Internal Rotation Involving a Preequilibrium Ring Inversion[1]

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3-Mesitylnaphthopyrans exhibit slow or locked internal rotation on the NMR time scale at ambient temperatures. Conformational analysis demonstrates that ground-state mesityl preferentially occupies the equatorial position of the nonplanar pyran ring and that rotation is blocked in this state. However, rotation is relatively unhindered in the higher energy axial state. A transannular substituent effect on the barrier height suggests that mesityl site exchange is a multistep process involving a preequilibrium inversion of the pyran ring followed by rotation of mesityl in the axial state and final relaxation to the site-exchanged equatorial ground state.

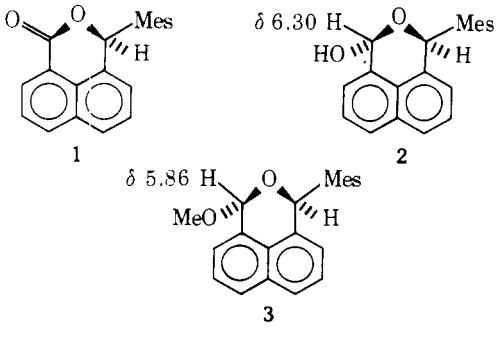
An interesting dynamical system results when internal rotation[3] and ring inversion[4] are interdependent. Two discrete cases can occur: (1) the rotational activated complex occurs in the low-energy inversion state, and (2) the rotational activated complex occurs in the high-energy inversion state. An example of case 1 is the 9-arylxanthene system,[5] and in such cases site exchange is a simple, single-step aryl rotation in the preferred conformation. An example of case 2 is the 3-arylnaphthopyran system described below, and in this case it is proposed that site exchange is a three-step process involving a preequilibrium ring inversion followed by aryl rotation in the high-energy inversion state and final relaxation to the site-exchanged inversion ground state.

Results and Discussion

The site-exchange mechanism of 3-mesitylnaphthopyrans is analyzed by studying the exchange barrier height as a function of the size of the pyran ring substituent at the 1 position. The compounds used in the study are naphthopyrans **1–3** shown in Chart I. Ground-state conformational analysis of **1–3** utilizes model 2-mesitylacenaphthenes, which have bond angles intermediate to the extremes of the pyran axial and equatorial bonds. In contrast to the six-membered pyran ring, the peri ring of acenaphthene is a rigid,[6] planar five-membered ring having bisectional aliphatic bonds that form an angle of about 50° with the plane of the ring.[7]

The mesityl group dominates the geometry of 3-mesitylnaphthopyrans and is placed equatorially in the ground state. This is clearly demonstrated by the chemical shift data in Table I for the mesityl methyl groups. The values are very similar for all three compounds. Parameter δ' is a measure of anisotropic shielding of a methyl group on a mesitylene ring, and a positive value indicates that a group absorbs upfield of (or is more shielded than) a methyl group in mesitylene, which by definition has $\delta' = 0$. The δ' values for the inside methyl (i.e., the methyl group that would lie over the naphthalene nucleus if mesityl were axial) varies from 0.28 to 0.36 for naphthopyrans **1–3**. In contrast, the values range from 0.73 to 1.07 for the acenaphthene models. Thus, the inside methyls of **1–3** are less "inside" than those for the acenaphthenes, and hence mesityl is equatorial. An equivalent argument can be applied to the outside and para methyls. Especially interesting is the sign change that occurs for the para methyls, suggesting that the para methyls of **1–3**, unlike those of the acenaphthenes, are outside of the shielding zone of the naphthalene rings. Mesityl is preferred in the equatorial position because an axial mesityl would encounter a strong nonbonded interaction of its inside methyl with the π orbitals of the naphthalene nucleus. This interaction would probably exceed the analogous interaction of about 12 kcal/mol that stabilizes the enol 2-mesitylacenaphthylenol.[8]

Chart I. 3-Mesitylnaphthopyrans 1–3 and H_1 Chemical Shifts



1 2 3

The ground-state hydroxyl and methoxyl substituents, in contrast, are axial and hence are trans to mesityl. The evidence for axial OH and OCH_3 is the NMR data in Chart I, which indicate that the benzylic protons H_1 in **2** and **3** are equatorial. The benzylic protons in the parent compound, 1*H*,3*H*-naphtho[1,8-*cd*]pyran,[9] absorb as a singlet at δ 4.95, which is necessarily the mean of the true chemical shifts for the equatorial and axial protons since the latter are rapidly exchanging on the NMR time scale. Since H_1 and H_3 in the derivative (evidently the cis isomer) 1,3-dimethoxy-1*H*,3*H*-naphtho[1,8-*cd*]pyran[10] absorb as a singlet at δ 6.42, it appears likely that an equatorial proton in naphthopyrans absorbs at around δ 6 and an axial proton at around δ 4.

