Regioselectivity in Diels–Alder reactions of pyranobenzoquinones

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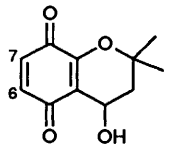
The pyranobenzoquinone **1** was reacted with the 1-azadiene **5** to give the pyranoquinolinquinone **9** that upon dehydration furnished quinone **10**. The structural assignment for **10** was established by an unambiguous method of synthesis. The treatment of the 7-hydroxy quinoline-5,8-dione with 3-methylbutanal gave significant amounts of the allylquinone **13** that, under reaction with 2,3-dichloro-5-6-dicyano-1,4-benzoquinone, afforded quinones **10** and **14**. We also report the reaction of pyranobenzoquinone **16** with trimethylsilyldiazomethane **15** to give **17**. All of our results are analysed in terms of the HSAB principle by calculating the resultant molecular hardnesses for a space charge separation transition state for each atom position of reagent by using semiempircal MO methods. We show that this procedure predicts always the main product for the cycloaddition reactions studied.

Recently, we reported a new method to obtain pyranonaphthoquinones through a Diels–Alder reaction of the pyranobenzoquinone **1** and 1-substituted electron-rich dienes.[1] Thus, the



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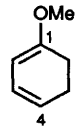

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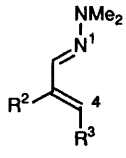

3 R^2 = Me; R^3 = H
4 R^2 = H; R^3 = Me
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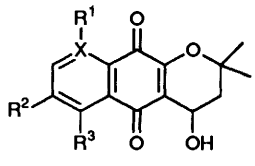
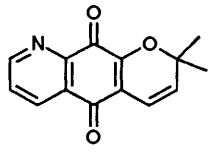


6 X = C; R^1 = OMe; R^2 = R^3 = H
7 X = N; R^2 = Me; R^3 = H
8 X = N; R^2 = H; R^3 = Me
9 X = N; R^2 = R^3 = H



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pyranonaphthoquinone **6** was obtained in 46% yield using this methodology through a regioselective reaction of the pyranobenzoquinone **1** with 1-methoxycyclohexa-1,3-diene (**2**). This result showed that the more nucleophilic terminus of the diene adds at the C-6 position of the quinone **1**. The regiochemistry of the cycloaddition was controlled probably by the electron-donating effect of the alkoxy moiety (pyran ring) making the C-6 atom the more electron deficient of the unsubstituted double bond in the quinone **1**.

On the reaction of the quinone **1** with the 1-azadienes **3** and **4**, the heterocyclic quinones **7** and **8** were obtained in 57% and 50% yield, respectively. The structures of **7** and **8** were proposed considering the above result and that C-4 atom of these dienes is the more electron rich centre.[1] In order to confirm the regiochemistry of the cycloaddition of the quinone **1** with 1-azadienes, in this paper we describe the synthesis of the pyranoquinone **10** by the cycloaddition route and by an unambiguous method.

The frontier molecular orbital theory (FMO) has been extensively used to rationalize the observed regioselectivities of Diels–Alder cycloaddition reactions in quinones.[2] For the cases involved in this work, there are no similar studies on pyranoquinones where the various electronic and steric effects of substituents and heteroatoms might make predictions of reaction sites difficult. In this paper we make use of chemical hardness concepts in a space charge separation transition state for each reagent to corroborate the observed regiochemistry in Diels–Alder reactions of pyranobenzoquinones.

