

PLATINUM COMPLEX CATALYZED SYNTHESIS OF UREA DERIVATIVES FROM NITROARENES AND AMINES UNDER CARBON MONOXIDE

YASUSHI TSUJI, RYO TAKEUCHI, and YOSHIHISA WATANABE*

Department of Hydrocarbon Chemistry, Faculty of Engineering, Kyoto University, Sakyo-ku Kyoto 606 (Japan)

(Received January 7th, 1985)

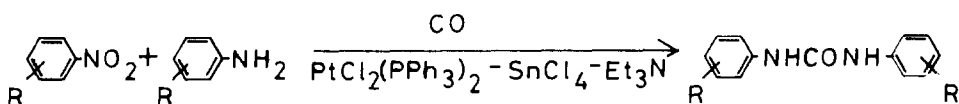
Summary

N,N'-Diarylureas were obtained in good yields from nitroarenes and aminoarenes at 140°C under carbon monoxide (initial 60 kg cm⁻²) in the presence of a catalytic amount of dichlorobis(triphenylphosphine)platinum(II), the yields of *N,N'*-diphenylurea, *N,N'*-bis(4-methylphenyl)urea, and *N,N'*-bis(4-chlorophenyl)urea were 65, 67 and 61%, respectively. Benzimidazole derivatives were obtained by the intramolecular cyclization reaction. An attempted synthesis of unsymmetric ureas resulted in the formation of a mixture of symmetric and unsymmetric products.

Introduction

The activation of carbon monoxide by transition metal catalysts is of current interest [1]. Complexes of Group VIII first and second row metals have been used as catalysts for wide varieties of transformations [2,3]. Compared with these metals, platinum complexes have had less attention as catalysts for carbonylations with carbon monoxide. Recently, Knifton and Schwanger [4] and Ogata and co-workers [5] have reported carbonylation of olefins in the presence of a platinum/tin(II) chloride systems. We also reveal that a homogeneous platinum catalyst system is highly active for a series of the reductive *N*-carbonylation of nitroarenes under carbon monoxide pressure affording phenylcarbamates [6], aminoarenes [7], or arylamides [8] as products.

This paper deals with platinum catalyzed synthesis of urea derivatives from nitroarenes and amines. Regarding transition metal catalyzed syntheses of urea derivatives from nitroarenes, only a few precedents are known. Heck et al. [9] have found that palladium catalysts show high catalytic activity for urea synthesis from nitroarenes and aminoarenes under carbon monoxide. Iqbal [10] obtained urea derivatives by carbonylation of aromatic azides under carbon monoxide.



SCHEME 1

Results and discussion

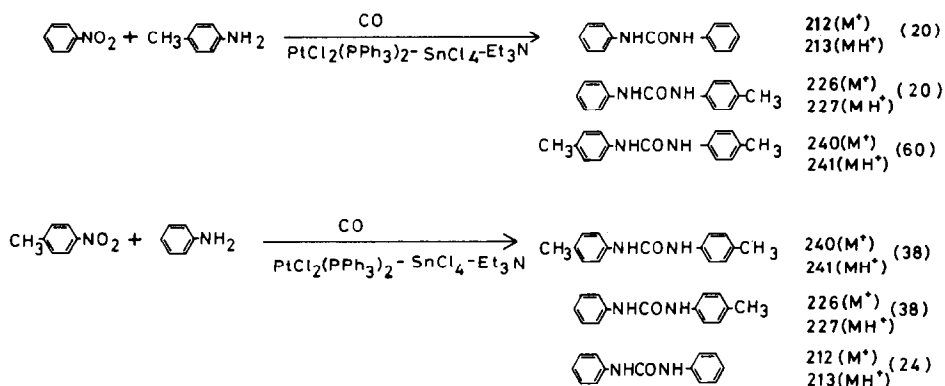
Nitrobenzene reacted with aniline in the presence of a platinum/tin(IV) chloride catalyst system at 140°C for 4 h under carbon monoxide (60 kg cm⁻²). *N,N'*-Diphenylurea was the product obtained. Effects of the catalyst components in this reaction were examined. The results are listed in Table 1. Dichlorobis(triphenylphosphine)platinum(II) combined with tin(IV) chloride and triethylamine showed the highest catalytic activity (Run 1). If one of these components, tin(IV) chloride or triethylamine, were removed from the catalyst system, the yield of urea was dramatically decreased (Runs 2–4). When the amount of triethylamine was reduced to 0.5 mmol ([Et₃N]/[SnCl₄]=0.5; Run 5), the yield of urea decreased to 14%. An excess of triethylamine over tin(IV) chloride was required for a good yield of urea. The optimum reaction temperature was 140°C, and the yield of urea decreased at 100°C. Use of aluminum(III) chloride or iron(III) chloride as a Lewis acid gave lower yields (Runs 7 and 8). Heck et al. claimed that tetrabutylammonium chloride was essential in the palladium catalyzed reaction [9]. Tetrabutylammonium chloride cannot replace tin(IV) chloride in the present platinum catalyst system. When the inorganic base, potassium carbonate, is used instead of triethylamine, the yield of urea is low (Run 9).

