ORGANIC
LETTERS

2001
Vol. 3, No. 4
557−559

Enantioselective Hydride Abstraction in Organic Substrates: A Novel Use for Chiral Carbenium Ions[†]

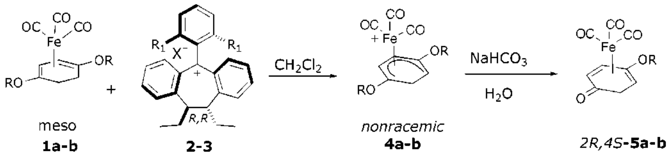
Derek Magdziak, Liping H. Pettus, and Thomas R. R. Pettus*

Department of Chemistry and Biochemistry, University of California at Santa Barbara,
Santa Barbara, California 93106

pettus@chem.ucsb.edu

Received December 5, 2000

ABSTRACT



It is surprising that chiral cations have not been used to distinguish between *prochiral* hydrides when converse notions, such as asymmetric addition of a hyride to a *prochiral* functional group or use of a chiral anion to distinghish between a pair of *prochiral* protons, are methods employed everyday in enantioselective synthesis. To the best of our knowledge, this Letter describes the first example of an oxidative enantioselective hydride transfer process.

Hydride transfer [H-T] from an organic substrate to a cation is a fundamental oxidation mechanism in organic chemistry.[1] The reaction is thought to occur by an ion transfer, or a single electron transfer [SET] followed by loss of [H$^+$] and another [SET], or some combination of these processes. The exact pathway depends on the steric and electronic attributes of the hydride donor. The majority of reactions involving [H-T]-oxidation have utilized Ar$_3$C$^+$ as the oxidant. Trityl salts corresponding to [BF$_4^-$] and [PF$_6^-$] dehydrogenate various types of ethers and ketals to carbonyl compounds,[2] promote the formation of lower energy cations,[3] convert enol ethers and enamines to enones,[4] and are often used in conjunction with organometallic substrates to increase the *hapto* number, η, of metal atoms such as Fe,[5] Cr,[6] Mo,[7] Rh,[8] Ir,[8] and Pd[8] in their respective metal complexes. In principle, each of these processes could provide optically enriched chiral material by subjecting a particular *meso* or *achiral* substrate to oxidation with a chiral surrogate of trityl cation.

[†] During the preparation of this Letter, we learned the Stephenson research group [University of East Anglia, Norwich, UK] was working on a similar concept and is establishing a method to recycle chiral *Ar$_3$CH into *Ar$_3$C$^+$.

(1) For a useful discussion of trityl cations, see: Connelly, N.; Geiger, W. *Chem. Rev.* **1996**, *96*, 877−910. For a review of hydride affinities of various triphenylcarbenium ions as well as other types of cations, see: (a) Hart, H.; Tomalia, D. A. *Tetrahedron Lett.* **1966**, *16*, 3383−3388. (b) Bordwell, F. G.; Cheng, J−P. *J. Org. Chem.* **1992**, *57*, 6542−6546. (c) Mayr, H.; Müller, K.-H.; Buhl, M. *J. Am. Chem. Soc.* **1999**, *121*, 2418−2424. (d) Arnett, E. *J. Phys. Org. Chem.* **1997**, *7*, 499−513. (e) Parker, V.; Handoo, K.; Cheng, J−P. *J. Am. Chem. Soc.* **1993**, *115*, 5067−5072. (f) Freedman, H. H.; Mckinley, S. V. *J. Am. Chem. Soc.* **1971**, *93*, 4715−4724.

(2) (a) Barton, D. H. R.; Magnus, P. D.; Smith, G.; Zurr, D. *J. Chem. Soc., Chem. Commun.* **1971**, 861−863. (b) Barton, D. H. R.; Magnus, P. D.; Smith, G.; Streckert, G.; Zurr, D. *J. Chem. Soc., Perkin Trans. 1* **1972**, 542−552. (c) Jung, M. E. *J. Org. Chem.* **1976**, *41*, 1479−1480.

