Stereochemistry of the Products from the Alkylation of 2-Naphthol with Glyoxal

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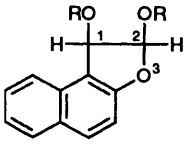
Structural analyses of the products formed in the base-catalysed alkylation of 2-naphthol with glyoxal were performed by IR, ^1H and ^{13}C NMR spectroscopy and mass spectrometry. The *final* product, 7a,14c-dihydrobenzo[*e*]benzo[4,5]benzofuro[2,3-*b*]benzofuran (**4**), was determined to be in the *cis* rather than the *trans* form. MO calculations of the heats of formation and geometrical parameters also favour the *cis* form for **4**. Two precursors of **4**, 1,2-dihydronaphtho[2,1-*b*]furan-1,2-diol and 1-(2-hydroxy-1-naphthyl)naphtho[2,1-*b*]furan-2-ol, have also been analysed and their stereochemistry is discussed.

We previously reported the base-catalysed alkylation of 2-naphthol with glyoxal.[1] In this reaction, four products, *i.e.*, 1,2-dihydronaphtho[2,1-*b*]furan-1,2-diol (**1a**), naphtho[2,1-*b*]-



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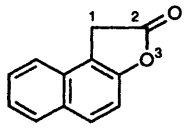
b R = Ac



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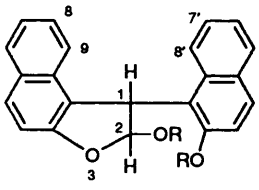

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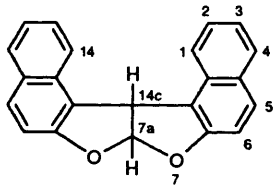
b R = Ac



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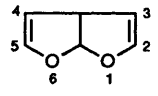

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furan-2(1*H*)-one (**2**), 1-(2-hydroxy-1-naphthyl)naphtho[2,1-*b*]furan-2-ol (**3a**) and 7a,14c-dihydrobenzo[*e*]benzo[4,5]-benzofuro[2,3-*b*]benzofuran (**4**) were isolated. Construction of these compounds with molecular models suggests the existence of various stereoisomers for compounds **1a**, **3a** and **4**. Structural studies on compound **4** have so far been reported by several authors,[2-5] but there have been no reports on its stereochemistry.

In this report, we examine the stereochemistry of compounds **1a**, **3a** and **4** and propose a possible process for their formation.

Results and Discussion

There may exist four stereoisomers of compound **1a** in regard to the orientation of two hydroxy groups on the C^1 and C^2 atoms. Two of these isomers, with both hydroxy groups directed either upwards or downwards (with respect to the plane of the naphthalene ring) (*cis* form) form a pair of mirror images. For the other two stereoisomers, the two hydroxy groups are directed in opposite directions to each other (*trans* form), forming another pair.

The ^1H NMR (250 MHz) spectrum (in [$^2H_6$]acetone) of compound **1a** gave four singlets and a multiplet (composed of four groups), ranging from 4.8 to 8.0 ppm (see Experimental section), with the proton ratio of 1:1:1:1:6. Six aromatic protons constitute the multiplet. Both signals at 4.81 and 6.37 ppm disappeared upon addition of deuterium oxide. Therefore, these two signals are attributed to C^1–O*H* and C^2–O*H*, respectively, and the others at 5.40 and 5.85 ppm to C^1–*H* (H^1) and C^2–*H* (H^2), respectively. Signals for H^1 and H^2 were both singlets, indicating that there is no coupling between them. Two small signals at 5.51 and 5.94 ppm did not disappear upon addition of D_2O and were coupled with each other, with a *J* value of nearly 0 Hz. Therefore, these signals were attributed to two hydrogens ($H^{1'}$ and $H^{2'}$, respectively) on the C^1 and C^2 atoms of the other stereoisomer. The proton signal ratios of H^1:$H^{1'}$ and H^2:$H^{2'}$ were both equal to 72:28.

Attempted separation of the stereoisomers of compound **1a** failed. Consequently, **1a** was transformed into its diacetate **1b** by acetylation with acetic anhydride.

Two peaks appeared in a liquid chromatogram of **1b**, indicating that **1b** consists of two stereoisomers. These stereoisomers **1b***t* and **1b***c* were successfully separated by recrystallization and column chromatography, respectively, and their geometrical structures (*cis* and *trans*) were analysed by a 250 MHz ^1H NMR spectrum.

