The iron-mediated intramolecular addition of carboxylates to conjugated dienes

Ming-Chang P. Yeh,* Li-Wen Chuang, Ya-Sheng Hsieh and Ming-Shan Tsai

Department of Chemistry, National Taiwan Normal University, 88 Sec. 4, Ding-Jou Road, Taipei, Taiwan, Republic of China. E-mail: cheyeh@scc.ntnu.edu.tw

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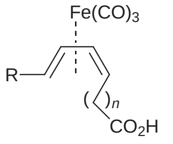
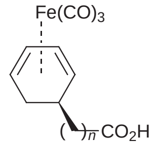
Treatment of carboxylic acid functionalized (η^4-diene)-$Fe(CO)_3$ complexes with 3.0 equiv. of $NOBF_4$ in the presence of Et_3N generates γ- and δ-lactones containing an α,β-unsaturated aldehyde or oxime functionality after NO^+ insertion.

Nucleophilic additions to conjugated dienes coordinated to a transition metal have attracted considerable interest in organic synthesis.[1] Transition metals, such as molybdenum, palladium or iron, have been used to activate dienes towards nucleophilic additions. The (η^4-cyclohexa-1,3-diene)$MoCp(CO)_2$ cations underwent reaction with a variety of carbon nucleophiles at the terminal position of the diene ligand to produce neutral (π-allyl)molybdenum complexes. Hydride abstractions from these complexes regenerated cationic diene complexes which again underwent intermolecular nucleophilic attack from the face opposite the metal, resulting in overall 1,3-stereocontrol in the six-membered ring.[2] With a pendant carboxylic acid group, neutral (π-allyl)molybdenum complexes underwent intramolecular addition with carboxylates by conversion of the neutral species to the cationic nitrosyl intermediates (exchange of neutral CO for NO^+) to afford γ- and δ-lactone derivatives.[3] In the palladium-catalyzed oxidation of conjugated dienes, two nucleophiles were added in a regio- and stereoselective manner across the diene. Nucleophiles that could be used in the overall 1,4-addition included carboxylates, amides, alcohols, and halides.[4] Conjugated dienes could also be activated towards nucleophilic additions by the $Fe(CO)_3$ moiety. The intermolecular addition of reactive ester or cyano stabilized carbanions to diene–iron complexes under CO afforded cyclopentanoids after acid quenching.[5] Recently, we have extended this chemistry into an intramolecular variant. Thus, sequential additions of carboester functionalized zinc–copper organometallics to (η^5-pentadienyl)$Fe(CO)_3$ cations furnished bicyclo[3.3.0]octanones or trisubstituted cyclopentanecarboxylic acid derivatives depending on the quenching process.[6] However, nucleophiles that could be used to add at the diene ligand of $Fe(CO)_3$ complexes have been restricted to stabilized carbanions. It would be of great synthetic interest to extend these regio- and stereoselective additions to other nucleophiles, such as oxygen and nitrogen nucleophiles. Here we report, for the first time, on the intramolecular addition of carboxylates to conjugated dienes by conversion of neutral (η^4-diene)$Fe(CO)_3$ complexes to the cationic nitrosyl intermediates (exchange of neutral CO and NO^+). The addition proceeded regiospecifically to form γ- and δ-lactones with an α,β-unsaturated aldehyde or oxime functionality after NO^+ insertion.

