namics. Processes with very low activation energies normally require the use of low temperatures and high magnetic fields to bring the time scale of the NMR experiment into a useful range (i.e., comparable to the lifetime of the species undergoing the rearrangement).[1] Obviously, there are limitations on achieving very low temperatures with solution NMR studies; in principle, however, the possibility of doing high-resolution NMR in solids removes this constraint. In this communiction, we report an effect which indicates that even in the most favorable cases (i.e., when geometry changes along the reaction pathway from one structure to the next are minimal), it may not be possible to treat a molecular solid at low temperature as a low-temperature solution (of infinite concentration). The implication is that the activation parameters for a degenerate electronic rearrangement (or any other kind of dynamic process, for that matter) derived from a temperature-dependent study of the NMR spectrum of the solid may be more complex than its solution counterpart. The degree to which this conclusion holds will, of course, be a function of molecular structure, the phyiscal nature of the sample (crystalline, glassy, etc.), the process involved, and the temperature. Nonetheless, the results presented here also suggest that it should be possible, by using this method, to distinguish in a very direct manner between equilibrating and symmetrical structures. This is particularly apropos for the study of certain semibullvalene derivatives, which, according to calculation, should have activation energies (for the Cope process) considerably lower than semibullvalene.[10] Furthermore, experiments designed to make these structural distinctions for other low activation energy processes (e.g., trivalent nitrogen inversion, rotation about carbon–carbon single bonds, pseudorotation) may now be carried out at very low temperatures in the solid state using NMR spectroscopy with near-liquid resolution. Studies of this type are in progress.

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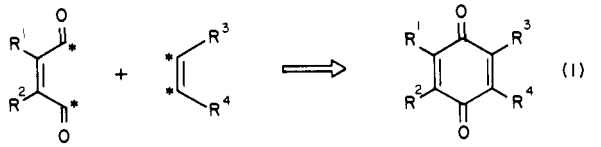
An Organotransition-Metal Synthesis of Naphthoquinones

Sir:

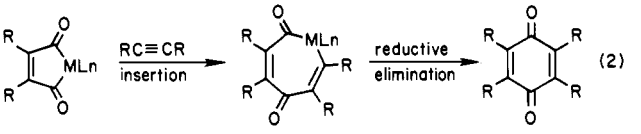
The quinone moiety is an important functionality in the area of bioactive natural products. It is represented in many different classes of biologically active molecules including the K vitamins,[1] ubiquinones,[2] and antibiotics and anticancer drugs.[3,4] The pervasive occurrence of the quinone functionality in nature has prompted the development of many synthetic approaches to such molecules, most of which depend upon oxidation of an appropriately substituted phenol or functionalization of a preexisting quinone.[5] A synthesis of quinones based upon the reaction of a 4-carbon maleoyl equivalent (**1**) with a 2-carbon unsaturated species (**2**) represents a potentially important, *convergent* route to substituted quinones (eq 1). If a mild and regiospecific means



1 **2**

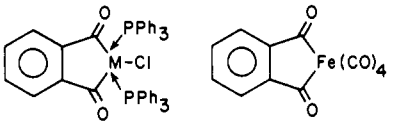
of joining equivalents of **1** and **2** could be found, then quinones of diverse structure could be synthesized by a common method.[6] We wish to report our preliminary results of a convergent approach to 1,4-naphthoquinones which utilizes organotransition-metal species for effecting the carbon–carbon bond formation depicted in eq 1.

The reaction of alkynes with metal carbonyls is known to produce quinones or quinone complexes in a number of cases,[7] and the intermediacy of metallacyclopent-3-ene-2,5-diones (**3**) has been postulated to account for the quinone formation.[7c,8] The reaction is proposed to occur by insertion of an alkyne into complex **3**, giving metallacycle **4** which then undergoes reductive elimination to the quinone (eq 2). We have shown that phthaloyl metal



3 **4**

complexes **5**–**7** (benzo analogues of metallacyclopent-3-ene-2,5-dione (**3**)) can be conveniently synthesized in high yield from



5 M = Rh
6 M = Co
7

benzocyclobutenedione,[9] and we have now found that cobalt complex **6** and iron complex **7** react with a wide variety of alkynes to give high yields of 1,4-naphthoquinones (Table I).

Cobalt complex **6** reacts with alkynes on treatment with $AgBF_4$ in CH_3CN under mild conditions (sealed tube, 110 °C, 20–40 h), while iron complex **7** produces naphthoquinones simply on heating in CH_3CN in the presence of an alkyne (sealed tube, 100 °C, 6 h). Table I lists our current results. The iron complex appears somewhat superior to the cobalt metallacycle in that it does not require Ag^+ to induce reaction and it also cleanly reacts with a wider variety of alkynes ranging from electron rich to electron deficient. However, cobalt complex **6** does have an advantage over the iron system in three cases. The sterically demanding alkynes 2,2-dimethyl-3-pentyne (entry 7) and 1-(trimethylsilyl)-1-hexyne (entry 10) give significantly higher yields

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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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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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