Ninhydrin as a Source of Naphthoquinone Acetals and Benzocycloheptenetrione Derivatives, and the Trapping of an Oxacarbene Derived from a Cyclopentanone

Dirk Leinweber,[a] Matthias Schnebel,[a] Rudolf Wartchow,[b] Hans G. Wey,[c] and Holger Butenschön*[a]

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1,3-Bis(ethylenedioxy)-2-indanone (**2**) was shown to react with some dienophiles to give naphthoquinone acetals under photochemical reaction conditions, presumably by photodecarbonylation via the corresponding *ortho*-quinodimethane. With maleic anhydride the highly oxygenated benzocycloheptane derivative *rac*-**12** was obtained in good yield. In a similar manner, upon irradiation in the presence of acrylonitrile a 2:1 mixture of ring-expanded regioisomers *rac*-**13** and *rac*-**14** was obtained. Irradiation in the presence of fumarodinitrile unexpectedly gave the spirocyclic compound *rac*-**15**, which was characterized by X-ray crystallography. *rac*-**15** is the trapping product of oxacarbene **16**, thus demonstrating a rare case of a ring expansion of a cyclopentanone to give a six-membered ring oxacarbene, here leading to an orthoester.

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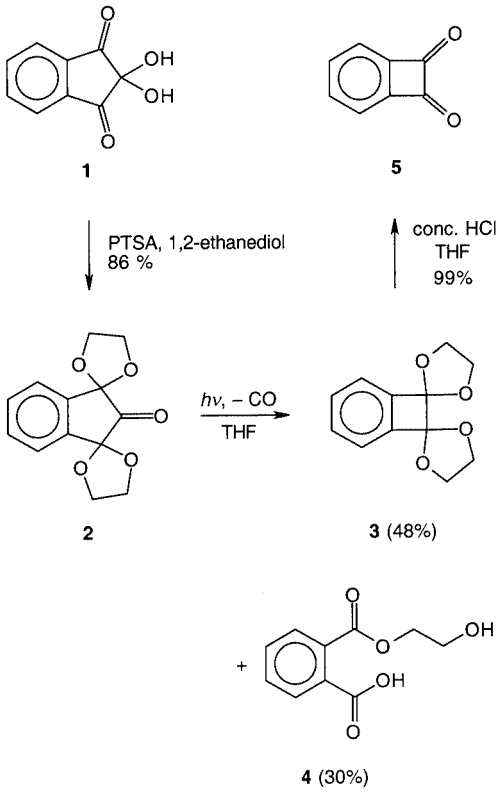
Introduction

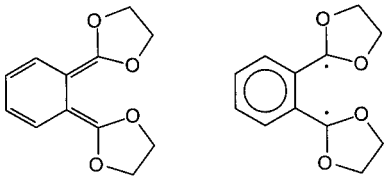
Ninhydrin (**1**), which is frequently used for the analysis of amino acids, can be transformed into 1,3-bis(ethylenedioxy)-2-indanone (**2**) in high yield. Recently we published a short synthesis of benzocyclobutenedione (**5**) on the basis of a photodecarbonylation of **2** giving bis(acetal) **3** only, which was hydrolyzed to give **5**.[1] Later, the phthalic acid monoester **4** was identified as a side product of the reaction, and the yield of **3** was raised to 57% by using benzene as the solvent.

It is reasonable to consider that the reaction proceeds via the corresponding *ortho*-quinodimethane **6** or the diradical **7**.[2–9] The importance of **5** in organic chemistry has been well documented in recent review articles.[10–16]

The intermediacy of **6** or **7** raises the question of whether the presence of dienophiles during the irradiation might allow the formation of the respective [4+2] cycloadducts. Given the importance of naphthoquinone derivatives the possibility of obtaining such compounds in a one-pot operation from readily accessible **2** is particularly attractive. The naphthoquinone building block can be found in many natural products, for example vitamin K,[17] and 1,4-naphthoquinone is pharmacologically active to moderate *Pneumocystis carinii* pneumonia (PCP).[18] Some 2-indanone de-



[a] Institut für Organische Chemie, Universität Hannover, Schneiderberg 1B, 30167 Hannover, Germany
Fax: (internat.) +49-(0)511/762-4616
E-mail: holger.butenschoen@mbox.oci.uni-hannover.de
[b] Institut für Anorganische Chemie, Universität Hannover, Callinstraße 9, 30167 Hannover, Germany
[c] Degussa AG, Paul-Baumann-Straße 1, 45476 Marl, Germany



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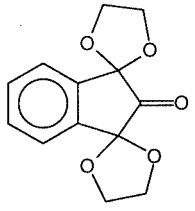
rivatives have been used by Sustmann et al. for the generation of *ortho*-quinodimethanes followed by cycloadditions with nitric oxide.[19,20]

With a number of dienophiles the intramolecular cyclization giving **3** prevailed over the desired cycloaddition: the use of diphenylethyne, tetracyanoethene, ethyl propynoate, and 3-sulfolene, resulted in the formation of the bis(acetal) **3** only. However, irradiation of **2** and 1.5 equivalents of dimethyl fumarate in benzene at 20 °C resulted in a 62% yield of the cycloadduct *rac*-**8**. This compound can also be obtained by heating **3** and dimethyl fumarate (neat) at 240 °C for 3 h; it was fully characterized. The reaction conditions and the possibility to skip intermediate **3** clearly demonstrate the value of the direct photolysis of **2** to give *rac*-**8**.



