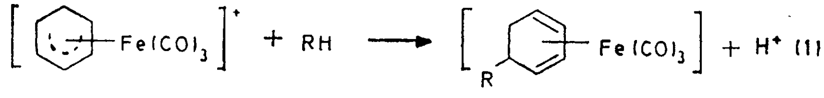
Kinetics of Nucleophilic Attack on Co-ordinated Organic Moieties. Part 4.† Mechanisms of Addition of Indole and Substituted Indoles to Tricarbonyl(cyclohexadienyl)-iron and -ruthenium Cations

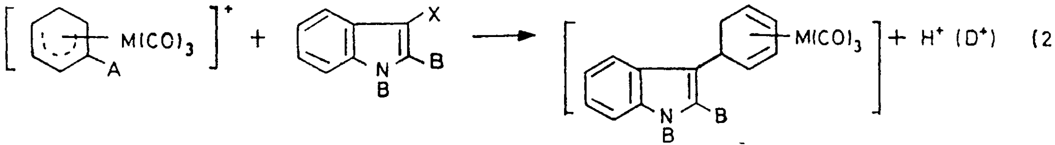
By **L. A. P. Kane-Maguire** * and **C. A. Mansfield**, Department of Chemistry, University College Cardiff, Cardiff CF1 1XL

A kinetic study of the addition of indoles to the dienyl cations $[M(C_6H_7)(CO)_3]^+$ (M = Fe or Ru) and related species in nitromethane reveals a change in mechanism with metal. The iron complexes obey the rate equation Rate = k[complex] [indole]. This observation together with substituent effects (*e.g.* deuteriation) and product stereochemistry supports direct electrophilic attack of the dienyl cation at C^3 of indole followed by rapid proton loss. On the other hand, kinetic evidence has been obtained for an intermediate prior to the rate-determining step in the ruthenium case. These differences are most readily rationalised in terms of rate-determining formation of a π complex for iron, whereas with ruthenium pre-equilibrium formation of a π-complex intermediate is followed by slow formation of a Wheland-type σ complex.

We recently reported[1,2] the synthetic utility of cationic organometallic complexes such as $[Fe(C_6H_7)(CO)_3]^+$ (1) as electrophilic reagents towards aromatic substrates, leading to a variety of substituted aromatic derivatives [equation (1); RH = indole, pyrrole, furan, thiophen, substituted indoles, 1,3,5-trimethoxybenzene, or 1,3-dimethoxybenzene]. These reactions may be alternatively regarded as involving nucleophilic addition of the aromatic species to the dienyl cations. In order to elucidate the mechanisms of these novel processes more fully, detailed kinetic studies have now been undertaken.



This paper reports kinetic data for the reactions of indole and substituted indoles with the cations (1), $[Fe(C_6H_6OMe)(CO)_3]^+$ (2), and $[Ru(C_6H_7)(CO)_3]^+$ (3) in nitromethane solvent [equation (2): A = H or OMe; M = Fe or Ru; B = H or Me; X = H, D, or Me).



(4)

EXPERIMENTAL

Materials.—The cations (1)—(3) were isolated as the $[BF_4]^-$ salts using published procedures.[3,4] These salts were converted into the appropriate tetraphenylborate salts immediately prior to use, as illustrated below for cation (1).

Tricarbonyl(*cyclohexadienyl*)*iron Tetraphenylborate*.—The complex $[Fe(C_6H_7)(CO)_3][BF_4]$ was dissolved in a minimum volume of water and an excess of sodium tetraphenylborate (also in water) was added. On cooling in ice a cream precipitate separated, which was filtered off and washed with water. The precipitate was dried in a vacuum desiccator (yield >95%) (Found: C, 72.6; H, 5.0. Calc. for $C_{33}H_{27}BFeO_3$: C, 73.6; H, 5.0. Found: C, 71.7; H, 5.3. Calc. for $C_{34}H_{29}BFeO_4$: C, 71.9; H, 5.3. Found: C, 68.1; H, 4.4. Calc. for $C_{33}H_{27}BO_3Ru$: C, 68.0; H, 4.4%).

