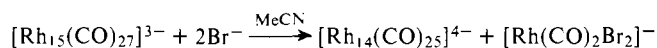Figure 5. A view of the $[Rh_{14}(CO)_{25}]^{4-}$ anion. A fourfold crystallographic axis passes through atoms 1 and 5.

$$[Rh_{15}(CO)_{27}]^{3-} + 2Br^- \xrightarrow{MeCN} [Rh_{14}(CO)_{25}]^{4-} + [Rh(CO)_2Br_2]^-$$

ν_{CO} 2040 (vw),
1998 (s, Br),
1850–1825–1805
(m, br) cm^{-1}

ν_{CO} 1960 (s),
1930 (sh, br),
1805 (m) cm^{-1}

This new tetraanion has been isolated as the crystalline Et_4N^+ salt in nearly quantitative yield. IR spectra suggest that addition of $[Rh(CO)_2(MeCN)_2]BF_4$ to an acetonitrile solution of $[Rh_{14}(CO)_{25}]^{4-}$ results in quantitative conversion of the tetranion to the starting $[Rh_{15}(CO)_{27}]^{3-}$ trianion.

The metallic skeleton of the $[Rh_{14}(CO)_{25}]^{4-}$ tetraanion is illustrated in Figure 4a, while Figure 4b shows the coordination around the central metal atom. The metallic polyhedron corresponds to an incomplete rhombic dodecahedron elongated along the crystallographic quaternary axis passing through atoms 1 and 5. Figure 4b clearly shows that this structure is essentially part of a body-centered cubic lattice. Of the independent metal–metal interactions 8 are normal bonds ranging from 2.63 to 2.79 Å (average 2.73 Å), 2 are intermediate (3.00 and 3.08 Å) and 2 are long (3.33 and 3.38 Å) contacts.

The complete anion is illustrated in Figure 5. There are 9 terminal and 16 edge-bridging CO groups, and all of the skeletal metal atoms, except 5, are bonded to 3 carbonyls; the low coordination of atom 5 is apparently compensated by the formation of 4 strongly asymmetric CO bridges (Rh(5)–C = 2.30 (4) Å, Rh(3)–C = 1.75 (4) Å). The mean values for the Rh–C and C–O bond lengths for the terminal and symmetric edge-bridging carbonyls are 1.77, 1.19 Å and 2.00, 1.18 Å, respectively. Comparison of Figures 3 and 5 shows that the metal atom which is removed on passing from the Rh_{15} to the Rh_{14} anion seems to be that labeled 15 in Figure 3, i.e., the metal which has two terminal CO groups. The disposition of the carbonyl groups in the remaining part of the Rh_{15} anion strictly resembles that in the Rh_{14} cluster and is similar to that previously observed in the $[Rh_{13}(CO)_{24}H_{5-n}]^{n-}$ ($n = 2, 3$) anions.

Comparison of the structures observed for the Rh_{13} and Rh_{14} clusters is analogous to the transformation between hcp and bcc lattices which is well known for many metals.[6] Comparison of the structures of Rh_{13} or Rh_{14} with the Rh_{15} structure is analogous to surface reconstruction, which is again well known for a number of metals.[7] Both analogies are in agreement with the belief that large clusters are real models of small

metallic crystallites covered (or poisoned) by ligands.

Further work is in progress on these families of clusters.

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(2) V. G. Albano, G. Ciani, S. Martinengo, and A. Sironi, *J. Chem. Soc., Dalton, Trans.*, in press.
(3) S. Martinengo, B. T. Heaton, R. J. Goodfellow, and P. Chini, *J. Chem. Soc., Chem. Commun.*, 39 (1977).
(4) The salt $[Me_4N]_3[Rh_{15}(CO)_{27}]$ crystallizes in the monoclinic space group $P2_1/n$ (No. 14) with cell constants $a = 12.658$ (4) Å, $b = 22.485$ (9) Å, $c = 22.848$ (8) Å, $\beta = 91.52$ (3)°, $Z = 4$. The structure has been solved by direct methods and refined by least squares using 3730 independent significant counter data. The refinements are in progress, the current R value being 8.3%.
(5) The salt $[Et_4N]_4[Rh_{14}(CO)_{25}]$ crystallizes in the tetragonal space group $P4/ncc$ (No. 130) with cell constants $a = 17.056$ (2) Å, $c = 27.186$ (4) Å, $Z = 4$. The structure has been solved by Patterson and Fourier methods on the basis of 876 independent significant counterdata. The refinements are in progress, the current R value being 5.2%.
(6) A. F. Wells, "Structural Inorganic Chemistry", Oxford University Press, London, 1975, p 1015.
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Diel–Alder Cycloaddition of Juglone Derivatives: Elucidation of Factors Influencing Regiochemical Control

