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ASYMMETRIC ALLYLBORATIONS OF DIENE ALDEHYDE Fe(CO)$_3$ DERIVATIVES: EFFICIENT KINETIC RESOLUTION OF RACEMIC COMPLEXES AND THE HIGHLY ENANTIOTOPIC GROUP AND FACE SELECTIVE ALLYLBORATION OF A MESO SUBSTRATE

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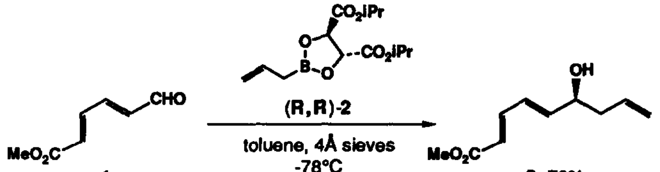
Abstract. Efficient kinetic resolutions of racemic diene aldehyde-Fe(CO)$_3$ complexes 4 and 5 and the highly enantiotopic group and face selective allylboration of meso complex 8 are described.

We recently reported that the enantioselectivity of the asymmetric allyl- and crotylborations of benzaldehyde and 2-decynal is significantly improved by using metal carbonyl complexes as substrate surrogates [e.g., benzaldehyde chromium tricarbonyl and 2-decynal dicobalt hexacarbonyl, respectively].[1] Seeking to explore the generality of these surprising results, attributed to an electronic (dipole) effect of the metal carbonyl ligand in the stereochemically favored allylboration transition state, we decided to examine the asymmetric allylborations of diene aldehyde-Fe(CO)$_3$ complexes.[2] Diene aldehydes, like other unsaturated aldehydes, are poor substrates in reactions with the tartrate ester modified allylboronates.[1,3] For example, the reaction of aldehyde **1** and (R,R)-**2** provides **3** with an enantiomeric purity of only 70% e.e. We hoped that significantly improved enantioselection would be realized by using the corresponding Fe(CO)$_3$ complexes (e.g., **4** and **5**), especially since allylic alcohols like **3** are of interest as precursors to triene substrates for the intramolecular Diels-Alder reaction.[4] The allylborations of *racemic* diene aldehyde complexes, however, are complicated by the chirality of the diene iron tricarbonyl unit. We are pleased to report, therefore, that racemic **4** and **5** undergo remarkably efficient kinetic resolutions in reactions with **2** (96% e.e. at 60% conversion) and that the fast reacting enantiomer exhibits exceptional diastereofacial selectivity (≥100 : 1) for the ψ-exo diastereomer **6**. This kinetic resolution technology constitutes a simple alternative to conventional resolution procedures,[2,5] and has the advantage that the absolute configuration of the resolved diene-Fe(CO)$_3$ complexes are easily predicted. Finally, the exceptional enantio- and diastereofacial selectivity of this resolution process is illustrated in the highly enantiotopic group and face selective allylboration of meso diene-Fe(CO)$_3$ complex **8**.



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3, 70% e.e.

We initiated this study anticipating that data regarding the influence of the -Fe(CO)$_3$ ligand on the enantioselectivity of the allylboration reactions could be determined by careful analysis of the ratio and enantiomeric purity of the two diastereomeric products, **6** and **7**.[6] Initial experiments with racemic **4** using excess (S,S)-**2** (toluene, -78°C, 4Å sieves) provided an easily separated 62 : 38 mixture of **6a** and (6R)-**7a** ($[\alpha]^{23}_{D}$ -24.7° (c 0.74, $CHCl_3$)) in a combined yield of 88% Table 1, entry 4). *Significantly, the minor diastereomer (6R)-7a, which is the major product of a mismatched double asymmetric reaction of (2S)-4 and (S,S)-2, was determined to be >99% e.e. by the Mosher ester technique.*[7] The enantiomeric purity of the major product **6a**, however, was estimated to be only ca. 60% e.e. These data enable one to calculate that the matched double asymmetric reaction of (2R)-**4** and (S,S)-**2** proceeds with greater than 100 : 1 selectivity for ψ-

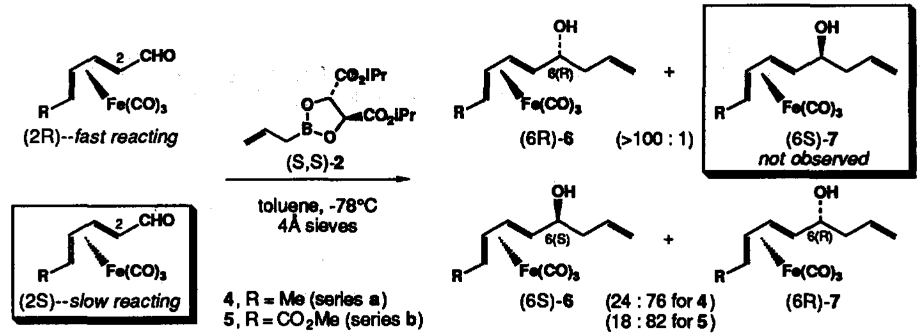


Table 1. Kinetic Resolution of Racemic Diene-Fe(CO)$_3$ Complexes 4 and 5.[a]