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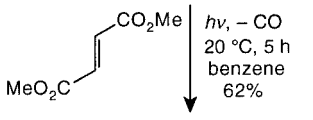
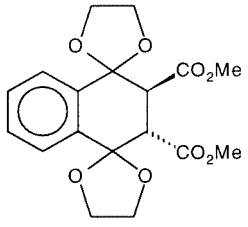
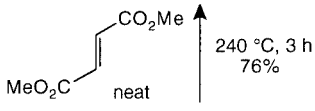
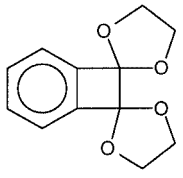




rac-**8**





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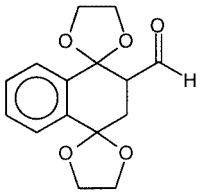
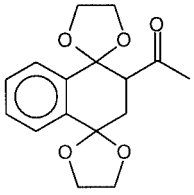
In the presence of 2.5 equivalents of propenal as the dienophile a 67% yield of the cycloadduct *rac*-**9** was achieved, and, in a similar way, the reaction with four equivalents of butenone gave the cycloadduct *rac*-**10** in 58% yield.

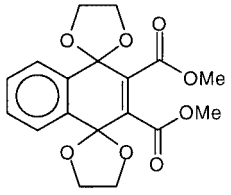
While *rac*-**8**−*rac*-**10** are dihydronaphthoquinone derivatives, the photolysis of **2** in the presence of 1.5 equivalents of dimethyl butynedioate gave the naphthoquinone diacetal **11** in 89% yield. Compound **11** is of interest because of the electron-poor double bond in the anellated ring, which might be used as a dienophile in another [4+2] cycloaddition leading to anthraquinone derivatives.



rac-**9**



rac-**10**



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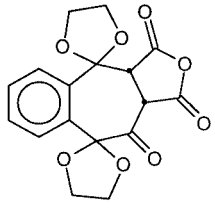
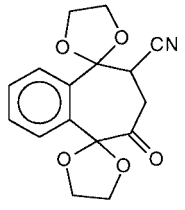
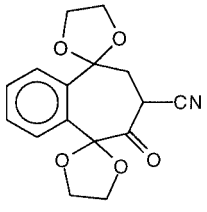
Interestingly, when maleic anhydride was tested as the dienophile, the highly oxygenated benzocycloheptene *rac*-**12** was obtained in 85% yield. *rac*-**12** is the product of a cyclization reaction between the diradical formed by the first photochemical α-cleavage and the dienophile. Apparently the reactivity of maleic anhydride makes the cyclization process faster than the second α-cleavage. In a similar fashion, the use of five equivalents of acrylonitrile resulted in a 2:1 regioisomeric mixture of nitriles *rac*-**13** and *rac*-**14** in 67% overall yield.



rac-**12**



rac-**13** 2:1



rac-**14**

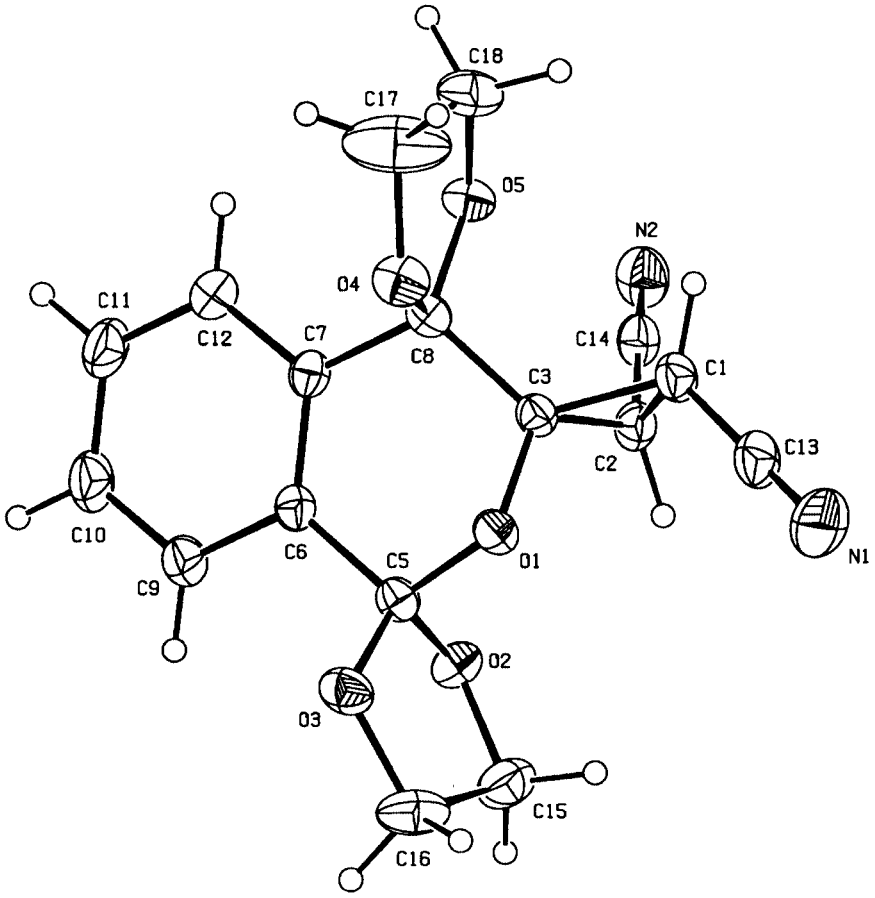
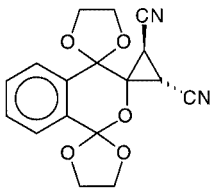
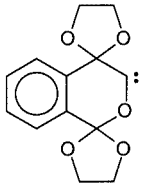


