Indirect Electroreductive Addition of Alkyl Radicals to Activated Olefins using a Nickel(II) Complex as an Electron-transfer Catalyst

Shigeko Ozaki,* Hidenori Matsushita and Hidenobu Ohmori
Faculty of Pharmaceutical Sciences, Osaka University, 1-6, Yamadaoka, Suita, Osaka-fu, 565 Japan

Indirect electroreductive intermolecular addition of primary and secondary alkyl radicals has been achieved using a nickel(II) complex as an electron-transfer catalyst.

Most metal-catalysed reactions leading to carbon–carbon bond formation (*e.g.* allylation or alkenylation of olefins, the Heck reaction,[1] or cross coupling of halides with Grignard reagents) have been successful with a palladium catalyst.[2] In such reactions, electrophiles such as halides, triflates, acetate or sulfones bearing an sp or sp^2 carbon either at the electrophilic centre or immediately adjacent to it have been used.

Recently, conjugated addition of alkyl radicals to electron-deficient olefins by means of tin hydride and closely related mercuric hydride methods have been described and their utility shown, especially in the addition to highly functionalized molecules such as natural products.[3] Vitamin B_{12}-catalysed carbon–carbon bond formation has been also developed by Scheffold[4] and proven particularly useful in the synthesis of C-glucosides by reductive addition of 1-bromo derivatives of glucose or ribose to Michael olefins added in excess. Usually, in the tin hydride method, reactions are conducted with equimolar amounts of alkyl halide and tin hydride, and an excess (*ca.* 5 equiv.) of an activated olefin.[3] This tin hydride method, however, requires a delicate balance among the starting halide, activated alkene and tin hydride to avoid hydrostannylation of the starting alkene, hydrogenation of the initially formed radical by tin hydride and telomerization caused by the reaction of the adduct radical with the activated olefin used in large excess to enhance the addition rate with the initial radical.

Few attempts have been made, in the area of intermolecular radical addition to olefins, to conduct reactions with catalytic amounts of tin hydride, although reduced consumption of harmful metals in chemical reactions is highly desirable.[5]

Pletcher has reported that a nickel(I) complex, [Ni (tet a)]⁺,†
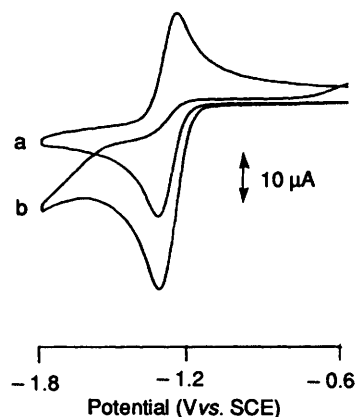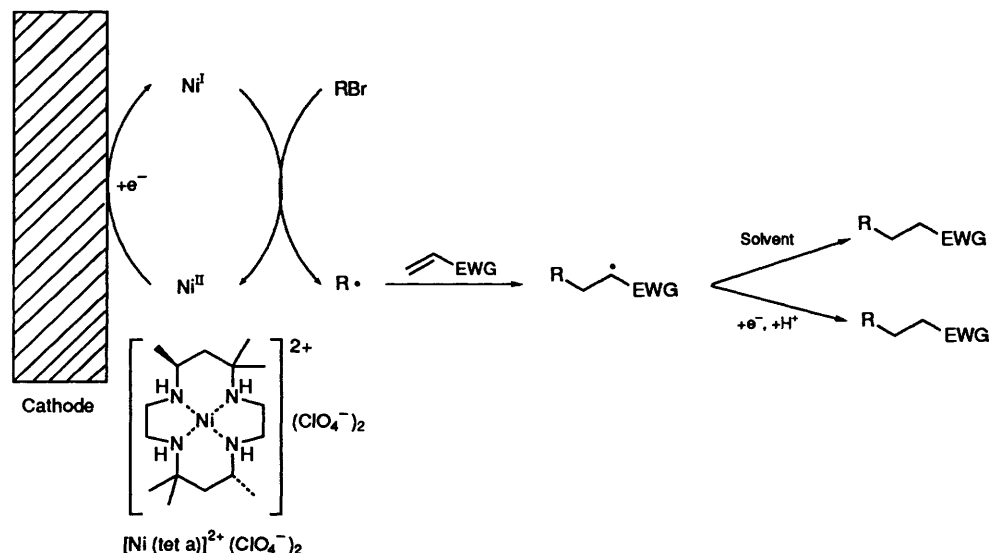
† Structure given in Scheme 1.