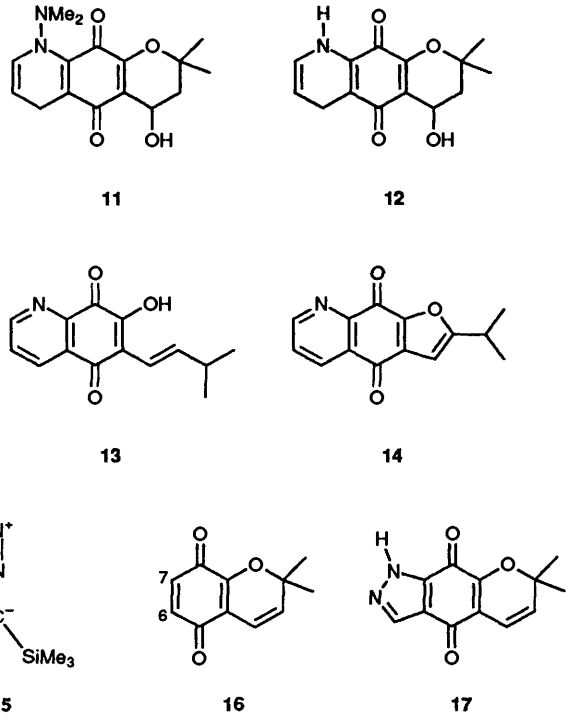
Results and discussion

The reaction of the quinone **1** with the 1-azadiene **5** gave[3] an unstable adduct, which was oxidized *in situ* with silver(I) oxide to afford the pyranoquinolinequinone **9** in 33% yield. We think that the low yield of this process may have been due to decomposition of the adduct during the reaction sequence. Fillion *et al.*,[4] obtained evidence that the initial adduct **11** easily lost dimethylamine affording a 1,4-dihydropyridine derivative such as **12**, which under oxidation conditions gave the corresponding azaquinone **9**. The use of 1-azadienes such as **3**–**5** to build nitrogen containing six-membered rings is well documented.[5] Dehydration of the alcohol **9** in the presence of toluene-*p*-sulfonic acid furnished the quinone **10** (68%). The structural assignment for the quinones **9** and **10** was verified after the unambiguous synthesis of the pyranoquinone **10**.

The synthesis of pyranonaphthoquinones through the reaction of 2-hydroxynaptho-1,4-quinones with aldehydes has been widely used,[6] but no examples are reported for heterocyclic hydroxyquinones. In view of the potential usefulness of this reaction for our purpose, we decided to study its applicability for the synthesis of the quinone **10**. The treatment of 7-hydroxy-5,8-dihydroquinoline-5,8-dione with 3-methylbutanal in an acid medium gave a complex mixture of products, however when the reaction was carried out in a basic medium the allylquinone **13** was obtained in 60% yield. After reaction of **13** with 2,3-dichloro-5,6-dicyanobenzo-1,4-quinone (DDQ) the quinones **10** and **14** were obtained in 38% and 12% yield, respectively.

The mp and spectral properties of pyranonaphthoquinone **10** obtained by both methods were identical. Therefore we confirmed that in the cycloaddition reaction of pyranobenzoquinone **1** with 1-azadienes, the C-4 atom of the diene became attached at the C-6 atom of the quinone.

Next, the 1,3-dipolar cycloaddition reactions of pyranobenzoquinone **16**, easily obtained by dehydration of **1**, with trimethylsilyldiazomethane **15**, was studied. The procedure for the reaction of **15** with quinones was described recently.[7] Thus,



the treatment of **16** with one equivalent of trimethylsilyldiazomethane gave an adduct that underwent desilylation and air oxidation during the purification process of silica gel column chromatography. The structure proposed for compound **17**, isolated in 83% yield, is based on the described regiochemistry for the quinone **1**, and on the prediction of theoretical calculations for the reaction of **15** with **16** as shown later on.

Model of calculations

The FMO calculations and full geometry optimizations for **1–5**, **15** and **16** were carried out by the semiempirical AM1 method implemented in the AMPAC package.[8] The results for the frontier π-orbital coefficients are given in Table 1.

