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Synthetic Use of a σ-Alkyl-π-Allyl Iron Complex Obtained by Stereospecific Ring Opening of α-Pinene

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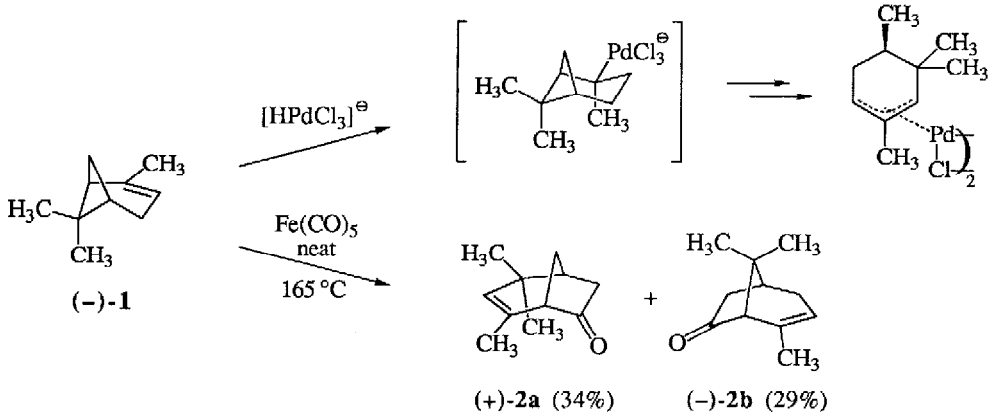
Key Words: Transition Metal Induced Ring Opening; Natural Product Transformation; Reactivity of Iron-Carbon σ-Bonds; CC Bond Formation; Ring Enlargement.

Abstract: *Insertion of iron carbonyl into the four-membered ring of α-pinene produces a versatile iron complex exhibiting an iron-carbon σ-bond. Reaction of this complex with various reagents, i.e. dimethyl butynedioate, produces the bicyclic ketones 2, 7, and 8 with moderate to high regioselectivity and full conservation of the optical purity of the starting terpene.*

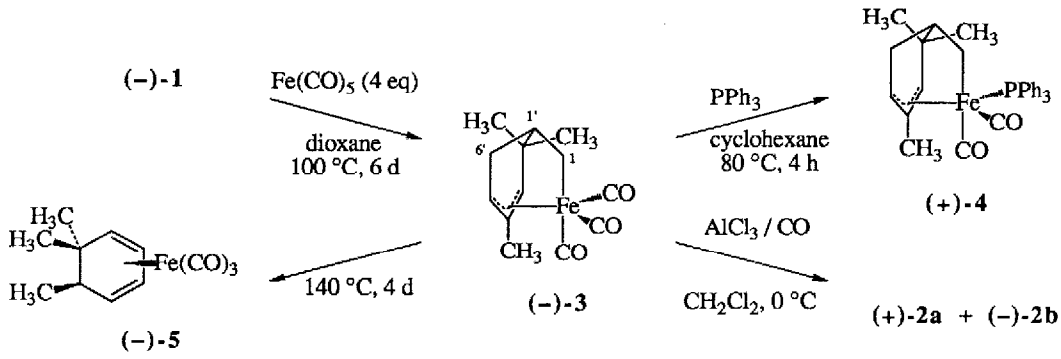
The metal assisted ring opening[1] or ring expansion[2] of α-pinene has previously been reported. Full conservation of optical purity had been noted during these transformations. They both yield skeletons different from the acid catalyzed reactions of pinenes which lead *via* the migration of the quaternary carbon center to the bornane ring system. The geminal dimethyl group therefore efficiently blocks any access of the bulkier metal reagents to the sterically more hindered side of the pinene double bond.

Whereas a synthetical application of the former reaction is precluded by the need for stoichiometric amounts of palladium hydride, the latter, stereospecific ring expansion by $Fe(CO)_5$ has been of little practical use either, since the optically active products **2a** and **2b** were formed in a nearly 1 : 1 ratio and proved extremely difficult to be separated. The similar physical properties are not surprising owing to the enantiomeric skeletons of the two ketones.