Fig. 1 Cyclic voltammograms of [Ni(tet a)](ClO₄)₂ in DMF containing 0.1 mol dm⁻³ of TEAP. Sweep rate of 0.1 V s⁻¹, at a glassy carbon electrode. a: [Ni(tet a)](ClO₄)₂ (2 mmol dm⁻³) alone. b: [Ni(tet a)](ClO₄)₂ (2 mmol dm⁻³) with BuBr (10 mmol dm⁻³).

formed by cathodic reduction of the corresponding nickel(II) complex, reacts rapidly with alkyl bromides and gives addition products with activated olefins upon electrolysis. However, the nickel species becomes electroinactive after passage of 2F mol⁻¹ of [Ni (tet a)]²⁺, since the syntheses are not catalytic with respect to the latter.[6]

In connection with the latter reaction we have described a useful catalytic synthesis of bicyclic ketones by intramolecular 1,4-addition of alkyl bromides[7a] and an alternative method to that using tin hydride for the radical cyclization of halogeno ethers;[7b] in these reactions we have used a variety of cobalt and nickel complexes as electron-transfer catalysts.

Scheme 1

Table 1 Electroreductive 1,4-addition of alkyl bromide to activated olefin using [Ni (tet a)]$^{2+}$ as an electron-transfer catalyst[a]

Run	RBr	$\nearrow$ EWG	F mol^{-1}	R$\searrow\diagup$ EWG		R–R	R–H
1	BuBr	$CH_2=CH(O)OCH_2Ph$	1.7	**1**	53	c	c
2	BuBr	$CH_2=CHC(O)OH$	1.8	**2**	32	c	c
3	$Ph(CH_2)_3Br$	$\overline{CH_2COCH=CH(CH_2)_2}CH_2$	1.9	**3**	14	18	11
4	$Ph(CH_2)_3Br$	$MeCH=CH(C(O)OMe$	1.7	**4**	13[d]	18	6
5	$Ph(CH_2)_3Br$	$CH_2=C(Me)C(O)OMe$	2.8	**5**	53	4	6
6	$Ph(CH_2)_3Br$	$CH_2=CHC(O)OMe$	2.0	**6**	57	4	Trace
7	$Ph(CH_2)_3Br$	$CH_2=CHCN$	2.6	**7**	72	3	Trace
8	$Ph(CH_2)_3Br$	$CH_2=CHC(O)Me$	2.5	**8**	37	6	6
9	$Ph(CH_2)_2CHMeBr$	$CH_2=CHC(O)OMe$	1.7	**9**	60	7	2

[a] Conditions: see text. [b] Isolated yield based on alkyl halide except for 1 which was determined by GCL. Product: **1**; benzyl heptanoate, **2**; heptanoic acid, **3**; 3-(3-phenylpropyl)cyclohexanone, **4**; methyl 3-methyl-6-phenylhexanoate, **5**; methyl 2-methyl-6-phenylhexanoate, **6**; methyl 6-phenylhexanoate **7**; 5-cyanopentylbenzene, **8**; 7-phenylheptan-2-one, **9**; methyl 4-methyl-6-phenylhexanoate. [c] Not determined. [d] Constant current electrolysis at 2.3 mA gave essentially the same results.

