as reaction between the radical cation[9] derived from the magnesium–macrocycle complex and the radical derived from the enolate. There is ample precedent[3] for subsequent incorporation of the 10-methoxy group under these conditions.

It is our intention to test the biosynthetical validity of this scheme with labeled 2-vinyl- and 2,4-divinylporphyrin 6-monomethyl esters, analogous to II, in the chloroplast system.[1]

(8) Identified by high-resolution mass spectrum and comparison with an authentic sample.[3]

(9) J-H. Fuhrhop and D. Mauzerall, *J. Am. Chem. Soc.*, **90**, 3875 (1968).

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Base-Catalyzed Carboxylation of Organic Halides by Nickel Carbonyl in Protic Media

Sir:

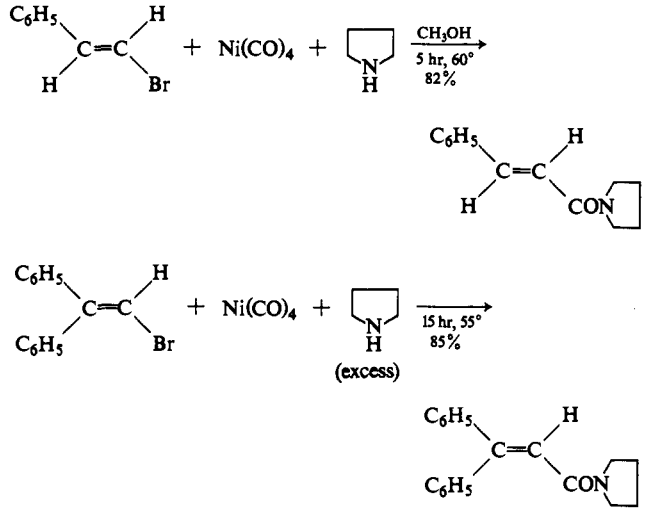
A new method for carbon–carbon bond formation in which halogen attached to trigonal or tetrahedral carbon is replaced by carbon, *e.g.*, *n*-alkyl, using organocopper–lithium complexes has recently been reported.[1] The copper reagents appear to function as electron donors to generate simultaneously two mutually reactive species which combine to form the observed coupling product. This concept suggested the possibility of finding electropositive, transition metal reagents which would function in a similar way to replace halogen by carbon functional groups. As a consequence of studies so directed, a new general method has been developed for the replacement of halogen bound to trigonal or tetrahedral carbon by *carboxylic* functional groups. The method depends on the well-known tendency of certain metal carbonyls to form more strongly electropositive anionic species under the influence of bases.[2,3]

Treatment of a wide variety of organic halides, RHal, with several equivalents of nickel carbonyl in alcoholic medium (R′OH) containing 2–3 equiv of the corresponding sodium or potassium alkoxide results in formation of the esters RCOOR′. The examples cited in Table I illustrate the synthesis of methyl esters using the indicated reactants and reaction conditions.[4] In general, and in accord with the expected reactivity sequence RI > RBr > RCl, the chlorides corresponding to the halides in Table I are unreactive under the conditions there listed. Bromobenzene is unaffected under the conditions which suffice for methoxycarbonylation of iodobenzene. Alkyl halides, including iodides, do not undergo methoxycarbonylation under even more forcing conditions than those given in Table I, and hence it appears that halogen attached to saturated carbon is much less reactive than that on trigonal carbon. Finally, the transformations outlined in Table I proceed much more slowly or (in most cases) not at all in the absence of the methoxide base under the conditions specified. Even iodobenzene, which is known to react with nickel carbonyl in methanol at reflux to form methyl benzoate,[5] is unchanged when sodium methoxide is omitted from the experiment outlined in Table I.[6]

A mixture of nickel carbonyl and potassium *t*-butoxide in *t*-butyl alcohol is a much more powerful carboxylating system than the methanol–methoxide–nickel carbonyl reagent.[7] As indicated in Table II the former mixture effectively *t*-butoxycarbonylates not only trigonal halides but also *alkyl* iodides. Furthermore, it can be seen that even vinylic chlorides can undergo the replacement reaction. Although the nickel carbonyl–*t*-butoxide reagent appears more general than the methoxide reagent, the observed yields of ester were often lower with the former for two reasons: (1) the presence of water in the reaction mixture which leads to formation of carboxylic acid rather than ester is much more critical in the *t*-butyl alcohol–*t*-butoxide system, and (2) dehydrohalogenation is a more serious side reaction in the more strongly basic *t*-butoxide system. Both systems fail in cases where the alkoxycarbonylation product is very reactive toward bases, *e.g.*, with 2-bromopropene as substrate.