The products from the reactions of indole with (1) and (2), and of 2-methylindole with (2), were isolated in good yield. All showed the two i.r. carbonyl bonds at *ca.* 2 040 and 1 970 cm^{-1} in nitromethane expected for neutral tricarbonyl(diene)iron complexes. Preparative details and their full characterisation using ^{1}H n.m.r. and mass spectroscopy are reported elsewhere.[5] The product from the reaction of (3) with indole also showed the expected carbonyl bands at *ca.* 2 040 and 1 970 cm^{-1}, but was an oily material which resisted attempts to crystallise it.

[1,3-$^2H_2$]Indole was prepared by the literature method[6] and its purity checked by i.r. and ^{1}H n.m.r. The degree of deuteriation was greater than 90%. The nitromethane solvent was distilled under nitrogen and stored over molecular sieves.

Kinetic Studies.—(*a*) The reactions of cations (1) and (2) with high concentrations of indole (≥0.4 mol dm^{-3}) were too rapid to follow by conventional methods. A thermostatted (±0.1 °C) stopped-flow apparatus of the type previously described[7] was therefore employed. Reactant solutions of the appropriate concentrations were prepared separately in nitromethane, and were thermostatted in the stopped-flow apparatus for at least 10 min prior to mixing. Incident light of wavelength 390 nm was provided by a Bausch and Lomb high-intensity monochromator. At this wavelength a large decrease in absorbance occurred during

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† Ref. 13 is Part 3.

[1] L. A. P. Kane-Maguire and C. A. Mansfield, *J.C.S. Chem. Comm.*, 1973, 540.

[2] C. A. Mansfield, K. M. Al-Kathumi, and L. A. P. Kane-Maguire, *J. Organometallic Chem.*, 1974, **71**, C11.

[3] A. J. Birch, P. E. Cross, J. Lewis, D. A. White, and S. B. Wild, *J. Chem. Soc.* (*A*), 1968, 332.

[4] R. J. H. Cowles, Ph.D. Thesis, University College London, 1969.

[5] C. A. Mansfield, R. Davis, and L. A. P. Kane-Maguire, unpublished work.

[6] R. L. Hinman and C. P. Bauman, *J. Org. Chem.*, 1974, **29**, 2437.

[7] L. A. P. Kane-Maguire and G. Thomas, *J.C.S. Dalton*, 1975, 1890.

the reactions of (1) and (2) with all the heterocyclic nucleophiles, the absorbance decreasing to almost zero. Attachment of a log-converter unit [8] to the oscilloscope permitted direct absorbance readout. Pseudo-first-order rate constants $k_{obs.}$ were estimated from the gradients of plots of log A_t against time, where A_t is the absorbance of the reaction solution at 390 nm at time t.

(*b*) The reactions of $[Ru(C_6H_7)(CO)_3][BPh_4]$ (3) with indole ($\geqslant$0.02 mol dm^{-3}), and of (1) and (2) with indole under equimolar conditions (3×10^{-3} mol dm^{-3}), were sufficiently slow to permit the use of an i.r. sampling technique. Details of the solution preparation (in the dark under nitrogen) and sampling methods have been previously described.[9] The reactions were followed by monitoring the decrease of the original dienyl carbonyl band at *ca.* 2 110 cm^{-1}.

When excess of nucleophile was employed, pseudo-first-order rate constants $k_{obs.}$ were calculated from the gradients of plots of log A_t against time. For runs carried out under equimolar conditions, second-order rate constants k were calculated from the gradients of plots of log $[x/a(a - x)]$, where a is the initial concentration of dienyl salt and x is the concentration of product at time t.

(*c*) All the tetraphenylborate salts (1)—(3) decompose slowly in the nitromethane solvent. However, only for the reaction of (2) with an equimolar concentration of indole (3×10^{-3} mol dm^{-3}) was this rate of background decomposition sufficient to influence the observed rate constant. For this reaction appropriate corrections were therefore applied.