Figure 1. Structure of one molecule of *rac*-**15** in the crystal;[21] the structure of the other one does not significantly deviate from this; selected bond lengths [Å] and angles [°]: O1−C3 1.392(2), O1−C5 1.444(2), O2−C5 1.383(2), O3−C5 1.384(2), C1−C2 1.519(2), C2−C3 1.505(2), C3−C8 1.506(2), C5−C6 1.502(2), C6−C7 1.388(2), C6−C9 1.389(2), C7−C8 1.511(2), C7−C12 1.391(2), C9−C10 1.367(3), C10−C11 1.383(3), C11−C12 1.368(3); C3−O1−C5 113.33(12), O1−C5−C6 111.53(14), C5−C6−C7 122.21(14), C6−C7−C8 120.20(14), C3−C8−C7 107.92(14), O1−C3−C8 111.81(12), C1−C3−C2 60.76(11)

Fumarodinitrile was tested next; the *spiro*-anellated orthoester *rac*-**15** was isolated in only 32% yield. Due to the number of directly connected quaternary carbon atoms an identification by NMR spectroscopy was not easy. An HR mass spectrum could not be obtained because of the low intensity of the molecular ion peak. The product was finally identified by an X-ray crystal structure analysis (Figure 1).



rac-**15**



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The asymmetric unit contains two molecules, which, in a first approximation, form an enantiomeric pair. The anisotropic displacement ellipsoid of atom C17 in the first molecule suggests a split position for this atom, although no split position was introduced in the refinement. The maximum of the difference Fourier synthesis is in the vicinity of C17 and H11 (bonded to C17) and is probably caused by the slight disorder of C17.

There is no doubt that *rac*-**15** is the result of a cycloaddition of the dienophile with the oxacarbene **16**. The formation of cyclic oxacarbenes by photolysis of cycloalkanones was first reported by Yates et al. in 1964 upon photolysis of cyclocamphanone.[22] Since then many cases of such ring expansions have been reported, although the vast majority describe the reactions of cyclobutanone derivatives.[23−26] Ring expansions of cyclopentenone derivatives leading to pyran systems via oxacarbene intermediates are rare. The scarce reports include reactions of cyclocamphanone,[22,27] a stereochemical study using 3-oxacyclopentanones,[28] photolysis of a spirocyclopropyl-anellated cyclopentanone in a synthesis of thromboxane A_2 [29] and a similar step in the synthesis of pederol,[30] and, finally, a photochemical ring expansion starting from a camphor derivative.[31] To the best of our knowledge the photolysis leading to *rac*-**16** is not only a rare case in that a cyclopentenone ring is expanded, but also the first case of such a reaction leading to an orthoester; it is possible that the formation of side product **4** of the irradiation of **2** can be explained along similar lines.

In summary, we have found a ready access to some naphthoquinone derivatives under rather mild reaction conditions as well as an example of a cyclopentenone ring expansion via an oxacarbene leading to the orthoester *rac*-**15**. We are currently investigating the possibilities to exploit this chemistry for the synthesis of naturally occurring or pharmacologically interesting substances as phthiokol or vitamin K derived compounds.[17]

Experimental Section

General: Pentane, petroleum ether (PE), *tert*-butyl methyl ether (TBME), diethyl ether (DEE), and THF were distilled under argon from sodium-potassium alloy/benzophenone. ^{1}H NMR: Bruker WP 200 SY (200.1 MHz), AM 400 (400.1 MHz). ^{13}C NMR: Bruker WP 200 SY (50.3 MHz), AM 400 (100.1 MHz). Signal multiplicities were determined with APT and DEPT techniques. Chemical shifts refer to $\delta_{TMS} = 0$ or to residual solvent signals.[32,33] IR: Perkin−Elmer FT-IR 580 and 1710. MS: Finnigan MAT 112, 312 at 70 eV. HRMS: Finnigan MAT 312, VG Autospec, peak matching with PFK. Combustion analyses: Heraeus CHN Rapid. Melting points (uncorr.) were determined in sealed glass tubes with an apparatus according to Dr. Tottoli. Column chromatography (col. chrom.): silica gel (J. T. Baker, 40 μm). Separations were performed using flash chromatography.[34] Column length (l) and diameter (ø) are given. Ninhydrin was a donation from Merck KGaA.

