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Regioselective 1,4-Functionalization of 1,3-Dienes via (η^3-1-Acetonylallylic)$Fe(CO)_2NO$ Complexes

Keiji ITOH, Saburo NAKANISHI,† and Yoshio OTSUJI†*
Department of Industrial Chemistry, Osaka Prefectural
College of Technology, Saiwaicho, Neyagawa, Osaka 572
†Department of Applied Chemistry, College of Engineering,
University of Osaka Prefecture, Mozu-Umemachi, Sakai, Osaka 591

1,4-Acylation-alkylation of 1,3-dienes occurred regioselectively via (η^3-1-acetonylallylic)$Fe(CO)_2NO$ complexes upon treatment of 1,3-dienes with iodomethane in the presence of $Bu_4NFe(CO)_3NO$ and then with carbon nucleophiles or carbon electrophile.

Regio- and stereoselective 1,4-functionalization of 1,3-dienes has found wide applications in organic synthesis. For example, Backvall et al. have developed several palladium-catalyzed 1,4-oxidations of 1,3-dienes and their synthetic applications.[1)] Hegedus et al. have reported the cobaltcarbonyl anion ($[Co(CO)_4]^-$)-mediated 1,4-acylation-alkylation of 1,3-dienes.[2)] Previously, we have reported that tetrabutylammonium tricarbonylnitrosylferrate $Bu_4N^+[Fe(CO)_3NO]^-$ (TBAF) serves as a useful reagent for the formation of a variety of (η^3-allylic)$Fe(CO)_2NO$ complexes from allylic halides, and the iron complexes thus produced can be utilized as intermediates for various organic transformations.[3)] We now report that 1,4-acylation-alkylation of 1,3-dienes can be effected by use of TBAF via (η^3-1-acetonylallylic)$Fe(CO)_2NO$ complexes. These complexes react not only with carbon nucleophiles but also with carbon electrophile at the 3-position of the allylic ligands to give a variety of 1,4-addition products.

Iodomethane (4.5 mmol) and 1,3-butadiene (3 mmol) were added successively to a solution of TBAF (3 mmol) in tetrahydrofuran (THF, 10 cm^3). The mixture was stirred at room temperature for 3 h, and then $NaCH(CO_2Me)_2$ (6 mmol) was added. The resulting mixture was further stirred at room temperature for 20 h, acidified with 4 M (1 M=1 mol dm^{-3}) hydrochloric acid and extracted with ether (30 cm^3). The ether extract was washed with water, dried (Na_2SO_4), and concentrated. The products were isolated by chromatography of the residue on silica gel with hexane/ethyl acetate (95/5), giving methyl 2-methoxycarbonyl-7-oxo-trans-4-octenoate (**2a**) in a 52% yield. Similarly, 1,3-dienes (**1b-c**) were treated with MeI in the presence of TBAF and then with carbon nucleophiles (NaNu). These treatments gave the corresponding 1,4-acylation-alkylation products (**2b-f**) in moderate yields. The structure of the products was determined by their spectral data[4)] and elemental analyses. The results are summarized in Table 1.

In these reactions, acetyl group and carbon nucleophiles were introduced

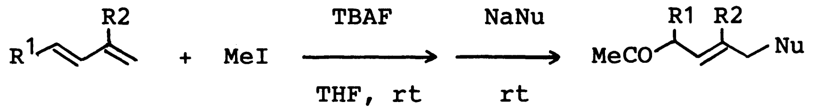

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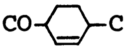
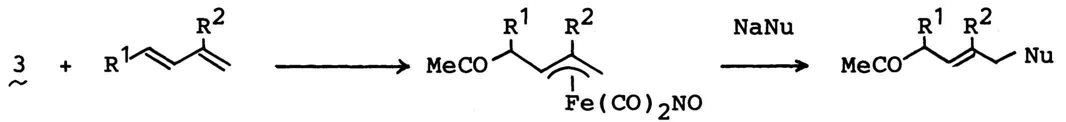
Table 1. The TBAF-mediated reaction of 1,3-dienes with iodomethane and carbon nucleophiles

