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Furo[3,4-*b*]benzodioxin Cycloadditions – A One-Pot Synthesis of Functionalized Bis-Adducts

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Furo[3,4-*b*]benzodioxin **1** was found to undergo a double Diels–Alder reaction with several dienophiles. The diene reacts directly with the suitable dienophile to give the mono-adduct intermediate that unexpectedly leads to a second cycloaddition at the internal, electron-rich, oxabicyclic C4a–C10a double bond. The resulting bis-adducts were formed under relatively mild conditions with dienophiles ranging from maleic anhydride and dimethyl acetylenedicarboxylate to the extremely reactive arynes. With this methodology of two uninterrupted sequential cycloaddition reactions, interesting formation of stable bis-adducts was observed. The dienophile behavior of 1,4-benzodioxin is described for the first time in this work.

Introduction

For more than 70 years, the Diels–Alder (DA) cycloaddition has been one of the most valuable and versatile reactions found in organic synthesis, particularly in the preparation of interesting heterocyclic compounds.[1] The energy differences of the HOMO/LUMO (the highest occupied molecular orbital/the lowest unoccupied molecular orbital) play important roles and allow three types of DA reactions to be described: *normal, inverse*, and *neutral*. In the *normal* reaction, a conjugated diene (HOMO) reacts with a dienophile (LUMO), which can be an alkene or an alkyne bearing electron-withdrawing groups. Through conjugation, the energy of the LUMO antibonding π orbital is lowered to an appropriate level for the reaction with the diene. Its counterpart, the *inverse* electron demand reaction, is a LUMO-diene/HOMO-dienophile controlled process. In the *neutral* DA reaction, the two molecular orbital interactions (HOMO-diene/LUMO-dienophile and LUMO-diene/HOMO-dienophile) are involved in the cycloaddition.[2,3] Highly reactive cyclic dienes such as isobenzofuran derivatives would be interesting and useful building blocks for the preparation of bioactive compounds.

Although additions of isobenzofurans to a number of dienophiles have already been reported,[4] to date and to the best of our knowledge, no reaction using 1,4-benzodioxin dienophiles has been described. Only a few examples of dienes containing the 1,4-benzodioxin substructure have been reported.[5] The chemistry of 1,4-benzodioxins and their 2,3-dihydro derivatives has attracted special attention due to the relevant biological activity of compounds possessing this nucleus.[6]

Results and Discussion

In this article, we report our studies on the cycloaddition of furo[3,4-*b*]benzodioxins focusing on the synthesis of bis-adducts.

In earlier work, we synthesized differently substituted dibenzo[*b,e*][1,4]dioxins by using Diels–Alder reactions.[5b–5d] The reaction of diene **1**[5d] with dimethyl acetylenedicarboxylate (DMAD) proceeds instantly in a low volume of toluene at 80 °C in a sealed tube (Scheme 1) to afford a mixture of products that was fractionated by column chromatography (hexane/ethyl acetate, 1:2).

Bis-adduct **3** was the major product isolated in moderate yield. Even with a large excess of the dienophile, the bis-adduct was the main compound obtained. The mono-adduct was not found in significant amounts even when the dienophile was used as the solvent. After the first cycloaddition, the 1,4-benzodioxin framework acts as a new dienophile for a second cycloaddition reaction. In fact, we observed that the C4a–C10a double bond is the only reactive site, and that the Diels–Alder reaction does not take place at the C2–C3 position under these conditions.

