Table I. Naphthoquinones[a]

entry	alkyne	product	from cobalt complex 6	from iron complex 7
1	MeC≡CMe	2,3-dimethyl-1,4-naphthoquinone[c]	73	99
2	EtC≡CEt	2,3-diethyl-1,4-naphthoquinone[d]	90	95
3	PhC≡CPh	2,3-diphenyl-1,4-naphthoquinone[e]	68	88
4	PhC≡CCH$_3$	2-methyl-3-phenyl-1,4-naphthoquinone[f]	78	100
5	*n*-BuC≡CH	2-*n*-butyl-1,4-naphthoquinone[g]	65	95
6	PhC≡CH	2-phenyl-1,4-naphthoquinone[h]	57	94
7	*t*-BuC≡CMe	2-*tert*-butyl-3-methyl-1,4-naphthoquinone[i,j]	72	37
8	EtC≡Callyl	2-ethyl-3-(3-propenyl)-1,4-naphthoquinone[k,j]	80	75
9	EtOC≡CEt[l]	2-ethoxy-3-ethyl-1,4-naphthoquinone[m,j]	89	low yield[n]
10	*n*-BuC≡CSiMe$_3$	2-*n*-butyl-3-(trimethylsilyl)-1,4-naphthoquinone[o,j]	68	22
11	PhC≡C(CH$_2$)$_2$OH	2-(2-hydroxyethyl)-3-phenyl-1,4-naphthoquinone[p,j]	27	81
12	MeC≡CCO$_2$Et	2-carbethoxy-3-methyl-1,4-naphthoquinone[q,j]	0	74
13	EtC≡CCOMe	2-acetyl-3-ethyl-1,4-naphthoquinone[r,j]		68

[a] Reactions with cobalt complex 6 were run in CH_3CN at 110 °C in a sealed tube for 20–40 h in the presence of alkyne (1.5 equiv) and $AgBF_4$ (2.0 equiv). Reactions with iron complex 7 were conducted in CH_3CN at 100 °C in a sealed tube for 6 h in the presence of alkyne (1.1 equiv). All previously known compounds were analyzed by IR and NMR spectroscopy and corroborated with literature data. New compounds were further identified by elemental analysis. [b] The indicated yields refer to isolated products purified by chromatography. [c] Reference 14. [d] Reference 10. [e] Reference 15. [f] Reference 11. [g] Reference 16. [h] Reference 17. [i] Mp 33.5–34 °C. [j] Satisfactory IR, NMR, and elemental analysis were obtained. [k] Mp 38–38.5 °C. [l] Four equivalents of $AgBF_4$ was used. [m] Mp 51–51.5 °C. [n] An iron complex derived by incorporation of one molecule of the alkyne into complex 7 was the major product of this reaction. [o] An oil. [p] Acetate derivative mp 106–107 °C. [q] Mp 97.5–98 °C. [r] Mp 69–70 °C.

of the naphthoquinone product using cobalt instead of iron. Also, 1-ethoxy-1-butyne (entry 9) gives a high yield of 2-ethoxy-3-ethyl-1,4-naphthoquinone in the cobalt system but forms an, as yet, unidentified iron complex on reaction with metallacycle **7**. As indicated in Table I, entry 8, both the iron and cobalt complexes react with 1-hepten-4-yne exclusively at the alkyne functionality without interference from the olefin to give 2-allyl-3-ethyl-1,4-naphthoquinone, and an alcohol β to the alkyne functionality, as in 4-phenyl-3-butyne-1-ol (entry 11), is carried through the reaction with iron complex **7** without trouble. Typical reaction conditions are as follows:

Reaction with Cobalt Complex 6. To a heavy-walled glass reaction tube, sealable by means of a two-piece threaded aluminum coupling and internal Teflon sealing disk, was added $AgBF_4$ (343 mg, 1.76 mmol) under a nitrogen atmosphere. The cobalt complex **6** (660 mg, 0.88 mmol), 3-hexyne (108 mg, 1.32 mmol), a small magnetic stirring bar, and CH_3CN (3 mL) were then added and the reaction vessel was sealed. The heavy-walled glass tube was immersed in an oil bath maintained at 110 °C and the reaction was magnetically stirred. After 40 h, the reaction was filtered with the aid of CH_2Cl_2 and condensed on a rotary evaporator, and the residue was passed through a 15 × 3 cm silica gel column with CH_2Cl_2. The resulting yellow solution was evaporated to dryness and the residue was chromatographed by medium-pressure LC (Merck Lobar prepacked column, 3:2 hexane–CH_2Cl_2) to yield 169 mg, 90%, of 2,3-diethyl-1,4-naphthoquinone, mp 70–71 °C, from petroleum ether (lit.[10] mp 72–73 °C).

