Site Selectivity of the Diels−Alder Reactions of 3-[1-(*tert*-Butyldimethylsilyloxy)vin-1-yl]furan and 3-(Propen-2-yl)furan. Synthesis of 4-Substituted Benzofurans†

Aída Benítez,‡ F. Ruth Herrera,§ Margarita Romero,|| and Francisco X. Talamás*

Syntex S. A. de C. V., División de Investigación, Apartado Postal 272 (CIVAC), 62500 Jiutepec, Morelos, México

Joseph M. Muchowski

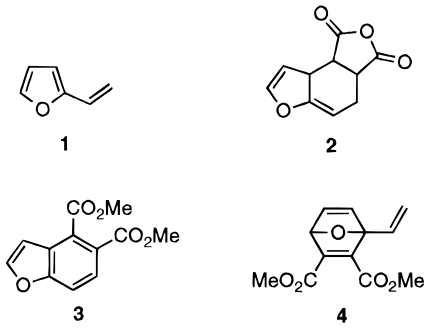
Syntex Research, Institute of Organic Chemistry, 3401 Hillview Avenue, Palo Alto, California 94304

Received August 22, 1995⊗

The Diels−Alder reaction of 3-vinylfurans **5** and **27** with DMAD, *N*-phenylmaleimide, and dimethyl maleate afforded products derived both from addition to the furan ring diene system (intraannular addition) and to the furan 2,3-double bond 3-vinyl group diene system (extraannular addition). For example, compounds **6** and **7** were obtained from **5** and DMAD. In contrast, dienophiles containing a phenylsulfinyl group, such as **19**−**21**, gave products derived exclusively from the extraannular reaction mode. These products are useful precursors of 4-substituted benzofurans, especially 4-hydroxybenzofurans.

Introduction

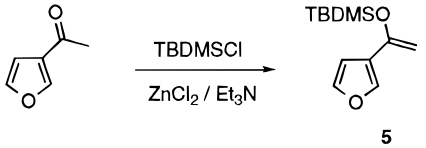
In connection with a synthetic program underway in our laboratories, we required benzofurans with various substituents in the benzene ring. The synthesis of such compounds has been achieved in the past in different ways.[1] One method which has been used for this purpose is the Diels−Alder reaction of vinylfurans with the appropriate dienophile followed by one or two oxidation steps. This cycloaddition reaction has been reported for 2-vinylfurans[2] as well as for 3-vinylfurans,[3] but 2-vinylfurans have been more extensively studied. The first example was reported by Paul[2a] in which 2-vinylfuran (**1**) was reacted with maleic anhydride to produce the adduct **2** in 79% yield. Later, it was reported[2b] that the reaction of 2-vinylfuran with dimethyl acetylenedicarboxylate (DMAD) gave the benzofuran **3** and the bicyclic adduct **4** in 5% yield each. Compound **3** is derived from the reaction of the dienophile with the vinyl group and the 2,3-double bond of the furan ring whereas compound **4** stems from a Diels−Alder reaction in which the furan ring served as the diene.[4] These results are representative of what is found in the literature for this system. In contrast, the 3-vinylfuran system has been studied to a lesser extent[3] in Diels−Alder reactions, and none of these studies has been systematic in nature.



One class of substituted benzofuran in which we were specifically interested was that with an hydroxy group at C-4. For this purpose, we decided to investigate the Diels−Alder reaction of the 3-[1-(*tert*-butyldimethylsilyloxy)vin-1-yl]furan (**5**).

Results and Discussion

The vinylfuran **5** was prepared from 3-acetylfuran and *tert*-butyldimethylchlorosilane (eq 1) under standard conditions[5] ($ZnCl_2$/Et_3N) in 54% yield. This furan can be stored in the refrigerator at 0 °C for months without decomposition.



(1)

We first investigated the reaction of **5** with excess DMAD (3 equiv) in toluene at rt. After 72 h, the benzofuran **6** and the tricyclic compound **7** were obtained in 39% and 16% yield, respectively. The structure of the

† Contribution No. 933 from the Syntex Institute of Organic Chemistry.

‡ Research completed in partial fulfillment for the degree of "Químico Industrial" in the Facultad de Ciencias Químicas e Industriales, Universidad Autónoma del Estado de Morelos, 1995.

§ Research completed in partial fulfillment for the degree of "Químico Farmaceutico Biólogo" in the Facultad de Química, Universidad Nacional Autónoma de México, 1993.

|| Present address: Facultad de Química, Estudios de Posgrado, Universidad Nacional Autónoma de México, México, D. F.

⊗ Abstract published in *Advance ACS Abstracts,* January 15, 1996.

(1) Donnelly, D. M. X.; Meegan, M. J. *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Ed.; Pergamon Press: New York, 1984; Vol. 4, p 678.

(2) (a) Paul, R. *Bull. Soc. Chim. Fr.* **1943**, 163. (b) Davidson, W. J.; Elix, J. A. *Aust. J. Chem.* **1973**, *26*, 1059. (c) Kotsuki, H.; Kondo, A.; Nishizawa, H.; Ochi, M; Matsuoka, K. *J. Org. Chem.* **1981**, *46*, 5454. (d) Sasaki, T.; Ishibashi, Y.; Ohno, M. *Heterocycles* **1983**, *20*, 1933. (e) Ancerewicz, J.; Vogel, P. *Heterocycles* **1993**, *36*, 537. (f) Kusurkar, R. S.; Bhosale, D. K. *Synth. Commun.* **1990**, *20*, 101.

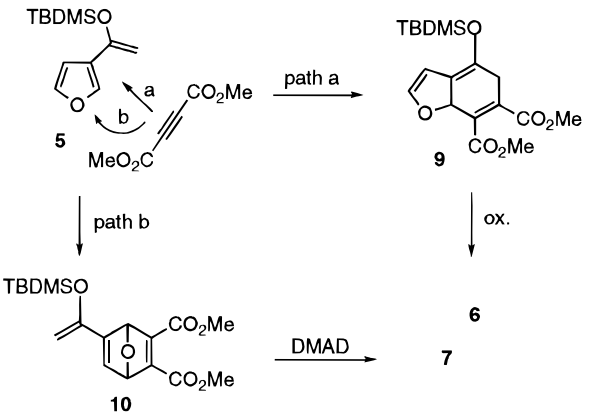
(3) (a) Freslon, G.; Lepage, Y. *Bull. Soc. Chim. Fr.* **1974**, 2105. (b) McNamara, J. M.; Kishi, Y. *Tetrahedron* **1984**, *40*, 4685. (c) Cooper, J. A.; Cornwall, P.; Dell, C. P.; Knight, D. W. *Tetrahedron Lett.* **1988**, *29*, 2107.

(4) (a) Gilchrist, T. L. *Heterocyclic Chemistry*; John Wiley & Sons: New York, 1992; p 209. (b) Wong, H. N. C. *Synthesis* **1984**, 787.