Here, we report that primary and secondary alkyl radicals add smoothly to activated olefins (see Scheme 1) upon electroreduction of equimolar proportions of alkyl halides and activated olefins in the presence of a catalytic amount of [Ni (tet a)]$^{2+}$; the latter exhibits the most negative redox potential of the three complexes used in our earlier work.[7b]

Cyclic voltammetry (Fig. 1) was used to check whether electron-transfer from reductively generated [Ni (tet a)]$^+$ to butyl bromide occurred. Thus on addition of butyl bromide (10 mmol dm^{-3}) to a solution of [Ni (tet a)]$^{2+}$ (2 mmol dm^{-3}), the reversible wave at -1.30 V vs. SCE which corresponds to the [Ni (tet a)]$^{2+}$/[Ni (tet a)]$^+$ couple became irreversible; an increase of the catalytic peak height corresponded to reduction of [Ni (tet a)]$^{2+}$, although butyl bromide is not electroactive below -2.20 V at a glassy carbon electrode. Addition of the activated olefins cyclohex-2-enone or benzyl acrylate caused no significant change in the reversible wave of the Ni^{II}/Ni^I couple.

Alkyl radicals added to activated olefins in dimethyl-formamide (DMF; 20 cm) containing a supporting electrolyte (Et$_4$NClO$_4$; 0.1 mol dm^{-3}), an alkyl bromide (2 mmol), an activated olefin (1.1 equiv. based on the bromide), a proton source (NH$_4$ClO$_4$; 2 equiv. based on the bromide), and a catalytic amount of [Ni (tet a)](ClO$_4$)$_2$ (0.02 equiv. based on the bromide) potentiostatically at -1.30 V using a graphite plate electrode as a cathode in an H-shaped divided cell under an inert gas.

As shown in Table 1, primary and secondary alkyl bromides gave the conjugated adducts in reasonable yield along with smaller amount of the radical coupling products and hydrogenated products except for runs 3 and 4. The results 3 and 4 indicate that in the case of substituted activated olefins, addition of the alkyl radical to the olefins occurs more slowly than that at an unsubstituted terminus, and dimerization of the initial radical becomes predominant, which must be ascribed, at least in part, to steric effects.

On the other hand, there seems to be little difference between the reactivity of primary and secondary alkyl radicals towards conjugated addition to activated olefins (runs 6 and 9).

The present method for indirect electroreductive addition of alkyl radicals to activated olefins offers advantage over the tin hydride method in that the reaction can be conducted with almost equimolar proportions of alkyl bromide and activated olefin at ambient temperature using a catalytic amount of easily prepared [Ni (tet a)]$^{2+}$.

Experimental

Instrumentation.—Gas chromatograph analyses (GLC) were performed on a JEOL JGC 20K chromatograph with a PEG 20

M glass column (2 m; 3 mm diam.). NMR spectra were taken on a JEOL EX-270 or a Varian VXR-200 instrument. IR spectra were taken on a Jasco A-202 instrument. Cyclic voltammetry was performed with a three-electrode system employing a linear scanning unit (Huso Electrochemical System HECS 321B) equipped with a potentiostat (Hokuto Denko PS-55B). Controlled potential electrolysis was carried out with a potentiostat (Hokuto Denko HA 301 or HA 105S), and the quantity of electricity consumed was recorded with a coulometer (Hokuto Denko HF-201).

Materials.—2-Bromo-4-phenylbutane was prepared by a literature method[8] from the reaction of 4-phenylbutan-2-ol (9.9 g, 66 mmol) and phosphorus tribromide (6.1 g, 22 mmol) under nitrogen at -10 °C. The crude product was purified by column chromatography (silica gel); δ_H(200 MHz; CDCl$_3$) 1.74 (3 H, d, MeCHBr), 2.10 (2 H, m, CH_2CHBr), 2.80 (2 H, m, CH_2Ph), 4.08 (1 H, m, CHBr) and 7.22 (5 H, m, Ph). Benzyl acrylate was prepared by the addition of benzyl bromide (8.55 g, 50 mmol) to a stirred mixture of HMPA (50 cm^3) containing acrylic acid (3.6 g, 50 mmol) and 25% aq. NaOH (70 mmol). The mixture was stirred for 5 h at room temperature after which it was worked up and the crude product purified by column chromatography (silica gel); δ(200 MHz; CDCl$_3$) 5.20 (2 H, s, CH_2Ph), 5.85 (1 H, dd, J 10 and 1.6, H^AH^BC=CH), 6.17 (1 H, dd, J 17 and 10, H^{2}C=CH), 6.46 (1 H, dd, J 17 and 1.6, H^AH^{B}C=CH) and 7.35 (5 H, m, Ph). Other reagents were purchased and used as received.