(3) Barua, P.; Barua, N. C.; Sharma, R. P. *Tetrahedron Lett.* **1983**, 5801.

(4) (a) Manis, P. A.; Rathke, M. W. *J. Org. Chem.* **1981**, *46*, 5348−5351. (b) Jung, M. E.; Pan, Y.-G. *J. Org. Chem.* **1977**, *42*, 3961−3963. (c) Reetz, M. T.; Stephan, W.; Maier, W. F. *Synth. Commun.* **1980**, *10*, 867−871.

(5) (a) Fu, Y.-T.; Chao, P.-C.; Liu, L.-K. *Organometallics* **1998**, *17*, 221−226. (b) Stephenson, G. R.; Finch, H.; Owen, D. A.; Swanson, S. *Tetrahedron* **1993**, *49*, 5649−5662. (c) Pearson, A. J.; Srinivasan, K. *J. Org. Chem.* **1992**, *57*, 3965−3973. (d) Pearson, A. J.; Gelormini, A. M.; Pinkerton, A. A. *Organometallics* **1992**, *11*, 936−938. (e) Owen, D. A.; Stephenson, G. R.; Finch, H.; Swanson, S. *Tetrahedron Lett.* **1990**, *31*, 3401−3404.

(6) (a) Fretzen, A.; Ripa, A.; Liu, R.; Bernardinelli, G.; Kundig, E. P. *Chem. Eur. J.* **1998**, *4*, 251−259. (b) Fretzen, A.; Kundig, E. P. *Helv. Chim. Acta* **1997**, *80*, 2023−2026.

(7) (a) Bjurling, E.; Johansson, M. H.; Andersson, C.-M. *Organometallics* **1999**, *18*, 5606−5613. (b) Bjurling, E.; Andersson, C.-M. *Tetrahedron Lett.* **1999**, *40*, 1981−1984. (c) Pearson, A. J.; Khan, M. N. I. *Tetrahedron Lett.* **1985**, *26*, 1407−1410.

(8) Barabotti, P.; Diversi, p.; Giovanni, I. *J. Chem. Soc., Dalton Trans.* **1984**, 2517.

10.1021/ol006963k CCC: $20.00

Because tricarbonyliron complexes afford excellent diastereomeric control for the stereospecific preparation of quaternary carbon stereocenters from species similar to **4**,[9] our preliminary efforts have focused on the transformation shown in Figure 1.

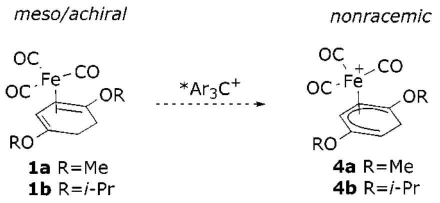
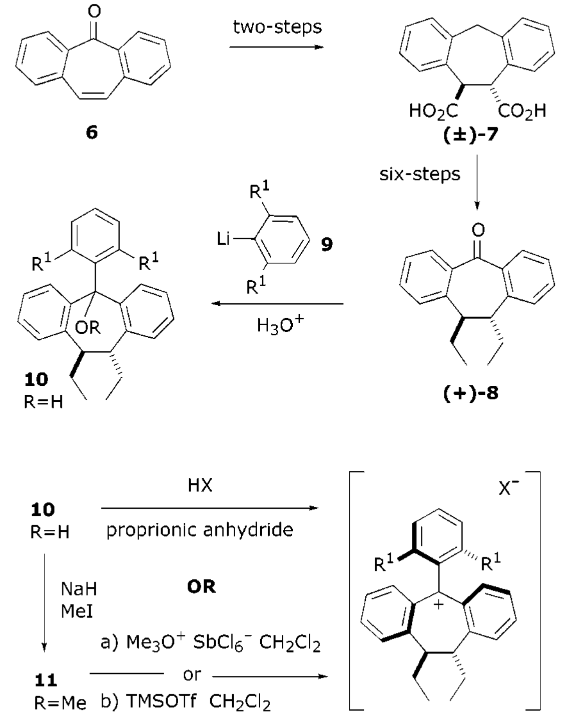


Figure 1.