RESULTS

Second-order rate constants k from the reaction of (1) with indole under equimolar conditions (3×10^{-3} mol dm^{-3}) at various temperatures are collected in Table 1. These values are the average of duplicate i.r. determinations, individual rate plots being linear for at least 80% completion of reaction. Pseudo-first-order rate constants $k_{obs.}$ for the same reaction at higher indole concentrations are also summarised in Table 1. Each $k_{obs.}$ value is the average of values from four separate stopped-flow runs. Primary rate plots were linear for at least 80% completion of reaction. The constant $k_{obs.}$ was dependent directly on the concentration of indole employed, confirming the rate equation (3). {The agreement between the k values

$$\begin{aligned} \text{Rate} &= k[\text{complex}][\text{indole}] \\ &= k_{obs.}[\text{complex}] \qquad (3) \end{aligned}$$

calculated at [indole] $\geqslant$0.4 mol dm^{-3} and those obtained directly under equimolar conditions ([Fe] = [indole] = 3×10^{-3} mol dm^{-3}) is good considering the different techniques, i.r. and u.v.–visible stopped-flow, employed in their estimation.}

TABLE 1

Kinetic data for reaction of $[Fe(C_6H_7)(CO)_3][BPh_4]$ (1) with indole in nitromethane. [Fe] = 3.0×10^{-3} mol dm^{-3}

θ_c/°C	[Indole]/mol dm^{-3}	10 $k_{obs.}$/s^{-1}	10 k/dm^3 mol^{-1} s^{-1}
20.9	0.0030		1.36
25.4	0.0030		1.70
30.0	0.0030		2.15
35.1	0.0030		3.31
21.5	0.40	0.714	1.78 *
	0.50	0.866	1.73 *
	0.80	1.36	1.70 *
	1.30	2.08	1.73 *
	1.50	2.41	1.61 *
	1.78	2.92	1.64 *

* Calculated from equation (3).

Second-order rate constants k for the reaction of (2) with indole, $[1,3\text{-}^2H_2]$indole, and various substituted indoles under equimolar conditions are collected in Table 2. Table 3 summarises the pseudo-first-order rate constants, $k_{obs.}$, obtained for the reaction of (3) with indole at various temperatures and indole concentrations. Figure 1(*a*) shows a plot of $k_{obs.}$ against [indole] for this reaction, while $1/k_{obs.}$ against 1/[indole] is plotted in Figure 1(*b*).

TABLE 2

Kinetic data for reaction of $[Fe(C_6H_6OMe)(CO)_3][BPh_4]$ (2) with indoles ([Fe] = [indole] = 3×10^{-3} mol dm^{-3}) in nitromethane

Heterocycle	θ_c/°C	10^2k/dm^3 mol^{-1} s^{-1}
Indole	50.7	11.1
	40.7	4.74
	30.7	2.83
	20.0	1.62
$[1,3\text{-}^2H_2]$Indole	20.0	1.25
2-Methylindole	20.0	11.6
N-Methylindole	20.0	9.66
3-Methylindole	20.0	No reaction

TABLE 3

Kinetic data for reaction of $[Ru(C_6H_7)(CO)_3][BPh_4]$ with indole in nitromethane

θ_c/°C	[Indole]/mol dm^{-3}	$10^4k_{obs.}$/s^{-1}
24.5	0.02	0.145 (0.148) [a]
	0.03	0.310
	0.05	0.554
	0.08	0.700
	0.10	0.900
	0.20	1.51
	0.40	2.28
	0.50	2.43
16.3	0.05	0.201
20.0	0.05	0.323
24.5	0.05	0.554
35.1	0.05	1.22
45.2	0.05	2.25 [b]

[a] Value in parentheses is for $[1,3\text{-}^2H_2]$indole. [b] Corrected for decomposition of (3).

TABLE 4

Activation parameters for reactions of dienyl salts with indole in nitromethane (1 cal = 4.184 J)

Complex	$\Delta H_{obs.}^{\ddagger}$/kcal mol^{-1}	$\Delta S_{obs.}^{\ddagger}$/cal K^{-1} mol^{-1}
$[Fe(C_6H_7)(CO)_3][BPh_4]$	10.4 ± 0.1	−27
$[Fe(C_6H_6OMe)(CO)_3][BPh_4]$	11.0 ± 0.3	−29
$[Ru(C_6H_7)(CO)_3][BPh_4]$	14.4 ± 0.2	−24

Activation parameters for each of the reactions studied are compared in Table 4. Activation enthalpies were obtained from the gradients of Arrhenius plots calculated by the least-squares method. The errors quoted are the standard errors of estimation derived from the least-squares analyses. Entropies of activation were calculated by standard procedures. In the case of the ruthenium complex the $\Delta H^{\ddagger}$ value was estimated from data at [indole] = 0.05 mol dm^{-3}. At this concentration the rate equation (3) was approximately obeyed [Figure 1(*a*)], permitting conversion of the $k_{obs.}$ values into second-order rate constants before calculation of $\Delta S^{\ddagger}$.