The structure of adduct **3** was identified by MS (m/z = 546) and ^{1}H NMR spectroscopy. The two singlets for the different methyl groups at δ = 1.53 and 1.74 ppm confirmed the surprising structure of adduct **3**. Analysis of the ^{13}C NMR spectrum of **3** showed three different quaternary carbon atoms bonded to oxygen {87.3 [C6(11)], 89.2 [C7(10)], and 92.6 [C6a(10a)] ppm}, which proved that the second

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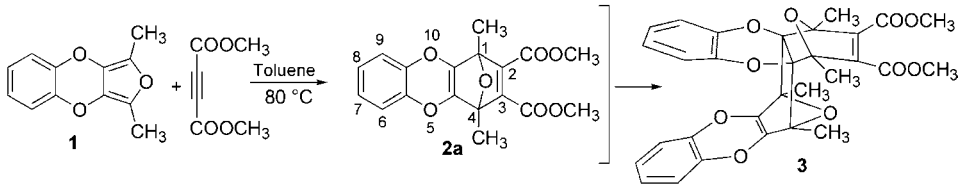


Scheme 1. Cycloaddition with DMAD.

intermolecular cycloaddition occurred on the C4a–C10a double bond of **2a**. Albeit four bis-adducts with different stereochemistries are theoretically possible, TLC and ^{1}H and ^{13}C NMR spectroscopic analysis of the crude products showed that only one single diastereomer was formed during the cycloaddition.[7] The formed adduct was not the expected linear bis-adduct structure such as **4** (Figure 1), as it was reported from the cycloaddition of other dienes with acetylenic dienophiles[8a] and in related derivatives.[8b]

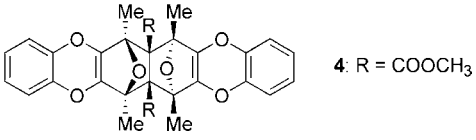


Figure 1. Bis-adduct **4**.

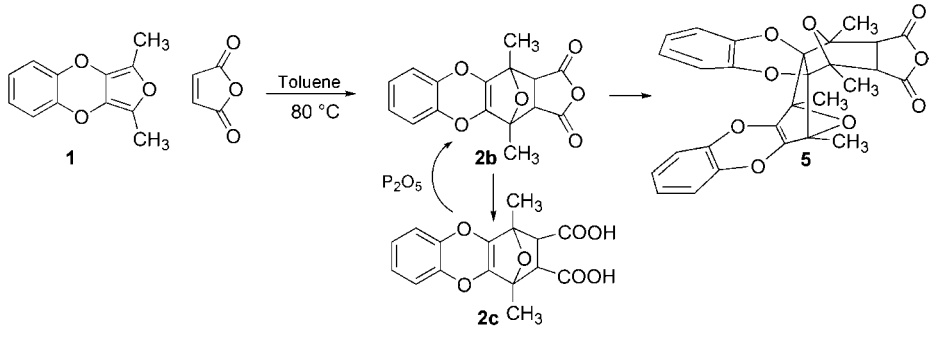
As our computational study indicates, a significant charge rearrangement upon formation of adduct **3** occurs outside of the near-neighboring reaction centers. The net charge transfer from diene **1** to dienophile **2a**, however, is close to zero. This suggest that the observed regioselectivity can be rationalized as not being HOMO–LUMO, but electrostatically controlled, favoring the electron-deficient C4a and C10a carbon atoms over the electrophilic C2–C3 atoms. Furthermore, computational methods that are known to fail in the modeling of weak contacts also fail to predict the stability of the product, which reinforces our hypothesis that intramolecular forces play a central role in both regioselectivity and stability.

The interactions controlling the *exo* or *endo* selectivity in these cycloadditions are the result of electronic and steric effects. The formation of the *endo* adduct suggests preferential approach from the more accessible face on the primary adduct, which implies a more favorable conformation by placing the carbonyl groups at the opposite side. The formation of this adduct appears thus favored by the close proximity of the two dioxygenated substructures separated of the bulky groups.[9] Bis-adduct **3** was detected after only 2 min of reaction at 60 °C (41% yield). This result confirms the high reactivity of mono-adduct **2a**.