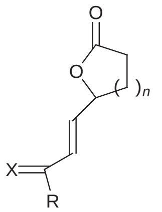
The starting acid complexes **1**–**3** were prepared in two steps according to literature procedures.[6,7] Addition of carboester functionalized zinc–copper reagents to the corresponding (η^5-dienyl)$Fe(CO)_3$ cationic salts followed by hydrolysis of the residue with KOH in MeOH–THF–H_2O at 30 °C produced complexes **1**–**3** as the major products in good yields (70–90%). Finally, our intramolecular addition involved the addition of an MeCN solution of $NOBF_4$ (3.0 equiv.) to **1a** in MeCN at 0 °C under nitrogen and then addition of Et_3N (2.0 equiv.). The addition was carried out for 30 min at 0 °C followed by workup with saturated aqueous NH_4Cl and CH_2Cl_2 extraction. After purification by flash column chromatography on silica gel and distillation under reduced pressure, γ-lactone **4**† bearing an α,β-unsaturated aldehyde at the γ-position of the ring was obtained as the major product in 60% yield (entry 1, Table 1). Under the same reaction conditions, intramolecular cyclization of **1b** with an additional methyl group at the terminal position of the diene ligand afforded γ-lactone **5** with an α,β-unsaturated oxime at the γ-position of the ring in 64% yield (entry 2, Table 1). The formation of **4** and **5** may result from NO^+ insertion. However, it is important to mention that the intramolecular addition of carboxylates to (η^3-allyl)MoCp(CO)(NO) cations to give γ and δ-lactones did not involve NO^+ insertion.[3] A mechanism for generation of **4** and **5** is suggested in Scheme 1. Addition of $NOBF_4$ to complexes **1a**,**b** may produce the cationic species **10**. Deprotonation of **10** with Et_3N gave carboxylate **11**, with attack exclusively at the terminal position of the diene ligand to



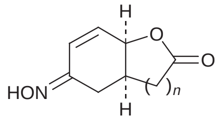
1a R = H, *n* = 2
b R = Me, *n* = 2
2a R = H, *n* = 3
b R = Me, *n* = 3



3a *n* = 1
b *n* = 2



4 R = H, X = O, *n* = 1
5 R = Me, X = NOH, *n* = 1
6 R = H, X = O, *n* = 2
7 R = Me, X = NOH, *n* = 2

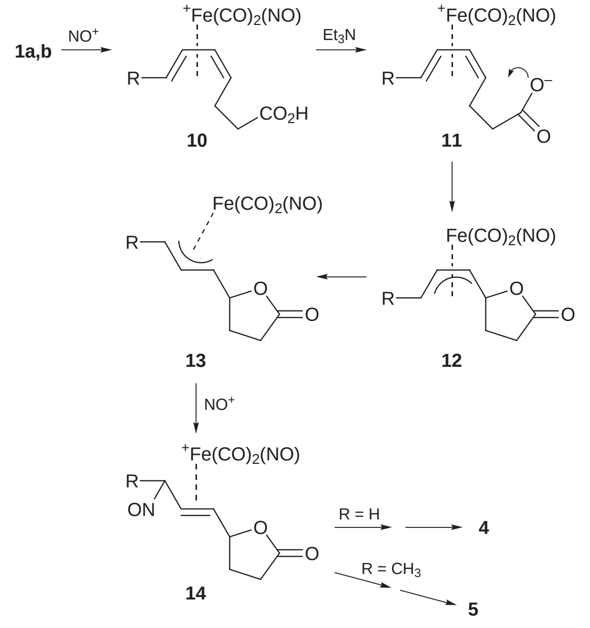


8 *n* = 1
9 *n* = 2

Table 1 Intramolecular additions of carboxylates to (η^4-Diene)$Fe(CO)_3$ complexes

Entry	Starting complex	Product	Yield (%)[a]
1	**1a**	**4**	60
2	**1b**	**5**	64
3	**2a**	**6**	55
4	**2b**	**7**	53
5	**3a**	**8**	50
6	**3b**	**9**	53

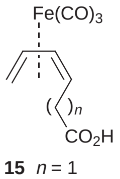
[a] All products were purified by flash column chromatography on silica gel and distillation under reduced pressure and have been fully characterized by ^1H and ^{13}C NMR, IR, mass and high resolution mass spectra.



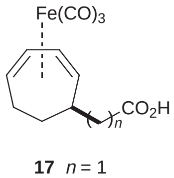
Scheme 1 Proposed reaction pathway for the formation of lactones **4** and **5**.

produce the postulated neutral (π-allyl)$Fe(CO)_2(NO)$ intermediate **12**. *Syn/anti* isomerization of **12** *via* π-allyl/σ-allyl interconversion of the allyl ligand produced **13**.[8] Intermediate **13** may undergo nitrosyl migration with an additional NO^+ to give **14**. However, neutral complexes, such as (η^3-allyl)$Fe(CO)_2NO$, underwent internal CO (rather than NO^+) insertion upon treatment with 1,2-bis(diphenylphosphino)ethane to give an iron acyl intermediate. Quenching the iron acyl intermediate with I_2/EtOH produced a β,γ-unsaturated carboxylic ester.[9] Thus, it is reasonable to suggest that complex (η^3-allyl)$Fe(CO)_2NO$ **13** may undergo nitrosyl insertion with an excess of $NOBF_4$ (3.0 equiv. of NO^+) to produce **14**. The primary nitroso compound (R = H) hydrolyzed to **4**, while the secondary nitroso derivative (R = CH_3) underwent nitroso–oxime tautomerization to produce **5** after aqueous workup and flash column chromatograph of the residue.