[8] D. O'Donnell, E. G. Phillips, and N. H. Rees, *Rev. Sci. Instr.*, 1974, **45**, 274.

[9] L. A. P. Kane-Maguire, *J. Chem. Soc.* (*A*), 1971, 1602.

DISCUSSION

Tetraphenylborate salts of the cations (1)—(3) were employed to avoid possible polymerisation of the indole substrate by liberated acid during reaction (2). Indole is a very weak base and is known to be converted by acid into dimeric or trimeric species.[10] The tetraphenylborate anion is expected to function as a proton scavenger since it reacts with protons to give benzene and triphenylboron.[11]

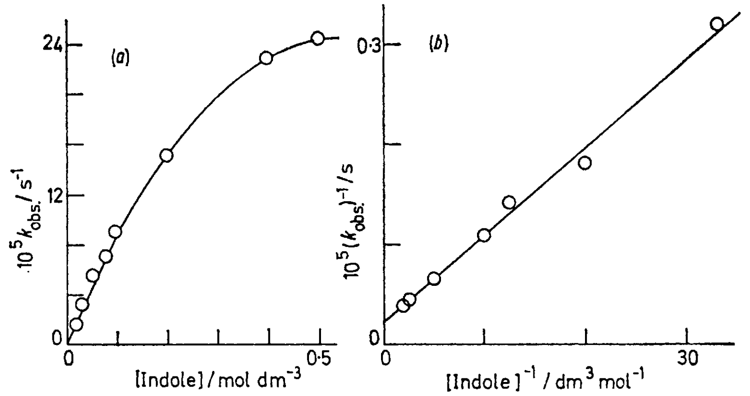
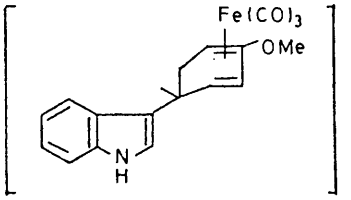


FIGURE 1 Dependence of $k_{obs.}$ on [indole] for reaction of $[Ru(C_6H_7)(CO)_3][BPh_4]$ with indole in nitromethane at 34.5 °C

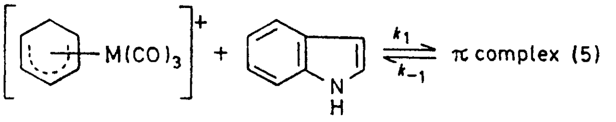
Mechanism of Indole Reaction with Iron Dienyl Cations.—Reactions of type (2) exhibit the characteristics expected for electrophilic substitution at indole. The products (4) were isolated as microcrystalline solids for the cases M = Fe, A = H or OMe, and B = H or Me. The ^{1}H n.m.r. spectrum [5] of (4; M = Fe, A = OMe, B = H) is consistent with the structure below in which electrophilic attack by $[Fe(C_6H_6OMe)(CO)_3]^+$ on C^3 of indole has occurred. This is the normal position for electrophilic substitution on indole, in agreement with molecular-orbital calculations showing C^3 to be the carbon atom of highest π-electron density in the heterocycle.[10] In addition, the i.r. spectra of all the solid products (4) showed the presence of an N–H stretching band at *ca.* 3 400 cm^{-1}, eliminating the possibility of electrophilic substitution at the nitrogen atom.



Kinetic data in Table 2 for reaction of $[Fe(C_6H_6OMe)(CO)_3]^+$ with various substituted indoles provide further strong evidence for electrophilic attack at C^3. The 2-methyl- and *N*-methyl-indoles are attacked considerably faster than indole, as expected due to donation of electron density by the methyl groups to the heterocyclic ring. However, no reaction was observed with 3-methylindole. While supporting attack at C^3, this latter observation contrasts with other reports [12] that blocking position C^3 can cause certain electrophiles to enter at C^2.