The fact that all these mono-adducts undergo subsequent addition of the second mol of diene to give stable bis-adducts and that the double bond of 1,4-benzodioxin is the dienophile instead of the classical double bond (conjugated with electron-attracting substituent such as CO, CO_2R, CN, and NO_2) constituted an unprecedented finding. With these results, we have now turned our attention to the finding that the double bond of the 1,4-benzodioxin framework is an effective Diels–Alder dienophile for simple dienes, and we decided to study the reaction of **1** with other dienophiles.

Following the same conditions described previously, the reaction of diene **1** with maleic anhydride gave bis-adduct **5** in 62% yield (Scheme 2). Intermediate mono-adduct **2b** possess only the double bond of the 1,4-benzodioxin substructure. This adduct showed spectroscopic characteristics similar to those of bis-adduct **3**.

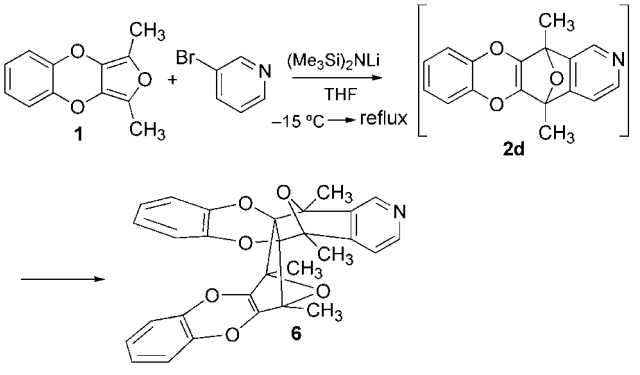
When the reaction time was decreased, mono-adduct **2b** was detected and differentiated from bis-adduct **5** by the ^{1}H NMR spectroscopic data corresponding to the α-carbonylic–CH signal at 3.54 (mono-adduct) and 3.88 ppm (bis-adduct). Several conditions were assayed for the preparation of mono-adduct **2b**, but this was difficult, as the mono-adduct is more reactive than the starting dienophile. Purification by column chromatography on silica gel results in hydrolysis of the anhydride. For this study, on the basis of our previous results, toluene was chosen as the solvent. The diene/dienophile equivalents ratio was studied, and the results showed that 1:3 was the best stoichiometry. The influence of the temperature and reaction time was investigated.



Scheme 2. Cycloaddition with maleic anhydride.

The best conditions for the formation of bis-adduct **5** were the maintenance of the reaction at 80 °C over 5 h. Indeed, we could not observe cycloaddition at room temperature. Then, we studied the cycloaddition without solvent, and the results showed that the formation of mono-adduct **2b** was increased and the obtention of bis-adduct **5** decreased. The formation of carboxylic acid **2c**, generated by hydrolysis of initial mono-adduct **2b**, was also observed under these last conditions. Diacid **2c** can be reverted to the anhydride by dehydration with P_2O_5.

As a part of our ongoing research program on Diels–Alder cycloadditions, we previously reported that 3,4-didehydropyridine (3,4-pyridyne) prepared from 3-bromopyridine, lithium bis(trimethylsilyl)amide, and diene **1** undergo Diels–Alder cycloaddition to furnish novel adducts.[5d–5e] In the same way, treatment of diene **1** with 3,4-didehydropyridine generated in situ from 3-bromopyridine gave bis-adduct **6** after 20 h (57% yield) (Scheme 3). The bis-adduct was easily purified by column chromatography and fully characterized. Finally, with a shorter reaction time mono-adduct **2d** of the crude reaction mixture was isolated, but it was unstable under the column chromatographic conditions; after several attempts we were able to isolate and characterize it properly. Adduct **2d** is trapped rapidly and in a diastereoselective manner undergoes a second cycloaddition reaction to give bis-adduct **6c** as a main compound. Our thermochemical calculations for the formation of **6a–d** indicated that **6c** is the most stable and plausibly formed bis-adduct (see Supporting Information), suggesting that **6** has the same structure as that suggested by NOESY experiments.