In the spectrum of **1b***t*, two singlets at 2.13 and 6.67 and a multiplet at 7.2 to 7.9 ppm gave a proton ratio of 6:2:6, indicating that the two acetyl groups have nearly the same chemical shift values and the two hydrogens (H^{1t} and H^{2t}) are also almost identical in their magnetic environment. As for **1b***c*, two singlets at 2.15 and 2.21 ppm were attributed to the acetyl protons and two doublets at 6.66 and 6.93 ppm to H^{1c} and H^{2c},

respectively. Two configurations, *cis* and *trans* forms, are possible for compound **1b**. An application of the Karplus equation to the J_{H^1,H^2} values[6] observed for **1b***t* (nearly zero) and **1b***c* (5.9 Hz) suggests that the dihedral angles of H^1–C^1–C^2–H^2 in these compounds are about 100° and 31°, respectively. Therefore, we conclude that **1b***t* and **1b***c* exist as the *trans* and *cis* forms, respectively. According to MNDO MO calculation, the dihedral angle of H^1–C^1–C^2–H^2 is 120° for **1b***t* and nearly zero for **1b***c*. These values are a little different from those obtained by the Karplus equation.

The *trans*:*cis* (**1b***t*:**1b***c*) ratio in the reaction mixture was estimated by calculation based on the integral values of either methyl protons or H^1 and H^2 signals in the ^1H NMR spectra of **1b** (a mixture of *c* and *t*). Signals for the methyl groups of **1b***t* and **1b***c* were well separated from each other and a *trans*/*cis* ratio of 69:31 was obtained. The integral ratios of two methine protons (H^{1t}:H^{1c} and H^{2t}:H^{2c}) both provide similar values (65:35). The signal height ratio of 64:36 for the C^2 atom at 158.7 (**1b***t*) to 156.1 (**1b***c*) ppm in the ^{13}C NMR spectrum was also favourable for the *trans* form. These isomer ratios, we conclude, may also be valid for compound **1a**, as described by the corresponding ratio of 72:28 for **1a** in the preceding paragraph.

In our previous report,[1] the C^1–OH group in **1a** is susceptible to attack by an acid to form protonated **1a**, followed by removal of a water molecule to leave the $(C^1)^+$ ion. This carbonium ion will lead to lactone **2** in the absence of 2-naphthol and to hemiacetal **3a** in the presence of 2-naphthol. In the latter case, the $(C^1)^+$ ion will make an electrophilic attack on the C^1 atom of 2-naphthol in an acidic medium, either from above or below the naphthalene ring. Accordingly, formation of both *cis* (**3a***c*) and *trans* (**3a***t*) isomers is possible for **3a** in regard to the direction of the two hydrogens, namely the methine (H^1) and hemiacetal (H^2) hydrogens. Both **3a***c* and **3a***t* isomers have their mirror images. Therefore, four stereoisomers for **3a** are possible.

A ^1H NMR study on **3a***c* and **3a***t* was conducted (see Experimental section). Two signals at 9.46 and 10.37 ppm were assigned to phenolic hydrogens (the integral ratio for the two signals was about 3:7). These signals disappeared upon addition of deuterium oxide. Signals for the hemiacetal hydroxy groups were located in the aromatic region.

For confirmation of the existence of stereoisomers for compound **3a**, it was converted into the corresponding acetate (**3b**) because **3a** was so unstable that it easily changed into **4** during post-treatment. Attempted separations of this isomeric mixture of **3b** by column chromatography were unsuccessful. Therefore, the stereochemistry of **3b** will be discussed in the following paragraph with the help of the result of the following discussion on compound **4**.

Various structural forms have so far been proposed for compound **4**. The ether and acetal types were typical. The former type was claimed by Rosenthal *et al.*[2] and McGowan *et al.*,[3] and the latter, shown above, was suggested by Thyagarajan *et al.*[4] and Coxworth[5] based on ^1H NMR studies. Although Coxworth gave an assignment for each proton signal in **4**, he did not refer to the possibility of the existence of the *cis* (**4***c*) and *trans* (**4***t*) isomers in regard to the direction of the two hydrogens on the C^{7a} and C^{14c} atoms.

An attempted construction of **4***t* with a STS molecular model failed due to severe distortion of its molecular framework. Compound **4***c* was constructed with a slight distortion of the two naphthalene rings, due to partial overlapping of hydrogens on the C^1 and C^{14} atoms (H^1 and H^{14}).

The difference between the heats of formation (Δ_fH) for isomers **4***t* and **4***c* was estimated by three semiempirical MO methods, namely MNDO, AM1 and PM3 (see Table 1);[7] all afforded very large Δ_fH values (averaging 44 kcal mol^{-1}). For reference, energy differences (about 48 kcal mol^{-1}) between the

Table 1 Heats of formation (Δ_fH/kcal mol^{-1})[a] of compounds **4** and **5** calculated by semiempirical MO methods

Compd.	Method	Δ_fH(*trans*)	Δ_fH(*cis*)	Difference
4	MNDO	60.05	17.24	42.81
	AM1	84.13	39.12	45.01
	PM3	66.53	23.36	43.15
5	MNDO	4.83	−42.20	47.03
	AM1	17.99	−31.71	49.70
	PM3	9.49	−37.07	46.56

[a] 1 cal = 4.184 J.