First of all, the ground state values for the LUMO π-coefficients of sites 6 and 7 for quinone **1** are not different enough to support the regioselective formation of quinone **6** through the cycloaddition reaction of **1** and **2**.[1] Moreover, similar trends are seen for **16** in spite of the fact that the latter one differs from quinone **1** because of a different substituent at position 4. Thus, these figures do not provide us with strong arguments in favour of the observed regiochemistry for these quinone compounds.

Then our attention was turned to another important theoretical treatment that can assess compound reactivity like the soft–hard acid–base theory as proposed some time ago by Pearson[9] and recently established on solid and almost quantitative grounds by means of Density Functional Theory (DFT).[10–13] Briefly stated, soft bases are donor atoms of high polarizability, low electronegativity and are easily oxidized while hard bases are difficult to polarize, highly electronegative and difficult to reduce. Soft acids are acceptor species of low positive charge, large in size and easily polarizable while hard acids have a high positive charge, small size and are poorly polarizable. For a molecular system made from electrons and nuclei reaching an equilibrium state DFT shows that the electronegativity χ and the absolute hardness η are the first and the second derivatives of the electronic energy with respect to the number of electrons, respectively. Namely

Table 1 Transition state electronegativity, χ, hardness, η, and ground state π-MO coefficients of molecules[a] for Diels–Alder reactions

Compound	Position	χ^{TS}/eV	η^{TS}/eV	π-Coefficient
1[b]	6	11.090	0.885[d]	0.3731[e]
(η^{G}_{n+2} = 1.706)	7	11.097	0.727	0.3490
2b	1	12.003	1.094	0.4108[f]
(η^{G}_{n} = 1.533)	4	11.759	1.218[d]	0.4476
3[c]	1	11.656	0.681	0.2831[f]
(η^{G}_{n} = 1.246)	4	11.725	0.803[d]	0.4330
4[c]	1	11.681	0.788	0.3074[f]
(η^{G}_{n} = 1.212)	4	11.935	0.804[d]	0.4038
5[c]	1	11.752	0.687	0.2949[f]
(η^{G}_{n} = 1.197)	4	11.931	0.803[d]	0.3852
15[c]	1	12.397	0.153	−0.1699[f]
(η^{G}_{n} = 0.934)	3	11.609	0.941[d]	0.3726
16[b]	6	10.944	0.774[d]	0.3627[e]
(η^{G}_{n+2} = 1.351)	7	11.037	0.674	0.3239

[a] Optimized geometry by AM1 Hamiltonian from the AMPAC package. [b] Values for the n molecular electrons TS. [c] Values for the n − 2 molecular electrons TS. [d] The hardest site. Orbital energies are calculated by EHT methods. [e] Ground State values from the AMPAC package for the LUMO level. [f] Ground State values from the AMPAC package for the HOMO level.

$$\chi = -\left(\frac{\delta E}{\delta n}\right)_v \quad \text{and} \quad \eta = \tfrac{1}{2}\left(\frac{\delta^2 E}{\delta n^2}\right)_v \qquad (1)$$

where v is the external potential due to the nuclei. Moreover, the electronegativity is not a simple function of the state of the system. Instead, it depends upon whether the system can only lose electrons ($\chi = E_i$, the ionization potential) or it can only gain electrons ($\chi = E_a$, the electron affinity). It turns out that when we deal with molecular systems for which both gaining and losing electrons are allowed, the finite approximation $\chi = (E_i + E_a)/2$ is used.[14] In DFT, Koopman's theorem is strictly obeyed so that E_i and E_a are replaced by the HOMO and LUMO energies.

On the other hand, the hardness measures the resistance of the electronegativity to a change in the number of electrons, $2\eta = (\delta\chi/\delta n)_v$ and it is intimately related to the HOMO–LUMO gap for doubly occupied energy orbitals.[9,13] Thus, eqn. (1) becomes

$$\chi = -\frac{\varepsilon_{HOMO} + \varepsilon_{LUMO}}{2} \quad \text{and} \quad \eta = \frac{-\varepsilon_{HOMO} + \varepsilon_{LUMO}}{2} \qquad (2)$$

We plan to use these concepts to predict the regiochemistry of cycloaddition of dienes to pyranobenzoquinones and fused heterocyclic ring systems. Like other theoretical treatments on this matter, steric effects are not considered here.