The parent cation $[Fe(C_6H_7)(CO)_3]^+$ reacts (Tables 1 and 2) with indole approximately nine times faster than does $[Fe(C_6H_6OMe)(CO)_3]^+$. A similar difference in reactivity of these two cations was noted in their reactions with pentane-2,4-dione.[9,13] This difference is due to the ability of the methoxy-substituent to share the positive charge, thus reducing the effective charge on the dienyl ring.

The second-order rate equation (3) observed for the reaction of $[Fe(C_6H_7)(CO)_3]^+$ with indole (Table 1) is consistent with the generalised mechanism in (4) and (5) (M = Fe). Formation of a π complex (5) could be rate determining, in which case the $k_{obs.}$ values refer to k_1[indole] [alternative (*a*), Figure 2]. On the other hand,



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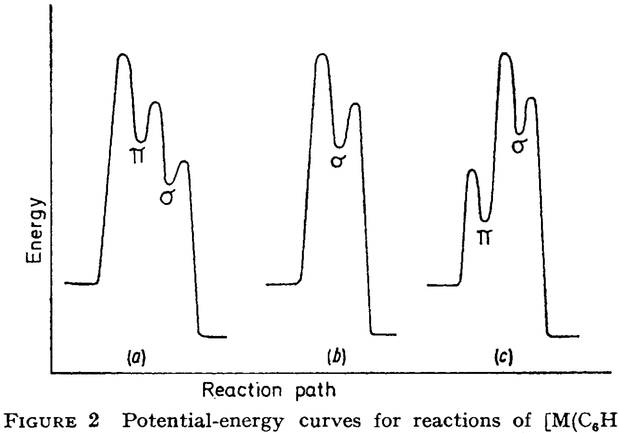

FIGURE 2 Potential-energy curves for reactions of $[M(C_6H_7)(CO)_3]^+$ with indole: (*a*) π-complex formation rate determining; (*b*) σ-complex formation rate determining; (*c*) pre-equilibrium formation of π-complex followed by slow formation of σ-complex

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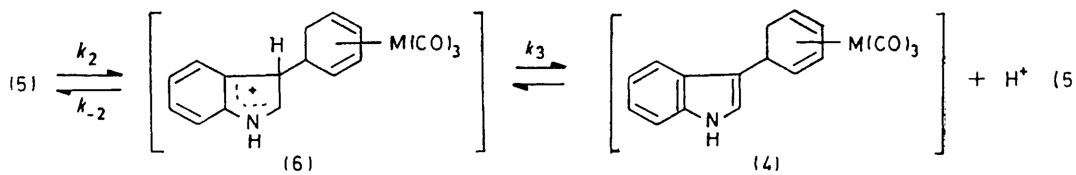
[10] R. M. Acherson, 'An Introduction to the Chemistry of Heterocyclic Compounds,' 2nd edn., Wiley, New York, ch. 4.

[11] J. N. Cooper and R. E. Powell, *J. Amer. Chem. Soc.*, 1963, **85**, 1590.

[12] A. H. Jackson and A. Smith, *Tetrahedron*, **1965**, **21**, 898 and subsequent papers of the series.

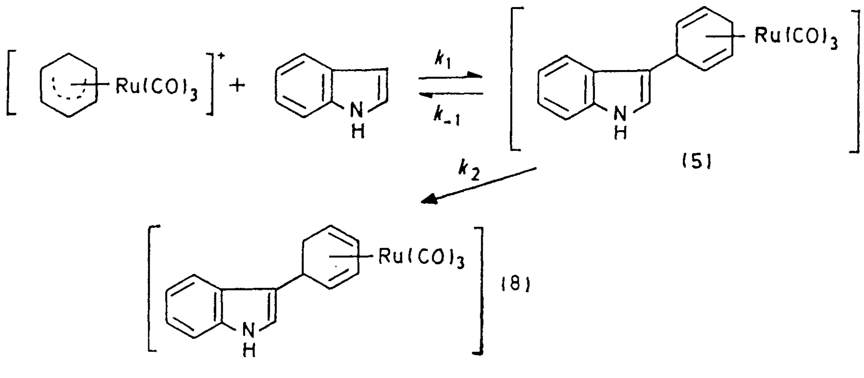
[13] C. A. Mansfield and L. A. P. Kane-Maguire, preceding paper.

rate-determining formation of the Wheland-type σ-complex intermediate (6) could be involved with $k_{obs.} = k_2$[indole] [alternative (*b*), Figure 2]. In order to explain the strict observation of the second-order rate equation (3) over a wide range of indole concentration, this latter mechanism [equations (4) and (5); (*b*)] requires a very small pre-equilibrium constant K ($= k_1/k_{-1}$) for π-complex formation.