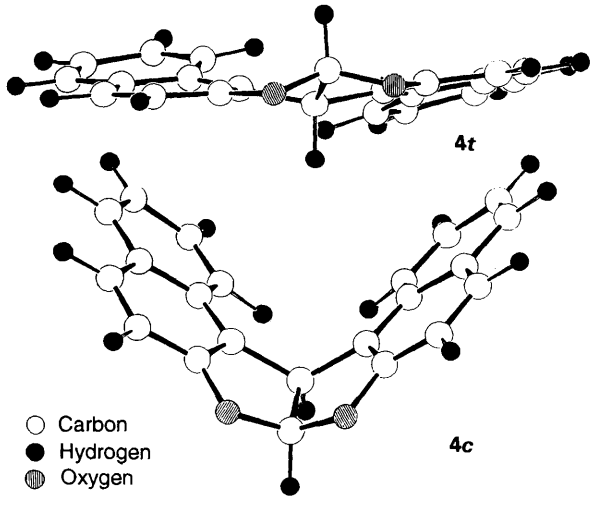

Fig. 1 Molecular structures of **4***c* and **4***t*

Δ_fH values of *cis*- and *trans*-3a,6a-dihydrofuro[2,3-*b*]furan (**5***c* and **5***t*) were also calculated by these three methods (Table 1). Virtually equal values of the difference for **4** and **5** indicate that the larger Δ_fH values for **4***t* should be attributed to the ring strain of the **5***t* skeleton contained in **4***t*. Also, formation of the C=C bond between C^{7a} and C^{14c} in compound **4** leads to an increase in the Δ_fH value up to 54.9 kcal mol^{-1}, by calculation. Consequently, **4***c* is a stable compound and would not suffer such dehydrogenation during the reaction.

Energetically optimized structures for **4***c* and **4***t* are depicted in Fig. 1 using the ORTEP routine.[8] According to this method, **4***c* is symmetrical, although **4***t* is not. Bond angles and bond lengths as well as atomic distances for **4***c* and **4***t* were also calculated (Table 2). Deviation of the bond angle from the standard value (109.5°) for **4***t* is larger than that for **4***c*. For example, angles C^{7a}–C^{14c}–C^{14b}, C^{7a}–C^{14c}–C^{14d} and C^{14b}–C^{14c}–C^{14d} for **4***t* were 94.9, 97.3 and 147.1°, respectively. If **4***t* has a symmetrical configuration, the distance between H^1 and H^{14} was calculated by the MNDO method to be 1.70 Å, less than twice the value of the van der Waals radius for hydrogen (1.2 Å),[9] compared with the corresponding distance of 2.07 Å for **4***c*. As depicted in Fig. 1, the **4***t* molecule is twisted to avoid overlapping between H^1 and H^{14}. This causes distortion of the bond angles involving C^{14c}. In practice, we found it extremely difficult to construct the **4***t* framework with the STS model.

Compound **4** was analysed by ^1H NMR spectroscopy in [$^2H_6$]DMSO. The methine proton (H^{14c}) appeared at 5.87 ppm as a doublet (*J* 5.9 Hz). A doublet at 7.30 ppm was assigned to H^{7a}, because irradiation of H^{14c} collapsed it into a singlet. Assignment of a signal at 8.37 ppm for H^1 and H^{14} by the NOE technique is described in the following paragraph. Upon successive irradiation, signals at 7.54, 7.35 and 7.89 ppm were assigned to H^2 (and H^{13}), H^3 (and H^{12}) and H^4 (and H^{11}),

Table 2 Bond angles (°) and lengths (Å)[a]

Angle	4c	4t	Length	4c	4t
C^6–C^{6a}–O^7	122.4	122.2	C^{6a}–O^7	1.366	1.384
O^7–C^{6a}–C^{14d}	114.0	114.8	C^{6a}–C^{14d}	1.413	1.430
C^{6a}–O^7–C^{7a}	109.3	102.4	O^7–C^{7a}	1.417	1.409
C^{6a}–C^{14d}–C^{14c}	107.9	104.7	C^{7a}–C^{14c}	1.610	1.603
O^7–C^{7a}–C^{14c}	107.8	105.7	C^{7a}–O^8	1.417	1.415
O^7–C^{7a}–O^8	106.6	119.2	O^8–C^{8a}	1.366	1.385
C^{7a}–C^{14c}–C^{14d}	100.6	97.3	C^{8a}–C^{14b}	1.413	1.435
C^{7a}–C^{14c}–C^{14b}	100.6	94.9	C^{14b}–C^{14c}	1.523	1.517
C^{7a}–O^8–C^{8a}	109.3	101.9	C^{14c}–C^{14d}	1.523	1.513
O^8–C^{8a}–C^{14b}	114.0	114.3	H^1–H^{14c}	2.707	3.086
C^{8a}–C^{14b}–C^{14c}	107.9	103.0	H^{7a}–H^{14c}	2.490	3.250
C^{14a}–C^{14b}–C^{14c}	133.5	137.7	H^{14}–H^{14c}	2.707	3.732
C^{14b}–C^{14c}–C^{14d}	118.5	147.1	H^1–H^{14}	2.068	2.193
C^{14c}–C^{14d}–C^{14e}	133.5	135.3			
	5c	**5t**		**5c**	**5t**
O^1–O^2–C^3	113.8	114.4	O^1–C^2	1.374	1.394
O^1–C^{6a}–C^{3a}	106.5	103.8	C^2–C^3	1.361	1.375
O^1–C^{6a}–O^6	108.7	122.7	O^1–C^{6a}	1.419	1.414
C^2–O^1–C^{6a}[b]	109.6	102.1	C^{3a}–C^{6a}	1.602	1.597
C^2–C^3–C^{3a}	111.2	105.5	C^3–C^{3a}	1.512	1.506
C^3–C^{3a}–C^4	116.9	145.5			
C^3–C^{3a}–C^{6a}	105.4	99.7	H^{3a}–H^{6a}	2.531	3.257
C^4–C^{3a}–C^{6a}	100.8	99.7			