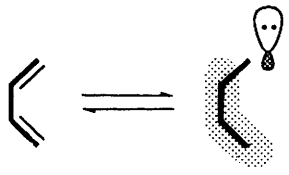
The rate-determining step for aromatic electrophilic or nucleophilic substitutions is the formation of a space charge separation in which the transition state (TS) strongly resembles the intermediate arenium ion of Wheland type.[15] Initially, these steps are (with few exceptions) rapid and reversible so that the formation of various isomers is dependent on the activation energy necessary to form this intermediate complex. Anything that increases the stability of the specific intermediate is expected to lower the activation energy required to attain it. This point has been stressed recently to introduce the activation hardness ($\Delta\eta^{\ddagger}$) concept and its relationship to the activation energy, $\Delta E^{\ddagger} = 2\Delta\eta^{\ddagger}$ for a two electrons process, as a guide to predict the predominant product of the electrophilic substitution in aromatic molecules.[16] For the nucleophile species the activation hardness can be written as eqn. (3), where

$$\Delta\eta^{\ddagger} = \eta^{G}_{n} - \eta^{TS}_{n-2} \qquad (3)$$

η_n^G is the molecular hardness in the ground state (G) with n electrons and η_{n-2}^{TS} is the molecular hardness in a transition state (TS) with $n - 2$ electrons since two of them are potentially available for an electrophile at a specific site. Obviously, for an electrophile species one simply changes n electrons by $n + 2$ electrons so that the argument that follows applies to both electrophile and nucleophile species: the harder is the transition state molecule the lower is the activation energy to achieve it. This argument provides us with a simple tool to determine the preferred reaction site within a molecule when there are several possible sites available. Besides, it agrees with the principle of maximum hardness.[9,12]

Our main interest here is to use a similar transition state model to support our experimental results that cycloaddition reactions with unsymmetrical dienes to a specific quinone double bond occur with a given regioselectivity that is dependent upon the molecular hardness values in the TS for each reagent. It will be shown that this approach together with the HSAB principle[10,11] that is, 'hard acid centres prefer to coordinate to hard base centres and soft acid centres to soft base centres', will allow us to determine the regiochemistry for the Diels–Alder reactions described in this paper. Accordingly, we will assign a preferential orientation for those positions that show the highest hardness for the transition states involved for both reagents.[16] In addition to this, the harder is the TS for both reacting molecules the faster is the reaction.

The manner to learn about the preferential site of a quinone molecule to add electron-rich asymmetric dienes is to allow for the localization—at a given quinone atom—of the charge induced on the TS diene molecule. Scheme 1 describes the case



Reactant
n molecular electrons

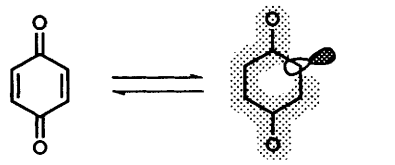
Transition state
$n - 2$ molecular electrons

Scheme 1

when two π-electrons from the diene ground state π-system are separated from the other π electrons to build a TS molecule with $n - 2$ electrons. These two electrons are bound to an atom position in a $2p_z$ local orbital where the electrophilic substitution will take place and they do not interact with the $n - 2$ remaining electrons from the molecular π and σ framework. In practice, this means that we neglect all the intramolecular interactions and overlap terms involving this orbital. This procedure yields a new basis set for the molecule (including a modified π-system) for which we calculate the TS eigenvalues to obtain the molecular hardness η_{n-2}^{TS} according to eqn. (2).