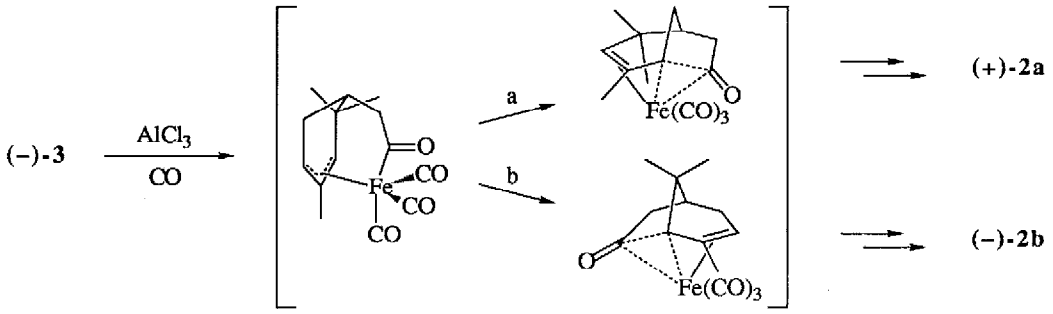


Using different reaction conditions, we isolated now the iron complex **3**, originally formulated as an intermediate[2] in the mechanism of the formation of the above ketones **2a** and **2b** from (–)-α-pinene,[3,4] which opens a

more selective and more versatile access to products of the type mentioned. The structure of **3** was deduced from its ^{1}H and ^{13}C NMR spectra as well as from IR and MS data.[5,6] The structural assignment was confirmed by the solid state structure of the phosphine substituted analog **4**.[7,8]



Despite the presence of a Fe–C σ-bond, complex **3** turned out to be very stable. Heating of **3** under a nitrogen atmosphere for 8 days to 140 °C converts it to the cyclohexadiene complex **5**.[9] Smooth conversion to the known ketones **2a** and **2b** was achieved by treatment of **3** with excess $AlCl_3$ in CH_2Cl_2 under an atmosphere of CO at r.t. or below. A remarkable regioselectivity (cf. Table 1.) for the CO insertion and ring closure was found. Under the assumption that the iron moiety stays complexed to the remaining double bond during ring closure, the formation of the preferred isomer **2b** can be rationalized by the smaller sterical hindrance in the corresponding transition state (**a** *vs.* **b**).



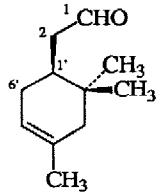
Application of the photoreductive complex degradation procedure introduced by Franck-Neumann[10] to complex **3** leads to a mixture of the isomeric optically active aldehydes **6a**[11] and **6b**[12] in high chemical yield. The enantiomer of aldehyde **6b** has been obtained previously in 9 steps starting from (–)-β-pinene.[13] The only moderate regioselectivity reflects the more open transition state in this transformation as compared to the above mentioned ring closure reaction. Moreover, the regioselectivity highly depends on the reaction conditions used: conducting the irradiation in diethyl ether solution containing 1% acetic acid, the ratio of **6a** and **6b** is reversed.

A surprising result was obtained from the photolysis of **3** in the presence of dimethyl butynedioate. The bicyclic product **7a**[14] which was collected after one cristallization from the reaction mixture is formed *via* the more hindered transition state (type **a**) by insertion of the acetylene prior to ring closure and contains only a minor amount (~1%) of the isomer which results from a transition state of type **b**. The structure of **7a** was deduced from NMR data including selectively decoupled ^{13}C NMR spectra. The reaction with other acetylenes only led to untractable mixtures of products so far.

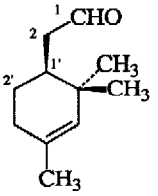
An other puzzling product (**8**) was obtained from the oxidation of **3** with $NaNO_2$ in the presence of benzaldehyde. The bicyclic ketones **8a**[15] and **8b**[16] formally derive from an aldol condensation of benzaldehyde on to the bicyclic ketones **2a** and **2b**. However, the observed regiospecificity renders a simple reaction pathway through preliminary formation of these ketones unlikely, since at the temperature used these ketones would be formed in a 1:1 ratio. The orientation of the phenyl substituent in **8b** was determined by identifying the long range coupling partners of the proton at C(1). Contrary to the other reaction products, **8a** and **8b** could be separated by column chromatography.