1,3-Diene	R^1	R^2	NaNu	Product	Yield/%[a)]
1a:	H	H	$NaCH(CO_2Me)_2$	2a: R^1=H, R^2=H, Nu=$CH(CO_2Me)_2$	58
1b:	H	Me	$NaCH(CO_2Me)_2$	2b: R^1=H, R^2=Me, Nu=$CH(CO_2Me)_2$	56
1b:	H	Me	$NaCH(CO_2Et)_2$	2c: R^1=H, R^2=Me, Nu=$CH(CO_2Et)_2$	60
1b:	H	Me	$NaCH(COMe)CO_2Me$	2d: R^1=H, R^2=Me, Nu=$CH(COMe)CO_2Me$	44
1b:	H	Me	$NaCMe(CO_2Et)_2$	2e: R^1=H, R^2=Me, Nu=$CMe(CO_2Et)_2$	55
1c:	Me	H	$NaCH(CO_2Me)_2$	2f: R^1=Me, R^2=H, Nu=$CH(CO_2Me)_2$	35
1d: 1,3-cyclohexadiene			$NaCH(CO_2Me)_2$	2g: MeCO--$CH(CO_2Me)_2$	42

a) Isolated yields based on 1,3-diene used.

regioselectively at 1- and 4-positions of 1,3-dienes. In addition, the carbon-carbon double bonds in the products were found to have E-configuration in all cases. Stereochemically rigid 1,3-cyclohexadiene (1d) reacted also in a similar manner. However, in this case a stereoisomeric mixture of compounds having cis- and trans-configuration at 1,4-substituents was obtained in a 1:1 ratio. These reactions presumably proceed via the pathway similar to that proposed for the $[Co(CO)_4]^-$-mediated reactions.[2)] Iodomethane reacts with TBAF to generate the methyliron complex $[MeFe(CO)_3NO]$, which inserts CO to produce the acetyliron complex $[MeCOFe(CO)_2NO]$. This species adds regioselectively to 1,3-dienes to give (η^3-1-acetonylallylic)$Fe(CO)_2NO$ complexes (4),[3a)] which are alkylated regioselectively by carbon nucleophiles at the less hindered site of the allylic ligands to result in overall 1,4-acetylation-alkylation of dienes (Scheme 1).

$$Bu_4NFe(CO)_3NO \xrightarrow[-Bu_4NI]{MeI} [MeFe(CO)_3NO] \longrightarrow \underset{3}{[MeCOFe(CO)_2NO]}$$



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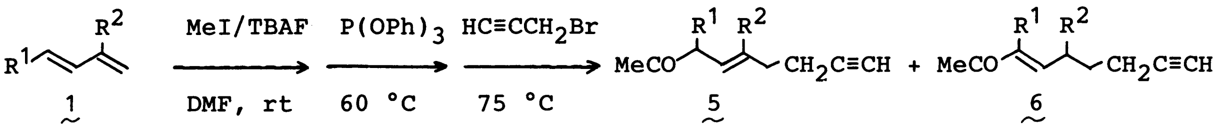
Scheme 1.

However, a striking feature, which is distinct from the $[Co(CO)_4]^-$-mediated reactions, was found when (η^3-1-acetonylallylic)$Fe(CO)_2NO$ complexes were used as intermediates. These complexes react even with a reactive carbon electrophile.

Iodomethane (4.5 mmol) and 1,3-butadiene (3 mmol) were added to a DMF solution (10 cm^3) of TBAF (3 mmol), and the mixture was stirred at room temperature for 3 h. Triphenyl phosphite (3 mmol) was then added and the mixture was heated at 60 °C for 1 h. After adding 2-propynyl bromide (6 mmol), the resulting mixture was heated at 75 °C for 15 h, and extracted with ether (30 cm^3). The ether extract was washed successively with 4 M hydrochloric acid , aqueous $NaHSO_3$ solution and water, dried (Na_2SO_4) and then evaporated. The residue was chromatographed on silica gel with hexane/ethyl acetate (97.5/2.5), giving 5-nonen-1-yn-8-one (5a, 10%) and 6-nonen-1-yn-8-one (6a, 41%). When the reaction mixture was heated at the same temperature for a much longer period of time (30 h), 6a was obtained as a single isolable product in a 62% yield. Other 1,3-dienes (1b-d) were also treated in a similar manner to give the corresponding 1,4-addition compounds (6b-d) as sole isolable products in moderate yields. The structure of the products was determined by their spectral data[5] and elemental analyses. The results are given in Table 2.