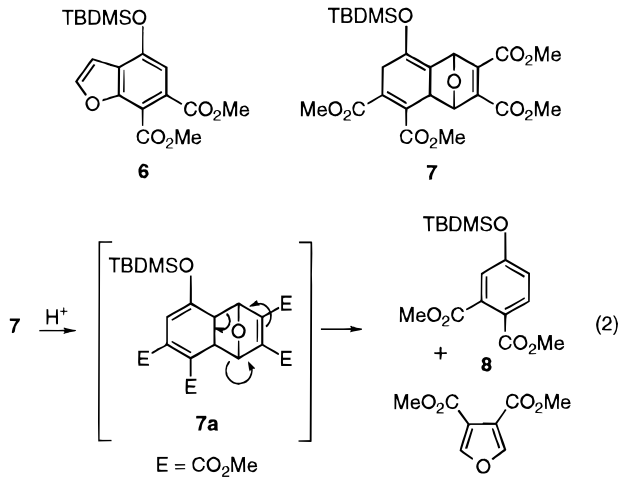
(5) Danishefsky, S.; Kitahara, T. *J. Am. Chem. Soc.* **1974**, *96*, 7807.

0022-3263/96/1961-1487$12.00/0

Scheme 1

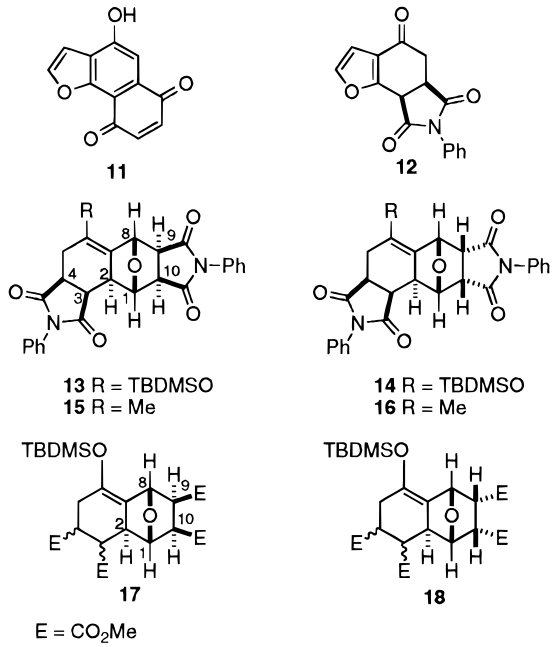


tricyclic compound **7** was supported by the ^{1}H NMR spectrum which showed signals for four methoxy groups, and by the ^{13}C NMR spectrum which showed absorptions for six sp^2 carbons, one of which, at 109.9 ppm, corresponded to one of the carbons of the enol system. In addition, the ^{13}C NMR spectrum had absorptions for the two bridgehead carbons at 82.1 ppm and 80.1 ppm. Furthermore, when compound **7** was treated with a catalytic amount of *p*-toluenesulfonic acid at rt, a mixture of dimethyl furan-3,4-dicarboxylate and the phthalate **8** (eq 2) was obtained. These compounds are derived from acid-catalyzed isomerization of **7** to **7a** followed by a retro Diels−Alder reaction. This result in conjunction with the NMR spectroscopic data confirm the structure assigned to **7**.



Scheme 1 shows the reaction pathways that should take place for the formation of **6** and **7**. Compound **6** was formed (path a) by the addition of the dienophile to the furan 2,3-double bond 3-vinyl group diene system (extraannular addition) to give adduct **9** (not detected) which was oxidized during the course of the reaction or during purification. The use of hydroquinone in the reaction at least helped to prevent the formation of complex mixtures.[2c] On the other hand, **7** stemmed from Diels−Alder addition of the dienophile to the furan ring diene system (path b; intraannular addition), followed by a second Diels−Alder reaction with the diene **10** thus produced (double addition adduct). This is an example of what has been termed the diene transmissive Diels−Alder reaction.[6]

The reaction of the vinylfuran **5** with 1, 4-benzoquinone afforded, after 5 days, the furonaphthoquinone **11** in 45% yield. The products of double addition could not be found in the reaction mixture. When *N*-phenylmaleimide was used as the dienophile, after 48 h, the ketone **12** and the double addition adducts **13** and **14** were isolated in 9%, 36%, and 19% yields, respectively. Thus, in contrast to DMAD, the double addition products predominated with *N*-phenylmaleimide. The formation of these compounds can be rationalized in a manner analogous to that described above for the formation of **7**. It should be noted that compound **12** is at one oxidation level higher than that of the primary Diels−Alder adduct. The relative configuration of **13** and **14** were determined by ^{1}H NMR spectroscopy. The protons at C-1 and C-8 in compound **13** are at δ 5.65 and δ 5.35 as singlets. The lack of coupling with the vicinal hydrogens indicates that these protons are at a 90° dihedral angle to H-2, H-9, and H-10. Compound **14** shows two doublets at δ 5.59 (J = 6.1 Hz) and δ 5.36 (J = 5.4 Hz) for the protons at C-1 and C-8. This indicates that these protons have a dihedral angle of approximately 30° to H-9 and H-10. The other vicinal hydrogen (H-2) must have a dihedral angle of 90° with H-1 because no coupling therewith was observed.[7] NOE experiments established that H-2, H-3, and H-4 are cis to one another in **13** and **14**. This type of stereochemistry has been observed by Vogel *et al.*[8] in similar systems.

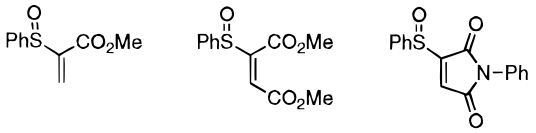


Reaction of the diene **5** with the less reactive dienophile dimethyl maleate in toluene at reflux temperature for 56 h gave an approximately 1:1 mixture of the double addition products **17** and **18** in 39% yield. In this case, none of the expected extraannular product was observed. The relative stereochemistry of **17** and **18** was assigned by ^{1}H NMR in the manner described above for **13** and **14**. When ethyl acrylate was used as dienophile in the reaction with **5** (neat, reflux, 120 h), only a complex mixture of the double addition products, which was not fully identified, was obtained.

The Diels−Alder reaction of the vinylfuran **5** with the dienophiles described above showed that the site selectiv-

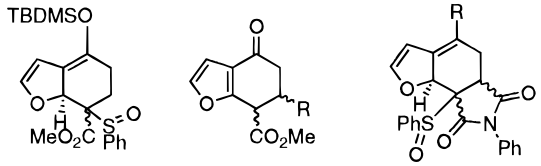
(6) Spino, C.; Liu, G.; Tu, N.; Girard, S. *J. Org. Chem.* **1994**, *59*, 5596 and reference cited therein.
(7) Slee, J. D.; LeGoff, E. *J. Org. Chem.* **1970**, *35*, 3897.
(8) Meerpoel, L.; Vrahami, M. M.; Deguin, B.; Vogel, P. *Helv. Chim. Acta* **1994**, *77*, 869.

ity may be dependent on their reactivity. The less reactive dienophiles usually showed a distinct preference for intraannular addition to the furan ring to give the bis-adducts as the major products. It was desirable to enhance the extraannular reaction pathway, and therefore we chose to examine more activated dienophiles. A sulfinyl group α to the electron-withdrawing group of the dienophile can be used to increase the reactivity in normal Diels–Alder reactions.[9] An advantage of this activating group is that after the cycloaddition it readily undergoes elimination (as PhSOH), thus effecting the introduction of a double bond.



