).

*(7RS,15RS)-7,15-Diethyl-7,15-methano-6H,7H,14H,15H-[1,5]dioxocino[3,2-c:7,6-c′]bis[1]benzopyran-6,14-dione (**5c**)*

M. p. 204 °C (dec.). – R_f = 0.65 (SiO_2; Et_2O). – UV/Vis (CH_3CN): λ_{max} ($\lg\varepsilon_{max}$) = 213 (4.65), 268 (4.22), 281 (4.09), 309 nm (4.12). – IR (ATR): ν = 2924 (CH_2, CH_3), 1713 (C=O), 1612, 1560 and 1492 (C=C), 1454 (CH_2, CH_3), 1391 (CH_3), 1229 and 1073 (C–O), 761 cm^{-1} (=C–H, 1,2-disub. ar.). – ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.03 (t, $^3J_{2'\text{-}H_3,1'\text{-}H_2}$ = $^3J_{2''\text{-}H_3,1''\text{-}H_2}$ = 7.6 Hz, 6 H, 2′-H_3, 2″-H_3), 2.27 (s, 2 H, 17-H_2), 2.54 (dq, $^2J_{1'\text{-}H_A,1'\text{-}H_B}$ = $^2J_{1''\text{-}H_A,1''\text{-}H_B}$ = 13.8 Hz, $^3J_{1'\text{-}H_A,2'\text{-}H_3}$ = $^3J_{1''\text{-}H_A,2''\text{-}H_3}$ = 7.5 Hz, 2 H, 1′-H_A, 1″-H_A), 3.09 (dq, $^2J_{1'-H_B,1'-H_A}$ = $^2J_{1''-H_B,1''-H_A}$ = 13.9 Hz, $^3J_{1'-H_B,2'-H_3}$ = $^3J_{1''-H_B,2''-H_3}$ = 7.6 Hz, 2 H, 1′-H_B, 1″-H_B), 7.24 (d, $^3J_{4\text{-}H,3\text{-}H}$ = $^3J_{12\text{-}H,11\text{-}H}$ = 8.3 Hz, 2 H, 4-H, 12-H), 7.27 (t, $^3J_{2\text{-}H,1\text{-}H}$ = $^3J_{2\text{-}H,3\text{-}H}$ = $^3J_{10\text{-}H,9\text{-}H}$ = $^3J_{10\text{-}H,11\text{-}H}$ = 7.7 Hz, 2 H, 2-H, 10-H), 7.54 (td, $^3J_{3\text{-}H,2\text{-}H}$ = $^3J_{3\text{-}H,4\text{-}H}$ = $^3J_{11\text{-}H,10\text{-}H}$ = $^3J_{11-H,12-H}$ = 7.8 Hz, $^4J_{3\text{-}H,1\text{-}H}$ = $^4J_{11\text{-}H,9\text{-}H}$ = 1.5 Hz, 2 H, 3-H, 11-H), 7.94 (dd, $^3J_{1\text{-}H,2\text{-}H}$ = $^3J_{9\text{-}H,10\text{-}H}$ = 7.9 Hz, $^4J_{1\text{-}H,3\text{-}H}$ = $^4J_{9\text{-}H,11\text{-}H}$ = 1.5 Hz, 2 H, 1-H, 9-H). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 8.82 (C-2′, C-2″), 28.26 (C-1′, C-1″), 36.94 (C-17), 77.75 (C-7, C-15), 100.86 (C-6a, C-14a), 115.05 (C-8b, C-16b), 116.52 (C-4, C-12), 124.30 (C-1, C-9 or C-2, C-10), 124.36 (C-1, C-9 or C-2, C-10), 133.36 (C-3, C-11), 153.36 (C-4a, C-12a), 160.00 (C-6, C-14), 164.14 (C-8a, C-16a). – MS (EI, 70 eV): *m/z* (%) = 416 (29) $[M]^+$, 387 (100) $[M–C_2H_5]^+$, 267 (10), 254 (8), 214 (52), 201 (6), 175 (6), 121 (36). – HRMS (EI, 70 eV): *m/z* = 416.12418 (calcd. 416.12598 for $C_{15}H_{24}O_3$, $[M]^+$).

*(7RS,15RS)-3,11-Dimethoxy-7,15-dimethyl-7,15-methano-6H,7H,14H,15H-[1,5]dioxocino[3,2-c:7,6-c′]bis[1]benzopyran-6,14-dione (**5d**)*

M. p. 219 °C (dec.). – R_f = 0.50 (SiO_2; *tert*-butyl methyl ether). – UV/Vis (CH_3CN): λ_{max} ($\lg\varepsilon_{max}$) = 206 (4.83), 219 (4.55), 284 (4.16), 313 (4.47), 325 nm (4.37). – IR (ATR): ν = 2924, 2852 (CH_2, CH_3), 1710 (C=O), 1607 and 1561 (C=C), 1439 (CH_2, CH_3), 1379 (CH_3), 1201 and 1069 (C–O), 831 cm^{-1} (=C–H). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.18 (s, 6 H, 7-CH_3, 15-CH_3), 2.27 (s, 2 H, 17-H_2), 3.83 (s, 6 H, 3-OCH_3, 11-OCH_3), 6.69 (d, $^4J_{4\text{-}H,2\text{-}H}$ = $^4J_{12\text{-}H,10\text{-}H}$ = 2.2 Hz, 2 H, 4-H, 12-H), 6.80 (dd, $^3J_{2\text{-}H,1\text{-}H}$ = $^3J_{10\text{-}H,9\text{-}H}$ = 8.9 Hz, $^4J_{2\text{-}H,4\text{-}H}$ = $^4J_{10\text{-}H,12\text{-}H}$ = 2.3 Hz, 2 H, 2-H, 10-H), 7.80 (d, $^3J_{1\text{-}H,2\text{-}H}$ = $^3J_{9\text{-}H,10\text{-}H}$ = 8.9 Hz, 2 H, 1-H, 9-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.60 (7-CH_3, 15-CH_3), 44.48 (C-17), 56.02 (3-OCH_3, 11-OCH_3), 74.44 (C-7, C-15), 99.58 (C-6a, C-14a), 100.23 (C-4, C-12), 108.18 (C-8b, C-16b), 112.60 (C-2, C-10), 125.63 (C-1, C-9), 155.18 (C-4a, C-12a), 160.64, 163.29 (C-6, C-14 or C-8a, C-16a), 164.10 (C-3, C-11). – MS (EI, 70 eV): *m/z* (%) = 448 (45) $[M]^+$, 433 (24) $[M–CH_3]^+$, 283 (8), 256 (10), 230 (100), 151 (35), 107 (5), 79 (4). – HRMS (EI, 70 eV): *m/z* = 448.11547 (calcd. 448.11581 for $C_{15}H_{24}O_3$, $[M]^+$).

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