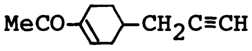
a: R^1=H, R^2=H, b: R^2=H, R^2=Me, c: R^1=Me, R^2=H.

Table 2. The TBAF-mediated reaction of 1,3-dienes with iodomethane and 2-propynyl bromide

1,3-Diene	Product(s)(Yield/%[a])	
1a	5a (10)[b]	6a (41)[b]
1a	—	6a (62)[c]
1b	—	6b (53)[c]
1c	—	6c (44)[c]
1d	—	6d[d] (54)[b]

a) Isolated yields based on 1,3-dienes used.

b) Reaction time: 15 h. c) Reaction time: 30 h.

d) 6d: 

The key intermediates of this reaction are also most likely to be (η^3-1-acetonylallylic)$Fe(CO)_2NO$ complexes (4). The electrophilic attack of 2-propynyl bromide on the less hindered site of the ligands of the iron complexes gives the corresponding 1,4-addition products. The regioselectivity in this reaction was extremely high, but the initial products 5 gradually isomerize to the conjugated ketones 6. The carbon-carbon double bonds of the products were found to have E-configuration.

All the above reactions can be carried out in one pot, so that the reactions appear to be useful in organic synthesis.

References

1) J. Backvall, J. Nystrom, and R. Nordberg, J. Org. Chem., 53, 5695 (1988). and references cited therein.

2) L. S. Hegedus and Y. Inoue, J. Am. Chem. Soc., 104, 4917 (1982); L. S. Hegedus, R. J. Perry, J. Org. Chem., 49, 2570 (1984).

3) a) T. Ueda, M. Kawakita, and Y. Otsuji, Nippon Kagaku Kaishi, 1985, 271; b) K. Ito, S. Nakanishi, and Y. Otsuji, Chem. Lett., 1987, 2103; c) K. Ito, S. Nakanishi, and Y. Otsuji, ibid., 1988, 473.

4) **2a**: IR(neat) 1730, 1710, 969 cm^{-1}. ^{1}H NMR(CDCl$_3$) δ 2.04 (s, 3H), 2.51 (t, J=7 Hz, 2H), 2.97 (d, J=7 Hz, 2H), 3.28 (t, J=7 Hz, 1H), 3.70 (s, 6H), 5.37 (m, J=15.4 Hz, 2H). **2b**: IR(neat) 1730, 1710 cm^{-1}. ^{1}H NMR(CDCl$_3$) δ 1.65 (br s, 3H), 2.09 (s, 3H), 2.58 (d, J=7 Hz, 2H), 3.04 (d, J=7 Hz, 2H), 3.47 (t, J=7 Hz, 1H), 3.70 (s, 6H), 5.32 (br t, J=7 Hz, 1H). **2c**: IR(neat) 1730, 1710 cm^{-1}. ^{1}H NMR(CDCl$_3$) δ 1.34 (t, J=7 Hz, 6H), 1.65 (br s, 3H), 2.09 (s, 3H), 2.58 (d, J=7 Hz, 2H), 3.04 (d, J=7 Hz, 2H), 3.47 (t, J=7 Hz, 1H), 3.92 (q, J=7 Hz, 4H), 5.32 (br t, J=7 Hz, 1H). **2d**: IR(neat) 1730, 1710 cm^{-1}. ^{1}H NMR(CDCl$_3$) δ 1.66 (br s, 3H), 2.06 (s, 3H), 2.18 (s, 3H), 2.63 (d, J=7 Hz, 2H), 3.04 (d, J=7 Hz, 2H), 3.46 (t, J=7 Hz, 1H), 3.76 (s, 3H), 5.32 (br t, J=7 Hz, 1H). **2e**: IR(neat) 1730, 1710 cm^{-1}. ^{1}H NMR(CDCl$_3$) δ 1.34 (t, J=7 Hz, 6H), 1.35 (s, 3H), 1.65 (br S, 3H), 2.09 (s, 3H), 2.56 (s, 2H), 3.07 (d, J=7 Hz, 2H), 4.13 (q, J=7 Hz, 4H), 5.41 (br t, J=7 Hz, 1H). **2f**: IR(neat) 1730, 1710, 968 cm^{-1}. ^{1}H NMR(CDCl$_3$) δ 1.18 (d, J=7 Hz, 3H), 2.07 (s, 3H), 2.46 (t, J=7 Hz, 2H), 3.07 (m, 1H), 3.46 (t, J=7 Hz, 1H), 3.78 (s, 6H), 5.37 (m, J=15.8 Hz, 2H). **2g**: The stereoisomers of this compound were difficult to isolate in pure forms, but their structures and distribution could easily be assigned from the ^{1}H NMR spectrum of the isomeric mixture. IR(neat) 1730, 1710, 845 cm^{-1}. ^{1}H NMR(CDCl$_3$) for the trans-isomer: δ 1.64-1.80 (m, 2H), 1.86-2.03 (m, 2H), 2.18 (s, 3H), 2.90 (m, 1H), 3.10 (m, 1H), 3.30 (d, J=9.4 Hz, 1H), 3.74 (s, 6H), 5.76-5.89 (m, 2H). ^{1}H NMR(CDCl$_3$) for cis-isomer: δ 1.64-1.80 (m, 2H), 1.86-2.03 (m, 2H), 2.19 (s, 3H), 2.90 (m, 1H), 3.10 (m, 1H), 3.31 (d, J=9.9 Hz, 1H), 3.75 (s, 6H), 5.76-5.89 (m, 2H).