Scheme 3. Cycloaddition with 3,4-pyridyne.

Reaction conditions such as time, amounts of substrate and base, order of addition of the components, and temperature were studied. The best results were obtained when diene **1** was initially mixed with bis(trimethylsilyl)amide (8 equiv.) and bromopyridine (8 equiv.) and heated at reflux in dry tetrahydrofuran for 5.5 h. The mono-adduct was always accompanied by the bis-adduct, but it can be isolated by column chromatography. When excess amounts of the three components were initially mixed and heated at reflux in dry tetrahydrofuran for 15 h, bis-adduct **6** (57%) was obtained and 28% of unreacted diene **1** was recovered, but the mono-adduct was not detected. The use of an excess amount of bromopyridine and a shorter reaction time (5 h) afforded **6** (49%) and mono-adduct **2d** (7%); diene **1** was also recovered (41%). Ultrasonic irradiation at room temperature gave bis-adduct **6** (11%) and mono-adduct **2d** (13%); **1** was also recovered (61%). MS in combination with 2D NMR heteronuclear (^1H–^{13}C HMQC) correlation experiments allowed us to assign the signals of all protons and carbon atoms and to establish the possible structures of these compounds.

The stereochemistry of bis-adduct **6** was determined by proton NOESY experiments. Protons H-9 and H-10 exhibit a NOESY correlation peak with H-4′ and H-5′, whereas H-8 and H-11 exhibit a correlation peak with H-3′ and H-6′, respectively. Proton H-4 exhibits a correlation peak with methyl at C-5, whereas H-6′ correlates with the methyl group at C-13, suggesting that the conformation indicated for **6** is in accordance with the spectral observations (Figure 2).

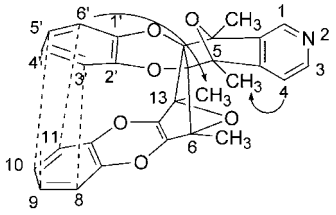
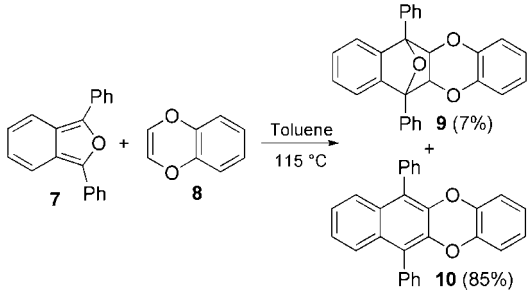


Figure 2. Correlation observed in the NOESY spectrum of bis-adduct **6**.

Spino et al. reported that dienophiles such as 2,3-dihydro-1,4-benzodioxine and 2,3-dihydro-1,4-dioxane were unreactive with electron-poor dienes such as (*E*)-methyl-(6-oxocyclohex-1-enyl)acrylate or dimethyl 2,3-dimethylenesuccinate in Diels Alder cycloadditions.[10] In spite of these results, the suggested reactivity of 1,4-benzodioxin as a dienophile was confirmed with the reaction of commercially available diene **7** and 1,4-benzodioxin **8**[11] in toluene at 115 °C. In this case, after complete consumption of the starting material expected cycloadduct **9** was obtained in only 7% yield together with main product **10** (85% yield). The aromatization takes place in one step by opening of the tetrahydrofuran ring and dehydration (Scheme 4). Here, the in situ ring-opening of the oxabridge in intermediate **9** occurs even in the absence of an acidic catalyst. Presumably, the ring-opening reaction is assisted by the adjacent phenyl



Scheme 4. Preparation of adducts from 1,4-benzodioxin.

groups driving the reaction in the desired direction. The higher stability of analogues of **9** without phenyl groups supports the latter suggestion.

Attempts to obtain suitable crystals of bis-adducts **3**–**6** to further validate the structure of the diastereoisomers by X-ray analysis proved unsuccessful. Efforts to further define the scope of this reaction by using other dienes are currently underway in this laboratory.