Irradiation of 1,3-Bis(ethylenedioxy)indan-2-one (2):[1] In a photochemical immersion reactor (Pyrex, Hg high-pressure lamp Philips HPK 125 W) a solution of **2**[1] (1000 mg, 4.0 mmol) in 100 mL of benzene was irradiated for 5 h at 20 °C with some argon bubbling through the mixture. After solvent removal a colorless oil was obtained, which was purified by column chromatography (l = 25 cm, ø = 30 mm, TBME). Yield: 254 mg (1.2 mmol, 30%) of (2-hydroxyethyl) phthalate (**4**), recrystallized from ethyl acetate, colorless solid (m.p. 120 °C), and 422 mg (1.92 mmol, 48%) of 1,2-bis(ethylenedioxy)benzocyclobutene (**3**).[35]

3: IR (KBr): $\tilde{\nu}$ = 3388 (s, OH) cm^{-1}, 3248 (w), 3132 (w), 2984 (w), 2940 (w), 2828 (w), 2640 (m), 2552 (m), 1740 (s), 1684 (s), 1580 (w), 1492 (w), 1408 (w), 1364 (w), 1308 (m), 1280 (s), 1260 (s), 1072 (m), 768 (w), 748 (w). ^{1}H NMR (400.1 MHz, [D$_6$]DMSO): δ = 3.67 (t, ^3J = 5.3 Hz, 2 H, 9-H), 4.23 (t, ^3J = 5.3 Hz, 2 H, 10-H), 4.88 (br, 1 H, OH), 7.58−7.82 (m, 4 H, arom. H), 13.31 (br, 1 H, COOH) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 58.8 (CH$_2$, C-9), 66.9 (CH$_2$, C-10), 128.4 (CH), 128.9 (CH), 131.1 (CH), 131.4 (CH), 132.2 (C$_q$), 132.5 (C$_q$), 167.7 (C=O), 168.2 (C=O) ppm. MS (70 eV, 120 °C): *m*/*z* (%) = 180 (6), 149 (100) [M$^+$ − OCH$_2$CH$_2$OH], 121 (9), 104 (29), 93 (10), 76 (20, C$_6$H$_4$). C$_{10}$H$_{10}$O$_5$ (210.19): calcd. C 57.14, H 4.80; found C 57.15, H 4.68.

Dimethyl 1,4-Bis(ethylenedioxy)-*trans*-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate (*rac*-8): a) In a photochemical immersion reactor (Pyrex, Hg high-pressure lamp Philips HPK 125 W) a solution of **2**[1] (1000 mg, 4.0 mmol) and dimethyl *trans*-butenedioate (860 mg, 6.0 mmol) in 100 mL of benzene was irradiated for 5 h at 20 °C with some argon bubbling through the mixture. After solvent removal a yellowish solid was obtained, which was purified by column chromatography (l = 25 cm, ø = 30 mm, TBME/PE, 1:1). Yield: 920 mg (2.5 mmol, 62%) of *rac*-**8** as a colorless solid (m.p. 156 °C).

b) In a Schlenk flask equipped with a Liebig condenser a mixture of 1,2-bis(ethylenedioxy)benzocyclobutene (**3**) (1090 mg, 5.0 mmol) and dimethyl *trans*-butenedioate (831 mg, 5.8 mmol) was heated at 240 °C for 3 h. Dimethyl *trans*-butenedioate, which sublimed into the condenser, was brought back into the reaction mixture by heating it with a heat gun. After the reaction time the temperature was reduced to 130−140 °C, and unchanged dimethyl *trans*-butenedioate was removed into a cold trap at 0.1 mbar. Residual dimethyl *trans*-butenedioate was removed into a cold trap over 14 h at 50 °C at 0.1 mbar. A brown, crystalline solid was obtained, which was recrystallized from toluene, washed with pentane and dried at 0.001 mbar. Yield: 1370 mg (3.8 mmol, 76%) of *rac*-**8** as colorless crystals (m.p. 155 °C). IR (KBr): $\tilde{\nu}$ = 3440 cm^{-1} (br), 3060 (w), 2980 (m), 2950 (m,), 2900 (m), 1735 (s), 1600 (w), 1575 (w), 1482 (m), 1440 (s), 1430 (s), 1368 (s), 1340 (s), 1280 (s), 1235 (s), 1215 (s), 1170 (s), 1165 (s), 1100 (s), 1060 (s), 1020 (s), 980 (m), 965 (m), 950 (s), 900 (m), 775 (s) 708 (w), 660 (w), 605 (m), 570 (m). ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 3.69 (s, 6 H, CH$_3$), 3.73 (s, 2 H, CH), 3.98 (m, 2 H, CH$_2$), 4.13 (m, 4 H, CH$_2$), 4.42 (m, 2 H, CH$_2$) 7.40 + 7.46 (AA′BB′ system, 2 × 2 H, arom. CH) ppm. ^{13}C NMR (100 MHz, [D$_6$]acetone): δ = 52.0 (d, $^1J_{C,H}$ = 137 Hz, CH), 52.4 (q, $^1J_{C,H}$ = 147 Hz, CH$_3$), 65.8 (t, $^1J_{C,H}$ = 150 Hz, CH$_2$), 67.7 (t, $^1J_{C,H}$ = 150 Hz, CH$_2$), 107.8 (s, benzyl-C), 126.1 (d, $^1J_{C,H}$ = 161 Hz, arom. *C*HCHC$_q$), 129.8 (d, $^1J_{C,H}$ = 162 Hz, arom. *C*HC$_q$), 139.0 (s, arom. C$_q$) 171.3 (s, C=O) ppm. MS (CI, 70 eV, NH$_3$): *m*/*z* (%) = 382 (100) [M$^+$ + NH$_4^+$], 365 (16) [M$^+$ + H$^+$], 338 (3), 310 (9), 280 (3). C$_{18}$H$_{20}$O$_8$ (364.36): calcd. C 59.34, H 5.53; found C 59.18, H 5.50.