Reaction with Iron Complex 7. To the reaction vessel described above were added iron complex **7** (60 mg, 0.20 mmol), 1-phenyl-1-propyne (26 mg, 0.22 mmol), CH_3CN (0.75 mL), and a small magnetic stirring bar. After stirring at 100 °C for 6 h, the reaction was allowed to cool and was partitioned between CH_2Cl_2 and 1.2 M aqueous HCl. The organic layer was dried (powdered Na_2SO_4), filtered, and condensed on a rotary evaporator, and the residue was chromatographed on Merck 20 × 20 cm × 2 mm silica gel plates (1:1 CH_2Cl_2–hexane) to yield 50 mg, 100% yield, of 2-methyl-3-phenyl-1,4-naphthoquinone, mp 111–112 °C, from petroleum ether (lit.[11] mp 112–113 °C).

The results described herein support the feasibility of metallacyclopent-3-ene-2,5-diones as intermediates in the formation of quinones from alkynes and metal carbonyls. From the perspective of synthetic organic chemistry, this work demonstrates one specific example of a potentially general, convergent route to organic ring compounds by the intentional design of metallacycles as synthetic reagents.[12] Since substituted benzocyclobutenediones can be synthesized in good yields by the vapor-phase pyrolysis of anthracene adducts of the corresponding phthalazine-1,4-diones,[13] convergent syntheses of diverse 1,4-naphthoquinones could be realized by using this organotransition-metal methodology if regioselective reaction with unsymmetrical alkynes could be demonstrated. We are currently investigating this aspect of the reaction as well as synthetic extentions of the chemistry described above.

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Lanny S. Liebeskind,* Sherrol L. Baysdon, Michael S. South
Department of Chemistry, Florida State University
Tallahassee, Florida 32306
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On Binding in Subunit Systems

Sir:

Interations between subunits in enzyme systems are regarded as *allosteric* when binding at one site induces conformational changes which alter the receptivity of a remote site.[1] Such interactions may be manisfested as *positive* cooperativity (as in hemoglobin), *negative* cooperativity,[2] or *noncooperativity*. We have recently shown that processes involving smaller molecules

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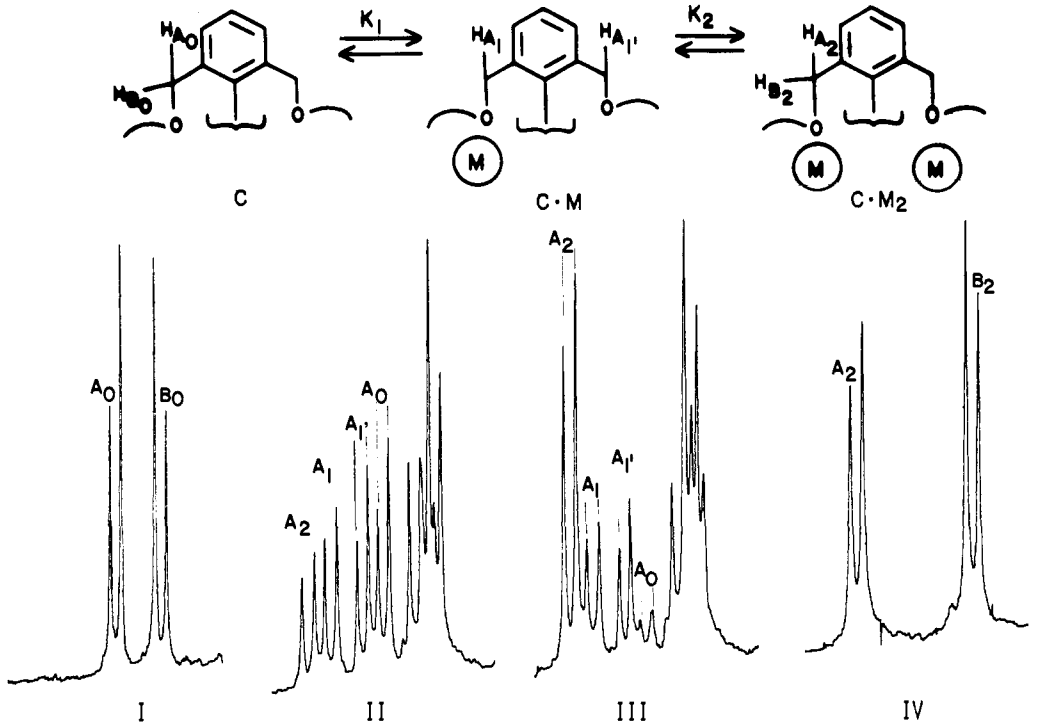
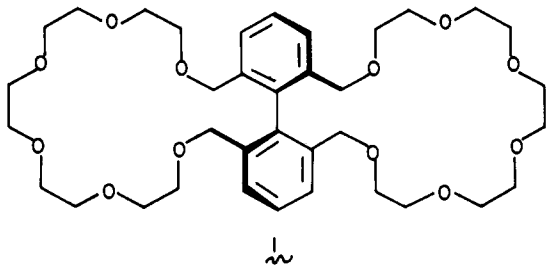