Sir:

In connection with studies directed toward tetracycline total synthesis, Inhoffen and Muxfeldt reported an interesting observation: the nature of the oxygen function in 5-hydroxy- (1) and 5-acetoxy-1,4-naphthoquinone (2) profoundly influenced the regiochemistry of the cycloaddition with 1-acetoxybutadiene.[1] This general trend has been noted subsequently for a variety of diene systems by several groups, notably Birch,[2] Kelly,[3] and Trost.[4a]

The rationale for this effect, alluded to initially by Inhoffen and further developed by Birch[2] and Kelly,[3] revolves around the concept that the strong hydrogen bond known to be present in quinone 1 serves as an "internal Lewis acid" polarizing the unsaturated system and resulting in the C-4 carbonyl serving as the dominant director of cycloaddition. Alternatively, electron donation by the oxygen is considered to dominate in the acetate 2 (and methyl ether 6) leading to reversal of the regiochemical result.
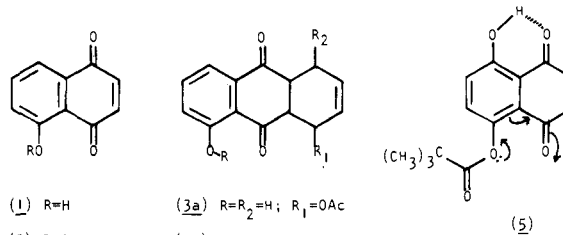
(**1**) R=H	(**3a**) R=R$_2$=H; R$_1$=OAc
(**2**) R=Ac	(**3b**) R=R$_1$=H; R$_2$=OAc
(**6**) R=CH$_3$	(**4a**) R=Ac; R$_1$=H; R$_2$=OAc
	(**4b**) R=Ac; R$_1$=OAc; R$_2$=H

Table I[a]

	R₁	R₂	R₃	Δ	BF₃·Et₂O	AlCl₃[b]	Δ	BF₃·Et₂O	AlCl₃[b]	Δ	BF₃·Et₂O	AlCl₃[c]
7	OCH₃	CH₃	OCH₃	1:1.8	1:4.5	4.7:1	2:1	4.7:1	2.75:1	1:1.9	1:2.4	1.3:1
10	H	OSi(CH₃)₃	OCH₃	only **11a**						only **12a**		
13	H	OCH₃	H	2.7:1[d]						1:2.8[e]		
14	H	CH₃	H	1.2:1	1:7.3	1:4.5	2.6:1	2.0:1		1.4:1	1.1:1	
17	OAc	CH₃	OAc	1:1			1.2:1	2.1:1		3.1:1	1:1.1	1:1

[a] See note 11. [b] For dienes **7, 14,** and **17,** results are reported as ratios of **8:9** (anti:syn). [c] See note 6. [d] Ratio of **11b:11c** (anti:syn). [e] Ratio of **12b:12c** (anti:syn).

Table II[a]

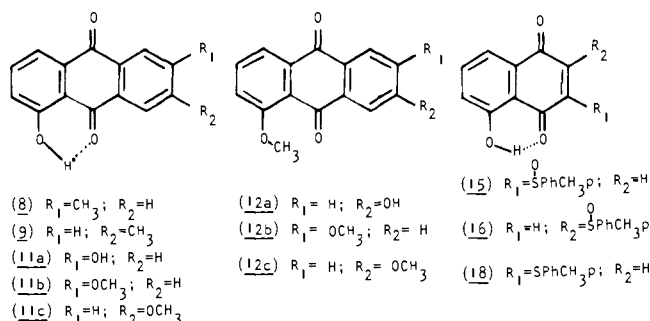|	Δ[b]	BF₃·Et₂O[b]
15 and **14**	2.9:1	5.4:1
16 and **14**	1:2.0	1:4.3

[a] See note 11. [b] Results are reported as ratios of **8:9** (anti:syn).

Considering all the known uncatalyzed cases of high regiocontrol with dienophiles **1, 2, 5,** and **6,** the diene components were always significantly polarized, electron rich, and terminally substituted with a good π-electron-donating substituent. Consequently, it appeared to us that, *for high regiocontrol to be observed, proper choice of the diene component might be a much more crucial design feature.* It is generally believed that diene–HOMO and dienophile–LUMO interactions are primarily responsible for the observed regiospecificity in cycloaddition processes such as these.[5] The expected differences in the coefficients for C-2 and C-3 of LUMO for **1, 2,** and **6** are not, however, obtained from molecular orbital calculations (CNDO/2) on these systems.[6] These results and some preliminary experiments suggested that the electronic structure of the diene component may be much more important for regiocontrol than the dienophile structure.