Conclusions

We found that 1,4-benzodioxins undergo Diels–Alder cycloadditions with isobenzofuran dienes to generate a range of new polycyclic systems. The intermolecular double cycloaddition protocol presented herein was applied to the preparation of complex bis-adducts. The first cycloaddition constructs a new substrate serving as a dienophile for the second Diels–Alder cycloaddition. Overall and unexpectedly, from the two starting compounds bridged yet stable cycloadducts were produced in remarkable yields. Finally, the cycloadducts reported herein possess the common pharmacophore 1,4-benzodioxin moiety, which has great potential in medicinal chemistry.

Experimental Section

General Data: ^{1}H NMR spectra were recorded with a Varian Gemini 300 or 500 spectrometer by using tetramethylsilane as internal standard and $CDCl_3$ as solvent; chemical shifts are given in ppm and coupling constants are expressed in Hz. ^{13}C NMR spectra were recorded with a Varian Gemini 50.3 or 75.5 MHz spectrometer. Melting points were determined with a Gallenkamp apparatus and are uncorrected. IR spectra were recorded with a FTIR Perkin–Elmer 1600 spectrophotometer. Mass spectra were recorded with a Hewlett–Packard spectrometer 5988-A (70 eV). Chromatography was carried out on SiO_2 (silica gel 60, SDS, 60–200 μm). Microanalyses were determined with a Carlo Erba 1106 Analyser at Serveis Cientifico-Tècnics, University of Barcelona, and all new compounds have given C, H, N analyses within ±0.4% of the theoretical values. All reagents were of commercial quality or purified before use, and the organic solvents were of analytical grade or purified by standard procedures.

Dimethyl 1,4-Dimethyl-1,4-dihydro-1,4-epoxydibenzeno[1,4]dioxin-2,3-dicarboxylate (2a) and Dimethyl 6a,10a-(*o*-Phenylenedioxy)-6,7,10,11-tetramethyl-6,6a,7,10,10a,11-hexahydro-6,11:7,10-diepoxynaphtho[2,3-*b*][1,4]benzodioxin-8,9-dicarboxylate (3): An oven-dried flask equipped with a magnetic stirring bar was charged with diene **1** (42 mg, 0.32 mmol) and dimethyl acetylenedicarboxylate (45 mg, 0.32 mmol) in dry toluene (drops). The reaction mixture was heated at 120 °C for 20 min after which the mixture was cooled to room temperature, adsorbed onto silica gel, and then purified by column chromatography (hexane/ethyl acetate, 85:15) to afforded dimer **3** as a white solid (30 mg, 0.055 mmol, 41%). Under these conditions, mono-adduct **2a** was not observed. Data for **3**: M.p. 236–238 °C. IR (KBr): $\tilde{\nu}$ = 1721 (CO, s) 1269, 1229 (Ar–O, s) 1085 (C–O–C, s) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.53 [s, 6 H, C6(11)-CH_3], 1.74 [s, 6 H, C7(10)-CH_3], 3.64 (s, 6 H, -OCH_3), 6.73 [m, 2 H, C1(4)H], 6.79 [m, 4 H, C3′(6′)H and C4′(5′)H], 6.87 [m, 2 H, C2(3)H] ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 12.6 (CH_3), 13.0 (CH_3), 52.1 (CH_3-O), 87.3 [C6(11)], 89.2 [C7(10)], 92.6 [C6a(10a)], 116.4 [CH, C3′(6′)], 117.1 [CH, C1(4)], 121.9 [C, C4′(5′)], 124.9 [C2(3)], 137.5 [CH, C5a(11a)], 142.2 and 142.3 [C1′(2′) and C4a(12a)], 148.4 [C, C8(9)], 163.2 (C, CO) ppm. MS (EI): *m*/*z* (%) = 546 (6) [M]$^+$, 285 (23). $C_{39}H_{26}O_{10}$ (654.63): calcd. C 65.93, H 4.80; found C 65.91, H 5.15.