Next, we perform a similar transition state calculation but this time the $2p_z$ orbital and charge are assigned to another centre of the diene molecule. The transition state hardnesses obtained in this manner for dienes **2–5** and **16** are given in Table 1.

Scheme 2 shows the corresponding model for the quinone electron acceptor molecule acting as dienophile. The transition state molecule keeps the original n π- and σ-electrons system in a modified basis set because one $2p_z$ empty orbital is localized as before at an atom position where the nucleophile will attack. Next, one calculates the TS orbital eigenvalues for each of the selected atom sites. Finally, transition state molecular hardnesses thus obtained are used as orientation indexes for the regioselective cycloaddition according to the HSAB principle.



Ground state
n molecular electrons

Transition state
n molecular electrons

Scheme 2

The theoretical description for the TS molecular hardnesses given above is suitable for direct methods of calculations like the extended Huckel method (EHT) using the single zeta Slater-type atomic orbitals.[17] Thus, for each ground state optimized geometry reagent the TS orbital energies were calculated by cancelling the overlap integral values between the isolated atomic orbital at the specific site (eventually holding the local charge) and all the other orbitals in the S-matrix (thereby their contributions to the non-diagonal elements of the H-matrix are cancelled out). The calculated TS molecular electronegativities and hardnesses [see eqn. (2)] are given in Table 1 and used as alternative regioselective indexes for cycloaddition reactions.

All of our experimental results are in agreement with the theoretical predictions given by the HSAB principle as stated above.[9–13] To show this, let us take the TS molecular hardness values for the electron-rich dienes. For example, it is seen that for **2** the activation hardness is smaller (the TS hardness is larger) when position 4 is the active electron donor centre according to Scheme 2, a fact that it is not so clear when comparing the ground state π-orbital coefficients (see Table 1). Similar trends are observed for the azadienes **3–5**. However, it is important to realize also that the influence of the aza group for all of them makes the use of ground state frontier π-orbital coefficients more predictable. In addition to this, for trimethylsilyldiazomethane (**15**) one finds a large difference in TS hardness when comparing positions 1 and 3: the lowest activation hardness is obtained when position 3 is the active centre.

The results for the electron acceptor molecules in Table 1 indicate that for **1** the activation hardness for the dienophile is smaller when the $2p_z$ accepting orbital is at the atom site 6 of the external quinone ring double bond. Table 1 shows that such a clear distinction between positions 6 and 7 is not provided by their π-LUMO coefficients. Thus, for **1** the TS molecule becomes harder when position 6 is the active local site. Similar findings are seen for **16** where, again, the hardest TS molecule is obtained when position 6 acts as the electrophilic centre.

Our theoretical results confirm that dienes like **2 – 5** in a transition state having $n - 2$ molecular electrons as shown in Scheme 1 achieve the highest value for TS molecular hardnesses when the two electrons are localized at site 4. Besides, quinones like **1** and **16** with n molecular electrons in a transition state, as shown in Scheme 2, show smaller activation hardnesses when the accepting centre is at site 6 thus yielding the experimentally observed main products described here: the C-4 atom of the dienes becomes attached at the C-6 atom of the quinone **1** whereas the C-3 atom of **15** becomes attached to C-6 of **16**. The experimental results are thus fully explained by the HSAB principle approach for Diels–Alder reactions when transition state reagents like the ones considered in this work, are invoked.

Experimental

Melting points were determined with a Kofler modified apparatus and are not corrected. IR spectra were obtained on a Perkin-Elmer Model 1310 spectrometer. NMR spectra (^{1}H and

^{13}C) were recorded on a Bruker AM-200 spectrometer, using tetramethylsilane as internal reference and coupling constants are given in Hz. Column chromatography was performed on Merck silica gel (70–230 mesh). Elemental analyses were performed at the *Instituto de Química Orgánica General* (CSIC), Madrid, Spain.