This procedure was applicable in the preparation of unsymmetric ureas, although a mixture of symmetric and unsymmetric products was obtained. Both the reaction of nitrobenzene with *p*-toluidine and the reaction of *p*-nitrotoluene with aniline gave

TABLE 1
PLATINUM CATALYZED SYNTHESIS OF *N,N'*-DIPHENYLUREA FROM NITROBENZENE AND ANILINE^a

| Run | Lewis acid | Base | Temperature (°C) | Yield (%) ^b |
|----------------|-------------------|---|------------------|------------------------|
| 1 | SnCl ₄ | Et ₃ N | 140 | 65 (61) ^c |
| 2 | SnCl ₄ | – | 140 | 5 |
| 3 | – | Et ₃ N | 140 | 27 |
| 4 | – | – | 140 | 1 |
| 5 ^d | SnCl ₄ | Et ₃ N | 140 | 14 |
| 6 | SnCl ₄ | Et ₃ N | 100 | 19 |
| 7 ^e | AlCl ₃ | Et ₃ N | 140 | 27 |
| 8 | FeCl ₃ | Et ₃ N | 140 | 37 |
| 9 | SnCl ₄ | K ₂ CO ₃ ^f | 140 | 7 |

^a A mixture of nitrobenzene (10 mmol), aniline (11 mmol), PtCl₂(PPh₃)₂ (0.10 mmol; 1.0 mol% based on nitrobenzene), SnCl₄ (1.0 mmol), Et₃N (1.8 mmol), and dioxane (20 ml) was stirred for 4 h under carbon monoxide (initial 60 kg cm⁻²). ^b Determined by HPLC based on the amount of nitrobenzene charged. ^c Isolated yield in parenthesis. ^d Et₃N (0.5 mmol). ^e Et₃N (5.0 mmol), benzene (20 ml). ^f K₂CO₃ (7.0 mmol).

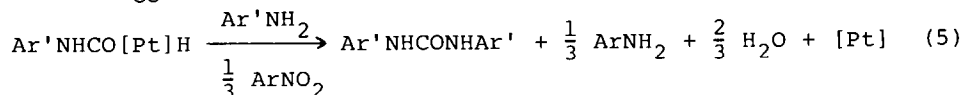
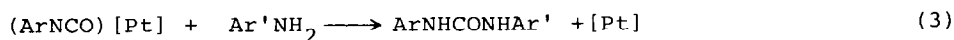
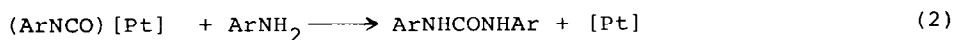
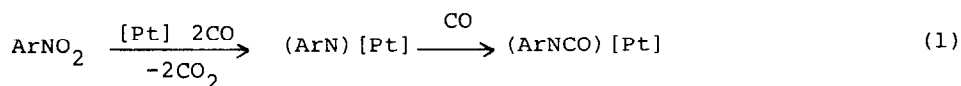


SCHEME 2

a mixture of three ureas (see Experimental). The proportions of these ureas could not be determined by ^{13}C NMR spectra. Therefore, these were estimated by FD-mass spectra (Scheme 2). Figures in parentheses in Scheme 2 show sums of relative intensities of M^+ and MH^+ for the ureas.