The absence of a primary kinetic-isotope effect for the reactions of $[Fe(C_6H_6OMe)(CO)_3]^+$ with indole and $[1,3\text{-}^2H_2]$indole (Table 2) supports either of these alternative mechanisms. The small $k_H : k_D$ ratio of 1.29 : 1 can be attributed to secondary isotope effects. In this respect, the overall mechanism for reaction (2) with M = Fe is similar to that previously found [14a] for electrophilic attack by *p*-nitrodiazonium salt on indole, *i.e.* rate-determining addition to indole followed by rapid proton loss from C^3. However, it constrasts with iodination of indole where a positive deuterium-isotope effect was observed.[14b] Rapid proton loss in step k_3 to give the product (4) may be facilitated by the tricarbonyl(dienyl)-iron moiety acting as an electron sink (it is known [15] to be an electron-withdrawing group).

From the present data for reaction (2; M = Fe) it is not possible to distinguish between the alternatives (*a*) and (*b*) of the mechanism in equations (4) and (5). Although most electrophilic aromatic substitutions proceed *via* rate-determining formation of σ-complex intermediates, some instances in which π-complex formation is dominant have been reported by Olah.[16] The formation of π complexes is expected to be favoured when the aromatic substrate is a powerful nucleophile as is the case with many five-membered heterocyclic rings.[17]



Hydrogen-1 n.m.r. evidence [5] shows the indole substituent in product (4; M = Fe, A = OMe) to be *exo*.

This is also consistent with the mechanism in (4) and (5) in which direct reaction on the dienyl ring has occurred.

Mechanism of Indole Reaction with $[Ru(C_6H_7)(CO)_3]^+$.—The kinetic data for reaction (2) with $[Ru(C_6H_7)(CO)_3]^+$ as electrophile (Table 3) reveal a more complicated rate law. Unlike the iron case, a plot of $k_{obs.}$ against [indole] became distinctly curved for [indole] $\geqslant 0.2$ mol dm^{-3} [Figure 1(*a*)]. An attractive explanation for this behaviour is the mechanism in (4) and (5) [Figure 2(*c*)] in which a significant concentration of the π complex (5) is formed in a rapid pre-equilibrium, followed by rate-determining formation of the δ-complex intermediate (6). Assuming a genuine pre-equilibrium, $k_{obs.}$ for this process is given by equation (6). Strong support for this mechanism comes from the excellent linearity of a plot of $1/k_{obs.}$ against

$$k_{obs.} = \frac{k_2K[\text{indole}]}{1 + K[\text{indole}]} \tag{6}$$

$$1/k_{obs.} = \frac{1}{k_2} + \frac{1}{k_2K[\text{indole}]} \tag{7}$$

1/[indole] for the ruthenium reaction at 24.5 °C [Figure 1 (*b*)]. A k_2 value of 4.8×10^{-4} s^{-1} is estimated from the intercept, while the gradient yields a pre-equilibrium constant K ($= k_1/k_{-1}$) of 2.32 dm^3 mol^{-1}. The present results might thus provide the first kinetic evidence for the formation of a π complex during electrophilic substitution at indole. Similar evidence has been recently obtained [18] for the chlorination of benzothiophen.

Alternative formulations for the intermediate (5) formed in the pre-equilibrium include a species with a direct ruthenium–indole bond. Such a mechanism, involving initial attachment of indole to the metal, would be expected to yield a product (4) with an *endo*-indole substituent. Unfortunately the inability to crystallise

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[14] (*a*) J. H. Binks and J. H. Ridd, *J. Chem. Soc.*, 1957, 2398; (*b*) E. C. R. DeFabrizio, *Ann. Chim.* (*Italy*), 1968, **58**, 1435.