The rate constants and free energies of activation for ortho methyl site exchange in **1–3** are shown in Table II. The variable-temperature NMR behavior can be explained only by the occurrence of a complete site exchange process equivalent to a 180° rotation of mesityl and not merely by changing conformer populations.[11] For example, the methyl signals of **1** at −15 °C consist of three sharp singlets (δ 1.95, 2.30, and 2.45), at 51 °C of a sharp singlet [δ 2.25 (the para methyl)] superimposed on a flat-topped coalescence peak and at 83 °C of two singlets (δ 2.29 and 2.21), the last of which is approximately the mean of δ 1.95 and 2.45. The kinetic parameters in the table were determined by the dynamic NMR method used previously;[6,8] other studies[12] report that the method gives $\Delta G^{\ddagger}$ to within about 0.1 kcal/mol of that obtained by complete line shape analysis. The main result in Table II is that the increasing order for the mesityl rotational barrier heights, **1** < **2** < **3**, is also the increasing order of size for the largest group at the 1 position across the pyran ring, that is, π orbital < OH < OCH_3.[13]

The transannular substituent effect on the barrier height is explicable if mesityl site exchange is a multistep process involving a preequilibrium ring inversion. Space-filling models demonstrate that rotation of equatorial mesityl in the inversion ground state is completely blocked by the H_4 ring proton, which resides over the face of the rotor. Such a barrier involving an aromatic ring proton is analogous to the large barriers observed for 9-arylxanthenes,[5] 9-arylfluorenes,[5] and 2-arylacenaphthenones.[8] The ground-state proximity of mesityl and H_4 is also indicated by the NMR spectra: H_4 ab-

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Table I. NMR Chemical Shifts and Shielding Parameters δ'[a]

compd[b]	mesityl methyl protons, ppm (δ)		
	outside, δ'	para, δ'	inside, δ'
1[c,d]	2.45, −0.22	2.30, −0.07	1.95, 0.28
2[d]	2.45, −0.22	2.30, −0.07	1.90, 0.33
2	2.44, −0.21	2.30, −0.07	1.87, 0.36
3[d]	2.46, −0.23	2.28, −0.05	1.90, 0.33
3	2.41, −0.18	2.25, −0.02	1.89, 0.34
2-hydroxy-2-mesitylacenaphthenone[d-f]	2.75, −0.52	2.21, 0.02	1.50, 0.73
2-mesitylacenaphthenone[e]	2.47, −0.24	2.18, 0.05	1.36, 0.87
2-mesityl-*trans*-1,2-acenaphthenediol[e]	2.49, −0.26	2.13, 0.10	1.16, 1.07
cis-2-mesityl-1-acenaphthenol[e]	2.40, −0.17	2.17, 0.06	1.40, 0.83

[a] Anisotropic shielding parameter δ' is defined as $\delta' = 2.23 - \delta$, where 2.23 is the chemical shift of the methyl protons of mesitylene in CCl_4 ("Sadtler Standard Spectra", Sadtler Research Labs, Philadelphia, Pa., 1971, no. 9910) and δ is the chemical shift of a given methyl group on mesityl. [b] Probe temperature was 41–44 °C and the solvent was CCl_4 unless otherwise noted. All concentrations were 100 mg of solute/450–500 μL of solvent. [c] Probe temperature was −15 °C. [d] $CDCl_3$ solvent. [e] Reference 6. [f] Probe temperature was −40 °C.