When nitrobenzene alone was treated with triethylamine in the presence of the platinum/tin(IV) chloride catalyst system, *N,N'*-diphenylurea was obtained in 64% yield. Nitrobenzene may be partly hydrogenated to aniline. The hydrogen source in this reaction is considered to be triethylamine. Several examples of hydrogen transfer from amines catalyzed by transition metals have been shown in the literature [11]. Molecular hydrogen (30 kg cm^{-2} initial) was not effective as the hydrogen source for this reaction. The urea was obtained only in 1% yield, but aniline was a major product (65% yield). When aniline alone was used in the reaction, aniline conversion was low and the yield of urea was only 9%. In the present reaction, therefore, the combination of a nitroarene and an aminoarene is indispensable for high yield of the urea.

The reaction features observed hitherto are consistent with the sequence represented by eq. 1–5 (Scheme 3). One of the key intermediates in the present reaction



SCHEME 3

TABLE 2
PLATINUM CATALYZED SYNTHESSES OF UREA DERIVATIVES ^a

| Run | Nitroarene | Aminoarene | Product | Yield (%) ^b |
|-------------------|------------------------------|------------------------------|---|------------------------|
| 10 | <i>p</i> -nitrotoluene | <i>p</i> -toluidine | <i>N,N'</i> -bis(4-methylphenyl)urea | 67 |
| 11 | <i>o</i> -nitrotoluene | <i>o</i> -toluidine | <i>N,N'</i> -bis(2-methylphenyl)urea | 49 |
| 12 | <i>p</i> -nitrochlorobenzene | <i>p</i> -chloroaniline | <i>N,N'</i> -bis(4-chlorophenyl)urea | 61 |
| 13 | <i>p</i> -nitroanisole | <i>p</i> -methoxyaniline | <i>N,N'</i> -bis(4-methoxyphenyl)urea | 20 |
| 14 ^c | | <i>o</i> -nitroaniline | 1,3-dihydro-2 <i>H</i> -benzimidazol-2-one | 56 |
| 15 ^{c,d} | | 2-nitro- <i>p</i> -toluidine | 1,3-dihydro-5-methyl-2 <i>H</i> -benzimidazol-2-one | 29 |

^a Nitroarene (10 mmol), aminoarene (10 mmol), PtCl₂(PPh₃)₂ (0.10 mmol), SnCl₄ (1.0 mmol), Et₃N (5 mmol), benzene (20 ml) at 140°C for 4 h under carbon monoxide (initial 60 kg cm⁻²). ^b Isolated yield.

^c Nitroaminoarene (10 mmol), Et₃N (1.8 mmol), dioxane (20 ml). ^d At 110°C.

seems to be a phenylisocyanate complex generated by carbonylation of a nitrene-platinum complex as shown by eq. 1. There have been several precedents for a nitrene intermediate from a nitroarene and carbon monoxide [12], and also for the carbonylation of a nitrene intermediate into an isocyanate [13]. The phenylisocyanate intermediate can react with an amine to give the corresponding urea derivatives (eq. 2 and 3). Another key intermediate would be a carbamoyl complex from the amine and carbon monoxide (eq. 4). Such a carbamoyl intermediate is presumed in urea synthesis from amines and carbon monoxide [14]. The carbamoyl intermediate reacts with the amine in the presence of the nitro compound to give the urea (eq. 5). Here, the nitro compound works as an oxidizing reagent by removing hydrogen from the carbamoyl intermediate. Yield of the urea is low without the nitro compound (*vide supra*). Oxidative *N*-carbonylation of aminoarenes has been reported recently [15].