4-Hydroxy-2,2-dimethyl-3,4,5,10-tetrahydro-2*H*-pyrano[3,2-*g*]quinoline-5,10-dione (9)

To a stirred solution of the azadiene **5** (380 mg, 3.88 mmol) in methylene chloride (15 cm^3) at room temperature was added a solution of the quinone **1** (400 mg, 1.92 mmol). After 1.5 h silica gel (1.5 g) was added and after a further 10 min Ag_2O (0.5 g) was added and the mixture was stirred for 5 h. Then the mixture was filtered and the solid filter was rinsed thoroughly with methylene chloride. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography [methylene chloride–ethyl acetate (20:1, then 9:1)] to give the quinone **9** (165 mg, 33%), mp 180–182 °C (decomp.) (Found: C 65.1; H, 5.3; N, 5.5. $C_{14}H_{13}NO_4$ requires C, 64.9; H, 5.05; N, 5.4%); ν_{max}(KBr)/cm^{-1} 3300s (OH), 1680s and 1640s (C=O); δ_H($CDCl_3$) 1.49 (3 H, s, CH_3), 1.59 (3 H, s, CH_3), 2.13 (2 H, eight lines, CH_2), 3.66 (1 H, br s, OH), 5.02 (1 H, t, *J* 6.3, 4-H), 7.68 (1 H, dd, *J* 7.9, 4.7, 7-H), 8.43 (1 H, dd, *J* 7.9, 1.7, 6-H) and 9.02 (1 H, dd, *J* 4.7, 1.7, 8-H); δ_C($CDCl_3$) 26.88, 26.94, 39.6, 59.8, 80.4, 120.2, 127.9, 129.1, 134.1, 147.0, 154.3, 154.7, 184.8 and 205.4.

Dehydration of the quinone 9

A mixture of the quinone **9** (35 mg, 0.14 mmol), toluene (15 cm^3) and toluene-*p*-sulfonic acid (5 mg) was heated to reflux for 4 h. The solvent was evaporated under reduced pressure and the residue was purified by preparative TLC (95% methylene chloride–5% ethyl acetate; silica gel) to give 2.2-dimethyl-5,10-dihydro-2*H*-pyrano[3,2-*g*]quinoline-5,10-dione (**10**) (22 mg, 68%) mp 170 °C (decomp.) (Found: C, 70.0; H, 4.7; N, 5.8. $C_{14}H_{11}NO_3$ requires C, 69.7; H, 4.6; N, 5.8%); ν_{max}(KBr)/cm^{-1} 1690s and 1640s (C=O), 1560 and 1530 (C=C); δ_H($CDCl_3$) 1.59 (6 H, s, 2 CH_3), 5.79 (1 H, d, *J* 10.0, 4-H), 6.65 (1 H, d, *J* 10.0, 3-H), 7.66 (1 H, dd, *J* 7.9, 4.7, 7-H), 8.43 (1 H, dd, *J* 7.9, 1.7, 6-H) and 9.00 (1 H, dd, *J* 4.7, 1.7, 8-H); δ_C($CDCl_3$) 28.5, 81.2, 115.0, 117.6, 127.6, 128.7, 131.6, 134.3, 147.4, 153.2, 154.0, 178.0 and 180.8.

7-Hydroxy-6-(3-methylbut-1-enyl)-5,8-dihydroquinoline-5,8-dione (13)