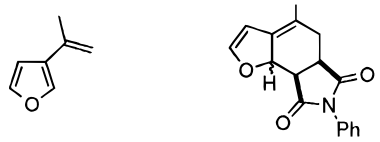
19 **20** **21**

The phenylsulfinylated dienophiles **19**,[10] **20**,[11] and **21**[12] were therefore prepared. Reaction of the sulfinyl acrylate **19** with **5** at rt for 5 h gave the extraannular Diels–Alder adduct **22** exclusively, in 67% yield. Similar results were obtained when the dienophiles **20** and **21** were used. Reaction of the maleate **20** with **5** at 55–60 °C for 24 h in the presence of trimethyl phosphite (to remove phenylsulfenic acid) afforded the cycloadduct **23** in 40% yield. In this case, the phenylsulfinyl group was lost during the reaction probably because of the higher reaction temperature. Reaction of the maleimide **21** with **5** at rt for 24 h gave the adduct **25** in 45% yield. Thus, the phenylsulfinyl group in dienophiles **19**-**21** has a pronounced effect on the site selectivity of the Diels–Alder reaction with **5**.



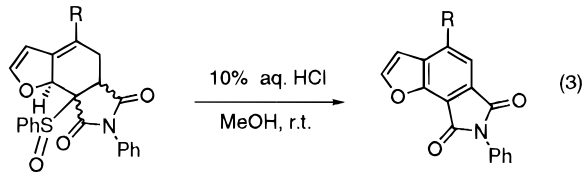
22 **23** R = CO_2Me, **24** R = H **25** R = TBDMSO, **26** R = Me

At this point, it was of interest to know what effect, if any, the *tert*-butyldimethylsilyloxy group in **5** had on the course of the Diels–Alder reaction.[13] For this reason, 3-(propen-2-yl)furan[14] (**27**) was prepared. Reaction of the vinylfuran **27** with *N*-phenylmaleimide under the standard conditions for 20 h afforded products **28**, **15**, and **16** in 22%, 30%, and 22% yield, respectively, derived from addition by both pathways. In contrast, reaction of **27** with the phenylsulfinylated maleimide **21** gave compound **26**, the product of extraannular addition, in 70% yield as the sole product. These results were very similar to those obtained with the diene **5**, indicating that the substituent on the vinyl group has no significant effect on the site selectivity.

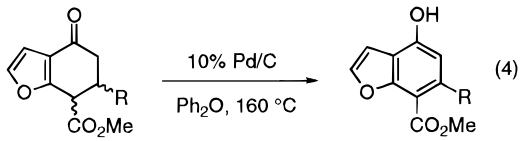


27 **28**

The Diels–Alder adducts were converted into the desired benzofurans as follows. Compound **22** was heated in toluene for 2 h to obtain the furyl ketone **24** in 84% yield. When the maleimides **25** and **26** were heated to eliminate the phenylsulfinyl group a complex mixture was produced, but under acidic conditions (10% aqueous HCl in MeOH; eq 3), the benzofurans **29** and **30** were obtained in 60% and 44% yields, respectively. Compounds **23** and **24** were oxidized with 10% Pd/C[15] to the benzofurans **31** and **32** in good yield (eq 4). Compound **28** was aromatized to benzofuran **30** in a similar manner.



25 R = TBDMSO
26 R = Me
29 R = OH (60%)
30 R = Me (44%)



23 R = CO_2Me
24 R = H
31 R = CO_2Me (60%)
32 R = H (70%)

In summary, we present here a study of the Diels–Alder reaction of 3-vinylfurans with various dienophiles. We demonstrate that a phenylsulfinyl group in the dienophile dramatically alters the site selectivity of the process from one in which cycloaddition occurs by both pathways a and b in favor of the exclusive formation of the extraannular Diels–Alder product (path a). The extraannular addition products are readily converted into 4-substituted benzofurans.

These findings have synthetic implications beyond that disclosed herein.

Experimental Section

General Methods. Flash chromatography was carried out as described by Still *et al.*[16] Toluene was dried over sodium and degassed with argon for 3 min previous use. All the Diels–Alder reactions were done in the presence of a few crystals of hydroquinone.

(9) (a) Alexandre, C.; Belkadi, O.; Maignan, C. *J. Chem. Res. (S)* **1992**, 48. (b) Watanabe, M.; Tsukazaki, M.; Hamada, Y.; Iwao, M.; Furukawa, S. *Chem. Pharm. Bull.* **1989**, *37*, 2948.

(10) (a) Leyendecker, F.; Comte, M. T. *Tetrahedron* **1986**, *42*, 1413. (b) Monteiro, H. J.; Gemal, A. L. *Synthesis* **1975**, 437.

(11) Kaydos, J. A.; Smith, D. L. *J. Org. Chem.* **1983**, *48*, 1096.

(12) Barry, J. F.; Wallace, T. W.; Walshe, N. D. A. *Tetrahedron Lett.* **1993**, *34*, 5329.

(13) Reaction of 3-[1-(trimethylsilyloxy)vin-1-yl]furan with DMAD in toluene for 72 h afforded 4-hydroxybenzofuran-6,7-dicarboxylic acid dimethyl ester and 4-hydroxyphthalic acid dimethyl ester in 17% and 13% yield, respectively. The benzofuran comes from the reaction of DMAD with the furan 2,3-double bond 3-vinyl group diene system and the phthalate from the reaction of DMAD with the furan ring diene system. The ratio for the preference of these two systems in this case is 1.3, and for **5**, as described above, is 2.4. The change of the silyl group had a small influence in the ratio. Unpublished results from F. R. Herrera and F. X. Talamás.

(14) Takaya, H.; Hayakawa, Y.; Makino, S.; Noyori, R. *J. Am. Chem. Soc.* **1978**, *100*, 1778.

(15) Linstead, R. P.; Michaelis, K. O. A. *J. Chem. Soc.* **1940**, 1134.

(16) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

3-[1-(*tert*-Butyldimethylsilyloxy)vin-1-yl]furan (5). A suspension of anhyd zinc chloride (2.7 g, 20.0 mmol) in triethylamine (5.3 mL , 40.0 mmol) was stirred at rt for 1 h until it became milky. A solution of 3-acetylfuran (2.2 g, 20.0 mmol) in benzene (20 mL) was added followed by *tert*-butyldimethylchlorosilane (6.0 g, 40.0 mmol). The reaction was stirred at rt for 1 h then at 70 °C for 4 h. The reaction was poured into ether (100 mL), filtered through Celite, and concentrated. The residue was distilled to give **5** as a colorless oil (2.12 g, 54%): bp 48−50 °C (0.5 mmHg); IR ($CHCl_3$) 2958, 2932, 1633, 1561, 1508, 1323, 1168, 1015, 833 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.52 (s, 1H), 7.34 (t, J = 1.8 Hz, 1H), 6.46 (dd, J = 1.8, 0.8 Hz, 1H), 4.57 (d, J = 1.5 Hz, 1H), 4.29 (d, J = 1.5 Hz, 1H), 0.98 (s, 9H), 0.21 (s, 6H); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 150.76, 143.60, 140.64, 125.97, 108.54, 90.92, 26.22, 18.67, −4.19; MS (EI) m/z (rel intensity) 224 (M^+, 18), 183 (100). Anal. Calcd for $C_{12}H_{20}O_2Si$: C, 64.24; H, 8.98. Found: C, 64.13; H, 9.16.