[a] Calculated by MNDO method. [b] The angle C^5–O^6–C^{6a} was the same as C^2–O^1–C^{6a}.

respectively. Signals at 7.85 and 7.29 ppm, assigned to H^5 and H^6, were found to couple with each other with a J value of 8.8 Hz by the double resonance method.

We have no direct means of determining which of these two chemical shifts should be assigned to H^5 or H^6 of **4**. For this purpose, we referred to the chemical shifts of naphthalene; H^1 (7.69 ppm) has a higher shift than H^2 (7.34 ppm). This trend is retained even with introduction of the methoxy group to the C^3 position of naphthalene ring (7.60 for H^1 and 7.04 for H^2 ppm).[10] Therefore, a doublet at 7.85 ppm was assigned to H^5 (and H^{10}) and a doublet at 7.29 ppm to H^6 (and H^9).

If **4** exists as a mixture of **4c** and **4t**, **4** should give a more complex signal pattern for H^{7a} and H^{14c}. The NMR spectrum of **4** in $[^2H_6]Me_2SO$ (see Fig. 2) gave a rather simple pattern, indicating that **4** should exist as a single form.

The NOE technique was applied to the $[^2H_6]Me_2SO$ solution of **4** to determine the *cis*/*trans* geometry of **4** (see Fig. 2). Irradiation of the methine proton (H^{14c}, 5.87 ppm) will enhance the signal of the acetal one (H^{7a}) if **4** takes the *cis* form, while the *trans* form will show none or a weaker enhancement for H^{7a}. Two doublets were observed at 7.30 (H^{7a}, 15.6%) and 8.37 (10.0%) ppm in the NOE spectrum. A significant enhancement of the H^{7a} signal strongly indicates that H^{7a} locates near H^{14c}; namely, **4** takes *cis* geometry. A signal at 8.37 ppm also locates close to H^{14c}, and was assigned to H^1 (and H^{14}). The atomic distance between H^{14c} and H^{7a}, H^1 or H^{14} of **4** was calculated by the MO method to be 2.49, 2.71 and 2.71 Å, respectively. Further support for the *cis* geometry for **4** comes from the structure of **3b**.

In the ^1H NMR spectrum of **3b** in $[^2H_6]Me_2SO$, both signals at 5.68 and 5.99 ppm can be assigned to the methine proton (H^1) based on the chemical shift (δ) values for **4**. Two signals at 6.69 and 6.83 ppm are attributed to H^2, because these were coupled with signals at 5.68 and 5.99 ppm, respectively. However, we cannot assign these protons to the *cis* or *trans* isomer by the ^1H NMR spectrum.

The NOE technique was applied to **3b**. Irradiation of the signal at 5.99 ppm caused enhancement of 4.3, 4.0 and 24.2% for signals at 6.69, 7.01 and 8.78 ppm, respectively. On the other hand, irradiation of the signal at 5.68 ppm caused enhancement

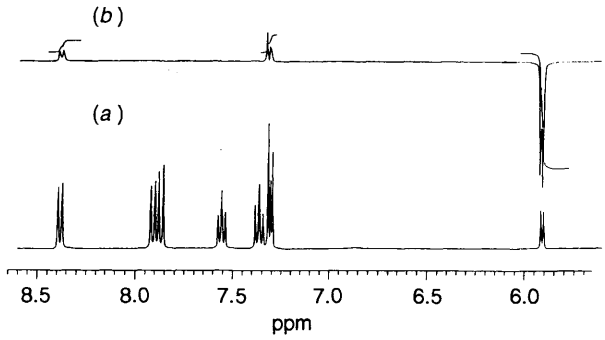

Fig. 2 (*a*) ^1H NMR and (*b*) NOE spectra of **4** (400 MHz in $[^2H_6]Me_2SO$)

of 3.3% for a signal at 6.83 ppm and 3.4% for a signal at 7.18 ppm. These observations suggest that the signals at 6.69, 6.83, 7.01, 7.18 and 8.78 ppm should be assigned to protons near H^1.