Table II. Kinetic Parameters for Mesityl Site Exchange[a]

compd	T_c, °C	$\Delta\nu$, Hz	k_1, s^{-1}	$\Delta G^{\ddagger}$, kcal/mol
1[b]	51 ± 1	30	67	16.3 ± 0.1
2[c,d]	175 ± 3	32	71	22.8 ± 0.2
3[c]	198 ± 3	32	71	24.0 ± 0.2

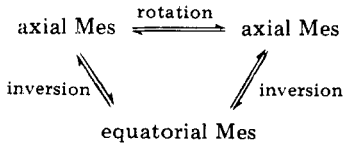
[a] Exchanging nuclei are the ortho methyl protons with a difference of $\Delta\nu$ in chemical shifts. [b] $CDCl_3$ solvent. [c] 1,2,4-Trichlorobenzene solvent. [d] Slowly self-condenses at this temperature to the bis ether (see Experimental Section).

sorbs at about 0.5 ppm upfield of the next highest naphthalene ring proton in all three compounds. Although equatorial rotation is blocked, axial rotation is relatively unhindered. Consequently, the H_4 barrier may be surmounted by a pyran ring inversion at the appropriate time followed by an axial-state rotation and final relaxation to the methyl-exchanged ground state. The three-step process is illustrated in Chart II. In the ideal case, the observed barrier height $\Delta G^{\ddagger}$ would therefore be given by eq 1, where ΔG_{inv} is the difference in free

$$\Delta G^{\ddagger} = \Delta G_{inv} + \Delta G^{\ddagger}_{rot} \quad (1)$$

energy of the axial and equatorial inversion states and $\Delta G^{\ddagger}_{rot}$ is the free energy of activation for mesityl rotation in the axial state. The space-filling models suggest that the lowest energy route for site exchange in **2** and **3** would be for mesityl to be in the axial-state energy well but for the pyran ring to be slightly flattened from its ideal conformation. The rotational activated complex would principally involve transannular engagement of the inside methyl with the H_1 proton and a simultaneous residual engagement of the outside methyl with the H_4 proton. The barrier is evidently higher in **3** than in **2** because of a greater buttressing effect on H_1 by OCH_3 vs. OH or a larger ΔG_{inv} term. Since naphthalide **1** has essentially no substituent at the 1 position, its rotational barrier is very slight in the axial state, and thus a large portion of its observed site-exchange barrier is probably due to the ΔG_{inv} term in eq 1.

Chart II. Proposed Site-Exchange Mechanism for 3-Mesitylnaphthopyrans



Experimental Section

General.[14] IR spectroscopy employed approximately 4% solutions in the solvents indicated; UV spectroscopy employed hexane solutions with λ_{max} reported. NMR spectra were recorded at 500-Hz sweep width (from Me_4Si) at concentrations of 100 mg of solute/450–500 μL of solvent and 41–44 °C probe temperature on Varian A-60A or A56/60 spectrometers unless otherwise noted.

Variable-Temperature NMR. High-temperature runs employed purified 1,2,4-trichlorobenzene as solvent. Temperature control employed a Varian V-6057 variable-temperature accessory; the probe temperature was measured by the peak separations of methanol or ethylene glycol or by thermocouple. Thermal equilibrium was allowed before a spectrum was recorded. Generally, several spectra were recorded below and above the coalescence temperature (T_c), and the bracketing spectra were used to interpolate T_c and estimate its error. Low-temperature spectra were recorded following the high-temperature runs to show that significant thermal decomposition did not occur. Variable-temperature spectra of **1** have been reproduced.[14] $\Delta G^{\ddagger}$ was calculated from the first-order rate constants[6,8] k_1 and the Eyring equation[15] $\Delta G^{\ddagger} = 4.576T(10.319 + \log T - \log k_1)$, where T is the coalescence temperature T_c in degrees kelvin; reported errors in $\Delta G^{\ddagger}$ were determined from the first derivative of the Eyring equation and the estimated errors in T_c.

NMR Spectrum of 3-Mesitylnaphthalide[16] (1): NMR ($CDCl_3$, −15 °C) δ 1.95 (s, 3 H, inside Me), 2.30 (s, 3 H, para Me), 2.45 (s, 3 H, outside Me), 6.83 (bd s with fine structure, inside Mes ring proton), 6.90 (bd s with fine structure overlapping the 6.83 peak, outside Mes ring proton), the 6.83 and 6.90 peaks together cover the H_4 naphthalene ring proton absorption, total area 3 H, 7.2–8.2 (complex m, 6 H, naphthalene ring protons with H_3 superimposed), 7.24 (H_3, see **1-*d*** below for assignment).