4,11-Dimethyl-1,3,3a,4,11,11a-hexahydro-4,11-epoxyisobenzofuro-[3,4-*b*][1,4]benzodioxin-1,3-dione (2b): Following the same conditions for the preparation of **5** but reducing the time of reaction to an 1 h, Yield: 12%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.71 (s, 6 H, -CH_3), 3.54 [s, 2 H, C3a(11a)], 6.78 [m, 2 H, C6(9)H], 6.93 [m, 2 H, C7(8)H] ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 13.1 (CH_3), 55.4 [C3a(11a)], 86.0 [C, C4(11)], 117.6 [CH, C6(9)], 125.3 [C7(8)], 139.0 [C, C4a(10a)], 142.1 [C5a(9a)], 167.7 (C, CO) ppm.

1,4-Dimethyl-1,2,3,4-tetrahydro-1,4-epoxydibenzo[1,4]dioxin-2,3-dicarboxylic Acid (2c): IR (KBr): $\tilde{\nu}$ = 3245 (OH, s), 1743 (CO, s), 1256 (Ar–O, s), 1100 (C–O–C, s) cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.66 (s, 6 H, -CH_3), 3.37 [s, 2 H, C2(3)H], 6.68 [m, 2 H, C6(9)H], 6.77 [m, 2 H, C7(8)H], 9.23 (br. s, COOH) ppm.

4a,12a-(*o*-Phenylenedioxy)-4,5,12,13-tetramethyl-1,3,3a,4,4a,5,-12,12a,13,13a-decahydro-5,12:4,13-diepoxyisobenzofuro[5,6-*b*]dibenzo[1,4]dioxin-1,3-dione (5): An oven-dried flask equipped with a magnetic stirring bar was charged with diene **1** (40 mg, 0.59 mmol) and maleic anhydride (58 mg, 0.59 mmol) in dry toluene (drops). The reaction mixture was heated at 80 °C for 5 h after which the mixture was cooled to room temperature, adsorbed onto silica gel, and then purified by column chromatography (hexane/ethyl acetate, 85:15) to afford dimer **5** as a yellow solid (31 mg, 0.0062 mmol, 62%). M.p. 247–248 °C. IR (KBr): $\tilde{\nu}$ 1741 and 1720 (CO, s), 1269, 1230 (Ar–O, s), 1084 (C–O–C, s) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.52 [s, 6 H, C5(12)-CH_3], 1.71 [s, 6 H, C4(13)-CH_3], 3.88 [s, 2 H, C3a(13a)], 6.70 [m, 2 H, C7(10)H], 6.90 [m, 6 H, C8′(9′)H, C3′(6′)H and C4′(5′)H] ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 12.4 (CH_3), 13.1 (CH_3), 50.6 [C3a(13a)], 87.9 [C, C5(12)], 88.9 [C4(13)], 89.9 [C4a(12a)], 116.4 [CH, C3′(6′)], 117.2 [CH, C7(10)], 122.9 [C, C4′(5′)], 125.2 [C8(9)], 137.7 [C, C5a(11a)], 142.1 and 142.7 [C1′(2′) and C6a(10a)], 169.6 (C, CO) ppm. MS (EI): *m*/*z* (%) = 502 (18) [M]$^+$, 202 (100). $C_{28}H_{22}O_9$ (502.48): calcd. C 66.93, H 4.41; found C 66.57, H 4.59.