Atomic distances between any two hydrogen atoms in **3b** were calculated by the MO method. The distances H^{1c}–H^{2c}, H^{1c}–H^{9c} and H^{1c}–$H^{8'c}$ for the *cis* form were 2.27, 2.86 and 2.03 Å and H^{1t}–H^{2t}, H^{1t}–H^{9t} and H^{1t}–$H^{8't}$ for the *trans* form were 3.07, 2.96 and 3.93 Å, respectively.

Based on the calculation, the atomic distance increases in the order H^1–$H^{8'c}$, H^1–H^{2c}, H^1–H^{9c}, H^1–H^{9t}, H^1–H^{2t} and H^1–$H^{8't}$. Thus, $H^{8'c}$ should give the strongest enhancement among them in the NOE spectrum with irradiation on the H^1 atom. Therefore, it is reasonable to assign the signal at 8.78 ppm to $H^{8'c}$; and in turn, the signals at 5.99, 6.69 and 7.01 ppm to the protons of the *cis* form. The other signals can be assigned to the protons of the *trans* form.

The signals at 7.01 and 7.18 ppm can be assigned to H^{9c} and H^{9t}, respectively, though the corresponding proton (H^{14}) for **4** appeared at 8.37 ppm. The STS molecular model and the MO calculations suggest that the H^{9c} atom locates over (or below) the π-electron cloud of the other naphthalene ring and, consequently, their δ values shifted to a higher magnetic field.

A signal for $H^{8't}$ was not observed in the NOE spectrum. MO calculation can explain this fact, because $H^{8't}$ locates at the farthest distance from H^1.

The *cis* isomer content of **3b** was estimated to be 73% (*trans*, 27%) based on the proton ratio of H^1 or H^2 and 75% based on that of $H^{8'}$.

The signals corresponding to those at 5.68 and 6.83 ppm characteristic of the *trans* form of **3b** were not found in the ^1H NMR spectrum of **4**. Therefore, we conclude that no *trans* form is present for **4**.

As for compound **3a**, signals at 5.63 and 5.93 ppm can be assigned to H^{1t} and H^{1c}, respectively, based on the ^1H NMR spectrum of **6**. The *cis*:*trans* ratio for compound **3b** is maintained in **3a**, because the proton ratio of signals at 5.93/5.63 ppm for **3a** gave a comparable ratio 75:25 to **3b** 73:27.

In the previous paper,[1] **4** was formed from 2-naphthol and glyoxal *via* **1** to **3a**. Transformations from **1** to **3** and from **3** to **4** both proceed in an acidic medium. In a simple synthesis, **4** can be prepared as it precipitates from 2-naphthol and glyoxal in ethylene glycol dimethyl ether (DME) solution without separation of **1** and **3**. DME was evaporated off from the filtrate after removal of **4** and the residue was analysed by ^1H NMR spectroscopy. The proton ratio of signals at 5.93/5.63 ppm was nearly the same (73:27) as that observed for the mixture of **3ac** and **3at** (75/25). This result suggests that there is an equilibrium between **3ac** and **3at**.

The reason why the *cis* isomer dominates over the *trans* one for compound **3a** can be explained as follows. An examination with a STS molecular model revealed that hydrogen bonding should play an important role in stabilization of the isomer. A

stable intramolecular hydrogen bond (a value of 2.71 Å was reported)[11] is possible for the *cis* form, in which the two naphthalene rings are free from steric hindrance. In marked contrast, in the *trans* form they must come too close and partially overlap for a favourable hydrogen bonding configuration, which will generate steric repulsion.

Experimental

^1H and ^{13}C NMR spectra were recorded on Bruker AC-250 and JEOL GX-400 spectrometers. Mass spectra were obtained at 70 eV. Liquid chromatography was performed with an EYELA PLC-7 (Tokyo Rikakikai) chromatograph (column, Kanto Lichrospher; MeOH–H_2O = 60:40; 5 cm^3 min^{-1}).

Improved procedures for synthesis of **1a** and **3a** are described, since their optimized reaction conditions were not established in our previous report.

Molecular Model.—A STS molecular model, a space-filling molecular model or Stuart model manufactured by Maruzen, Tokyo, Japan, was used.