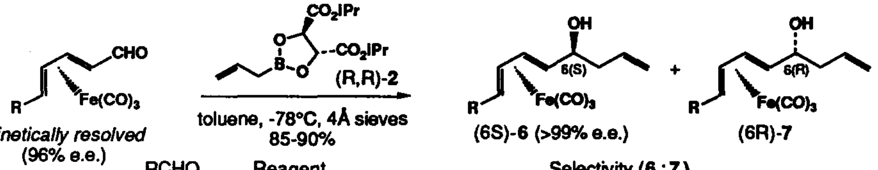
Entry	RCHO	% Conv.[b,c]	Ratio 6 : 7[c]	% e.e. (6)[d]	% e.e. (7)[e]	% e.e. (RCHO)[f]	% Yield[g]
1	4	25%	94.5 : 5.5	96%	--	--	--
2	4	45%	91 : 9	94%	--	--	36% (**6a**)
3	4	60%	86 : 14	ca. 90%	--	96%	37% (**4**)
4	4	100%	62 : 38	ca. 60%	>99%	--	31% (**7a**)
5	5	52%	92.5 : 7.5	96%	--	86%	47% (**6b**)
6	5	60%	88 : 12	ca. 94%	--	96%	38% (**5**)
7	5	100%	59 : 41	ca. 70%	>99%	--	39% (**7b**)

[a] All reactions were performed using (S,S)-**2** and 4Å mol. sieves in toluene at -78°C. Best results were obtained using (S,S)-**2** that had been purified by distillation. [b] The % conversion was controlled by the amount of **2** that was used (see ref. 3c for the preparation of standardized solutions). [c] The % conversion and the ratio of **6** : **7** were determined by 500 MHz ^{1}H NMR analysis. [d] E.e.'s for **6** were determined by Mosher ester analysis (ref. 7) or by $[\alpha]_D$ comparisons with samples of >99% e.e. The enantiomeric purity of **7** is also easily calculated from the reaction diastereoselectivity and the known stereoselectivities of the matched and mismatched double asymmetric reactions. [e] E.e.'s for **7** were determined by Mosher ester analysis. [f] Enantiomeric purity of kinetically resolved **4** and **5** was determined as described in text. [g] All isolated yields are absolute and are *uncorrected* for the amounts theoretically possible.

exo diastereomer (6R)-**6a** [ψ-endo isomer (6S)-**7a** is not detected in the Mosher ester analysis of **7a**, indicating that <0.5% of this isomer is produced from (2R)-**4**], while the mismatched double asymmetric reaction of (2S)-**4** and (S,S)-**2** provides a 76 : 24 mixture of (6R)-**7a** and (6S)-**6a**, respectively.[8,9] Similar results were obtained in the reaction of racemic **5** and excess (S,S)-**2** (entry 7), with the exception that the mismatched double asymmetric reaction is somewhat more selective, providing an 82 : 18 mixture of (6R)-**7b** and (6S)-**6b**, respectively.

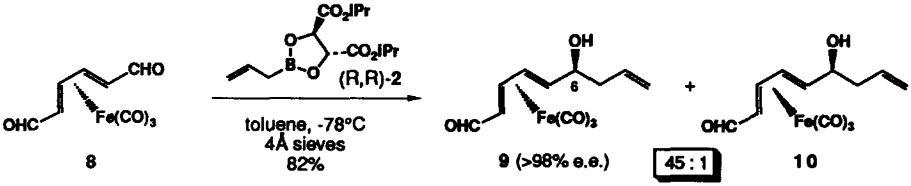
The observation that the reactions of the (2R)-**4** and (2R)-**5** with (S,S)-**2** proceed with outstanding diastereoselectivity (>100 : 1, entries 4, 7) prompted us to test the hypothesis that these stereochemically matched pairs[9] might also be kinetically matched. Indeed, when the reaction of racemic **4** and (S,S)-**2** was allowed to proceed to 25% conversion (by limiting the amount of **2** that was used), the diastereoselectivity was 17 : 1 (**6a** : **7a**) and (6R)-**6a** ($[\alpha]_D^{23}$ +43.3 (c 1.2, CHCl$_3$)) was isolated with an enantiomeric purity of 96% e.e. (entry 1). When allowed to proceed to 45% conversion, a 10 : 1 mixture of **6a** and **7a** was obtained, from which 94% e.e. (6R)-**6a** ($[\alpha]_D^{23}$ +43.4 (c 1.1, CHCl$_3$)) was obtained in 36% yield (entry 2). Finally, and most significantly, reactions allowed to proceed to 60% conversion provided a 6 : 1 mixture of (6R)-**6a** (ca. 90% e.e.) and (6R)-**7a**, plus kinetically resolved (2S)-**4** (96% e.e.; $[\alpha]_D^{23}$ +88.8° (c 1.1, MeOH)) that was isolated in 37% yield (entry 3).[10] Very similar results were obtained in the kinetic resolutions of racemic **5** (entries 5, 6). Noteworthy are the data in entry 5 for a reaction terminated at 52% conversion that provided a 12.5 : 1 mixture of (6R)-**6b** (48% yield; 96% e.e.; $[\alpha]_D^{23}$ +186° (c 0.6, $CHCl_3$)) and (6R)-**7b**, plus kinetically resolved (2S)-**5** (46% yield) that was shown to be 86% e.e.[11] Recrystallization of the latter material provided (2S)-**5** in 37% overall yield with enantiomeric purity ≥96% e.e. (m.p. 47-48°C; $[\alpha]_D^{23}$ -58° (c 0.3, MeOH)).[11] At 60% conversion, the enantiomeric purity of kinetically resolved (2S)-**5** is 96% (38% yield; entry 6).