1,4-Bis(ethylenedioxy)-1,2,3,4-tetrahydronaphthalene-2-carbaldehyde (*rac*-9): In a photochemical immersion reactor (Pyrex, Hg high-pressure lamp Philips HPK 125 W) a solution of **2**[1] (1000 mg, 4.0 mmol) and propenal (580 mg, 10.3 mmol) in 100 mL of benzene was irradiated for 5 h at 20 °C with some argon bubbling through the mixture. After solvent removal a yellowish solid was obtained, which was purified by column chromatography (l = 25 cm, ø = 30 mm, TBME/PE, 1:1). Yield: 740 mg (2.7 mmol, 67%) of *rac*-**9** as a colorless oil. IR (film): $\tilde{\nu}$ = 2892 (m) cm^{-1}, 1776 (m), 1720 (s), 1360 (m), 1316 (m), 1284 (m), 1228 (m), 1152 (m), 1116 (m), 1056 (s), 1008 (m), 944 (m), 892 (m). ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 2.24 (dd, ^2J = −13.7, ^3J = 11.2 Hz, *trans*-CHH), 2.41 (dd, ^2J = −13.7, ^3J = 3.3 Hz, *cis*-CHH), 3.19 (ddd, ^3J = 11.7, 3.3, 1.5 Hz, 1 H, CHCHO), 4.05−4.25 (m, 7 H, CH$_2$), 4.44−4.53 (m, 1 H, CH$_2$), 7.38−7.43 (m, 2 H, arom. CH), 7.45−7.53 (m, 2 H, arom. H), 9.87 (d, ^3J = 1.5 Hz, 1 H, CHO) ppm. ^{13}C NMR (BB, 100 MHz, [D$_6$]acetone): δ = 32.0 (CCH$_2$CH), 54.1 (aliph. CH), 64.3 (CH$_2$ acetal), 64.4 (CH$_2$ acetal), 65.3 (CH$_2$ acetal), 66.7 (CH$_2$ acetal), 105.3 (benzyl C$_q$), 106.7 (benzyl C$_q$), 124.9 (arom. CH), 126.1 (arom. CH), 128.6 (arom. CH), 128.7 (arom. CH), 137.9 (arom. C$_q$), 138.4 (arom. C$_q$), 200.1 (C=O) ppm. MS (70 eV): *m*/*z* (%) = 276 (1) [M$^+$], 248 (1) [M$^+$ − CO or M$^+$ − C$_2$H$_4$], 247 (2) [M$^+$ − CHO], 220 (13) [M$^+$ − CO − C$_2$H$_4$ or M$^+$ − 2 C$_2$H$_4$], 149 (15), 148 (100) [C$_6$H$_4$C(O$_2$C$_2$H$_4$)], 132 (11), 104 (64), 76 (31, C$_6$H$_4$).

2-Acetyl-1,4-bis(ethylenedioxy)-1,2,3,4-tetrahydronaphthalene (*rac*-10): In a photochemical immersion reactor (Pyrex, Hg high-pressure lamp Philips HPK 125 W) a solution of **2**[1] (1000 mg, 4.0 mmol) and butanone (1130 mg, 16.0 mmol) in 100 mL of benzene was irradiated for 5 h at 20 °C with some argon bubbling through the mixture. After solvent removal a yellow oil was obtained, which was purified by column chromatography (l = 250 mm, ø = 30 mm, TBME/PE, 1:2). Yield: 634 mg (1.8 mmol, 58%) of *rac*-**10** as a colorless solid (m.p. 113 °C). IR (ATR): $\tilde{\nu}$ = 2963 cm^{-1} (w), 2890 (w), 1704 (m), 1452 (w), 1372 (w), 1356 (w), 1304 (m), 1217 (m), 1180 (m), 1144 (m), 1061 (s), 1045 (s), 1026

(s), 946 (s), 927 (s), 853 (w), 775 (s). ^{1}H NMR (200.1 MHz, $CDCl_3$): δ = 2.22 (dd, $^2J_{cis\text{-}3,trans\text{-}3}$ = −13.8, $^3J_{cis\text{-}3,2}$ = 3.1 Hz, 1 H, *cis*-3-H), 2.31 (s, 3 H, CH_3), 2.61 (dd, $^2J_{trans\text{-}3,cis\text{-}3}$ = −13.8, $^3J_{trans\text{-}3,2}$ = 11.7 Hz, 1 H, *trans*-3-H), 3.50 (ddd, $^3J_{2,trans\text{-}3}$ = 11.7, $^3J_{2,cis\text{-}3}$ = 3.1 Hz, 1 H, 2-H), 4.01−4.30 (m, 8 H, acetal-H), 7.36−7.46 (m, 4 H, arom. H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, APT): δ = 31.3 (−, CH_3), 34.1 (+, CH_2CH), 54.6 (−, CH), 64.5 (+, acetal CH_2), 64.6 (+, acetal CH_2), 65.8 (+, acetal CH_2), 66.6 (+, acetal CH_2), 106.1 (+, C_qCH_2), 107.6 (+, C_qCH), 124.4 (−, arom. C), 126.2 (−, arom. C), 129.1 (−, arom. C), 129.2 (−, arom. C), 137.1 (+, arom C_q), 138.8 (+, arom. C_q), 207.9 (+, C=O) ppm. MS (70 eV, 60 °C): *m*/*z* (%) = 290 (2) [M^+], 247 (3) [$M^+ - CH_3CO$], 220 (42), 203 (3), 176 (9), 148 (100) [$C_6H_4C(O_2C_2H_4)$], 133 (17), 104 (41), 76 (16) [C_6H_4]. HRMS $C_{16}H_{18}O_5$: calcd. 290.1154; found. 290.1158.