Table 1. Regioselectivity in the Reactions of Complex **3**

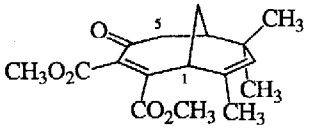
Reagents	Reaction Conditions	Product	Ratio of Isomers **a** : **b**	Yield (%)
$AlCl_3$ / CO	CH_2Cl_2, 20 °C, 6 h	**2**	15 : 85	35
$AlCl_3$ / CO	CH_2Cl_2, 0 °C, 24 h	**2**	6 : 94	36
CH_3CO_2H	CH_3CO_2H, hν, 20 °C	**6**	38 : 62	82
CH_3CO_2H	Diethyl ether, hν, 20 °C	**6**	60 : 40	68
$(CCO_2CH_3)_2$	Benzene, hν, 20 °C	**7**	99 : 1	35
$NaNO_2$, NaOH, PhCHO	Dioxane, 100 °C, 4 h	**8**	16 : 84	25



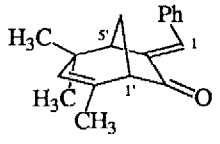
(+)-6a



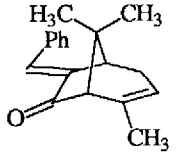
(+)-6b



(–)-7a



(–)-8a



(–)-8b

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2. Stockis, A.; Weissberger, E. *J. Am. Chem. Soc.* **1975**, *97*, 4288-92.
3. The optical purity of commercial (–)-α-pinene ($[\alpha]_D^{20} = 42.0°$) was increased to 96.4% *e.e.* using the method of ref. 4. All attempts to replace the dangerous $AgClO_4$ by other silver salts remained unsuccessful.
4. Comyns, A. E.; Lucas, H. J. *J. Am. Chem. Soc.* **1957**, *79*, 4339-41.
5. All new compounds gave satifactory elemental analyses. A more detailed discussion of the structural assignments will appear in ref. 7. All products exibit within the error limit of determination the same enantiomeric purity as the starting α-pinene.
6. **(–)-3:** Pale yellow liquid, $[\alpha]_D^{20} = -80°$ (c = 0.1, pentane); IR (pentane, cm^{-1}) ν (CO) 2049 (*vs*), 1986 (*vs*), 1978 (*vs*); ^1H NMR (C_6D_6) δ 3.96 (*m*, 1 H, H-C(5')), 3.62 (*t*, *J* = 2 Hz, 1 H, H-C(3')), 1.71 (*dm*, *J* = 14 Hz, 1 H, H_{exo}-C(6')), 1.66 (*dt*, *J* = 10 Hz, 3 Hz, 1 H, H_R-C(1)), 1.45 (*s*, 3 H, H_3-C($4'^1$)), 1.31 (*m*, 1 H,

H-C(1')), 1.14 (*dd*, *J* = 10 Hz, 2 Hz, 1 H, H_S-C(1)), 1.02 (*dt*, *J* = 14 Hz, 4 Hz, 1 H, H_{endo}-C(6')), 0.84 (*s*, 3 H, H_3-C($2'^1_{endo}$)), 0.70 (*s*, 3 H, H_3-C($2'^1_{exo}$)); ^{13}C NMR (C_6D_6) δ 217.1 (*s*, C≡O), 215.7 (*s*, C≡O), 207.4 (*s*, C≡O), 103.6 (*s*, C(4')), 87.3 (*d*, C(3')), 77.1 (*d*, C(5')), 49.5 (*d*, C(1')), 40.4 (*s*, C(2')), 34.1 (*t*, C(1)), 34.0 (*t*, C(6')), 28.2 (*q*, C($2'^1_{exo}$)), 27.2 (*q*, C($4'^1$)), 27.1(*q*, C($2'^1_{endo}$)).