MO Calculations.—Geometrical parameters and the heats of formation for compounds **1a**, **3a** and **4** and related compounds were obtained from energetically optimized calculations by the semiempirical MNDO MO method[12] and, if necessary, by AM1[13] and PM3[14] MO methods using MOPAC ver. 6.01.[15]

1,2-*Dihydronaphtho*[2,1-b]*furan*-1,2-*diol* (**1a**) (*Improved Method of Preparation*).—In a 500 cm^3 flask equipped with a mechanical stirrer was placed a solution of 2-naphthol (20.0 g, 0.139 mol) in 280 cm^3 aqueous KOH (0.139 mol). To the solution, aqueous glyoxal (40%; 120 g, 0.83 mol) was added dropwise at 18–21 °C over 1.5 h and the mixture was stirred for 3 h at 18–21 °C (when heated at above 30 °C, product **1a** was difficult to crystallize; in such a case, cooling in an ice-bath was effective.) Precipitates were collected and washed successively with $CHCl_3$ and hexane to give the monohydrate of **1a** (27.6 g; 90.2% as monohydrate).

1a. δ_H(250 MHz; [$^2H_6$]acetone) 4.81 (br s, 1 H, C^1OH), 5.40 (s, 0.72 H, H^{1t}) +5.51 (s, 0.28 H, H^{1c}), 5.85 (s, 0.72 H, H^{2t}) +5.94 (s, 0.28 H, H^{2c}), 6.37 (br s, 1 H, C^2OH) and 7.1–8.0 (m, 6 H, ArH). The proton ratio was 1:1:1:1:6. Signals at δ 4.81 and 6.37 disappeared upon addition of D_2O. Thermogravimetric analysis of compound **1a** (sample weight, 18.20 mg; *T*, room temp. to 800 °C, heating rate, 25 °C min^{-1}): weight loss, 8.18% at room temp. to 180 °C and 8.38% at 180 to 209 °C. Above 250 °C, the weight loss occurred at a faster rate. Calculated weight loss; 8.18% for **1a**·H_2O to **1a** (anhydrous) and 16.4% for **1a**·H_2O to **2** (lactone). For other analytical data (m.p., IR, ^{13}C NMR and MS), see ref. 1.

1-(2-*Hydroxy*-1-*naphthyl*)*naphtho*[2,1-b]*furan*-2-*ol* (**3a**) (*Improved Method of Preparation*).—In a 100 cm^3 flask equipped with a stirrer, a mixture of **1a**·H_2O (2.20 g, 0.0100 mol), 2-naphthol (1.44 g, 0.0100 mol), $CHCl_3$ (30 cm^3) and HCl (3 mol dm^{-3}; 20 cm^3) was refluxed for 3 h. After cooling, precipitates were collected by suction and washed with water and then with hexane to give **3a** (m.p. 96 °C, 1.16 g, 35%).

3a. (A mixture of **3ac** and **3at**): δ_H(250 MHz; [$^2H_6$]Me_2SO) 5.63 (d, 0.25 H, H^{1t}), 5.93 (d, 0.75 H, H^{1c}), 6.29 (d, 1 H, H^{2c} + H^{2t}), 7.0–8.6 (m, 13 H, ArH + C^2-OH), 9.46 (s, 0.26 H, C^2-OH) and 10.37 (s, 0.74 H, ArOH). For the other spectroscopic data, see ref. 1.

MO Calculation for **3a**.—The atomic distances of the *cis* and *trans* forms in Å: H^1–H^2, 2.28 and 3.07; H^1–H^9, 2.85 and 2.87; H^1–$H^{8'}$, 1.96 and 3.94.

7a,14c-*Dihydrobenzo*[e]*benzo*[4,5]*benzofuro*[2,3-b]*benzofuran* (**4**) (*Improved Method for Preparation*).—A mixture of 2-naphthol (28.8 g, 0.200 mol), aqueous glyoxal (40%; 29 g, 0.200 mol), DME (100 cm^3) and aqueous KOH (3 mol dm^{-3}; 2 cm^3) was stirred at room temp. After 1 h, CH_3SO_3H (25 cm^3) was added dropwise over 3 h with stirring. The precipitate formed was collected on a filter, washed with water, ethanol and dried. Yield, 22.6 g (72.9%). δ_H(400 MHz; [$^2H_6$]Me_2SO) 5.87 (d, 1 H, H^{14c}), 7.29 (d, 2 H, H^6 + H^9), 7.30 (d, 1 H, H^{7a}), 7.35 (dd, 2 H, H^3 + H^{12}), 7.54 (dd, 2 H, H^2 + H^{13}), 7.85 (d, 2 H, H^5 + H^{10}), 7.89 (d, 2 H, H^4 + H^{11}) and 8.37 (d, 2 H, H^1 + H^{14}); $J_{1,2}$ 8.4, $J_{2,3}$ 6.8, $J_{3,4}$ 8.4, $J_{5,6}$ 8.8 and $J_{7a,14c}$ 5.9 Hz. The proton signal ratio was 1:2:1:2:2:2:2:2. δ_H(250 MHz; $CDCl_3$) 5.58 (d, 1 H, H^{14c}), 7.12 (d, 1 H, H^{7a}), 7.23 (d, 2 H, H^6 + H^9), 7.33 (dd, 2 H, H^3 + H^{12}), 7.53 (dd, 2 H, H^2 + H^{13}), 7.75 (d, 2 H, H^5 + H^{10}), 7.81 (d, 2 H, H^4 + H^{11}) and 8.29 (d, 2 H, H^1 + H^{14}); $J_{1,2}$ 8.5, $J_{2,3}$ 6.7, $J_{3,4}$ 8.3, $J_{5,6}$ 8.8 and $J_{7a,14c}$ 5.9 Hz. The NOE spectrum (400 Hz in [$^2H_6$]Me_2SO at 35 °C) was obtained by irradiating H^{14c} (5.87 ppm). The enhancements of H^{7a} and H^1 (H^{14}) were 15.6% and 10.0% (see Fig. 2).