Dimethyl 1,4-Dihydro-1,4-bis(ethylenedioxy)naphthalene-2,3-dicarboxylate (11): In a photochemical immersion reactor (Pyrex, Hg high-pressure lamp Philips HPK 125 W) a solution of **2**[1] (1000 mg, 4.0 mmol) and dimethyl butynedioate (850 mg, 6.0 mmol) in 100 mL of benzene was irradiated for 7 h at 20 °C with some argon bubbling through the mixture. After solvent removal a yellowish solid was obtained, which was purified by column chromatography (l = 25 cm, ø = 30 mm, TBME/PE, 1:1). Yield: 1290 mg (3.6 mmol, 89%) of **11** as a colorless solid (m.p. 184 °C). IR (KBr): ṽ = 2956 (w) cm^{-1}, 2908 (w), 1716 (s), 1664 (w), 1488 (w), 1436 (m), 1332 (m), 1284 (s), 1224 (s), 1208 (s), 1160 (m), 1140 (m), 1064 (s), 1024 (s), 976 (m), 960 (s), 780 (m), 724 (w), 612 (w). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 3.81 (s, 6 H, CH_3), 4.26 (m, 8 H, CH_2), 7.39 + 7.50 (AA′BB′, 2 × 2 H, arom. H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 52.5 (CH_3), 66.8 (CH_2), 101.9 (C_q, OCO), 124.7 (CH, arom. $CHCHC_q$), 128.9 (CH, arom. $CHCHC_q$), 137.0 (C_q, arom. C_q), 140.7 (C_q, C_qC=O), 165.1 (C_q, C=O) ppm. MS (70 eV, 140 °C): *m*/*z* (%) = 363 (6) [M^+ +1], 362 (13) [M^+], 331 (7), 319 (17), 303 (40), 287 (12), 274 (77), 259 (21), 244 (17), 231 (57), 215 (26), 187 (21), 148 (100) [$C_6H_4C(O_2C_2H_4)$], 133 (17), 104 (44).

4,9-Bis(ethylenedioxy)-3a,4,9,10a-tetrahydro-2-oxabenzo[*f*]-azulene-1,3,10-trione (*rac*-12): In a photochemical immersion reactor (Pyrex, Hg high-pressure lamp Philips HPK 125 W) a solution of **2**[1] (1000 mg, 4.0 mmol) and maleic anhydride (784 mg, 8.0 mmol) in 100 mL of benzene was irradiated for 4 h at 20 °C with some argon bubbling through the mixture. After solvent removal a colorless solid was obtained, which was purified by column chromatography (l = 25 cm, ø = 30 mm, TBME). Yield: 1180 mg (3.4 mmol, 85%) of *rac*-**12** as a colorless solid. IR (KBr): ṽ = 2904 (m) cm^{-1}, 1872 (m, C=O cycl. anhydride) 1796 (s, cycl. C=O anhydride), 1732 (m, C=O, ketone), 1236 (m), 1216 (m), 1048 (m), 1020 (m), 988 (m), 944 (m), 908 (m). ^{1}H NMR (200 MHz, [D$_6$]acetone): δ = 3.5−4.6 (m, 10 H, CH, CH_2), 7.3−7.9 (m, 4 H, arom. CH) ppm. ^{13}C NMR (50 MHz, [D$_6$]acetone): δ = 52.0 (aliph. CH), 52.9 (aliph. CH), 106.1 (aliph. C_q), 106.5 (aliph. C_q), 125.6 (arom. CH), 129.3 (arom. CH), 129.7 (arom. CH), 129.9 (arom. CH), 134.1 (arom. C_q), 138.0 (arom. C_q), 165.7 (anhydride C=O), 166.2 (anhydride C=O), 193.9 (ketone C=O) ppm. MS (70 eV): *m*/*z* (%) = 347 (4) [M^+ + 1], 346 (18) [M^+], 220 (47), 176 (12), 149 (23), 148 (100) [$C_6H_4C(O_2C_2H_4)$], 133 (17), 104 (29), 76 (15) [C_6H_4], 66 (16).

***rac*-5,9-Bis(ethylenedioxy)-5,7,8,9-tetrahydro-6-oxobenzocyclohepten-8-carbonitrile (*rac*-13) and *rac*-5,9-Bis(ethylenedioxy)-5,7,8,9-tetrahydro-6-oxobenzocyclohepten-7-carbonitrile (*rac*-14):** In a photochemical immersion reactor (Pyrex, Hg high-pressure lamp Philips HPK 125 W) a solution of **2**[1] (1000 mg, 4.0 mmol) and acrylonitrile (1130 mg, 8.0 mmol) in 100 mL of benzene was irradiated for 5 h at 20 °C with some argon bubbling through the mixture. After solvent removal a red oil was obtained, which was purified by column chromatography (l = 250 mm, ø = 30 mm, TBME/PE, 1:1). Yield: 806 mg (2.7 mmol, 67%) of a 2:1 mixture of *rac*-**13** and *rac*-**14** as a colorless solid.