Figure 1. Changes in the NMR spectrum (300 MHz) of the benzyl protons of 1 in benzene-d_6 at 273 K as $Hg(CF_3)_2$ is added. (I) Free 1, (II) 44% sites occupied, (III) 65% sites occupied, (IV) saturated.

in solution can be controlled by allosteric effects[3] and here we record the binding behavior of a subunit system.

The macrobicyclic **1** incorporates the minimum requirements



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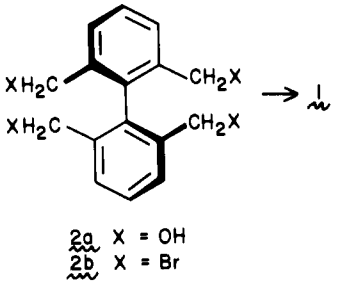
for a subunit model: symmetrically disposed polyether binding sites and a mechanism by which information at one such receptor can be transmitted to the other by conformational changes. Specifically, that distance between the benzyl carbons which is optimum for binding to one site is faithfully reproduced at the other by the rigidity of the biphenyl system. This simple, mechanical action available to **1** is precisely the feature which distinguishes it from the host of other known macrobicyclic polyethers. Substance **1** was obtained as a heavy oil in >50% yield through the action of KH and pentaethylene glycol[4] on the tetrabromide[5,6] **2b**, itself prepared from the tetraalcohol **2a**. The latter is readily available from pyrene through ozonolysis followed by reduction.[6]

In subunit systems such as **1**, the quantitative description of binding requires measurements over a large range, i.e., from a small fraction of sites occupied to near saturation.[7] A number



2a X = OH
2b X = Br

of techniques, such as extraction of alkali pictrates,[8] did not meet this requirement. Moreover, the magnitude of the association constants with alkali metals precluded accurate potentiometric titrations[9] with ion-selective electrodes. An ideal method was provided by NMR using the new guest, $Hg(CF_3)_2$.[10] Unlike alkali metals, which give only averaged spectra due to rapid exchange, equilibria with $Hg(CF_3)_2$ and this ether involve processes which are relatively slow. For example, in benzene-d_6, gradual addition of $Hg(CF_3)_2$ at 273 K gave a series of NMR spectra for the benzyl protons summarized in Figure 1. The individual species, unbound **1** (C), the 1:1 complex (C·M), and the 2:1 complex ($C·M_2$) were resolved in the NMR spectra and could be determined by integration over the range 20–90% of sites occupied. By use of ^{19}F NMR, the concentrations of the free and complexed $Hg(CF_3)_2$ could be determined simultaneously from their resonances at −36.4 (from $CFCl_3$) and −37.3 ppm, respectively.

The structures of these Hg complexes are unknown. If binding involved only a few of the oxygens of **1**, other crowns should also be effective, yet no NMR evidence for complexation was observed either with 18-crown-6 or with smaller (19-crown-5) homologues of **1**. Moreover, such complexes would be expected to show low kinetic stability. Space-filling models barely permit the passage of the CF_3 group through the 22-membered ring of **1** but not

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through smaller rings. We therefore favor a rotaxane-like structure for the complexes.

The definitions of the macroscopic association constants, $K_1 = [C{\cdot}M]/([C][M])$, $K_2 = [C{\cdot}M_2]/([C{\cdot}M][M])$, yield the ratio $K_1/K_2 = [C{\cdot}M]^2/([C]\,[C{\cdot}M_2])$ which can be determined directly from the proton NMR spectra. We find $K_1 = 4(\pm 0.1)K_2$. However, these constants must be corrected for statistical effects since C·M has two ways to form and $C{\cdot}M_2$ has two ways to dissociate. Therefore the statistically corrected (intrinsic) association constants K_1^i and K_2^i are equal; the system is noncooperative. Hill plots of the data[7] indeed give straight lines with slope $\bar{n} = 1$, with midpoints between 10^{-3} and 10^{-4} M free metal.

The finding that the two sites act independently in the present case may be rationalized in entropic terms. Binding at one site fixes only one of the many rotational degrees of freedom enjoyed by the remote polyether ring. In order for positive cooperativity ($K_2 > K_1$) to be observed, binding at one site must fix a larger fraction of the variables at the remote site. We are pursuing this goal through the construction of more rigid subunit systems.[11]

Acknowledgment. We are indebted to Professor J. Coetzee for advice and to the National Institutes of Health for financial support.