NMR ($CDCl_3$, 44 °C) δ 2.0 (very broad s, inside Me), 2.30 (s, para Me), 2.4 (very broad s, outside Me) (total preceding area 9 H), 6.9 (unresolved m, total area 3 H, H_4 naphthalene ring proton superimposed on Mes ring protons), 7.26 (s, 1 H, H_3), 7.25–8.6 (complex m, remaining naphthalene ring protons).

3-Mesitylnaphthalide-3-d (1-*d*). A solution of 1.0 g of 2-hydroxy-2-mesitylacenaphthenone[6] in 25 mL of benzene was extracted three times with 2-mL portions of deuterium oxide (99.7%) and dried by filtration through Na_2SO_4 on glass wool. The solution was then treated with potassium *tert*-butoxide analogously to the preparation[16] of **1** to give **1-*d***: NMR ($CDCl_3$, ~30 °C, Varian T-60 spectrometer) diminished or absent δ 7.24–7.26 peak.

***trans*-1-Hydroxy-3-mesityl-1*H*,3*H*-naphtho[1,8-*cd*]pyran (2).** To a stirred mixture of 0.2 g of $LiAlH_4$ and 100 mL of ethyl ether was added 2.0 g of naphthalide **1**. The mixture was stirred for 5 min, and 100 mL of benzene was added followed by ethyl acetate dropwise. The mixture was poured into saturated NH_4Cl and worked up to give a colorless syrup, which crystallized from *n*-heptane to give 2.0 g (99%) of white material, mp 169–172 °C. Recrystallization from toluene–heptane gave pure hemiacetal **2**: mp 176–177 °C; IR ($CHCl_3$) 3580 cm^{-1}; UV 206 nm (ϵ 38 000), 229 (70 700), 288 (8000); NMR ($CDCl_3$) δ 1.90 (s, 3 H, inside Me), 2.30 (s, 3 H, para Me), 2.45 (s, 3 H, outside Me), 3.52 (d, J = 4 Hz, 1 H, OH), 6.30 (d, J = 4 Hz, 1 H, H_1), 6.7–7.0 (4 H, H_3, H_4, and Mes ring protons), 6.8 (approximate position for both H_3 and H_4), 6.92 (both Mes ring protons), 7.1–7.9 (complex m, 5 H, remaining naphthalene ring protons); mass spectrum (low eV),

m/e (rel intensity) 304 (18), 147 (100). Anal. Calcd for $C_{21}H_{20}O_2$: C, 82.86; H, 6.62. Found: C, 82.68; H, 6.61.

Hemiacetal **2** readily undergoes self-condensation to **bis[3-mesityl-1*H*,3*H*-naphtho[1,8-*cd*]pyran-1-yl] ether.** For example, 2.2 g of **2** under argon was heated at 200 °C for 3 h and the yellow glass was crystallized from toluene–heptane (or acetone) to give 0.8 g of white material, which may be recrystallized from methyl ethyl ketone to give the bis ether: mp 265–267 °C; IR (CCl_4) no OH or CO absorption; NMR ($CDCl_3$) δ 1.99 (s, inside Mes methyl), 2.36 (s, para Me), 2.57 (s, outside Me), 6.7–7.9 (complex m, naphthalene ring protons); mass spectrum *m/e* 590, 589, 572. Adventitious DCl in unpurified stock $CDCl_3$ NMR solvent appears to cause significant self-condensation of **2** to the ether.

***trans*-1-Methoxy-3-mesityl-1*H*,3*H*-naphtho[1,8-*cd*]pyran (3). Method A.** A mixture of 0.3 g (1 mmol) of hemiacetal **2** and 2 mL of absolute methanol was warmed briefly and filtered to give a quantitative yield of pure acetal **3**: mp 146–147 °C; IR ($CHCl_3$) no OH or CO absorption; NMR ($CDCl_3$) δ 1.90 (s, 3 H, inside Me), 2.28 (s, 3 H, para Me), 2.46 (s, 3 H, outside Me), 3.66 (s, 3 H, OMe), 5.86 (s, 1 H, H_1), 6.7–7.0 (4 H, H_3, H_4, and Mes ring protons), 6.79 (H_3), 6.87 (inside Mes ring proton), 6.93 (outside Mes ring proton), 7.3–7.9 (5 H, remaining naphthalene ring protons). Anal. Calcd for $C_{22}H_{22}O_2$: C, 82.98; H, 6.97. Found: C, 82.98; H, 6.75.