Allylic halides, which undergo rapid alkoxycarbonylation by treatment with nickel carbonyl in alcohol solvents,[8] react similarly in the presence of added alkoxide, *e.g.*, 3-bromocyclooctene affords esters of 2-cyclooctenylcarboxylic acid.

Aminocarbonylation has been observed with mixtures of amines and nickel carbonyl as reagents, the following cases being typical.



In addition, direct formation of nitriles is possible as indicated by the following reaction,[9]

(1) (a) E. J. Corey and G. H. Posner, *J. Am. Chem. Soc.*, **89**, 3911 (1967); (b) *ibid.*, **90**, 5615 (1968).

(2) (a) R. B. King, *Advan. Organometal. Chem.*, **2**, 157 (1964); (b) T. A. Manuel, *ibid.*, **3**, 181 (1965).

(3) F. Calderazzo, R. Ercoli, and G. Natta in "Organic Synthesis via Metal Carbonyls," Vol. 1, I. Wender and P. Pino, Ed., Interscience Publishers, New York, N. Y., 1968, pp 1–200.

(4) Reaction products were identified by infrared, nuclear magnetic resonance, and mass spectra and elemental analysis and, for known compounds, comparison with authentic samples.

(5) N. L. Bauld, *Tetrahedron Letters*, 1841 (1963).

(6) All of the experiments described in this note were conducted on a scale of *ca.* 1 mmol, and so the use of excess nickel carbonyl (to compensate for volatilization losses during reaction) was not inconvenient. In larger scale work a modest excess (*e.g.*, 1.5 mol equiv based on halide) would be more satisfactory.

(7) Addition of *t*-butoxide to a solution of nickel carbonyl in *t*-butyl alcohol at 20° produces an immediate deep red coloration, whereas solutions of methoxide and nickel carbonyl in methanol remain colorless for at least 24 hr at 20°.

(8) R. F. Heck, *J. Am. Chem. Soc.*, **85**, 2013 (1963), has demonstrated that these reactions proceed *via* π-allyl- and σ-acylnickel intermediates.

Table I. Methoxycarbonylation of Organic Halides

$$RHal \xrightarrow[CH_3OH,\ CH_3O^-]{Ni(CO)_4} RCOOCH_3$$

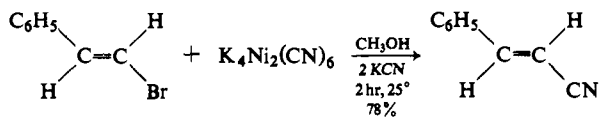
RX	Reaction time, hr, and temp, °C	Methyl ester, % yield
trans-1-Bromo-2-phenylethylene	2, 25[a]	*trans*-Cinnamate, 95
cis-1-Bromo-2-phenylethylene	1, 45[b]	*cis*-Cinnamate, 96;[c] *trans*-cinnamate, 4[c]
1-Bromo-2,2-diphenylethylene	12, 25[a]	β-Phenylcinnamate, 84
1-Bromocyclohexene	70, 25[a]	1-Cyclohexenecarboxylate, 65
1-Bromo-4-*t*-butylcyclohexene	6, 60[a]	4-*t*-Butyl-1-cyclohexenecarboxylate, 71
cis-1-Bromo-2-ethoxyethylene	1.6, 45[b]	β-Ethoxyacrylate, 62[d]
Iodobenzene	24, 25[a]	Benzoate, 88

[a] Molar ratio halide:nickel carbonyl:methoxide 1:6:3. [b] Molar ratio halide:nickel carbonyl:methoxide 1:6:1. [c] Based on reacted bromide; longer reaction time caused increasing isomerization of *cis* ester to *trans*. [d] Based on reacted bromide; longer reaction time led to formation of methyl β-ethoxy-β-methoxypropionate.