A stirred mixture of 7-hydroxy-5,8-dihydroquinoline-5,8-dione[18] (300 mg, 1.7 mmol), triethylamine (1.5 cm^3), 3-methylbutanal (1.21 g, 14 mmol) and molecular sieves 4A (2.0 g) was heated to reflux for 7 h. The reaction mixture was evaporated under reduced pressure and the blue residue was partitioned between methylene chloride and hydrochloric acid (1 mol dm^{-3}). The aqueous layer was extracted with methylene chloride (4 × 50 cm^3) and the combined extracts were washed with brine, dried (magnesium sulfate) and filtered. The solvent was removed under reduced pressure to give the quinone **13** (276 mg, 66%) in pure form. Recrystallization of a sample from benzene–cyclohexane (1:1) gave orange needles, mp 162–163 °C (Found: C, 69.0; H, 5.5; N, 5.8. $C_{14}H_{13}NO_3$ requires C, 69.1; H, 5.4; N, 5.8%); ν_{max}(KBr)/cm^{-1} 3320s (OH), 1680s and 1650s (C=O); δ_H($CDCl_3$) 1.13 (6 H, d, *J* 6.7, 2 CH_3), 2.54 (1 H, m, 3′-H), 6.59 (1 H, dd, *J* 1.3, 16.3, 1′-H), 7.12 (1 H, dd, *J* 16.3, 7.3, 2′-H), 7.69 (1 H, dd, *J* 7.9, 4.7, 3-H), 8.46 (1 H, dd, *J* 7.9, 1.7, 4-H) and 8.99 (1 H, dd, *J* 4.7, 1.7, 2-H); δ_C($CDCl_3$) 22.1, 33.6, 115.6, 118.9, 128.4, 129.7, 134.9, 146.0, 151.7, 152.2, 153.9, 179.9 and 183.4.

Reaction of the allylquinone 13 with DDQ

DDQ (120 mg, 0.53 mmol) was added to a stirred solution of the allylquinone **13** (115 mg, 0.47 mmol) in methylene chloride (35 cm^3). After the mixture had been stirred overnight at room temperature, 50 cm^3 of 5% $NaHCO_3$ was added. The aqueous layer was extracted with methylene chloride (2 × 50 cm^3) and the combined organic extracts were dried (anhydrous magnesium sulfate) and filtered. The filtrate was evaporated under reduced pressure and the residue after preparative TLC (70% methylene chloride–30% ethyl acetate; silica gel) gave the pyranoquinone **10** (56 mg, 49%) and furoquinone **14** (18 mg, 16%), mp 213–215 °C (Found: M^+, 243.0739. $C_{14}H_{11}NO_3$ requires M^+, 241.0739); ν_{max}(KBr)/cm^{-1} 1670s (C=O); δ_H($CDCl_3$) 1.39 (6 H, d, *J* 6.9, 2 CH_3), 3.16 [1 H, m, C*H*(CH_3)$_2$], 6.66 (1 H, d, *J* 0.9, 3-H), 7.68 (1 H, dd, *J* 7.9, 4.7, 6-H), 8.50 (1 H, dd, *J* 7.9, 1.8, 5-H) and 9.05 (1 H, dd, *J* 4.7, 1.8, 7-H); δ_C($CDCl_3$) 20.7, 28.5, 102.4, 118.8, 127.1, 130.0, 131.5, 134.8, 148.8, 154.2, 170.7, 171.1 and 179.6.

2,2-Dimethyl-5,8-dihydro-2*H*-1-benzopyran-5,8-dione (16)

A mixture of the quinone (**1**) (150 mg, 0.72 mmol), toluene (40 cm^3) and toluene-*p*-sulfonic acid (5 mg) was heated to reflux for 2.5 h. The solvent was evaporated under reduced pressure and the residue was purified by preparative TLC (95% methylene chloride–5% ethyl acetate; silica gel) to give the quinone **16** (115 mg, 84%), mp 78–80 °C (lit.,[19] 79–80 °C).