MO Calculations of the Heat of Formation and Geometrical Parameters for **4c** *and* **4t**.—The heat of formation and geometrical parameters for the energetically optimized structures of **4c** and **4t** (Fig. 1) were estimated by the MNDO MO method (Tables 1 and 2). The MNDO MO calculation on the assumption that **4t** has a symmetrical structure was also carried out for reference and gave 1.7024 Å for the atomic distance of H^1–H^{14}.

1,2-*Diacetoxy*-1,2-*dihydronaphtho*[2,1-b]*furan* (**1b**).—A mixture of **1a**·H_2O (10.0 g, 0.0455 mol), acetic anhydride (50 cm^3) and pyridine (10 cm^3) was refluxed for 24 h. After cooling, the mixture was extracted with diethyl ether (total volume, 200 cm^3) and the ether solution was washed successively with 1 mol dm^{-3} $NaHCO_3$ and water. Evaporation of the ether gave nearly a quantitative yield of **1b** (13.0 g).

1b (A mixture of **1bc** and **1bt**): ν_{max}(KBr)/cm^{-1} 1740s (with a shoulder). An absorption at 3400 cm^{-1} (br) characteristic of compound **1a** disappeared; δ_H(250 MHz; $CDCl_3$) 2.13 (s, 4.2 H) +2.15 (s, 0.9 H) +2.21 (s, 0.9 H) (total 6 H, 2 CH_3CO_2), 6.658 (d, 0.35 H, H^1), 6.664 (s, 1.3 H, H^1 + H^2), 6.93 (d, 0.35 H, H^2, for assignment of the three signals see **1bc** and **1bt**) and 7.1–7.9 (m, 6 H, ArH) (Found: C, 66.8; H, 5.02. $C_{16}H_{14}O_5$ requires C, 67.12; H, 4.93%). Liquid chromatography gave two peaks at 18.8 s (area ratio, 37.5%) for the *cis* form and 21.1 s (62.5%) for the *trans* form.

Calculation of the Dihedral Angle of H^1–C^1–C^2–H^2 *for* **1b**.—Dihedral angles calculated by MNDO, AM1 and PM3 methods are arranged in this order. H^1–C^1–C^2–H^2; 0, 2 and −3° for **1bc** and 120, 113 and 116° for **1bt**. AcO–C^1–C^2–OAc; 0, 8 and 3° for **1bc** and −131, −139 and −142° for **1bt**. The bond angles were also estimated by the Karplus equation, where $J_{vic} = 8.5 \cos^2 \theta - 0.28$ (Hz) ($0° < \theta < 90°$) and $J_{vic} = 9.5 \cos^2 \theta - 0.28$ (Hz) ($90° < \theta < 180°$).[6]

Stereoisomers of **1b**.—A liquid chromatogram of compound **1b** showed two peaks, indicating the presence of at least two stereoisomers for **1b**. One isomer (**1bt**), which corresponds to the peak with a shorter retention time, was obtained in a yield of 30.5% (3.96 g) by recrystallization of the crude mixture (13.0 g) from ethanol (50 cm^3). The other product (**1bc**) with a longer retention time was obtained in a yield less than 0.4% (0.05 g) by chromatographic separation of the filtrate on a silica gel column (silica gel 60, 70–230 mesh, Merck; eluent, benzene–$CHCl_3$ = 3:2).

1bc. ν_{max}(KBr)/cm^{-1} 1763s, 1740s, 827m and 756m; δ_H(250

MHz; $CDCl_3$) 2.15 (s, 3 H, $CH_3CO_2C^1$), 2.21 (s, 3 H, $CH_3CO_2C^2$), 6.66 (d, 1 H, H^1), 6.93 (d, 1 H, H^2) and 7.2–7.9 (m, 6 H, ArH), $J_{1c,2c}$ 5.9 Hz; δ_C(62.9 MHz, [$^2H_6$]Me_2SO) 20.1 (q) + 20.3 (q), (both are assigned to CH_3CO), 71.9 (d, C^1), 94.5 (d, C^2) and 183 (s, C^2OCO); *m/z* 286 (M^+, 7%), 226 (11), 184 (100), 173 (24), 156 (21) and 128 (50) (Found: C, 66.8; H, 5.0. $C_{16}H_{14}O_5$ requires C, 67.12; H, 4.93%).