To test this idea further, and to learn more about ways to influence the observed regiospecificity in 5-oxygenated-1,4-naphthoquinones for our own approach to anthracyclinone synthesis, we have undertaken the studies described below.

We were interested in exploring the potential for regioselectivity in relatively unpolarized dienes. Our initial choice was 1,4-dimethoxyisoprene (**7**),[7a] whose calculated polarization based upon terminal coefficients was small.[6-9] The results shown in Table I indicate that, in the product mixture of **8** and **9,** the *unexpected regioisomer predominates* in the thermal process based upon the calculated direction of polarization of **7** and the previously observed tendencies of **1** and **2** (vide supra)[10] (Table I).

On the other hand, the strong and complementarily polar-

(**8**) R₁=CH₃; R₂=H
(**9**) R₁=H; R₂=CH₃
(**11a**) R₁=OH; R₂=H
(**11b**) R₁=OCH₃; R₂=H
(**11c**) R₁=H; R₂=OCH₃

(**12a**) R₁= H; R₂=OH
(**12b**) R₁= OCH₃; R₂= H
(**12c**) R₁= H; R₂= OCH₃

(**15**) R₁=ṠPhCH₃P; R₂=H
(**16**) R₁=H; R₂=ṠPhCH₃P
(**18**) R₁=SPhCH₃P; R₂=H

ized diene **10** on reaction with **1** affords a single product (**11a,** mp 272–275 °C) in accord with prediction.[3,10] The expected reversal of regiocontrol, as was previously observed, does occur with **6** providing **12a** (mp 185–186 °C) exclusively.[10] This case is analogous to those reported by Birch[2] and Branville[13] and strongly implicates the role of diene as the major factor in the observed regiospecificity. 2-Methoxybutadiene (**13**) would be expected to afford substantial regiocontrol based upon polarity as judged from the calculated terminal orbital coefficients.[8,14] However, the observed magnitude of that control is modest (Table I). The expected reversal occurs in going from **1** to **6** and confirms the result reported previously.[15] The case of isoprene (**14**) is also informative in that this diene lacks a π-activating substituent. In this case, all three dienophiles (**1, 2,** and **6**) are largely unselective (cf. Table I) and again the unexpected regioisomer predominates for **2** and **6.** These results add further reinforcement to the idea that diene rather than dienophile structure dominates the regioselectivities for quinones **1, 2,** and **6,** Current theory cannot account completely for the relatively small changes in regioselectivities observed; however, consideration of secondary orbital effects permits one to rationalize the greater part of the experimental results.[16,17]

In an attempt to test the *effect of further polarizing the dienophile,* sulfoxides **15** and **16** were prepared.[18] The results of reaction of these much more strongly polarized dienophiles with isoprene (**14**) providing **8** and **9** are given in Table II.[19] The observed regioselectivities are in the anticipated direction based upon the apparent polarization, however, of much smaller magnitude (2–3-fold increase), again emphasizing the role of diene polarization.[20]

Trost recently reported the effects of Lewis acids upon the reaction of **1** with several dienes.[4] We have concurrently been studying the effects of Lewis acids on the cycloadditions of **1, 2,** and **6** with several dienes. The results are reported in Table I. It is most interesting that catalysis of the reaction between juglone (**1**) and diene **2** with AlCl₃ and BF₃·Et₂O leads to significantly increased regioselectivity but different predominant regioisomers (see Table I). These results can conceivably be attributed to different sites of complexation of BF₃ and AlCl₃ with the dienophile. Although Trost has invoked a rationale based upon an equilibrium among the sites of complexation of the dienophile and diene,[4] Valenta's suggestion that steric hindrance plays a significant role in determining the site of complexation may also be important in this case.[21] If one considers these results within the context of the Inhoffen–Kelly model[3] and assumes that polarization of the dienophile occurs primarily by complexation of the syn carbonyl owing to chelation, the regiochemical result should be in the same direction as the thermal result for both catalyzed reac-

tions of **1** and **7**. The results (Table I), therefore, suggest that site of complexation in **1** differs for BF$_3$·Et$_2$O and AlCl$_3$ and/or that the polarization of **7** has been significantly altered by complexation. The results with diene **17**[7b] are consistent with this picture since diene **17** should be significantly less susceptable to complexation.[21] Furthermore, for the corresponding reactions of isoprene (**14**) with **1**, no reversal of orientation occurs in line with the expectation that (1) the less hindered carbonyl should be the site of preferential complexation[21] and that (2) isoprene (**14**) should exhibit little or no tendency toward complexation.[22]