Increasing the tether length by one with complexes **2a** and **2b** (entries 3 and 4, Table 1) also allowed intramolecular cyclisation to provide δ-lactones **6** (55%) and **7** (53%), respectively, as the only product in each case. The results are consistent with complexes **1a** and **1b**. Thus, the substrate with an additional methyl group at the diene ligand, **2b**, produced lactone **7** with an α,β-unsaturated oxime functionality at the δ-position of the ring, while complex **2a** generated δ-lactone **6** bearing an α,β-unsaturated aldehyde functionality. However, preliminary attempts to prepare β- and ω-lactones were unsuccessful. No cyclization has been observed for acid complexes **15** and **16**.



15 $n = 1$
16 $n = 4$



17 $n = 1$
18 $n = 2$

Using the same methodology, we are able to construct fused bicyclic lactones **8** and **9** *via* intramolecular addition of carboxylates to cyclic diene–iron complexes **3a** and **3b**, respectively. Fused bicyclic lactones **8**† (50%) and **9** (64%) bearing an α,β-unsaturated oxime functionality were obtained as the only diastereoisomer in each case. The *cis*-stereochemistry at the ring juncture in lactones **8** and **9** was fixed by *anti* addition of carboxylates at the terminal position of the diene ligands and ^{1}H NMR studies provided evidence supporting the structure assignments. The coupling constants of 5.3 and 4.8 Hz, respectively, of the adjacent fused protons in **8** and **9** demand *cis*-fused bicyclic skeletons. These values are consistent with the couling constants observed for the *cis* fused bicyclo γ- and δ-lactones reported in the literature.[8] Rigorous proof of the structure of **8** was further accomplished by X-ray diffraction analysis.‡ Although the iron-mediated intramolecular cyclisation works well for the formation of fused bicyclic lactones **8** and **9** from (η^4-cyclohexa-1,3-diene)-$Fe(CO)_3$ acid complexes, attempts to obtain fused bicyclo γ- and δ-lactones from intramolecular cyclisation of (η^4-cyclohepta-1,3-diene)$Fe(CO)_3$ acid complexes **17** and **18** have thus far failed.

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Notes and references

† *Selected data* for **4**: $\delta_H(CDCl_3)$ 9.63 (1H, d, J 7.3), 6.80 (1H, dd, J 15.6, 4.4), 6.37 (1H, dd, J 15.6, 7.3), 5.21 (1H, m), 2.61 (3H, m) and 2.05 (1H, m); $\delta_C(CDCl_3)$ 192.2, 175.6, 150.9, 131.8, 77.5 and 27.8; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3040w, 3012w, 2959w, 2928, 2872, 1779m, 1732m, 1603m, 1460w, 1375w, 1236w, 1198w, 1113w and 1045m; m/z (EI) 140 (M^+, 48%), 123 (38), 111 (42), 98 (29), 95 (47), 85 (43), 81 (82), 70 (13), 67 (25), 56 (23) and 55 (57); HRMS: calc. for $C_7H_8O_3$ 140.0437, found 140.0471.

‡ *Crystal data* for **8**: $C_8H_9NO_3$, M = 167.16, monoclinic, a = 9.535(2), b = 7.052(1), c = 12.691(3) Å, U = 791.4(3) Å^3, T = 298 K, space group $P2_1/c$, Z = 4, μ(Mo-Kα) = 0.71073 mm^{-1}, 2395 reflections measured, 2298 unique (R_{int} = 0.012), which were used in all calculations. The final $wR(F^2)$ was 0.078 (all data). Single crystals of compound **8** were recrystallised from hexane–EtOAc. The structure was solved using direct methods and refined by full-matrix least-squares on F^2. CCDC 182/1211. See http://www.rsc.org/suppdata/cc/1999/805/ for crystallographic files in .cif format.