4-(*tert*-Butyldimethylsilyloxy)benzofuran-6,7-dicarboxylic Acid Dimethyl Ester (6) and (1*SR*,2*RS*,8*RS*)-6-(*tert*-butyldimethylsilyloxy)-11-oxatricyclo[6.2.1.$0^{2,7}$]-undeca-3,6,9-triene-3,4,9,10-tetracarboxylic Acid Tetramethyl Ester (7). A solution of vinylfuran **5** (250 mg, 1.1 mmol) and dimethyl acetylenedicarboxylate (0.41 mL, 3.3 mmol) in toluene (4 mL) was stirred at rt for 72 h. The solvent was removed and the residue purified by flash chromatography (hexane−EtOAc, 9:1) to obtain the benzofuran **6** (156 mg, 39%) and compound **7** (90 mg, 16%) as oils. Spectroscopic data for **6**: IR ($CHCl_3$) 3024, 2958, 1729, 1438, 1272, 1044 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.67 (d, J = 2.2 Hz, 1H), 7.12 (s, 1H), 6.82 (d, J = 2.2 Hz, 1H), 3.99 (s, 3 H), 3.91 (s, 3H), 1.02 (s, 9H), 0.25 (s, 6H); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 167.63, 166.79, 153.69, 151.12, 147.19, 127.69, 124.97, 113.83, 112.85, 104.99, 53.52, 53.23, 26.06, 18.73, −3.88; MS (EI) m/z (rel intensity) 364 (M^+, 60), 307 (100). Anal. Calcd for $C_{18}H_{24}O_6Si$: C, 59.32; H, 6.64. Found: C, 59.22 ; H, 6.77. Spectroscopic data for **7**: IR ($CHCl_3$) 3026, 2955, 1722, 1639, 1437, 1265, 842 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 5.59 (d, J = 1.2 Hz, 1H), 5.08 (d, J = 1.2 Hz, 1H), 3.70 (s, 3 H), 3.67 (s, 3H), 3.64 (s, 3H), 3.61 (s, 3H), 2.93 (br s, 3H), 0.81 (s, 9H), 0.01 (s, 3H), 0.004 (s, 3H); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 167.44, 166.34, 162.67, 162.24, 145.54, 143.98, 142.00, 138.18, 135.14, 109.91, 82.12, 80.07, 52.50, 52.37, 44.31, 34.80, 25.54, 18.06, −4.09, −4.46; MS (EI) m/z (rel intensity) 324 (M^+ − 184, 19), 153 (100). Anal. Calcd for $C_{24}H_{32}O_{10}Si$: C, 56.67; H, 6.34. Found: C, 56.63; H, 6.42.

Dimethyl Furan-3,4-dicarboxylate and 4-(*tert*-butyldimethylsilyloxy)phthalic Acid Dimethyl Ester (8). A solution of **7** (0.5 g, 0.98 mmol) and *p*-toluenesulfonic acid (18 mg, 0.098 mmol) in CH_2Cl_2 (12 mL) was stirred at rt for 2 h. The solvent was removed and the residue purified by prep TLC (hexane−acetone, 7:3) to give dimethyl furan-3,4-dicarboxylate (76 mg, 42%) which was identical to a commercial sample and compound **8** (140 mg, 49%) as an oil: IR ($CHCl_3$) 3028, 2955, 1723, 1603, 1305, 1125, 845 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.74 (d, J = 8.5 Hz, 1H), 7.21 (d, J = 2.4 Hz, 1H), 6.93 (dd, J = 8.5, 2.5 Hz, 1H), 3.91 (s, 3H), 3.87 (s, 3H), 0.98 (s, 9H), 0.23 (s, 6H); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 168.59, 166.96, 158.70, 135.47, 131.43, 123.01, 121.59, 119.89, 52.67, 52.33, 25.51, 18.16, −4.44; MS (EI) m/z (rel intensity) 324 (M^+, 6), 235 (100). Anal. Calcd for $C_{16}H_{24}O_5Si$: C, 59.23; H, 7.45. Found: C, 59.57; H, 7.75.

4-Hydroxynaphtho[1,2-*b*]furan-6,9-dione (11). A solution of vinylfuran **5** (0.5 g, 2.2 mmol) and 1,4-benzoquinone (0.71 g, 6.6 mmol) in toluene (10 mL) was stirred at rt for 5 days. The solvent was removed, and the dark residue was purified by prep TLC (hexane−acetone, 7:3) to give compound **11** (278 mg, 45%) as a red solid, mp 220 °C dec. (toluene); IR ($CHCl_3$) 3115, 1658, 1572, 1361, 1336, 1277, 1079 cm^{-1}; ^1H NMR ($CDCl_3$−DMSO-d_6, 200 MHz) δ 10.80 (br s, 1H, D_2O exchange), 7.82 (d, J = 2.2 Hz, 1H), 7.39 (s, 1H), 7.05 (d, J = 2.1 Hz, 1H), 6.85 (s, 2H); ^{13}C NMR ($CDCl_3$−DMSO-d_6, 25 MHz) δ 187.97, 182.71, 156.71, 153.67, 147.53, 138.94, 137.11, 130.65, 122.65, 110.51, 106.42, 104.32; MS (EI) m/z (rel intensity) 214 (M^+, 100), 186 (26), 158 (18). Anal. Calcd for $C_{12}H_6O_4 \cdot {}^1/_7H_2O$: C, 66.49; H, 2.92. Found: C, 66.19; H, 2.93.