Method B. A mixture of 1.0 g of the bis ether, formed from **2** as above, and 40 mL of absolute methanol containing 1 drop of concentrated H_2SO_4 was refluxed for 20 min and worked up to give acetal **3**.

1-Hydroxy-1-methyl-3-mesityl-1*H*,3*H*-naphtho[1,8-*cd*]pyran.[13] To a stirred mixture of 9.0 mmol of methyllithium (from Alfa) and ether was rapidly added 0.6 g (2.0 mmol) of naphthalide **1**. After being stirred for 1 h, the mixture was worked up (as for hemiacetal **2**) to give pure methyl hemiketal: mp 148–149 °C; IR ($CHCl_3$) 3575 cm^{-1}; UV 206 nm (ε 38 200), 229 (70 300), 288 (7600); NMR ($CDCl_3$) δ 1.93 (s, 3 H, inside Me), 1.95 (s, 3 H, ketal methyl), 2.29 (s, 3 H, para Me), 2.44 (s, 3 H, outside Me), 2.84 (s, 1 H, OH), 6.6–7.0 (4 H, H_3, H_4, and Mes ring protons), 7.1–7.9 (5 H, remaining naphthalene ring protons); mass spectrum (30 eV), *m/e* (rel intensity) 318 (16), 300 (24), 171 (21), 147 (100). Anal. Calcd for $C_{22}H_{22}O_2$: C, 82.98; H, 6.97. Found: C, 82.87; H, 6.97.

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Registry No.—**1**, 69502-46-1; **1d**, 69502-49-4; **2**, 69502-47-2; **3**, 69502-48-3; bis[3-mesityl-1*H*,3*H*-naphtho[1,8-*cd*]pyran-1-yl ether, 69502-50-7; 1-hydroxy-1-methyl-3-mesityl-1*H*,3*H*-naphtho[1,8-*cd*]pyran, 69502-51-8; 2-hydroxy-2-mesitylacenaphthenone, 59261-60-8.

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Multiple Horner–Emmons Cyclizations as a Route to Nonbenzenoid Aromatics. Synthesis of Polycyclic Dodecalenes

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Quadruple Horner–Emmons cyclization reaction between the tetraaldehyde **6** and the bis phosphonate **7** afforded (9*E*,14*E*,24*E*,29*E*)-hexabenzo[*d,f,jk,o,q,uv*]dodecalene (**1a**) and its 9*E*,14*Z*,24*Z*,29*E* isomer (**1b**) in 4.2 and 0.4% yield, respectively. The analogous reaction between the tetrakis phosphonate **8** and the dialdehyde **4** afforded **1a** in 0.3% yield. The double Horner–Emmons reaction between **4** and **7** afforded (9*E*,19*E*)-tetrabenzo[*a,c,g,i*]cyclododecene (**2a**) in 8.0% yield. The advantages of the multiple Horner–Emmons reaction in the synthesis of polycyclic nonbenzenoid aromatics as compared with the conventional multiple Wittig reaction are discussed.

The ISNA 3 demonstrated that annulenoannulenes are currently one of the major topics of interest and activity in the field of nonbenzenoid aromatic chemistry.[1] An annulenoannulene results from the fusion of two aromatic rings to form a π system with one or more bonds in common. It appears that the aromaticity of all annulenoannulenes is determined by the nature of the fused rings rather than by the size of the periphery.[2] Vogel's magnificant synthesis of octalene, the prototype of the [4*n*]annuleno[4*n*]annulenes, is considered a milestone of "aromaticity".[3] Octalene was characterized as a very reactive polyolefin. The proposal that two anti-Hückel rings fused might yield an aromatic system[4] has been shown to be invalid.

The present article describes a synthesis of hexabenzo[*d,f,jk,o,q,uv*]dodecalene (**1**), a polycyclic [12]-annuleno[12]annulene.

One of the valuable methods for the synthesis of nonbenzenoic aromatic systems is the bis Wittig reaction.[5] The reaction involves double intermolecular Wittig reactions between 1 mol of a dicarbonyl and 1 mol of a bis(alkylidenetriphenylphosphorane) leading to the unsaturated cyclic compounds. Polycarbocyclic and heterocyclic systems are par-

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