Finally, it can be shown that substituents on the double bond are capable of influencing the site of complexation in the quinones. Catalysis of the reaction of **15** and **16** with isoprene (**14**) results in an increase in regiospecificity consistent with enhanced complexation of the carbonyl syn to the sulfoxide. Remarkably, use of sulfide **18** with **14** at 0 °C provides only **8**, although in low yield (20%). This would appear to be at odds with the results based on expected Lewis basicities.[23]

Taking into consideration the above experiments and all other data available at this time, it becomes clear that the simple picture, developed by Inhoffen, Birch,[2] and Kelly,[3] of the factors influencing the regiospecificity of cycloaddition of juglone and related systems is inadequate for a broad range of dienes, although the rationale appears applicable to the class of highly activated, polarized dienes for which it was developed. Certainly, the actual picture is much more complex. However, several generalizations may apparently be drawn at this time: (1) *the regiochemistry seems dominated by diene polarity;* (2) juglone (**1**) and related systems are relatively weakly polarized, and effects due to hydrogen bonding, resonance, etc., are insufficient to exert substantial influence upon the regiochemical outcome except for strongly polarized dienes; (3) through the use of Lewis acid catalysis it is possible to markedly influence regiochemical control by proper choice of quinone and catalyst even for weakly polarized dienes; (4) complexation equilibria are highly substrate dependent, leading to dramatic reversals of regiospecificity; (5) diene complexation, previously implicated by Trost,[4a] may be the dominant factor in the observed regiospecificity of catalyzed reactions in some cases, although the observed results are not clearly correlatable with expected Lewis basicities.

From a synthetic point of view, *proper choice of the diene component is paramount,* although significant improvement can be effected in regiocontrol by suitable choice of the dienophile and the use of catalysis. Trost has suggested that a change in mechanism may be responsible in part for the observed results,[4] and it appears that charge-transfer complexation could also conceivably play a significant role in cases where the diene is a good π donor.[24] These and other concepts remain to be tested as we continue to explore the range of control possible in these intriguing dienophiles.