An aliphatic amine such as *n*-butylamine reacted similarly with nitrobenzene. A mixture of three ureas was obtained and the proportion of each urea was estimated by ¹³C NMR spectra; *N,N'*-dibutylurea/*N*-butyl-*N'*-phenylurea/*N,N'*-diphenylurea: 46/46/8. Generally the formation of the carbamoyl complex is favored with an aliphatic amine [16]. This may lead to the considerable formation of the *N,N'*-dialkylurea.

Several symmetric aromatic ureas were obtained by the present catalytic system. Results are listed in Table 2. Methyl and chloro substituents at the *para* position did not affect the reaction. However, the methoxy substituent reduced the yield considerably (Run 13). Benzimidazole derivatives were also produced intramolecularly, although yields were rather moderate (Runs 14 and 15).

Experimental

Materials

The reagents employed in this study were purified before use. Carbon monoxide (> 99.9%) was used without further purification. The platinum complex was prepared by the literature method [17]. ¹H NMR spectra are given in δ(ppm), 100 MHz; ¹³C NMR in δ(ppm), 25.05 MHz in DMSO-*d*₆.

General procedure

A 100 ml stainless steel autoclave (Nitto Koatsu) equipped with a magnetic stirrer was used. A glass liner was set in the autoclave and the inside of it was heated with a

heat gun (400 W) for 2 min. After the reactor was cooled under argon, the reagents were charged in the following order: solvent (20 ml), nitroarene (10 mmol), aminoarene (10 mmol), triethylamine (0.25 ml, 1.8 mmol), $\text{PtCl}_2(\text{PPh}_3)_2$ (79 mg, 0.10 mmol; 1.0 mol% based on the nitroarene), and SnCl_4 (0.12 ml, 1.0 mmol). After being sealed and flushed with carbon monoxide, the reactor was pressurized with carbon monoxide to 60 kg cm^{-2} . The autoclave was heated to 140°C in 15 min and then held at this temperature for 4 h. The reaction was terminated by rapid cooling and the autoclave was discharged. The resulting brown solution was analyzed by HPLC. The products were isolated by recrystallization from ethanol. The products were identified by elemental analysis, IR, ^1H NMR, ^{13}C NMR, and mass spectra.

Analytical procedure

The ^{13}C NMR and ^1H NMR spectra were recorded at 25.05 and 100 MHz respectively with a JEOL JNM FX 100 spectrometer. Samples were dissolved in $\text{DMSO}-d_6$, and the chemical shift values were expressed relative to Me_4Si as internal standard. The HPLC analysis was performed on a Shimadzu LC-5A equipped with Merck Hibar RP-18 ($5 \mu\text{m}$). A mixture of methanol and water (6/4 v/v) was used as an eluant. The product yields were determined by HPLC with phenetole as the internal standard. The IR spectra were measured on a Nicolet 5MX Fourier transform infrared spectrophotometer. The FD-mass spectra were measured on a Hitachi M-80. Elemental analyses were performed at the Microanalytical Center of Kyoto University.

N,N'-Diphenylurea from nitrobenzene (in the absence of aniline). A mixture of nitrobenzene (1.2 g, 10 mmol), $\text{PtCl}_2(\text{PPh}_3)_2$ (79 mg, 0.10 mmol), SnCl_4 (0.12 ml, 1.0 mmol), Et_3N (0.7 ml, 5 mmol), and benzene (20 ml) was stirred under the same conditions described in the general procedure. *N,N'*-Diphenylurea was obtained in 64% yield.

N,N'-Diphenylurea from aniline (in the absence of nitrobenzene). Aniline (0.95 g, 10 mmol), $\text{PtCl}_2(\text{PPh}_3)_2$ (79 mg, 0.10 mmol), SnCl_4 (0.12 ml, 1.0 mmol), Et_3N (0.25 ml, 1.8 mmol), and benzene (20 ml) were stirred under the same reaction conditions as described in the general procedure. *N,N'*-Diphenylurea was obtained in 9% yield.