Controlled Potential Electrolysis and Product Analysis.—An alkyl bromide (2 mmol), an activated olefin (2.2 mmol), NH$_4$ClO$_4$ (4 mmol) and [Ni (tet a)](ClO$_4$)$_2$ (0.04 mmol) were dissolved in DMF (20 cm^3) containing Et$_4$NClO$_4$ (0.1 mol dm^{-3}) in an H shaped divided cell. The electrolyte was degassed by bubbling nitrogen through it for 20 min, after which it was electrolysed potentiostatically using a graphite plate as a cathode at the redox potential of [Ni (tet a)](ClO$_4$)$_2$ (-1.30 V) vs. SCE at room temperature under nitrogen gas until complete consumption of the alkyl bromide.

The products, extracted with ether from the electrolyte which had been diluted with water, were separated by chromatography (silica gel). Spectral data for the products are as follows. Benzyl heptanoate: δ_H(270 MHz; CDCl$_3$) 0.87 (3 H, t, Me), 1.28 [6 H, m, (CH_2)$_3$Me], 1.68 (2 H, m, CH_2CH$_2$CO), 2.35 (2 H, t, CH$_2$CO), 5.11 (2 H, s, CH_2Ph) and 7.35 (5 H, m, Ph); heptanoic acid: δ_H(270 MHz; CDCl$_3$) 0.89 (3 H, t, Me), 1.30 (6 H, m, [CH$_2$]$_3$), 1.63 (2 H, m, CH_2CH$_2$CO) and 2.35 (2 H, t, CH$_2$CO), location of hydroxy proton not established; 3-(3-phenylpropyl)-cyclohexanone: δ_H(200 MHz; CDCl$_3$) 1.2–1.5 [2 H, m,

651

Ph(CH$_2$)$_2$CH_2], 1.5–2.0 (7 H, m, CH_2CH$_2$Ph, β and γ protons of cyclohexanone), 2.0–2.5 (4 H, m, α protons of cyclohexanone), 2.6 (2 H, t, CH_2Ph) and 7.24 (5 H, m, Ph); δ$_C$(270 MHz; CDCl$_3$) 38.89 (CH), 41.39 (COCH_2CH$_2$), 48.05 (COCH_2CH); 1,6-diphenylhexane: δ$_H$(270 MHz; CDCl$_3$) 1.30–1.50 [4 H, m, (CH$_2$)$_2$(CH_2)$_2$(CH$_2$)$_2$], 1.50–1.70 (4 H, m, 2 × CH_2CH$_2$Ph), 2.59 (4 H, t, 2 × CH_2Ph) and 7.20 (10 H, m, 2 × Ph); m/z 238 (M$^+$, 34%); methyl 3-methyl-6-phenylhexanoate: δ$_H$(200 MHz; CDCl$_3$) 0.93 (3 H, d, Me), 1.20–1.40 (2 H, m, CH$_2$CH_2CHMe), 1.54–1.70 (2 H, m, CH$_2$CH_2CH$_2$), 2.00 (1 H, m, CHMe), 2.10 (1 H, dd, CH_aH$_b$COMe), 2.30 (1 H, dd, CH$_a$CH_bCOMe), 2.59 (2 H, t, CH_2Ph), 3.64 (3 H, s, OMe) and 7.20 (5 H, m, Ph); δ$_C$(270 MHz; CDCl$_3$) 30.19 (CH), 41.55 (CH_2CO); methyl 2-methyl-6-phenylhexanoate: δ$_H$(200 MHz; CDCl$_3$) 1.14 (3 H, d, MeCH), 1.2–1.8 [6 H, m, (CH_2)$_3$CH], 2.44 (1 H, m, CHMe), 2.60 (2 H, t, CH_2Ph), 3.65 (3 H, s, OMe) and 7.20 (5 H, m, Ph); 5-cyanopentylbenzene: δ$_H$(270 MHz; CDCl$_3$) 1.4–1.5 [2 H, m, CH_2(CH$_2$)$_2$CN], 1.5–1.8 (4 H, m, CH_2CH$_2$CH_2CH$_2$CN), 2.32 (2 H, t, CH$_2$CN), 2.63 (2 H, t, CH_2Ph) and 7.20 (5 H, m, Ph); methyl 6-phenylhexanoate: δ$_H$(200 MHz; CDCl$_3$) 1.37 [2 H, m, CH_2(CH$_2$)$_2$CO], 1.62 (4 H, m, CH_2CH$_2$CH_2CH$_2$CO), 2.31 (2 H, t, CH_2CO), 2.61 (2 H, t, CH_2Ph), 3.64 (3 H, s, OMe) and 7.20 (5 H, m, Ph); 7-phenylheptan-2-one: δ$_H$(200 MHz; CDCl$_3$) 1.34 [2 H, m, CH_2(CH$_2$)$_2$CO], 1.60 (4 H, m, CH_2CH$_2$CH_2CH$_2$CO), 2.10 (3 H, s, MeCO), 2.4 (2 H, t, CH$_2$CO), 2.60 (2 H, t, CH_2Ph) and 7.20 (5 H, m, Ph); methyl 4-methyl-6-phenylhexanoate: δ$_H$(200 MHz; CDCl$_3$) 0.95 (3 H, d, MeCH), 1.3–1.9 (5 H, m, CH_2CHMeCH_2) 7.20 (5 H, m, Ph); 3,4-dimethyl-1,6-diphenylhexane (mixture of diastereoisomers): δ$_H$(200 MHz; CDCl$_3$) 0.88 (6 H, dd, 2 × MeCH), 1.25–1.80 (6 H, m, CH_2CHMe × 2),