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(3) (a) T. R. Kelly, J. Gillard, and R. Goerner, Jr., *Tetrahedron Lett.*, 3873 (1976); (b) T. R. Kelly, J. Gillard, R. Goerner, Jr., and J. Lyding, *J. Am. Chem. Soc.*, **99**, 5513 (1977); (c) T. R. Kelly, *Tetrahedron Lett.*, 1387 (1978).
(4) (a) B. M. Trost, J. Ippen, and W. Vladuchick, *J. Am. Chem. Soc.*, **99**, 8116 (1977); (b) G. Stork, *ibid.*, **100**, 3609 (1978).
(5) K. Houk, *J. Am. Chem. Soc.*, **95**, 4092 (1973).
(6) Unpublished calculations by R. K. Boeckman, Jr., and T. M. Dolak utilizing a CNDO/2 treatment. The details of these calculations will be presented in a forthcoming paper.
(7) (a) Prepared from 3-methoxy-2-methlacrolein (c; V. T. Klimko, T. V. Protopopova, N. V. Smirnova, and A. P. Skoldinov, *Zh. Obsch. Khim.*, **32**, 2961 (1962)) by Wittig reaction with Ph$_3$P=CHOCH$_3$ in THF (84%): bp 53–54 °C (3 mm); NMR (CDCl$_3$), mixture *E,E* and *E,Z*, δ 6.2–5.3 (m, 2 H), 4.55 (d, *J* = 7 Hz, 1 H), 3.50 (s, 6 H), 1.70 (d, *J* = 10 Hz, 3 H). (b) J. F. W. Keana and P. Eckler, *J. Org. Chem.*, **41**, 2625 (1976).
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(9) The magnitude of the difference for 1-methoxy- (or acetoxy-) butadiene is much larger than the difference for diene 7: R. K. Boeckman, Jr., and T. M. Dolak, unpublished calculations.
(10) The structure of **8** was verified by preparation of an authentic sample by two independent routes. Quinone **8** (mp 147 °C) was prepared by a route analogous to that described by P. C. Mitter and A. K. Sarkar, *J. Indian Chem. Soc.*, **2**, 619 (1930), from 3-methoxyphthalic anhydride. In as much as rearrangements are known to sometimes occur during acid-catalyzed cyclizations (see A. S. Kende, J. L. Belletine, J. L. Herrmann, R. F. Romanet, E. L. Hume, R. H. Schlessinger, J. Fayos, and J. Clardy, *Synth. Commun.*, **3**, 387 (1973)), **8** was also prepared from 2-methylanthraquinone via 1-amino-5-hydroxy-2-methylanthraquinone (cf. N. R. Agyangar, D. S. Bapert, and B. S. Joshi, *J. Sci. Ind. Res., Sect. B*, **20**, 493 (1961)) by diazotization and reduction (ethanol, Δ). The identical substance (**8**) (TLC, I R, NMR, melting point, mixture melting point) was obtained from this route also. Quinones **12b** and **12c** were obtained from the crude Diels–Alder adducts by hydrolysis and methylation (NaOH/(CH$_3$)$_2$SO$_4$).
(11) In general, the uncatalyzed Diels–Alder reactions were performed by heating the diene (1.2 equiv) and dienophile (1.0 equiv) in benzene or toluene for periods of 1–16 h. The catalyzed reactions were run in toluene at −78 °C (AlCl$_3$) or 0 °C (BF$_3$). The catalyst (0.5 equiv) and dienophile (1.0 equiv) were stirred at the appropriate temperature prior to the dropwise addition of a solution of the diene (1.2 equiv). In all cases, the crude products were treated with base (and oxygen for dihydro cases) to complete aromatization. The products from dienes 7, **14**, and 17 produced in yields of 60–90% were converted to mixtures of **8** and **9** and analyzed by NMR (integration of the phenolic proton; accuracy ±5%). All new compounds had satisfactory spectral data and combustion or mass spectral analysis.
(12) E. Schenk and H. Roeman, *Chem. Ber.*, **10**, 1225 (1977); also cf. ref 15.
(13) J. Branville and P. Bassard, *J. Chem. Soc., Perkin Trans. 1*, 1852 (1976).
(14) Calculations of the orbital coefficients confirm the experimental observations for several dienes. Details will be discussed in a forthcoming paper.
(15) A. S. Onishenko, M. Shemyakin, M. Kolosov, Y. Arbuzov, M. Karapetyam, and E. Chamian, *Proc. Acad. Sci. USSR*, 1802 (1959).
(16) (a) P. V. Alston, R. M. Ottenbrite, and D. D. Shillady, *J. Org. Chem.*, **38**, 4075 (1973); (b) P. V. Alston and R. M. Ottenbrite, *ibid.*, **40**, 1111 (1975); (c) I. Fleming, J. P. Michael, L. E. Overman, and G. F. Taylor, *Tetrahedron Lett.*, 1313 (1978).
(17) The trends are consistent with the concept that 2-substituted dienes are dominated by primary effects (terminal coefficient), but 1-substituted systems are dominated by the difference in coefficients at the internal atoms (secondary effects for 2-substituted dienes oppose the primary effect; cf. ref 16).
(18) R. Thompson, *J. Org. Chem.*, **16**, 1082 (1951); the sulfoxides were prepared by oxidation with MCPBA at 25 °C in CH$_2$Cl$_2$.
(19) Evidence of the polarization can be deduced from the shift of the proton β to sulfur from ~6.1 to ~7.3 upon conversion of sulfide to sulfoxide for both isomers 15 and 16.
(20) This result is not totally unexpected, since sulfoxide is a somewhat poorer π-electron-withdrawing group than carbonyl or nitrile as judged by the resonance vs. polar contribution to the acidity of an adjacent C–H bond; cf. F. Bordwell, M. Van Der Puy, and N. Vanier, *J. Org. Chem.*, **41**, 1883 (1976).
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(23) The sulfide dienophile is predicted to be a somewhat poorer Lewis base (cf. ref 22); however, this result may be due to a temperature effect. The sulfoxide 15 reaction was run at 0 °C. When the temperature is raised to 25 °C, regioselectivity for the sulfide 18 falls off to 4.9:1, more in line with expectations based on Lewis basicities. See ref 4a, and 4b also, for an example of a substantial temperature effect.
(24) Charge-transfer complexation has been implicated in some very polar, possibly nonsynchronous, concerted cycloadditions; cf. C. K. Bradsher, C. L. B. Carlson, N. A. Porter, I. J. Westerman, and T. G. Wallis, *J. Org. Chem.*, **43**, 822 (1978). Professor Trost had previously considered this possibility in his systems, and is actively pursuing experimental verification of this effect (private communication).
(25) Fellow of the Alfred P. Sloan Foundation (1976–1980); recipient of a Career Development Award (CA-00273) from the National Cancer Institute of the National Institutes of Health (1976–1981).

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