7. Jenny, T. A.; Ma, L.; Stoeckli-Evans, H. *Helv. Chim. Acta*, to be submitted.
8. **(+)-4:** Yellow solid, mp 90-94 °C; $[\alpha]_D^{20}$ = +150° (c = 0.4, pentane); IR (pentane, cm^{-1}) ν (CO) 1929 (*vs*), 1981 (*vs*); ^{1}H NMR (C_6D_6) (spectrum not resolved due to chemical exchange) δ 7.7 (*m*, 6 H, Ph), 7.0 (*m*, 9 H, Ph), 3.50 (*m*, 1 H, H-C(3')), 3.48 (*m*, 1 H, H-C(5')), 1.97 (*s*, 3 H, H_3-C($4'^1$)), 1.93 (*br d*, *J* = 9.5 Hz, 1 H, H_a-C(1)), 1.67 (*br d*, *J* = 14.0 Hz, H_a-C(6')), 1.41 (*m*, 1 H, H-C(1')), 1.22 (*br s*, 3 H, H_3-C($2'^{1a}$)), 0.89 (*s*, 3 H, H_3-C($2'^{1b}$)), 0.84 (*br dd*, J_{PH} = 15.1 Hz, *J* = 9.5 Hz, 1 H, H_b-C(1)).
9. **(–)-5:** Pale yellow liquid, $[\alpha]_D^{20}$ = -72° (c = 0.4, pentane); IR (film, cm^{-1}) ν (CO) 2040 (*vs*), 1960 (*vs*), 1955 (*vs*); ^{1}H NMR (C_6D_6) δ 4.73 (*dm*, *J* = 6 Hz, 1 H, H-C(3)), 2.50 (*d*, *J* = 2 Hz, 1 H, H-C(1)), 2.38 (*dd*, *J* = 6 Hz, 2 Hz, 1 H, H-C(4)), 1.67 (*s*, 3 H, H_3-C(2^1)), 1.42 (*qm*, *J* = 7 Hz, 1 H, H-C(5)), 0.89 (*s*, 3 H, H_3-C(6^1_{endo})), 0.83 (*d*, *J* = 7 Hz, 3 H, H_3-C(5^1_{endo})), 0.74 (*s*, 3 H, H_3-C(6^2_{exo})); ^{13}C NMR (C_6D_6) δ 213.1 (*s*, C≡O), 101.4 (*s*, C(2)), 85.4 (*d*, C(3)), 80.5 (*d*, C(1)), 66.2 (*d*, C(4)), 41.7 (*d*, C(5)), 40.4 (*s*, C(6)), 35.7 (*q*, C(5^1)), 25.6 (*q*, C(6^{1a})), 21.9 (*q*, C(6^{1b})), 17.5 (*q*, C(2^1)).
10. Franck-Neumann, M.; Martina, D.; Brion, F. *Angew. Chem., Int. Ed.*, **1978**, *17*, 690-1.
11. **(–)-6a:** IR ($CHCl_3$, cm^{-1}) ν (CO) 1720 (*vs*); ^{1}H NMR ($CDCl_3$) δ 9.77 (*dd*, *J* = 3.1 Hz, 1.5 Hz, 1 H, H-C(1)), 5.28 (*m*, 1 H, H-C(3')), 2.55 (*dm*, *J* = 16.1 Hz, 1 H, H_a-C(2)), 2.16 (*ddd*, *J* = 16.1 Hz, 8.9 Hz, 3.1 Hz, 1 H, H_b-C(2)), 1.55 - 1.95 (*m*, 5 H), 1.64 (*s*, 3 H, H_3-C($4'^1$)), 0.94 (*s*, 3 H, H_3-C($6'^{1a}$)), 0.81 (*s*, 3 H, H_3-C($6'^{1b}$)).
12. **(+)-6b:** IR ($CHCl_3$, cm^{-1}) ν (CO) 1720 (*vs*); ^{1}H NMR ($CDCl_3$) δ 9.80 (*dd*, *J* = 3.3 Hz, 1.3 Hz, 1 H, H-C(1)), 5.10 (*m*, 1 H, H-C(3')), 2.55 (*dm*, *J* = 16.1 Hz, 1 H, H_a-C(2)), 2.13 (*ddd*, *J* = 16.1 Hz, 8.1 Hz, 3.3 Hz, 1 H, H_b-C(2)), 1.37 - 2.05 (*m*, 5 H), 1.64 (*s*, 3 H, H_3-C($4'^1$)), 0.99 (*s*, 3 H, H_3-C($2'^{1a}$)), 0.82 (*s*, 3 H, H_3-C($2'^{1b}$)).