5) **5a**: IR(neat) 3280, 2100, 1710, 964 cm^{-1}. ^{1}H NMR(CDCl$_3$) δ 1.98 (t, J=2.4 Hz, 1H), 2.13 (s, 3H), 2.15 (q, J=7 Hz, 2H), 2.42 (td, J=7, 2.4 Hz, 2H), 3.03 (d, J=7 Hz, 2H), 5.35 (m, J=15.6 Hz, 2H). **6a**: IR(neat) 3280, 2100, 1670, 970 cm^{-1}. ^{1}H NMR(CDCl$_3$) δ 1.71 (m, 2H), 1.99 (t, J=2.4 Hz, 1H), 2.24 (s, 3H), 2.24(td, J=7, 2.4 Hz, 2H), 2.37 (qd, J=7.0, 1.6 Hz, 2H), 6.12 (dt, J=16.3, 1.6 Hz, 1H), 6.80 (dt, J=16.3, 7 Hz, 1H). **6b**: IR(neat) 3280, 2100, 1670, 968 cm^{-1}. ^{1}H NMR(CDCl$_3$) δ 1.15 (d, J=7 Hz, 3H), 1.72 (q, J=7 Hz, 2H), 1.98 (t, J=2.4 Hz, 1H), 2.13 (S, 3H), 2.17 (td, J=7, 2.4 Hz, 2H), 2.35 (m, 1H), 6.12 (dd, J=16.2, 1.4 Hz, 1H), 6.80 (dd, J=16.2, 7 Hz, 1H). **6c**: IR(neat) 3280, 2100, 1675 cm^{-1}. ^{1}H NMR(CDCl$_3$) δ 1.58 (s, 3H), 1.72 (m, 2H), 1.98 (t, J=2.4 Hz), 2.12 (s, 3H), 2.18 (td, J=7, 2.4 Hz, 2H), 2.36 (q, J=7 Hz, 2H), 6.72 (br t, J=7 Hz, 1H). **6d**: IR(neat) 3280, 2100, 1665, 845 cm^{-1}. ^{1}H NMR(CDCl$_3$) δ 1.80-1.93 (m, 3H), 2.00 (t, J=2.4 Hz, 1H), 2.22 (dd, J=7, 2.4 Hz, 2H), 2.29 (S, 3H), 2.41-2.51 (m, 4H), 6.88 (m, 1H).

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