The enantiomeric purity of kinetically resolved **4** and **5** was assessed by comparison of optical rotation data with literature values[10,11] as well as by performing double asymmetric reactions with both enantiomers of **2** (see below). Results of these experiments are in excellent agreement with expectations based on the diastereoselectivity data deduced from the experiments summarized in entries 4 and 7 of Table 1. The matched double asymmetric reactions, in particular, provide strong evidence of the enantiomeric purity of the kinetically resolved aldehyde complexes.[12]



RCHO	Reagent		Selectivity (6 : 7)
(2S)-4	(R,R)-2	*matched case*	99 : 1
(2S)-4	(S,S)-2	*mismatched case*	25 : 75
(2S)-5	(R,R)-2	*matched case*	98.5 : 1.5
(2S)-5	(S,S)-2	*mismatched case*	18 : 82

The data summarized in Table 1 clearly demonstrate that these kinetic resolutions exhibit high enantio- and diastereoselectivity. These criteria are characteristic of the special class of group and face selective reactions in which one of four nonequivalent (heterotopic) carbonyl (or olefin) faces reacts preferentially,[13] and they also constitute necessary conditions for the most successful examples of double stereodifferentiation involving two racemic reactants.[14] It seemed possible, therefore, that the asymmetric allylboration of the meso complex **8** would also proceed with exceptional enantio- and diastereoselectivity. Indeed, treatment of **8**[15] with 0.95 equiv. of (R,R)-**2** under standard conditions provided a 45 : 1 mixture of **9** and **10**. Allylboration products of **9** or **10** were not detected. The enantiomeric purity of the major product **9** ($[\alpha]_D^{23}$ -133° (c 0.8, $CHCl_3$)), isolated in 82% yield, was shown to be >98% e.e. by Mosher ester analysis of the derived diol, and the absolute configuration was established by correlation with **6b** prepared by the allylboration of **5**.[16]



In summary, we have shown that the enantioselectivity of the asymmetric allylboration of diene aldehydes is significantly improved by using the $Fe(CO)_3$ complexes as substrate surrogates. This is clearly demonstrated by the group and face selective allylboration of **8** that proceeds with $\Delta\Delta G^{\neq} \geq 1.7$ kcal mol^{-1}, compared to the allylboration of **1** (70% e.e.) for which $\Delta\Delta G^{\neq} = 0.7$ kcal mol^{-1}. Highly selective kinetic resolutions of racemic complexes **4** and **5** also have been demonstrated, defining a very efficient and convenient method for the synthesis of this interesting class of chiral organometallic complex.[2]

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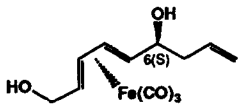
16. The relative and absolute stereochemistry of (6S)-**9** was determined by correlation with (6R)-**6b** ($[\alpha]_D^{23}$ +186° (c 0.6, $CHCl_3$); 96% e.e.), the major product from Table 1, entry 5. Thus, reduction of (6S)-**9** with $NaBH_4$ in MeOH provided (6S)-diol ***i*** ($[\alpha]_D^{23}$ -24.5° (c 0.2, $CHCl_3$)) in 95% yield that was enantiomeric but otherwise identical to a sample of (6R)-***i*** ($[\alpha]_D^{23}$ 23.7° (c 0.2, $CHCl_3$)) prepared by $LiAlH_4$ reduction of (6R)-**6b**.



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