(5a*RS*,8a*RS*)-7-Phenyl-5,5a,8a,8b-tetrahydro-3a*H*-1-oxa-7-aza-*as*-indacene-4,6,8-trione (12), *N*,*N*-diphenyl (1*SR*,2*SR*,8*SR*,9*SR*,10*RS*)-6-(*tert*-butyldimethylsilyloxy)-11-oxatricyclo[6.2.1.$0^{2,7}$]undec-6-ene-3,4,9,10-tetracarboximide (13), and *N*,*N*-Diphenyl (1*SR*,2*SR*,8*SR*,9*RS*,10*SR*)-6-(*tert*-butyldimethylsilyloxy)-11-oxatricyclo[6.2.1.$0^{2,7}$]-undec-6-ene-3,4,9,10-tetracarboximide (14). A solution of the vinylfuran **5** (0.3 g, 1.3 mmol) and *N*-phenylmaleimide (0.7 g, 4.0 mmol) in toluene (8 mL) was stirred at rt for 48 h. Compound **13** precipitated from the reaction (220 mg) mixture and was collected by filtration. The filtrate was evaporated in vacuo, and the residue was purified by flash chromatography (hexane−acetone, 9:1) to yield compound **12** (33 mg, 9%), compound **13** (53 mg; total 273 mg, 36%), and compound **14** (146 mg, 19%) as solids. Spectroscopic data for **12**: mp 173−175 °C (hexane−EtOAc); IR ($CHCl_3$) 3021, 1723, 1693, 1500, 1380 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.54 (d, J = 2.5 Hz, 1H), 7.52−7.34 (m, 3H), 7.28−7.18 (m, 2H), 6.76 (d, J = 2.1 Hz, 1H), 4.52 (d, J = 8.1 Hz, 1H), 3.84 (dt, J = 8.4, 2.9 Hz, 1H), 3.35 (dd, J = 17.8, 2.9 Hz, 1H), 2.87 (dd, J = 17.8, 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 189.41, 175.89, 171.43, 156.69, 146.28, 131.63, 129.74, 129.50, 126.61, 122.98, 107.40, 40.70, 39.19, 34.99; MS (EI) m/z (rel intensity) 281(M^+, 40), 134 (100). Anal. Calcd for $C_{16}H_{11}NO_4 \cdot {}^1/_{10}H_2O$: C, 67.89; H, 3.99; N, 4.95. Found: C, 67.82; H, 4.06; N, 4.84. Spectroscopic data for **13**: mp 260−262 °C (CH_2Cl_2−hexane); IR ($CHCl_3$) 3025, 2932, 1780, 1719, 1501, 1387, 1192, 829 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.52−7.33 (m, 6H), 7.37−7.16 (m, 4H), 5.65 (s, 1H), 5.35 (s, 1H), 3.43 (t, J = 8.4 Hz, 1H), 3.31 (ddd, J = 8.7, 5.8, 1.9 Hz, 1H), 3.21 (d, J = 7.1 Hz, 1H), 3.14 (d, J = 7.1 Hz, 1H), 2.79 (dd, J = 15.4, 1.8 Hz , 1H), 2.50 (d, J = 8.4 Hz, 1H), 2.35 (dd, J = 15.4, 5.6 Hz, 1H), 0.94 (s, 9H), 0.20 (s, 3H), 0.14 (s, 3H); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 177.71, 176.30, 176.18, 175.55, 142.94, 132.27, 129.63, 129.27, 129.12, 126.97, 126.88, 115.62, 80.77, 78.02, 49.97, 44.83, 41.25, 40.86, 30.20, 25.98, 18.56, −3.35,−3.61; MS (CI) m/z (rel intensity) 588 (M^+ + 18, 100). Anal. Calcd for $C_{32}H_{34}N_2O_6Si$: C, 67.43; H, 6.00; N, 4.91. Found: C, 67.28; H, 5.97; N, 4.89. Spectroscopic data for **14**: mp 204−205 °C (CH_2Cl_2−hexane); IR ($CHCl_3$) 3020, 2932, 1778, 1718, 1500, 1386, 1367, 1186, 829 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.56−7.31 (m, 6H), 7.27−7.09 (m, 4H), 5.59 (d, J = 6.1 Hz, 1H), 5.36 (d, J = 5.4 Hz, 1H), 3.74 (dd, J = 9.3, 6.1 Hz, 1H), 3.65 (dd, J = 9.2, 5.7 Hz, 1H), 3.29 (m, 2H), 2.86 (d, J = 15.1 Hz, 1H), 2.51 (m, 1H), 2.31 (dd, J = 15.4, 3.7 Hz, 1H), 0.94 (s, 9H), 0.20 (s, 3H), 0.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 177.51, 176.37, 175.07, 173.25, 144.82, 132.36, 132.05, 129.80, 129.61, 129.42, 129.08, 126.78, 113.20, 79.57, 77.10, 51.57, 50.84, 42.45, 41.23, 41.02, 29.98, 26.00, 18.47, −3.37, −3.44; MS (EI) m/z (rel intensity) 588 (M^+ − 57, 100). Anal. Calcd for $C_{32}H_{34}N_2O_6Si \cdot {}^1/_4\ H_2O$: C, 66.82; H, 6.04; N, 4.87. Found: C, 66.68; H, 6.00; N, 4.92.

(1*SR*,2*SR*,8*SR*,9*SR*,10*RS*)-6-(*tert*-Butyldimethylsilyloxy)-11-oxatricyclo[6.2.1.$0^{2,7}$]undec-6-ene-3,4,9,10-tetracarboxylic Acid Tetramethyl Ester (17) and (1*SR*,2*SR*,8*SR*,9*RS*,10*SR*)-6-(*tert*-butyldimethylsilyloxy)-11-oxatricyclo-[6.2.1.$0^{2,7}$]undec-6-ene-3,4,9,10-tetracarboxylic Acid Tetramethyl Ester (18). A solution of the vinylfuran **5** (500 mg, 2.2 mmol) and dimethyl maleate (0.96 mL, 6.6 mmol) in toluene (10 mL) was heated at reflux for 56 h. The solvent was removed, and the crude product was purified by flash chromatography (hexane−acetone, 4:1) to obtain the double addition adducts **17** and **18** (0.44 g, 39%). A pure sample of each was obtained by flash chromatography (hexane−EtOAc, 7:3). Spectroscopic data for **17**: IR ($CHCl_3$) 3026, 2955, 1739, 1438, 1364, 1259, 1169, 841 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 5.30 (s, 1H), 4.88 (s, 1H), 3.74 (s, 3H), 3.69 (s, 3H), 3.68 (s, 3H), 3.67 (s, 3H), 3.40 (ddd, J = 7.8, 3.5, 1.4 Hz, 1H), 3.25 (d, J = 9.5 Hz, 1H), 3.14 (d, J = 9.2 Hz, 1H), 2.61 (dt, J = 18.0, 1.7 Hz, 1H), 2.45−2.25 (m, 3H), 0.94 (s, 9H), 0.14(s, 3H), 0.12 (s, 3H); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 173.62, 173.46, 171.28, 141.58, 117.80, 81.56, 78.54, 53.51, 52.63, 49.98, 43.69, 42.40, 41.74, 31.50, 26.02, 18.50, −3.88; MS (EI) m/z (rel intensity) 512 (M^+, 6), 455 (68), 367 (100). Anal. Calcd for $C_{24}H_{36}O_{10}Si$: C, 56.23; H, 7.08. Found: C, 56.48; H, 7.10. Spectroscopic data for **18**: IR ($CHCl_3$) 3027, 2954, 1739, 1438, 1361, 1258, 1175, 841 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 5.22 (d, J = 5.6

Hz, 1H), 4.86 (d, J = 4.8 Hz, 1H), 3.79 (s, 3H), 3.72 (s, 3H), 3.69 (s, 3H), 3.63 (s, 3H), 3.47 (dd, J = 11.5, 5.5 Hz, 1H), 3.48−3.40 (m, 1H), 3.26 (dd, J = 11.5, 4.7 Hz, 1H), 3.15 (dt, J = 11.6, 2.1 Hz, 1H), 2.67 (dt, J = 17.6, 1.8 Hz, 1H), 2.41 (dd, J = 11.6, 3.9 Hz, 1H), 2.31 (ddd, J = 17.6, 7.4, 2.5 Hz, 1H), 0.94 (s, 9H), 0.16 (s, 3H), 0.12 (s, 3H); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 172.94, 172.87, 170.36, 170.07, 141.28, 118.19, 80.26, 78.88, 52.23, 51.99, 51.68, 50.39, 47.64, 43.57, 41.63, 38.16, 31.46, 25.67, 18.13, −3.78; MS (EI) m/z (rel intensity) 512 (M^+, 1), 455 (16), 367 (100). Anal. Calcd for $C_{24}H_{36}O_{10}Si$: C, 56.23; H, 7.08. Found: C, 56.29; H, 7.20.