2.30–2.80 (4 H, m, CH_2Ph) and 7.20 (10 H, m, 2 × Ph); m/z 266 (M$^+$, 49%).

References

1 (a) R. F. Heck and J. P. Nolly, Jr., J. Org. Chem., 1972, 37, 2320; (b) H. A. Dieck and R. F. Heck, J. Am. Chem. Soc., 1974, 96, 1133.
2 (a) J. Tsuji, Organic Synthesis with Palladium Compounds, Springer-Verlag, Berlin, 1980; (b) B. M. Trost, Acc. Chem. Res., 1980, 13, 385; (c) J. Tsuji, Pure Appl. Chem., 1982, 54, 197; (d) R. F. Heck, Palladium Reagents in Organic Synthesis, Academic Press, New York, 1985.
3 (a) R. M. Adlington, J. E. Baldwin, A. Basak and R. P. Kozyrod, J. Chem. Soc., Chem. Commun., 1983, 944; (b) G. Stork and P. M. Sher, J. Am. Chem. Soc., 1986, 108, 303; (c) B. Giese and R. Rupaner, Liebigs Ann. Chem., 1987, 231; (d) B. Giese, J. Dupuis and M. Nix, Org. Synth., 1987, 65, 236; (e) B. Giese and Rupaner, Synthesis, 1988, 219.
4 S. Arbrecht and R. Scheffold, Chimia, 1985, 39, 211.
5 (a) D. B. Gerth and B. Giese, J. Org. Chem., 1986, 51, 3726; (b) B. Giese, J. A. González-Gómez and T. Witzel, Angew. Chem., Int. Ed. Engl., 1984, 23, 69.
6 K. P. Healy and D. Pletcher, J. Organomet. Chem., 1978, 161, 109.
7 (a) S. Ozaki, T. Nakanishi, M. Sugiyama, C. Miyamoto and H. Ohmori, Chem. Pharm. Bull., 1991, 39, 31; (b) S. Ozaki, H. Matsushita and H. Ohmori, J. Chem. Soc., Chem. Commun., 1992, 1120.
8 (a) J. Cason and J. S. Correia, J. Org. Chem., 1961, 26, 3645; (b) E. J. Coulson, W. Gerrard and H. R. Hudson, J. Chem. Soc., 1965, 2364.