Reaction with molecular hydrogen. Nitrobenzene (1.2 g, 10 mmol), $\text{PtCl}_2(\text{PPh}_3)_2$ (79 mg, 0.10 mmol), SnCl_4 (0.12 ml, 1.0 mmol), Et_3N (0.25 ml, 1.8 mmol), benzene (20 ml) were charged in the autoclave. The autoclave was then pressurized with carbon monoxide (60 kg cm^{-2}) and hydrogen (30 kg cm^{-2}), the reactor was heated to 140°C and held at this temperature for 4 h. *N,N'*-Diphenylurea was obtained in 1% yield as well as aniline in 65% yield.

Synthesis of unsymmetric urea

A mixture of nitroarene (10 mmol), amine (10 mmol), triethylamine (0.25 ml, 1.8 mmol), $\text{PtCl}_2(\text{PPh}_3)_2$ (79 mg, 0.1 mmol), SnCl_4 (0.12 ml, 1.0 mmol), dioxane (20 ml) was stirred under the same conditions as described in the general procedure. From nitrobenzene (1.3 g, 10 mmol), and *p*-toluidine (1.1 g, 10 mmol), 1.78 g of a mixture of three ureas (*N,N'*-diphenylurea, *N*-(4-methylphenyl)-*N'*-phenylurea, *N,N'*-bis(4-methylphenyl)urea) was isolated by recrystallization from ethanol. From *p*-nitrotoluene (1.4 g, 10 mmol), and aniline (1.0 g, 10 mmol), 1.86 g of a similar mixture of the three ureas was isolated. The proportion of each urea was estimated by the FD-mass spectra (see Scheme 2). From nitrobenzene (1.3 g, 10 mmol) and

n-butylamine (0.73 g, 10 mmol), 1.06 g of a mixture of three ureas (*N,N'*-diphenylurea, *N*-butyl-*N'*-phenylurea, *N,N'*-dibutylurea) was isolated by Kugelrohr distillation. The proportion of each urea was estimated by ^{13}C NMR spectra (gated decoupling method).

The analytical data of the products are described below. The phenyl carbon resonance in the ^{13}C NMR spectra were tentatively assigned by calculating their chemical shifts with additive parameters [18].

N,N'-Diphenylurea. White crystals. ^1H NMR: δ 6.89–7.50 (m, 12H, phenyl and NH). ^{13}C NMR: δ 139.6 (s, phenyl, 1,1'), 118.0 (d, phenyl 2,6,2',6'), 128.6 (d, phenyl 3,5,3',5'), 121.6 (d, phenyl 4,4') 152.4 (s, C=O). IR (KBr): 3330 cm^{-1} ($\nu(\text{N-H})$), 1650 cm^{-1} ($\nu(\text{C=O})$). MS (m/e): 212 (M^+). Found: C, 73.19; H, 5.63; N, 12.74. $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}$ calcd.: C, 73.57; H, 5.70; N, 13.20%.

N,N'-Bis(4-methylphenyl)urea. White crystals. ^1H NMR: δ 2.23 (s, 3H, $-\text{CH}_3$), 7.06 (d, 4H, phenyl, J 8.07 Hz), 7.32 (d, 4H, phenyl, J 8.07 Hz), 8.49 (s, 2H, NH). ^{13}C NMR: δ 20.4 (q, $-\text{CH}_3$), 137.3 (s, phenyl, 1,1'), 118.3 (d, phenyl, 2,6,2',6'), 129.2 (d, phenyl, 3,5,3',5'), 130.6 (s, phenyl, 4,4'), 152.7 (s, C=O). IR (KBr): $\nu(\text{N-H})$ 3300 cm^{-1} ; $\nu(\text{C=O})$ 1635 cm^{-1} . Found: C, 75.15; H, 6.62; N, 11.62. $\text{C}_{15}\text{H}_{16}\text{N}_2\text{O}$ calcd.: C, 74.97; H, 6.71; N, 11.66%.