***N*-Phenyl 3-(Phenylthio)maleimide.** To a solution of 3-(phenylthio)maleic anhydride[11] (16.0 g, 82 mmol) in anhyd Et_2O (100 mL) was added dropwise a solution of aniline (7.4 mL, 82 mmol) in anhyd Et_2O (100 mL). The reaction mixture was stirred at rt for 2 h and then cooled to 0 °C for 1 h to crystallize the product acid which was collected by filtration (17.1 g, 70%). A solution of the acid (12.6 g, 42.1 mmol) and sodium acetate (1.7 g, 21.0 mmol) in acetic anhydride (22 mL) was heated at 70 °C for 30 min. The mixture was cooled to rt and poured onto ice−water. The product precipitated as a bright yellow solid which was filtered and washed with water (2×) to obtain the maleimide (7.0 g, 60%): mp 162−164 °C (CH_2Cl_2−Et_2O); IR ($CHCl_3$) 3060, 1790, 1730, 1410 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.70−7.30 (m, 10H), 5.79 (s, 1H); MS (EI) m/z (rel intensity) 281 (M^+, 100). Anal. Calcd for $C_{16}H_{11}NO_2S$: C, 68.25; H, 3.91; N, 4.97; S, 11.37. Found: C, 67.94; H, 3.94; N, 4.95; S, 11.15.

***N*-Phenyl 3-(Phenylsulfinyl)maleimide (21).** To a solution of *N*-phenyl 3-(phenylthio)maleimide (2.0 g, 7.1 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added a solution of MCPBA (2.3 g, 10.65 mmol) in CH_2Cl_2 (10 mL). The reaction was stirred at this temperature for 1 h and allowed to reach rt. The reaction was diluted with CH_2Cl_2 and washed with 10% aqueous $NaHSO_3$, 10% aqueous $NaHCO_3$ (3×), and brine (2×), dried over anhyd Na_2SO_4, and concentrated to obtain the unstable compound **21** as a yellow foam (2.1 g, quantitative): IR ($CHCl_3$) 1783, 1718, 1643, 1384, 1192, 1161, 1086, 1055 cm^{-1}; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 8.30−7.00 (m, 11H); MS (EI) m/z (rel intensity) 297 (M^+, 60), 249 (100).

(7a*SR*)-7-(Phenylsulfinyl)-4-(*tert*-butyldimethylsilyloxy)-5,6,7,7a-tetrahydrobenzofuran-7-carboxylic Acid Methyl Ester (22). A solution of the vinylfuran **5** (0.5 g, 2.2 mmol) and the methyl 2-(phenylsulfinyl)acrylate[10] (1.4 g, 6.6 mmol) in toluene (5 mL) was stirred at rt for 5 h. The solvent was removed and the residue purified by flash chromatography (hexane−acetone, 9:1) to yield compound **22** (0.65 g, 67%) as a slight yellow oil: IR ($CHCl_3$) 3014, 2956, 2932, 1728, 1694, 1569, 1355, 1235, 1083, 1050, 843 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.60−7.45 (m, 5H), 6.56 (d, J = 2.8 Hz, 1H), 5.65 (d, J = 2.8 Hz, 1H), 5.41 (t, J = 3.6 Hz, 1H), 3.60 (s, 3H), 2.41−2.26 (m, 2H), 2.05 (ddd, J = 17.7, 9.6, 8.2 Hz, 1H), 1.71 (ddd, J = 13.7, 7.2, 1.9 Hz, 1H), 0.89 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 167.28, 148.91, 139.15, 136.26, 132.37, 129.32, 126.14, 117.07, 102.96, 80.12, 70.75, 52.91, 28.59, 26.06, 18.51, 18.08, −3.56; MS (CI) m/z (rel intensity) 452 (M^+ + 18, 28), 435 (M^+ + 1, 8). Anal. Calcd for $C_{22}H_{30}O_5SSi$: C, 60.80; H, 6.96. Found: C, 61.07; H, 6.83.

4-Oxo-4,5,6,7-tetrahydrobenzofuran-6,7-dicarboxylic Acid Dimethyl Ester (23). A solution of the vinylfuran **5** (0.5 g, 2.2 mmol), dimethyl 2-(phenylsulfinyl)maleate (1.8 g, 6.6 mmol), and trimethyl phosphite (0.17 g, 3.34 mmol) in toluene (8 mL) was heated at 55−60 °C for 24 h . The solvent was removed and the crude product was purified by flash chromatography (hexane−EtOAc, 3:1) to give ketone **23** (0.22 g, 40%) as a mixture of 2 stereoisomers in a ratio of 7:3: IR ($CHCl_3$) 3024, 2957, 1741, 1688, 1439, 1274, 1124 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.44 (d, J = 2.1 Hz, 0.3H), 7.42 (d, J = 2.4 Hz, 0.7H), 6.72 (d, J = 2.2 Hz, 0.3H), 6.70 (d, J = 2.0 Hz, 0.7H), 4.46 (d, J = 6.1 Hz, 0.7H), 4.45 (d, J = 4.2 Hz, 0.3H), 3.84 (s, 2.1H), 3.79 (s, 0.9H), 3.76 (s, 0.9H), 3.73 (s, 2.1H), 3.82−2.75 (m, 3H); MS (EI) m/z (rel intensity) 252 (M^+, 22), 192 (100). Anal. Calcd for $C_{12}H_{12}O_6$: C, 57.14; H, 4.80. Found: C, 57.07; H, 4.86.

4-Oxo-4,5,6,7-tetrahydrobenzofuran-7-carboxylic Acid Methyl Ester (24). A solution of **22** (0.5 g, 1.2 mmol) in toluene (5 mL) was heated at reflux temperature for 2 h. The solvent was removed and the residue purified by prep TLC (hexane−acetone, 4:1) to give the ketone **24** (198 mg, 84%) as a yellow oil: IR ($CHCl_3$) 3020, 2957, 1741, 1682, 1454, 1283, 1176 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.33 (d, J = 2.3 Hz, 1H), 6.60 (d, J = 2.1 Hz, 1H), 3.91 (t, J = 5.4 Hz, 1H), 3.69 (s, 3H), 2.71−2.28 (m, 4H); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 193.70, 170.73, 161.93, 144.25, 122.45, 106.96, 53.17, 40.36, 35.99, 26.80; MS (EI) m/z (rel intensity) 194 (M^+, 100). Anal. Calcd for $C_{10}H_{10}O_4$: C, 61.85; H, 5.19. Found: C, 61.45; H, 5.15.