5,12-Dimethyl-5,12-dihydro-5,12-epoxy[1,4]benzodioxino[2,3-*g*]isoquinoline (2d) and 5a,13a-(*o*-Phenylenedioxy)-5,6,13,14-tetramethyl-5,5a,6,13,13a,14-hexahydro-5,14:6,13-diepoxydibenzo[1,4]dioxino-[2,3-*g*]isoquinoline (6): To a 50-mL flask equipped with a magnetic stirring bar and condenser, previously flamed and purged with argon, was added bromopyridine (0.27 mL, 2.80 mmol) in dry THF (1 mL). The solution was cooled externally with a bath of ice and NaOAc, and a solution Li(Me_3Si)$_2$N was slowly added (1 M in THF, 7.40 mL, 7.40 mmol). Then, the mixture was immersed in a 45 °C oil bath; typically, the internal temperature of the reaction was 38 °C. At this temperature, diene **1** (250 mg, 1.24 mmol) was added by a funnel over 30 min, and the resulting mixture was heated at reflux until bromopyridine was completely consumed as judged by TLC (5 h). The mixture was cooled to room temperature, adsorbed onto silica gel, and then purified by column chromatography (hexane/ethyl acetate, 70:30). Monomer **2d** was obtained as an oil (27 mg, 7% yield) and dimer **6** was isolated as a white solid (168 mg, 49%). Also starting diene **1** was recovered (70 mg, 28%). Data for mono-adduct **2d**: IR (KBr): $\tilde{\nu}$ = 1753 (C=C, s) 1600 (C=N, s) 1220 and 1278 (Ar–O, s) 1081 (C–O–C, s) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.82 (s, 3 H, C5-CH_3), 1.87 (s, 3 H, C12-CH_3), 6.70 (m, 2 H, C7H, C10H), 6.83 (m, 2 H, C8H, C9H), 7.19 (dd, *J* = 4.5 Hz, *J* = 1 Hz, 2 H, 1 H, C4H), 8.40 (d, *J* = 4.5 Hz, 1 H, C3H), 8.40 (d, *J* = 4.5 Hz, 1 H, C3H), 8.42 (d, *J* = 1 Hz, 1 H,

C1H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 12.4 (CH_3,C5-CH_3), 12.7 (CH_3, C12-CH_3), 84.8 (C12), 85.0 (C5), 114.0 (CH, C4), 117.3 (CH, C7), 117.4 (CH, C10), 124.8 (CH, C8 and C9), 137.9 (CH, C1), 142.3 (C, C6a and C10a) 144.4 (C, C5a), 145.6 (C, C11a), 145.7 (C, C12a), 148.4 (CH, C3), 160.6 (C, C4a) ppm. MS (EI): *m*/*z* (%) = 279 (30) $[M]^+$, 264 (5) $[M-CH_3]^+$, 251(11), 202 (4), 148 (100), 77 (11). $C_{17}H_{13}NO_3$ (279.29): calcd. C 73.11, H 4.69, N 5.01; found C 73.45, H 4.98, N 4.97. Data for bis-adduct **6**: M.p. 244–246 °C. IR (KBr): $\tilde{\nu}$ = 1748 (CO, s) 1606 (C=N, s) 1233 and 1271 (Ar–O, s) 1088 (C–O–C, s) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.56 (s, 3 H, C6-CH_3), 1.58 (s, 3 H, C13-CH_3), 1.85 (s, 3 H, C5-CH_3), 1.90 (s, 3 H, C14-CH_3), 6.59 (m, 4 H, C3′H, C4′H, C5′H, C6′H), 6.77 (m, 2 H, C8H, C11H), 6.87 (m, 2 H, C9H, C10H), 7.05 (dd, *J* = 4.5 Hz, *J* = 0.5 Hz, 1 H, C4H), 8.31 (d, *J* = 4.5 Hz, 1 H, C3H), 8.40 (d, *J* = 0.5 Hz, 1 H, C1H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 12.6 (CH_3,C5-CH_3, C6-CH_3, C13-CH_3), 12.9 (CH_3, C14-CH_3), 87.0 (C14), 87.2 (C5), 87.4 (C6 and C13), 116.0, 116.2, 116.3 (CH, C4, C3′, C6′), 117.0 (CH, C8), 117.1 (CH, C11), 121.6 and 121.8 (C, C4′ and C5′), 124.9 (C9 and C10), 137.5 and 137.7 (C, C6a and C12a), 141.7 and 141.9 (C1′ and C2′), 142.1 (C1), 142.4 (C7a and C11a), 142.7 (C, C14a), 148.5 (CH, C3), 156.2 (C, C4a) ppm. MS (EI): *m*/*z* (%) = 481 (3) $[M]^+$, 279 (100), 264 (14) $[279 - CH_3]^+$, 251 (41), 202 (27), 147 (9). $C_{29}H_{23}NO_6$ (481.50): calcd. C 72.34, H 4.81, N 2.91; found C 72.16, H 4.90, N 2.97.