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J. Rebek, Jr.,* R. V. Wattley, T. Costello, R. Gadwood L. Marshall

Department of Chemistry, University of Pittsburgh Pittsburgh, Pennsylvania 15260

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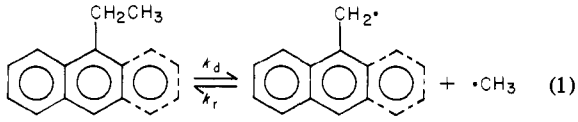
Highly Stabilized Radicals: Benzylic Radicals in Polycyclic Aromatic Systems

Sir:

We wish to report (1) measurements of the rates and equilibria of gas-phase benzylic bond scission for ethylbenzene, 1-ethylnaphthalene, and 9-ethylanthracene (reaction 1), (2) the enthalpies



(1)

of formation of the highly stabilized arylmethyl radicals produced in these reactions, and (3) the extent to which these values validate a recently developed technique[1] for estimating resonance-stabilization energies in polycyclic aromatic hydrocarbon radicals.

In recent publications, Herndon and co-workers have shown[2] that π-bonding energies in polycyclic aromatic hydrocarbons (PCAH) calculated by highly parameterized SCF-MO procedures are reproduced with an average deviation of 1.0 kcal/mol for 27 polycyclic aromatic hydrocarbons by means of a one-parameter equation involving the number of stable Kekule isomers [CSC(RH)]: $E_\pi(\mathrm{RH})/(\mathrm{kcal\ mol^{-1}}) = 27.33 \ln [\mathrm{CSC(RH)}]$. Stein and Golden have speculated[1] that a similar relationship holds for benzylic radicals in these same polycyclic aromatic systems. They have suggested an expression of the form

$$R_{\mathrm{RSE}}/(\mathrm{kcal/mol}) = A \ln [\mathrm{CSC(R\cdot)}] - B \ln [\mathrm{CSC(RH)}] \quad (2)$$

The values of the constants A and B were derived by (1) taking

Table I. Bond Dissociation Data and Derived Thermochemical Values

Substrate	Temp., K	k_d^{uni}, s^{-1}	K_d, m/l	k_r^∞, l-m/s	$\Delta H^0_{d,300}$	$\Delta(\Delta H^0_{d,300})$	k/k^∞	log $A_{d,T}$	$E_{d,T}$	$\Delta H^0_{d,300}$	$\Delta(\Delta H^0_{d,300})$	$\Delta(\Delta H^0_{d,300})$ (calc.)[d]	$\Delta H^0_{f,300}$ ArCH_2·
ØEt	1000	0.11	- - - - -	- - - - -	(75.0)[a]	(0)	0.30	15.85[b]	(74.7)[c]	(75.00)	(0)	(0)	
ØØEt	1000	0.60	- - - - -	- - - - -	- - - - -	- - - - -	0.52	- - -	- - -	- - -	- - -	- - -	- - -
	1100	8.9	1.01×10^{-8}	2×10^9	70.5 ± 1.8	4.5 ± 1.5	0.37	15.65[e]	71.8	72.1 ± 1.3[f]	2.9 ± 1.0	2.9	59.6 ± 1.5[f]
ØØØEt	1000	5.9	3.24×10^{-9}	4×10^9	66.7 ± 1.8	8.3 ± 1.5	0.45[g]	15.60[e]	66.5	66.8 ± 1.3	8.3 ± 1.0	7.8	79.9 ± 1.5

[a] Based on $\Delta H^0_{f,300} = 47.3$ for the benzyl radical (Reference 6). Units in kcal $mole^{-1}$.
[b] Derived from the RRK fitting of experimental values of k_d^{uni} and an assumed value[6] of 74.7 kcal $mole^{-1}$ for $E_{d,1000}$.
[c] Derived from $\Delta H^0_{d,300} = 75.0$ kcal $mole^{-1}$ (Ref. 6) and the considerations outlined in Reference 12a and Note 13.
[d] Calculated with equation (2), where A = 14.21 and B = 17.14.
[e] Derived by adjustment of log $A_{d,1000} = 15.85$ for ethylbenzene, where the most important consideration is the fact that increase in the external moments of inertia as the complex is formed gets smaller as the size of the aromatic system increases.
[f] Error limits assigned on basis of one standard deviation in rate constants and probable error limit in estimated A factors.
[g] k/k_∞ is slightly less for ethylanthracene than it is for ethylnaphthalene because the lower activation energy and a lower collision frequency for ethylanthracene outweigh the effect of the larger number of oscillators.

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