13. Wolleb, H.; Pfander, H. *Helv. Chim. Acta* **1986**, *69*, 646-58.
14. **(–)-7a:** White solid, mp 155 - 159 °C; $[\alpha]_D^{20}$ = -199° (c = 0.72, $CHCl_3$); IR (KBr, cm^{-1}) ν (CO) 1732 (*vs*), 1721 (*vs*), 1683 (*vs*); ^{1}H NMR ($CDCl_3$) δ 5.11 (*sextet*, *J* = 1.4 Hz, 1 H, H-C(8)), 3.77 (*s*, 3 H, OCH_3), 3.71 (*s*, 3 H, OCH_3), 3.31 (*ddq*, *J* =.6.8 Hz, 1.4 Hz, 0.8 Hz, 1 H, H-C(6)), 2.79 (*dd*, *J* = 11.9 Hz, 6.2 Hz, 1 H, H_{endo}-C(2)), 2.67 (*dd*, *J* = 11.9 Hz, 6.7 Hz, 1 H, H_{exo}-C(2)), 2.34 (*dd*, *J* = 14.3 Hz, 3.4 Hz, 1 H, H_R-C(10)), 2.03 (*tt*, *J* = 6.5 Hz, 3.4 Hz, 1 H, H-C(1)), 1.94 (*ddd*, *J* = 14.3 Hz, 6.8 Hz, 3.4 Hz, 1 H, H_S-C(10)), 1.61 (*s*, 3 H, H_3-C(6^1)), 1.03 (*s*, 3 H, H_3-C(11^{1a})), 0.98 (*s*, 3 H, H_3(11^{1b}); ^{13}C NMR ($CDCl_3$) δ 201.4 (*s*, C(3)), 168.4 (*s*, C(5^1)), 165.5 (*s*, C(4^1)), 146.9 (*s*, C(5)), 139.6 (*s*, C(4)), 132.1 (*d*, C(8)), 130.3 (*s*, C(7)), 47.4 (*t*, C(2)), 40.2 (*d*, C(6)), 39.5 (*d*, C(1)), 29.7 (*t*, C(10)), 29.4 (*q*, C(9^{1a})), 26.6 (*q*, C(9^{1b})), 22.3 (*q*, C(7^1)).
15. **(–)-8a:** White solid, mp 97-102 °C; $[\alpha]_D^{20}$ = -95° (c = 0.256, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.63 (*m*, 2 H, Ph), 7.41 (*m*, 3 H, Ph), 7.37 (*br s*, 1 H, H-C(1)), 5.07 (*quintet*, *J* = 1.4 Hz, 1 H, H-C(3')), 3.51 (*d*, *J* = 5.0 Hz, 1 H, H-C(5')), 2.70 (*dd*, *J* = 4.3 Hz, 1.3 Hz, 1 H, H-C(1')), 2.17 (*d*, *J* = 11.3 Hz, 1 H, H_a-C(8')), 1.92 (*dt*, *J* = 4.7 Hz, 1 H, H_b-C(8')), 1.78 (*d*, *J* = 1.5 Hz, 3 H, H_3-C($2'^1$)), 1.24 (*s*, 3 H, H_3-C($4'^{1a}$)), 0.87 (*s*, 3 H, H_3-C($4'^{1b}$)).
16. **(–)-8b:** White solid, mp 109-112 °C; $[\alpha]_D^{20}$ = -249° (c = 0.354, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.53 (*m*, 2 H, Ph), 7.46 (*br s*, 1 H, H-C(1)), 7.39 (*m*, 3 H, Ph), 5.48 (*m*, 1 H, H-C(3')), 2.93 (*m*, 1 H, H-C(5')), 2.61 (*dm*, *J* = 17.6, 1H, H_a-C(4')), 2.45 (*d*, *J* = 1.9 Hz, 1 H, H-C(1')), 2.31 (*dm*, *J* = 17.6, 1H, H_b-C(4')), 1.78 (*m*, 3 H, H_3-C($2'^1$)), 1.09 (*s*, 3 H, H_3-C($8'^{1a}$)), 0.95 (*s*, 3 H, H_3-C($8'^{1b}$)).

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