Table II. *t*-Butoxycarbonylation of Organic Halides

$$RHal \xrightarrow[t\text{-BuOH},\ t\text{-BuO}^-]{Ni(CO)_4} RCOO\text{-}t\text{-Bu}$$

RX	Ratio RX : $Ni(CO)_4$: *t*-BuO^-	Reaction time, hr, and temp, °C	*t*-Butyl ester, % yield
trans-1-Bromo-2-phenylethylene	1:3:1	2, 25	*trans*-Cinnamate, 60
trans-1-Chloro-2-phenylethylene	1:6:1.5	60, 60	*trans*-Cinnamate, 50
1-Chlorocyclohexene	1:6:3	48, 60	1-Cyclohexenecarboxylate, 64
1-Bromo-4-*t*-butylcyclohexene	1:6:3	16, 60	4-*t*-Butyl-1-cyclohexenecarboxylate, 76
1-Iodoheptane	1:6:2	24, 50	Octanoate, 66
1,6-Diiodohexane	1:6:3	40, 60	Octane-1,8-dioate, 61



The experimental execution of the alkoxycarbonylation reaction is illustrated by the procedure for the synthesis of methyl 4-*t*-butyl-1-cyclohexenecarboxylate. (*All operations involving nickel carbonyl were performed in a well-ventilated hood.*) To a solution of sodium methoxide (3.0 mmol, 0.16 g) in 5 ml of dry methanol under argon in a 25-ml flask fitted with side arm and reflux condenser was added nickel carbonyl (*danger, toxic*) (6.0 mmol, 0.8 ml) followed by 1-bromo-4-*t*-butylcyclohexene (1.0 mmol, 0.22 g). The mixture was heated to 60° and held there for 6 hr, during which time a deep red color developed. After cooling to 25°, carbon monoxide was bubbled through the mixture for 0.5 hr to dispel any remaining nickel carbonyl and to decompose nickel-containing side products which interfere with isolation. The exit gas stream was passed through a trap containing concentrated nitric acid to decompose the volatile nickel complexes. The resulting green solution was poured into 50 ml of 0.1 *N* HCl and 50 ml of ether in a separatory funnel and thoroughly shaken. The ether phase was washed with two 50-ml portions of distilled water, dried over anhydrous magnesium sulfate, concentrated, and distilled to give 0.14 g (71%) of methyl 4-*t*-butyl-1-cyclohexenecarboxylate as a colorless liquid having identical infrared and nmr spectra with a pure sample and homogeneous by vapor phase and thin layer chromatographic analysis.[10-12]

(9) For preparation of the cyanonickel(I) reagent see W. M. Burgess and J. W. Eastes, *Inorg. Syn.*, **5**, 197 (1957).

(10) 1-Bromo-4-*t*-butylcyclohexene[4] was prepared by a new method from 4-*t*-butylcyclohexanone (E. J. Corey and L. S. Hegedus, in preparation).

(11) A modified procedure was used for work-up when potassium *t*-butoxide was used as base, since treatment with carbon monoxide failed to free the reaction mixture of volatile nickel complexes. In these instances the reaction mixture was subjected directly to ether–water extraction, and the ether layer was evaporated to dryness under aspirator vacuum using a liquid nitrogen trap. The nonvolatile residue was then subjected to the standard isolation procedure.

(12) This work was supported by the National Science Foundation.

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Migrations of the Trimethylsilyl Group upon Electron Impact in Steroids

Sir:

Trimethylsilylation is used extensively by the chemist and biochemist in the gas–liquid partition chromatographic separation and mass spectrometric identification of a wide range of biologically important substances.[1] In the course of studies on the metabolism of C_{19} steroids in rat liver microsomes,[2] an intense and unexplained peak at *m/e* 191 was encountered frequently in the mass spectra of various dihydroxy and trihydroxy steroid trimethylsilyl (TMS) ethers. Because of both the key role that such TMS derivatives play in analytical mass spectrometry and

(1) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day Inc., San Francisco, Calif., 1967, pp. 471–476.

(2) J.-Å. Gustafsson, B. P. Lisboa, and J. Sjövall, *Eur. J. Biochem.*, **5**, 437 (1968).