1 J. E. Bäckvall, in *Advances in Metal-Organic Chemistry*, ed. L. S. Liebeskind, JAI, London, 1989, vol. 1, p. 135; L. S. Hegedus, *Tetrahedron*, 1984, **40**, 2415; B. M. Trost, *Angew. Chem., Int. Ed. Engl.*, 1989, **28**, 1173.
2 J. W. Faller, H. H. Murray, D. L. White and K. H. Chao, *Organometallics*, 1983, **2**, 400; A. J. Pearson, M. N. I. Kahn, J. C. Clardy and H. Ciu-Heng, *J. Am. Chem. Soc.*, 1985, **107**, 2748; A. J. Pearson and M. N. I. Kahn, *Tetrahedron Lett.*, 1985, **26**, 1407; S. Hansson, J. F. Miller and L. S. Liebeskind, *J. Am. Chem. Soc.*, 1990, **112**, 9660.
3 A. J. Pearson, S. Mallik, R. Mortezaei, M. W. D. Perry, D. J. Shively, Jr. and W. J. Youngs, *J. Am. Chem. Soc.*, 1990, **112**, 8034; A. J. Pearson and M. N. I. Kahn, *Tetrahedron Lett.*, 1984, **25**, 3507; M. C. P. Yeh, C. J. Tsou, C. N. Chuang and H. C. Lin, *J. Chem. Soc., Chem. Commun.*, 1992, 890.
4 J. E. Bäckvall, J. E. Nyström and R. E. Nordberg, *J. Am. Chem. Soc.*, 1985, **107**, 3676; J. E. Bäckvall, S. E. Byström and R. E. Nordberg, *J. Org. Chem.*, 1984, **49**, 4619; J. E. Bäckvall and J. O. Vågberg, *J. Org. Chem.*, 1988, **53**, 5695; J. E. Bäckvall, P. G. Andersson and J. O. Vågberg, *Tetrahedron Lett.*, 1989, **30**, 137; J. E. Bäckvall, *Pure Appl. Chem.*, 1992, **64**, 429; J. E. Bäckvall, and P. G. Andersson, *J. Am. Chem. Soc.*, 1990, **112**, 3683; 1992, **114**, 6374.
5 M. F. Semmelhack and J. W. Herndon, *Organometallics*, 1983, **2**, 363; M. F. Semmelhack, J. W. Herndon and J. K. Liu, *Organometallics*, 1983, **2**, 1885; M. F. Semmelhack, J. W. Herndon and J. P. Springer, *J. Am. Chem. Soc.*, 1983, **15**, 2497; M. F. Semmelhack and H. T. M. Le, *J. Am. Chem. Soc.*, 1984, **106**, 2715; M. F. Semmelhack and J. W. Herndon, *J. Organomet. Chem.*, 1984, **265**, C15; M. F. Semmelhack and H. T. M. Le, *J. Am. Chem. Soc.*, 1985, **107**, 1455; M. C. P. Yeh, K. K. Kang and C. C. Hwu, *J. Chin. Chem. Soc.*, 1991, **38**, 475.
6 M. C. P. Yeh, B. A. Sheu, H. W. Fu, S. I. Tau and L. W. Chuang, *J. Am. Chem. Soc.*, 1993, **115**, 5941; M. C. P. Yeh, L. W. Chuang, C. C. Hwu, J. M. Sheu and L. C. Row, *Organometallics*, 1995, **14**, 3396; M. C. P. Yeh and L. W. Chuang, *J. Org. Chem.*, 1995, **61**, 3874.
7 M. C. P. Yeh, L. W. Chuang, S. C. Chang, M. L. Lai and C. C. Chou, *Organometallics*, 1997, **16**, 4435.
8 J. K. Becconsall and S. J. O'Brien, *J. Chem. Soc., Chem. Commun.*, 1966, 302; P. Corradini, G. Maglio, A. Musco and G. Paiaro, *J. Chem. Soc., Chem. Commun.*, 1966, 618.
9 S. Nakanishi, T. Yamamoto, N. Furukawa and Y. Otsuji, *Synthesis*, 1994, 609.

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