8a-(Phenylsulfinyl)-4-(*tert*-butyldimethylsilyloxy)-7-phenyl-5,5a,8a,8b-tetrahydro-1-oxa-7-aza-*as*-indacene-6,8-dione (25). A solution of the vinylfuran **5** (0.4 g, 1.8 mmol) and sulfoxide **21** (1.6 g, 5.3 mmol) in toluene (7 mL) was stirred at rt for 24 h. The solvent was removed and the residue purified by flash chromatography (hexane−acetone, 3:1) to give compound **25** (0.42 g, 45%) as a yellow solid: IR ($CHCl_3$) 3019, 2958, 2932, 1779, 1714, 1689, 1383, 1369, 1083, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.72−7.48 (m, 5H), 7.35−7.28 (m, 3H), 6.78 (br d, J = 2.4 Hz, 1H), 6.61−6.54 (m, 2H), 5.78 (d, J = 2.9 Hz, 1H), 5.58 (d, J = 2.9 Hz, 1H), 3.45 (dd, J = 7.0, 1.6 Hz, 1H), 2.89 (dd, J = 16.0, 1.6 Hz, 1H), 2.44 (dddd, J = 16.0, 7.3, 2.8, 1.0 Hz, 1H), 0.89 (s, 9H), 0.09 (s, 3H), 0.06 (s, 3H); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 175.44, 168.94, 151.37, 138.27, 134.11, 133.18, 131.14, 130.05, 129.40, 126.57, 126.06, 117.49, 101.95, 79.99, 75.02, 36.74, 33.44, 25.94, 18.48, −3.63, −3.71; MS (EI) m/z (rel intensity) 395 (M^+ − 126, 54), 338 (96), 219 (100). Anal. Calcd for $C_{28}H_{31}NO_5SSi$: C, 64.46; H, 5.99; N, 2.68. Found: C, 64.75; H, 6.19; N, 2.59.

(5a*RS*,8a*RS*)-4-Methyl-7-phenyl-5,5a,8a,8b-tetrahydro-1-oxa-7-aza-*as*-indacene-6,8-dione (28), *N*,*N*-diphenyl (1*SR*,2*SR*,8*SR*,9*SR*,10*RS*)-6-methyl-11-oxatricyclo[6.2.1.0^{2,7}]-undec-6-ene-3,4,9,10-tetracarboximide (15), and *N*,*N*-diphenyl (1*SR*,2*SR*,8*SR*,9*RS*,10*SR*)-6-methyl-11-oxatricyclo[6.2.1.0^{2,7}]undec-6-ene-3,4,9,10-tetracarboximide (16). A solution of vinylfuran **27** (1.0 g, 9.24 mmol) and *N*-phenylmaleimide (4.8 g, 13.9 mmol) in toluene (45 mL) was stirred at rt for 20 h. A precipitate of **15** was formed and collected by filtration (0.27 g), the filtrate was evaporated in vacuo, and the residue was purified by flash chromatography (CH_2Cl_2−EtOAc, 98:2) to give compound **28** (0.58 g, 22%), compound **15** (0.63 g; 0.9 g in total; 22%), and compound **16** (1.25 g, 30%) as a white solids. Spectroscopic data for **28**: mp 149−153 °C (CH_2Cl_2−hexane); IR ($CHCl_3$) 3025, 1778, 1716, 1386, 1228, 1204 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.60−7.30 (m, 5H), 7.13 (d, J = 2.5 Hz, 1H), 5.77 (d, J = 2.8 Hz, 1H), 5.02 (dt, J = 8.3, 3.0 Hz, 1H), 3.82 (t, J = 8.1 Hz, 1H), 3.24 (ddd, J = 8.0, 5.9, 1.6 Hz, 1H), 2.89 (dd, J = 15.0, 1.7 Hz, 1H), 2.25−2.05 (m, 1H), 1.85 (br s, 3H); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 177.65, 173.18, 153.56, 134.81, 131.77, 129.02, 128.53, 126.31, 116.42, 102.12, 79.28, 42.69, 36.97, 30.88, 19.61; MS (EI) m/z (rel intensity) 281 (M^+, 100). Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.26; H, 5.43; N, 4.95. Spectroscopic data for **15**: mp 175−178 °C (hexane−EtOAc); IR ($CHCl_3$) 3021, 1779, 1716, 1500, 1387, 1190 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.54−7.34 (m, 6H), 7.34−7.22 (m, 2H), 7.22−7.15 (m, 2H), 5.64 (s, 1H), 5.29 (s, 1H), 3.49 (t, J = 8.6 Hz, 1H), 3.30 (ddd, J = 11.1, 4.6, 2.4 Hz, 1H), 3.24 (d, J = 7.2 Hz, 1H), 3.15 (d, J = 7.2 Hz, 1H), 2.77 (dd, J = 14.8, 2.2 Hz, 1H), 2.40 (d, J = 8.8 Hz, 1H), 2.21 (dd, J = 15.0, 4.8 Hz, 1H), 1.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 177.54, 175.89, 175.50, 175.29, 133.09, 131.68, 131.63,129.13, 129.08, 128.81, 128.67, 128.57, 126.48, 126.23, 80.26, 77.65, 49.38, 49.14, 43.51, 40.60, 40.03, 29.40, 20.54; MS (EI) m/z (rel intensity) 454 (M^+, 100). Anal. Calcd for $C_{27}H_{22}N_2O_5$: C, 71.29; H, 4.84; N, 6.16. Found: C, 71.11; H, 4.79; N, 6.14. Spectroscopic data for **16**: mp 262−263 °C (hexane−EtOAc); IR ($CHCl_3$) 3023, 1777, 1715, 1383, 1183 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.55−7.35 (m, 6H), 7.22 (dd, J = 8.4, 1.8 Hz, 2H), 7.10 (dd, J = 8.2, 2.0 Hz, 2H), 5.62 (d, J = 5.5 Hz, 1H), 5.31 (d, J = 5.2 Hz, 1H), 3.78 (m, 2H), 3.45 (t, J = 8.5 Hz, 1H), 3.21 (ddd, J = 8.3, 4.8, 2.2 Hz, 1H), 2.82 (dd, J = 15.0, 2.2 Hz, 1H), 2.44 (d, J = 8.6 Hz, 1H), 2.17 (dd, J = 15.2, 4.8 Hz, 1H), 1.86 (d, J = 1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 177.39, 175.87, 174.28, 173.37, 131.66, 131.62, 131.40, 131.25, 129.34, 129.05, 128.95, 128.56, 126.13, 126.06, 79.03.