***rac*-13 and *rac*-14:** IR (ATR): ṽ = 2970 cm^{-1} (w), 2892 (w), 2118 (w, CN), 1703 (m, ketone), 1679 (m, ketone), 1599 (m), 1456 (w), 1402 (w), 1357 (m), 1286 (s), 1252 (m), 1221 (m), 1175 (m), 1140 (m), 1083 (s), 1027 (s), 986 (m), 947 (s), 893 (w), 767 (s), 653 (w), 577 (m), 537 (m) ppm. MS (70 eV, 130 °C): *m*/*z* (%) = 302 (1) [M^+ + 1], 301 (3) [M^+], 271 (4), 248 (2), 237 (7), 220 (70), 201 (18), 187 (65), 162 (39), 148 (100) [$C_6H_4C(O_2C_2H_4)$], 133 (53), 104 (60), 76 (52, C_6H_4). HRMS $C_{16}H_{15}NO_5$: calcd. 301.0950; found. 301.0950.

***rac*-13:** ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 2.81 (m, 2 H, CH_2C=O), 3.40 (dd, ^3J = 7.65 Hz, 1 H, CH), 3.89−4.30 (m, 8 H, acetal H), 7.40−7.80 (m, 4 H, arom. H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, APT): δ = 36.6 (+, CH_2CO), 37.6 (−, CHCN), 65.8 (+, acetal CH_2), 65.9 (+, acetal CH_2), 66.2 (+, acetal CH_2), 66.6 (+, acetal CH_2), 106.6 (+, C_qCH), 106.9 (+, C_qCO), 117.3 (+, CN), 125.7 (−, arom. C), 128.4 (−, arom. C), 129.7 (−, arom. C), 129.9 (−, arom. C), 134.8 (+, arom. C_q), 135.4 (+, arom. C_q), 197.4 (+, C=O).

***rac*-14:** ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 3.13 (m, 2 H, CH_2CH), 3.70 (dd, $^3J_{trans}$ = 14.2, $^3J_{cis}$ = 6.9 Hz, 1 H, CH), 3.89−4.30 (m, 8 H, acetal H), 7.40−7.80 (m, 4 H, arom. H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, APT): δ = 30.9 (−, CH), 45.0 (+, CH_2CH), 65.6 (+, acetal CH_2), 65.8 (+, acetal CH_2), 65.9 (+, acetal CH_2), 67.2 (+, acetal CH_2), 108.4 (+, C_qCH_2), 109.6 (+, C_qCO), 118.8 (+, CN), 126.8 (−, arom. C), 127.4 (−, arom. C), 128.2 (−, arom. C), 129.7 (−, arom. C), 131.1 (+, arom. C_q), 135.6 (+, arom. C_q), 199.0 (+, CO).

6:7-Benzo-Anellated 4-Oxaspiro[2.5]octane-*trans*-1,2-dicarbonitrile (*rac*-15): In a photochemical immersion reactor (Pyrex, Hg high-pressure lamp Philips HPK 125 W) a solution of of **2**[1] (1000 mg, 4.0 mmol) and fumarodinitrile (1570 mg, 20.0 mmol) in 100 mL of benzene was irradiated for 5 h at 20 °C with some argon bubbling through the mixture. After solvent removal a red oil was obtained, which was purified by column chromatography (l = 250 mm, ø = 30 mm, TBME/PE, 1:1). Yield: 404 mg (1.3 mmol, 32%) of *rac*-**15** as a colorless solid (m.p. 123 °C). IR (ATR): ṽ = 3043 cm^{-1} (w), 2977 (w), 2906 (w), 2251 (w), 1477 (w), 1452 (w), 1318 (m), 1210 (m), 1146 (m), 1049 (s), 1033 (s), 976 (m), 945 (s), 871 (w), 763 (m), 732 (w), 653 (w). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 2.44 (d, ^3J = 7.0 Hz, 1 H, CH), 2.63 (d, ^3J = 7.0 Hz, 1 H, CH), 4.25−4.41 (m, 8 H, acetal H), 7.37−7.48 (m, 4 H, arom. H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, BB): δ = 14.5 (CH), 15.2 (CH), 65.1 (acetal CH_2), 65.6 (acetal CH_2), 66.2 (acetal CH_2), 66.7 (acetal CH_2), 68.1 (C_qCHCN), 101.3 (OC_qC_qCHCN), 114.1 (CN), 114.6 (CN), 119.6 (C_qO_3), 123.6 (arom. C), 127.4 (arom. C), 129.9 (arom. C), 130.4 (arom. C), 131.1 (arom. C_q), 135.5 (arom. C_q).) ppm. MS (70 eV, 140 °C): *m*/*z* (%) = 326 (2) [M^+], 283 (2), 253 (2), 220 (27), 200 (6), 176 (10), 148 (100) [$C_6H_4C(O_2C_2H_4)$], 104 (31), 76 (15) [C_6H_4].