7,7-Dimethyl-1,4,7,9-tetrahydropyrano[3,2-f]indazole-4,9-dione (17)

To a stirred solution of the quinone **16** (120 mg, 0.63 mmol) in methylene chloride (25 cm^3) at 0 °C was added trimethylsilyldiazomethane (2 mol dm^{-3} in hexanes; 0.35 cm^3, 0.70 mmol). After 2 h the solvent was evaporated and the residue was purified by column chromatography (R_f 0.30, 85% methylene chloride–15% ethyl acetate; silica gel) to give the quinone **17** (120 mg, 83%) mp 170 °C (decomp.) (Found: C, 62.5; H, 4.5; N, 12.0. $C_{12}H_{10}N_2O_3$ requires C, 62.6; H, 4.4; N, 12.2%); ν_{max}(KBr)/cm^{-1} 3240s (NH and enol OH), 1670s and 1640s (C=O); δ_H([$^2H_6$]DMSO) 1.53 (6 H, s, 2 CH_3), 5.93 (1 H, d, *J* 10.0, 5-H), 6.55 (1 H, d, *J* 10.0, 6-H), 8.54 (1 H, s, 3-H) and 14.4 (1 H, s, enol OH); δ_C([$^2H_6$]DMSO) 31.6, 84.0, 119.0, 121.6, 123.6, 133.6, 134.6, 149.9, 156.7, 178.6 and 181.8.

Computational details

The fully optimized geometries of all the reagents **1**–**5**, **15** and **16** were calculated by the semiempirical method AM1 implemented in the AMPAC program[8] and have been deposited as supplementary material.† The Fletcher–Powell minimization to a self-consistent field that satisfied Herbert's test was accomplished using the 'PRECISE' option. In general, the interatomic distances and angles are not very far from the expected average values. Fig. 1 shows the spatial structures obtained for all of them after optimization.

The input geometry for a given transition state calculation by the EHT method[17] was constructed from the AM1 optimized geometry with the key atom positions moved to the *xy* plane.

† For details of the Supplementary Publications Scheme, see 'Instructions for Authors (1995)', *J. Chem. Soc., Perkin Trans. 2*, 1995, issue 1 [Supp. Pub. No. 57070 (8 pp.)].

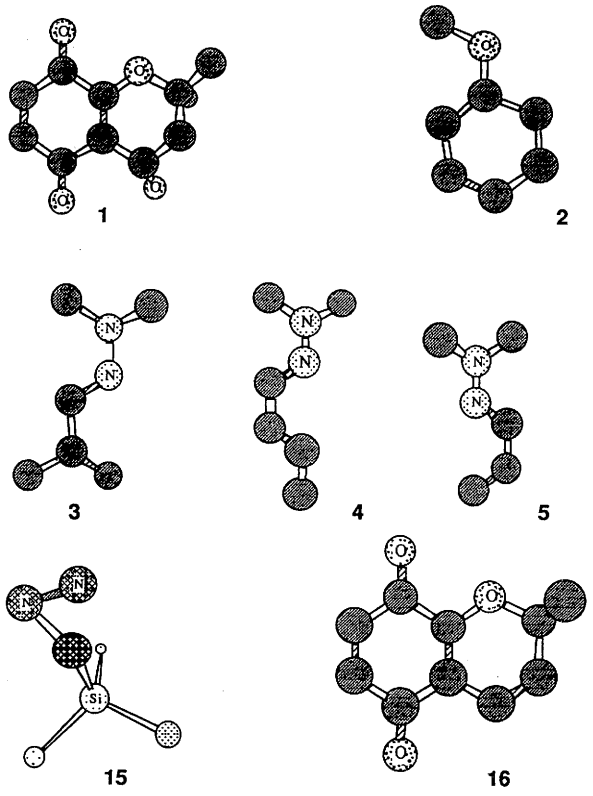


Fig. 1 Ground state optimized structures for reagents **1**–**5**, **15** and **16**. The AMPAC version 2.10 of the AM1 Hamiltonian was used for all of them.

Acknowledgements

We thank *Fondo de Desarrollo Científico y Tecnológico* (Research Grants 91/792 and 1930436) for financial support. We also thank CONICYT and *Dirección de Postgrado Pontificia Universidad Católica de Chile* for a fellowship to C. Q.

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Paper 4/05912C
Received 27*th September* 1994
Accepted 24*th November* 1994