1b*t*. M.p. 157 °C (from EtOH); ν_{max}(KBr)/cm^{-1} 1740s (with shoulders), 818m and 742m; δ_H(250 MHz; $CDCl_3$) 2.13, (s, 6 H, 2 CH_3CO_2), 6.670 + 6.676 (2 s, 2 H, H^1 + H^2) and 7.2–7.9 (m, 6 H, ArH), $J_{1,2}$ 0 Hz; δ_C(62.9 MHz; $CDCl_3$) 20.5 (s, $CH_3CO_2C^1$ + $CH_3CO_2C^2$), 76.5 (d, C^1), 101.5 (d, C^2) and 167.0 + 170.1 (s, C^1OCO + C^2OCO); *m/z* 286 (M^+, 5%), 226 (12), 184 (100), 173 (19), 156 (19) and 128 (48) (Found: C, 66.8; H, 5.0. $C_{16}H_{14}O_5$ requires C, 67.12; H, 4.93%).

Diacetate **3b**.—A mixture of **3a** (1.00 g, 0.003 05 mol), acetic anhydride (50 cm^3) and pyridine (10 cm^3) was stirred at 50 °C for 24 h. After cooling, the reaction mixture was extracted with diethyl ether (200 cm^3) and the ether extract was washed with aq. $NaHCO_3$, dilute HCl and finally with water. Evaporation of the ether gave crude diacetate **3b** (1.0 g, 80%). Recrystallization (hexane) gave pure **3b** (0.10 g).

3b. M.p. 138–145 °C (from hexane): ν_{max}(KBr)/cm^{-1} 1760s and 1190s (broad, with shoulders). A broad absorption at 3450–3350 cm^{-1} observed for compound **3a** completely disappeared; δ_H(400 MHz: [$^2H_6$]Me_2SO) 1.87 (s, 2.2 H) + 2.13 (s, 2.2 H) + 2.14 (s, 0.8 H) + 2.49 (s, 0.8 H) (total 6 H, 2 CH_3CO_2), 5.68 (d, 0.27 H, H^{1t}), 5.99 (d, 0.73 H, H^{1c}), 6.69 (d, 0.73 H, H^{2c}), 6.83 (d, 0.27 H, H^{2t}), 7.01 (d, 0.69 H, H^{9c}), 7.1–8.1 (m, ArH, 11 H + H^{9t}) and 8.78 (d, 0.75 H, $H^{8'c}$), $J_{1c,2c}$ 2.2, $J_{1t,2t}$ 3.7, $J_{8c,9c}$ 8.4 and $J_{7'c,8'c}$ 8.4 Hz; δ_C(62.9 MHz; $CDCl_3$) 21.0 (q), 21.1 (q), 46.5 (d, C^{1c}), 46.9 (d, C^{1t}), 104.0 (d), 105.1 (d), 111.6 (d), 112.0 (d), 119.3–132.7 (aromatic C), 146.9 (s), 148.0 (s), 155.8 (s), 168.5 (s) and 169.7 (s); NOE spectrum (400 MHz in [$^2H_6$]Me_2SO at 35 °C) was obtained by irradiating H^1 (5.68 and 5.99 ppm). Enhanced signals (in ppm; the intensity in % in parentheses) were as follows; 6.83 (3.3), 7.18 (3.4) and 8.78 when the signal at 5.68 ppm was irradiated and 6.69 (4.3), 7.01 (4.0), 7.80 (−1.7) and 8.78 (24.2) when the signal at 5.99 ppm was irradiated. *m/z* 412 (M^+, 7%), 352 (25), 310 (100) and 281 (28) (Found: C, 75.7; H, 5.0. $C_{26}H_{20}O_5$ requires C, 75.71; H, 4.89%).

MO Calculation for **3b**.—Atomic distances calculated by MNDO, AM1 and PM3 methods are arranged in this order. H^1–H^2; 2.27, 2.37 and 2.33 Å for **3bc** and 3.07, 3.05 and 3.05 Å for **3bt**. H^1–H^9; 2.86, 2.79 and 2.76 Å for **3bc** and 2.96, 2.79 and 2.80 Å for **3bt**. H^1–$H^{8'}$; 2.03, 1.86 and 1.72 Å for **3bc** and 3.93, 3.79 and 3.81 Å for **3bt**.

MO Calculation for cis- *and* trans-3a,6a-*Dihydrofuro*[2,3-b]*furan* (**5c** *and* **5t**).—Calculations were carried out by the method described for **4** and the results are summarized in Table 2.

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