Crystal Structure Analysis of *rac*-15:[21] $C_{17}H_{14}N_2O_5$, crystal size 0.85 × 0.63 × 0.15 mm, a = 9.984(2), b = 21.952(4), c = 28.004(6) Å, α = β = γ = 90°, V = 6138(2) Å^3, Z = 16, $d_{calcd.}$ = 1.413 gcm^{-3}, T = 300(2) K, crystal system orthorhombic, space group *Pcab* (No. 61), Stoe IPDS diffractometer, $\lambda_{Mo\text{-}K_\alpha}$ = 0.71073 Å, θ_{max} = 26.01, 68463 measured reflections, 6014 independent (R_{int} = 0.0895) and 3491 observed reflections [$I > 2\sigma(I)$], 434 refined parameters, $R_{gt}(F)$ = 0.0378, w$R(F^2)$ = 0.0777.

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[1] D. Leinweber, H. Butenschön, *Tetrahedron Lett.* **1997**, *38*, 6385−6386.
[2] G. Quinkert, K. Opitz, W. W. Wiersdorff, J. Weinlich, *Tetrahedron Lett.* **1963**, 1863−1868.
[3] G. Quinkert, W.-W. Wiersdorff, M. Finke, K. Opitz, F.-G. v. d. Haar, *Chem. Ber.* **1968**, *101*, 2302−2325.
[4] C. R. Flynn, J. Michl, *J. Am. Chem. Soc.* **1973**, *95*, 5802−5803.
[5] K. K. de Fonseka, J. J. McCullough, A. J. Yarwood, *J. Am. Chem. Soc.* **1979**, *101*, 3277−3282.
[6] D. S. Weiss, in *Organic Photochemistry* (Ed.: A. Padwa), Marcel Dekker, Inc., New York, **1981**; Vol. 5; pp 347−420.
[7] J. J. McCullough, *Acc. Chem. Res.* **1980**, *13*, 270−276.
[8] J. E. Starr, R. H. Eastman, *J. Org. Chem.* **1966**, *31*, 1393−1402.
[9] J. C. Netto-Ferreira, V. Wintgens, J. C. Scaiano, *Tetrahedron Lett.* **1989**, *49*, 6851−6854.
[10] M. A. Bennett, E. Wenger, *Chem. Ber./Recueil* **1997**, *130*, 1029−1042.
[11] F. Toda, P. Garratt, *Chem. Rev.* **1992**, *92*, 1685−1707.
[12] H. W. Moore, B. R. Yerxa, *Chemtracts Org. Chem.* **1992**, *5*, 273−313.
[13] H. Knorr, W. Ried, *Synthesis* **1978**, 649−666.
[14] I. L. Klundt, *Chem. Rev.* **1970**, *70*, 471−487.
[15] N. Martin, C. Seoane, M. Hanack, *Org. Prep. Proc. Int.* **1991**, *23*, 139−272.
[16] H. Butenschön, *Synlett* **1999**, 680−691.
[17] *The Merck Index*; 10th ed. (Eds.: M. Windholz, S. Budavari, R. F. Blumetti, E. S. Otterbein), Merck & Co., Inc.: Rahway NJ, **1983**.
[18] http://www.ama-assn.org/special/hiv/treatmnt/druginfo/mepron.htm
[19] H.-G. Korth, S. Sustmann, P. Lommes, T. Paul, A. Ernst, H. d. Groot, L. Hughes, K. U. Ingold, *J. Am. Chem. Soc.* **1994**, *116*, 2767−2777.
[20] T. Paul, M. A. Hassan, H.-G. Korth, R. Sustmann, D. V. Avila, *J. Org. Chem.* **1996**, *61*, 6835−6848.
[21] CCDC-177352 (*rac*-**15**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].
[22] P. Yates, L. Kilmurry, *Tetrahedron Lett.* **1964**, *5*, 1739−1742.
[23] P. Yates, R. O. Loutfy, *Acc. Chem. Res.* **1975**, *8*, 209−216.
[24] W.-D. Stohrer, P. Jacobs, K. H. Kaiser, G. Wiech, G. Quinkert, *Top. Curr. Chem.* **1974**, *46*, 181−236.
[25] P. Heinrich, in *Houben Weyl Methoden der Organischen Chemie* (Ed.: E. Müller), Georg Thieme Verlag, Stuttgart, **1975**; Vol. IV/5b; pp 822−829.
[26] M. C. Pirrung, V. K. Chang, C. V. DeAmicis, *J. Am. Chem. Soc.* **1989**, *111*, 5824−5831.
[27] P. Yates, L. Kilmurry, *J. Am. Chem. Soc.* **1966**, *88*, 1563−1564.
[28] R. S. Grewal, D. J. Burnell, P. Yates, *J. Chem. Soc., Chem. Commun.* **1984**, 759−760.
[29] S. W. Jones, F. Scheinmann, B. J. Wakefield, D. Middlemiss, R. F. Newton, *J. Chem. Soc., Chem. Commun.* **1986**, 1260−1261.
[30] M. C. Pirrung, P. M. Kenney, *J. Org. Chem.* **1987**, *52*, 2335−2336.
[31] K. Switlak, D. He, P. Yates, *J. Chem. Soc., Perkin Trans. 1* **1992**, 2579−2580.
[32] H. Günther, *NMR-Spektroskopie*; 2nd ed., Georg Thieme Verlag, Stuttgart **1983**.
[33] H.-O. Kalinowski, S. Berger, S. Braun, *13C NMR-Spektroskopie*, Georg Thieme Verlag, Stuttgart **1984**.
[34] W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem.* **1978**, *43*, 2923−2925.
[35] M. P. Cava, R. P. Stein, *J. Org. Chem.* **1966**, *31*, 1866−1869.

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