[15] J. M. Landesberg and L. Katz, *J. Organometallic Chem.*, 1971, **33**, C15.

[16] G. A. Olah, *Accounts Chem. Res.*, 1971, **4**, 240 and refs. therein.

[17] G. Marino, *Adv. Heterocyclic Chem.*, 1971, **13**, 235.

[18] E. Baciocchi and L. Mandolini, *J. Chem. Soc.* (*B*), 1968, 397.

the ruthenium product has so far prevented stereochemical analysis. Another possible explanation for intermediate (5) is that it arises *via* initial attack by indole at the 3-position of the dienyl ring in $[Ru(C_6H_7)(CO)_3]^+$ to give a substituted 1,4-diene species, which then slowly rearranges to the observed 1,3-diene product [equation (8)]. A two-step process of this type has recently been demonstrated by Johnson *et al.*[19] for the addition of hydride ion to the carbonyl(cycloheptadienyl)(cyclohexa-1,3-diene)iron cation. A 1,4-diene of this type should exhibit a distinct i.r. spectrum in the carbonyl region.[19] However, the only i.r. carbonyl bands observed during reaction (2) were those assignable to the dienyl cation and the neutral 1,3-diene product.

Comparison of Iron and Ruthenium Reactions.—Mechanistically, the most significant difference between the reactions of cations (1) and (3) with indole is the detection of a kinetic intermediate only in the ruthenium case. If one assumes a π-complex formulation for intermediate (5), this difference may be rationalised in terms of the mechanism in (4) and (5), route (*a*) for iron and (*c*) for ruthenium. While formation of the π-complex intermediate is rate-determining for iron, with the less electrophilic $[Ru(C_6H_7)(CO)_3]^+$ (see below) a greater degree of charge transfer is necessary to reach the transition state resulting in greater σ-bond formation and mechanism (*c*). An alternative explanation invoking mechanisms (*b*) and (*c*) [equations (4) and (5)] for iron and ruthenium, respectively, seems less likely since it is difficult to see why π-complex formation should be significant only in the ruthenium case. It is interesting that studies[3,20] of the related reactions of methoxide ion with $[M(C_6H_7)(CO)_3]^+$ (M = Fe or Ru) also indicated a change in mechanism on varying the metal. While direct attack on the dienyl ring occurred with iron, in the ruthenium case initial methoxide addition at a carbonyl ligand was observed yielding an ester species which then rearranged to give the methoxydiene product.

The variation in mechanism of reaction (2) with the nature of the metal precludes direct comparison of the rate and activation parameters. However, the overall observed rate constant ([indole] = 0.05 mol dm^{-3}) for ruthenium is seen from Tables 1 and 3 to be *ca.* 10^2 times slower than that with iron. Related studies of the reaction of (1) and (3) with pentane-2,4-dione have similarly shown a lower electrophilicity for the ruthenium (dienyl) cation. These observations, however, contrast sharply with recent kinetic data for the reaction of iodide ion with $[M(C_6H_7)(CO)_3]^+$ (M = Fe or Ru) to yield $[M(C_6H_7)(CO)_2I]$.[21] In this latter process (apparently involving bimolecular displacement at the metal) attack at ruthenium was several hundred times faster than at iron.

While the $\Delta H_{obs.}^{\ddagger}$ and $\Delta S_{obs.}^{\ddagger}$ values in Table 4 refer directly to step k_1 (or k_2) for the iron cations, they are composite parameters for $[Ru(C_6H_7)(CO)_3]^+$ (*e.g.* $\Delta H_{obs.}^{\ddagger} = \Delta H_1^{\ominus} + \Delta H_2^{\ddagger}$). All the reactions have relatively low activation enthalpies. The large negative entropies of activation are as expected for the associative mechanism [equations (4) and (5)], since solvation effects are not expected to be large in reactions of type (2) involving a neutral reactant.

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[6/755 *Received, 15th April, 1976*]

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[19] B. F. G. Johnson, J. Lewis, and T. W. Matheson, *J.C.S. Chem. Comm.*, 1974, 269.

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[21] G. R. John and L. A. P. Kane-Maguire, unpublished work.