N,N'-Bis(4-chlorophenyl)urea. White crystals. ^1H NMR: δ 7.31 (d, 4H, phenyl, J 9.0 Hz), 7.51 (d, 4H, phenyl, J 9.0 Hz), 8.84 (s, 2H, NH). ^{13}C NMR: δ 138.6 (s, phenyl, 1,1'), 120.0 (d, phenyl, 2,6,2',6'), 128.7 (d, phenyl, 3,5,3',5'), 125.7 (s, phenyl, 4,4'), 152.5 (s, C=O). IR (KBr): $\nu(\text{N-H})$ 3300 cm^{-1} , $\nu(\text{C=O})$ 1630 cm^{-1} . Found: C, 55.43; H, 3.42; N, 10.01; Cl, 24.97. $\text{C}_{13}\text{H}_{10}\text{N}_2\text{OCl}$ calcd.: C, 55.54; H, 3.59; N, 9.96; Cl, 25.22%.

N,N'-Bis(4-methoxyphenyl)urea. White crystals. ^1H NMR: δ 3.38 (s, 6H, CH_3O), 6.85 (d, 4H, phenyl, J 9.0 Hz), 7.35 (d, 4H, phenyl, J 9.0 Hz), 8.37 (s, 2H, NH). ^{13}C NMR: δ 55.8 (q, $-\text{OCH}_3$), 133.0 (s, phenyl, 1,1'), 120.1 (d, phenyl, 2,6,2',6'), 114.1 (d, phenyl, 3,5,3',5'), 153.1 (s, phenyl, 4,4'), 154.4 (s, C=O). IR (KBr): $\nu(\text{N-H})$ 3270 cm^{-1} , $\nu(\text{C=O})$ 1630 cm^{-1} . Found: C, 66.38; H, 5.73; N, 10.34. $\text{C}_{15}\text{H}_{16}\text{N}_2\text{O}_3$ calcd.: C, 66.16; H, 5.92; N, 10.29%.

N,N'-Bis(2-methylphenyl)urea. White crystals. ^1H NMR: δ 2.26 (s, 6H, $-\text{CH}_3$), 6.92–7.85 (m, 8H, phenyl) 8.22 (s, 2H, NH). ^{13}C NMR: δ 17.9 (q, $-\text{CH}_3$), 137.3 (s, phenyl, 1,1'), 127.6 (s, phenyl, 2,2'), 130.0 (d, phenyl, 3,3'), 122.5 (d, phenyl, 4,4'), 125.9 (d, phenyl, 5,5'), 121.4 (d, phenyl, 6,6'), 152.8 (s, C=O). IR (KBr): $\nu(\text{N-H})$ 3300 cm^{-1} , $\nu(\text{C=O})$ 1635 cm^{-1} . Found: C, 74.38; H, 6.76; N, 11.60. $\text{C}_{15}\text{H}_{16}\text{N}_2\text{O}$ calcd.: C, 74.97; H, 6.71; N, 11.66%.

1,3-Dihydro-2H-benzimidazol-2-one. Brown crystals. ^1H NMR: δ 6.94 (s, 6H, phenyl, NH). ^{13}C NMR: δ 129.6 (s, phenyl, 1), 108.4 (d, phenyl, 4,7), 120.3 (d, phenyl, 5,6), 155.3 (s, C=O). IR (KBr): $\nu(\text{N-H})$ 3180 cm^{-1} , $\nu(\text{N-H})$ 3140 cm^{-1} , $\nu(\text{C=O})$ 1740 cm^{-1} .

1,3-Dihydro-5-methyl-2H-benzimidazol-2-one. Brown crystals. ^1H NMR: δ 2.28 (s, 3H, $-\text{CH}_3$), 6.76–6.79 (m, 3H, phenyl). ^{13}C NMR: δ 21.0 (q, $-\text{CH}_3$), 108.0 (d, phenyl, 7), 108.9 (d, phenyl, 4), 120.7 (d, phenyl, 6), 127.3 (s, phenyl, 8), 129.2 (s, phenyl, 5), 129.8 (s, phenyl, 9), 155.3 (s, C=O). IR (KBr): $\nu(\text{N-H})$ 3132 cm^{-1} , $\nu(\text{C=O})$ 1749 cm^{-1} .