77.11, 50.84, 50.18, 41.47, 40.73, 40.01, 29.42, 20.37; MS (EI) *m/z* (rel intensity) 454 (M^+, 100). Anal. Calcd for $C_{27}H_{22}N_2O_5 \cdot {}^1/_4H_2O$: C, 70.65; H, 4.94; N, 6.10. Found: C, 70.30; H, 4.79; N, 6.05.

8a-(Phenylsulfinyl)-4-methyl-7-phenyl-5,5a,8a,8b-tetrahydro-1-oxa-7-aza-*as*-indacene-6,8-dione (26). A solution of vinylfuran **27** (0.17 g, 1.57 mmol) and the sulfoxide **21** (1.4 g, 4.72 mmol) in toluene (3 mL) was stirred at rt for 72 h. The solvent was removed and the crude product was purified by flash chromatography (hexane−EtOAc, 9:1) to give the compound **26** (0.45 g, 70%) as a yellow solid: mp 137−138 °C (hexane−EtOAc); IR ($CHCl_3$) 3019, 1780, 1712, 1384, 1083, 1053, 1023 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.74−7.66 (m, 2H), 7.62−7.48 (m, 3H), 7.36−7.27 (m, 3H), 6.97 (br s, 1H), 6.60−6.49 (m, 2H), 5.81 (d, J = 2.6 Hz, 1H), 5.51 (br t, J = 2.8 Hz, 1H), 3.45 (dd, J = 6.3, 1.4 Hz, 1H), 2.88 (dd, J = 15.3, 1.4 Hz, 1H), 2.36−2.20 (m, 1H), 1.79 (br s, 3H); MS (CI) *m/z* (rel intensity) 406 ($M^+ + 1$). Anal. Calcd for $C_{23}H_{19}NO_4S \cdot {}^1/_5H_2O$: C, 67.47; H, 4.77; N, 3.40. Found: C, 67.24; H, 4.62; N, 3.33.

4-Hydroxy-7-phenyl-1-oxa-7-aza-*as*-indacene-6,8-dione (29). To a solution of **25** (0.5 g, 0.95 mmol) in methanol (10 mL) was added 10% aqueous HCl (10 mL) dropwise at rt. The reaction mixture was stirred for 24 h, the solvent was removed, and the residue was purified by flash chromatography (hexane−acetone, 3:2) to give compound **29** (0.16 g, 60%) as a yellow foam: IR ($CHCl_3$) 3320, 1773, 1701, 1640, 1613, 1429, 1103, 753 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz) δ 11.72 (s, 1H, D_2O exchange), 8.21 (d, J = 2.1 Hz, 1H), 7.60−7.37 (m. 5H), 7.20 (d, J = 2.0 Hz, 1H), 7.10 (s, 1H); ^{13}C NMR (DMSO-d_6, 25 MHz) δ 167.75, 165.06, 158.11, 150.12, 148.54, 132.56, 131.41, 129.34, 128.32, 127.87, 122.69, 106.57, 105.54, 103.62; MS (EI) *m/z* (rel intensity) 279 (M^+, 100), 235 (34). Anal. Calcd for $C_{16}H_9NO_4 \cdot 1.25H_2O$: C, 63.68; H, 3.84; N, 4.64. Found: C, 63.97; H, 3.68; N, 4.33.

4-Methyl-7-phenyl-1-oxa-7-aza-*as*-indacene-6,8-dione (30). To a solution of **26** (0.5 g, 1.23 mmol) in methanol (10 mL) was added 10% aqueous HCl (10 mL) dropwise at rt. The reaction was stirred for 24 h, the solvent was removed, and the residue was purified by flash chromatography (hexane−EtOAc, 4:1) to give compound **30** (0.15 g, 44%) as a yellow solid: mp 213−214 °C (CH_2Cl_2−hexane); IR ($CHCl_3$) 3029, 1770, 1716, 1502, 1374 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.93 (d, J = 2.2 Hz, 1H), 7.66 (br s, 1H), 7.58 (m, 5H), 6.98 (d, J = 2.2 Hz, 1H), 2.70 (s, 3H); MS (EI) *m/z* (rel intensity) 277 (M^+, 100). Anal. Calcd for $C_{17}H_{11}NO_3$: C, 73.57; H, 3.99; N, 5.04. Found: C, 73.60; H, 3.99; N, 5.01.

4-Hydroxybenzofuran-6,7-dicarboxylic Acid Dimethyl Ester (31). A mixture of compound **23** (0.15 g, 0.6 mmol) and 10% Pd/C (0.15 g) in diphenyl ether (1.0 g) was heated in an oil bath at 160 °C until the starting material was consumed. The reaction mixture was diluted with CH_2Cl_2 and filtered through Celite and the filtrate concentrated. The residue was purified by flash chromatography (hexane−acetone, 4:1) to give the benzofuran **31** (90 mg, 60%) as a solid: mp 77−79 °C (CH_2Cl_2−hexane); IR ($CHCl_3$) 3384, 3025, 1719, 1610, 1438, 1325, 1274 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 8.15 (br s, 1H, D_2O exchange), 7.62 (d, J = 2.2 Hz, 1H), 7.07 (s, 1H), 6.89 (d, J = 2.2 Hz, 1H), 3.99 (s, 3H), 3.87 (s, 3H); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 168.72, 167.32, 153.97, 152.41, 146.93, 128.38, 120.91, 110.67, 109.63, 104.58, 53.46; MS (EI) *m/z* (rel intensity) 250 (M^+, 44), 219 (100). Anal. Calcd for $C_{12}H_{10}O_6$: C, 57.60; H, 4.02. Found: C, 57.78; H, 3.85.

4-Hydroxybenzofuran-7-carboxylic Acid Methyl Ester (32). Same procedure as for compound **31**. Ketone **24** (0.12 g, 0.6 mmol), 10% Pd/C (0.15 g), diphenyl ether (2.0 g). Purification by flash chromatography (hexane−acetone 9:1) yielded **32** (84 mg, 70%): mp 178−80 °C (MeOH−CH_2Cl_2); IR ($CHCl_3$) 3330, 1686, 1605, 1502, 1443, 1293, 756 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz) δ 11.00 (br s, 1H, D_2O exchange), 8.00 (d, J = 2.3 Hz, 1H), 7.90 (d, J = 8.5 Hz, 1H), 7.07 (d, J = 2.4 Hz, 1H), 6.75 (d, J = 8.4 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (DMSO-d_6, 25 MHz) δ 164.71, 156.53, 154.97, 145.02, 129.19, 117.65, 108.39, 106.33, 104.36, 51.82; MS (EI) *m/z* (rel intensity) 192 (M^+, 60), 161 (100). Anal. Calcd for $C_{10}H_8O_4$: C, 62.50; H, 4.20. Found: C, 62.87; H, 4.55.

Compound 30 from Compound 28. Same procedure as for compound **31**. Compound **28** (0.15 g, 0.54 mmol), 10% Pd/C (0.15 g), diphenyl ether (0.5 g). Purification by flash chromatography (hexane-acetone, 9:1) yielded **30** (63 mg, 42%). The spectroscopic data is the same as reported above.

JO951546K