6,11-Diphenyl-5a,6,11,11a-tetrahydro-6,11-epoxinaphtho[2,3-*b*][1,4]-benzodioxin (9): IR (KBr): $\tilde{\nu}$ = 1267 (Ar–O, s) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.09 [s, 2 H, H5a(11a)], 6.74 [m, 2 H, C1(4) H], 6.83 [m, 2 H, C2(3)H], 7.04 [br. s, 4 H, C7(10) and C8(9)H], 7.24 (m, 2 H, CH_{para}), 7.52 (m, 4 H, CH_{meta}), 7.87 (m, 4 H, CH_{ortho}) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 77.7 [CH, C5a(11a)], 117.1 [CH, C1(4)], 121.7 [CH, C2(3)], 122.2 [C, C8(9)], 126.2 (CH, C_{para}), 127.6 (CH, C_{ortho}), 128.5 [CH, C7(10)], 128.6 (CH, C_{meta}) ppm. The quaternary C was not distinguished. MS (EI): *m*/*z* (%) = 404 (1) $[M]^+$, 270 (100). $C_{28}H_{20}O_3$ (404.46): calcd. C 83.15, H 4.98; found C 83.43, H 4.62.

6,11-Diphenylnaphtho[2,3-*b*][1,4]benzodioxin (10): An oven-dried flask equipped with a magnetic stirring bar was charged with 1,4-benzodioxin (110 mg, 0.82 mmol) and isobenzofuran (180 mg, 0.67 mmol) in dry toluene (1 mL). The reaction mixture was heated at 115 °C for 21 h after which the mixture was cooled to room temperature, adsorbed onto silica gel, and then purified by column chromatography (hexane/ethyl acetate, 90:10). Title compound **10** was isolated as a white solid (219 mg, 85%) together with the adduct **9** (7%). M.p. 246–247 °C. IR (KBr): $\tilde{\nu}$ = 1278 (Ar–O, s) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.74 [m, 2 H, C1(4)H], 6.83 [m, 2 H, C2(3)H], 7.24 [m, 2 H, C8(9)H], 7.45–7.58 [m, 12 H, CH_{para}, CH_{meta}, CH_{ortho} and C7(10)H] ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 116.3 [CH, C1(4)], 123.4 [CH, C2(3)], 124.2 [C, C6(11)], 125.0 (CH) and 125.5 [(CH) C8(9) and C7(10)], 127.5 (CH, C_{para}), 128.2 (CH, C_{ortho}), 130.1 [CH, C6a(10a)], 130.9 (CH, C_{meta}), 134.4 [C, C1(1′′)], 138.4 [C, C5a(11a)], 141.5 [C, C4a(12a)] ppm. MS (EI): *m*/*z* (%) = 386 (100) $[M]^+$, 276 (15) $[M - 15]^+$. $C_{28}H_{18}O_2 \cdot ½H_2O$ (395.47): calcd. C 85.04, H 4.84; found C 84.82, H 4.67.

Supporting Information (see footnote on the first page of this article): Computational studies and NMR spectra of the compounds.

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