Acknowledgement

We thank Dr. H. Yatagai for measuring FD-mass spectra.

References

- 1 P.C. Ford (Ed.), *Catalytic Activation of Carbon Monoxide*, ACS Symposium Series 152, American Chemical Society, Washington, D.C., 1981.
- 2 I. Wender and P. Pino (Eds.), *Organic Syntheses via Metal Carbonyls*, Wiley-Interscience, New York, Vol. 2, 1977.
- 3 I. Tkatchenko, in G. Wilkinson, F.G.A. Stone, and E.W. Abel (Eds.), *Comprehensive Organometallic Chemistry*, Vol. 8, Pergamon Press, Oxford, 1982, p. 107.
- 4 (a) I. Schwanger and J.F. Knifton, *J. Catal.*, 45 (1976) 256; (b) J.F. Knifton, *J. Org. Chem.*, 41 (1976) 793.
- 5 T. Hayashi, Y. Kawabata, T. Isoyama, and I. Ogata, *Bull. Chem. Soc. Jpn.*, 54 (1981) 3483.
- 6 (a) Y. Watanabe, Y. Tsuji, R. Takeuchi, and N. Suzuki, *Bull. Chem. Soc. Jpn.*, 56 (1983) 3343; (b) Y. Watanabe, Y. Tsuji, and R. Takeuchi, *ibid.*, 57 (1984) 3011.
- 7 Y. Watanabe, Y. Tsuji, T. Ohsumi, and R. Takeuchi, *Bull. Chem. Soc. Jpn.*, 57 (1984) 2867.
- 8 Y. Watanabe, Y. Tsuji, T. Kondo, and R. Takeuchi, *J. Org. Chem.*, 49 (1984) 4451.
- 9 H. Dieck, R.M. Laine, and R.F. Heck, *J. Org. Chem.*, 40 (1975) 2819.
- 10 A.F.M. Iqbal, *Helv. Chim. Acta*, 55 (1972) 2637.
- 11 (a) Y. Shvo and R.M. Laine, *J. Chem. Soc. Chem. Commun.*, (1980) 753; (b) Y. Shvo, D.W. Thomas and R.M. Laine, *J. Am. Chem. Soc.*, 103 (1981) 2461; (c) R.M. Laine, D.W. Thomas and L.W. Cary, *ibid.*, 104 (1982) 1763; (d) R.B. Wilson, Jr. and R.M. Laine, *ibid.*, 107 (1985) 361.
- 12 A.F.M. Iqbal, *J. Org. Chem.*, 37 (1972) 2791; *Helv. Chim. Acta*, 55 (1972) 26, 798, 2637.
- 13 (a) R.B. Bennett and W.B. Hardy, *J. Am. Chem. Soc.*, 90 (1968) 3295; (b) J.P. Collman, M. Kubota, D.F. Vastine, T.Y. Sun, and W. J. Kang, *ibid.*, 90 (1968) 5430.
- 14 I. Tkatchenko, in G. Wilkinson, F.G.A. Stone, and E.W. Abel (Eds.), *Comprehensive Organometallic Chemistry*, Vol. 8, Pergamon Press, Oxford, 1982, p. 173–179.
- 15 (a) S. Fukuoka, M. Chono, and M. Kohno, *J. Org. Chem.*, 49 (1984) 1458; (b) S. Fukuoka, M. Chono, and M. Kohno, *J. Chem. Soc., Chem. Commun.*, (1984) 399; (c) Japan Kokai 80–120551 (1980), 80–120552 (1980), 80–124750 (1980).
- 16 R.J. Angelici, *Acc. Chem. Res.*, 5 (1972) 335.
- 17 J.C. Bailar and H. Itatani, *Inorg. Chem.*, 4 (1965) 1618.
- 18 J.B. Stothers, *Carbon-13 NMR Spectroscopy*, Academic Press, New York, p. 197.