We began our investigation with the only known example of a nonracemic trityl cation surrogate. Chen, using Snatzke's nonracemic ketone **(+)-8**,[10] had reported the preparation of several chiral trityl species, by implementing Dauben's procedure[11] (HX + Ph_3COH + propionic anhydride) with **10** or by combining $Me_3O^+SbCl_6^-$ with derivatives of the methyl ether **11**. Chen subsequently described the effectiveness of carbenium ions **12**−**16** and **2**−**3** as catalyst for Mukaiyama-type aldol reactions.[12] From the malleable synthesis of these species, we concluded that a range of chiral cations would be accessible from this sequence and that the capacity for hydride abstraction as well as the enantioselectivity of this event could be tuned by choice of the substituents introduced through **9**.[13] Although no X-ray data have been presented in regard to the conformation of **12**−**16** and **2**−**3**, we surmised after extensive molecular modeling that the top and bottom hemispheres of these chiral carbenium ions are identical because of S_2-symmetry about the seven-membered ring. Thus, only one side of the cation need be considered when contemplating combination with **1**.[14] Furthermore, it appears that the S_2-[*R*,*R*] stereocenters confer a new element of asymmetry on the carbenium species, establishing the direction of inclination of the blades in the phenyl propeller (Scheme 1).

Scheme 1



12: R^1 = H; X^- = ClO_4^-
13: R^1 = H; X^- = OTf^-
2: R^1 = H; X^- = BF_4^-
3: R^1 = H; X^- = PF_6^-
14: R^1 = H; X^- = $SbCl_6^-$
15: R^1 = CH_3; X^- = $SbCl_6^-$
16: R^1 = OCH_3; X^- = $SbCl_6^-$

Our intentions in regard to **1**, however, limited the counterions available to us and precluded several of these from further consideration. The explosive nature of perchlorates barred examination of **12**. The poor hydride affinity of the [$SbCl_6^-$] species excluded **14**−**16**.[15] Thus, we focused our attention on the [OTf^-], [BF_4^-], and [PF_6^-] cations **13**, **2**, and **3**, aiming to construct these along with their counterparts to **15**−**16**. While **2** and **3** formed smoothly as reported in the literature,[12a] 55% and 79%, respectively, in our hands, we were unsuccessful in preparing the [OTf^-] **13** or the [BF_4^-] and [PF_6^-] derivatives corresponding to **15** and **16**.[16]

To test the capability of **2**−**3** for the enantioselective hydride abstraction proposed in Figure 1, **1a** and **1b** were constructed using a procedure outlined by Stephenson.[9a] Commercially available hydroquinone ethers were subjected to reduction using lithium in ammonia. Diene **17** emerges

---

[9] For application of generic **4a** in synthesis, see: (a) Stephenson, G. R.; Finch, H.; Owen, D. A. *Tetrahedron* **1993**, *49*, 5649−5662. (b) Stephenson, G. R.; Sandoe, E.; Swanson, S. *Tetrahedron Lett.* **1996**, *37*, 6283−6288. (c) Stephenson, G. R.; Osborne, S. A.; Smyth, D. G.; Anson, C.; Hudson, R. *Tetrahedron Lett.* **1998**, *39*, 7603−7606. (d) Stephenson, G. R.; Owen, D. A. *Tetrahedron Lett.* **1991**, *32*, 1291−1294. (e) For a general review of tricarbonyliron chemistry, see: Pearson, A. J. *Iron Compounds in Organic Synthesis*; Academic Press: San Diego, 1994.

[10] Snatzke, G.; Platzek, J. *Tetrahedron* **1987**, *43*, 4947−4968.

[11] Dauben, H. J., Jr.; Honnen, L. R.; Harmon, K. *J. Org. Chem.* **1960**, *25*, 1442−1445.

[12] (a) Chen, C.-T.; Chao, S.-D.; Yen, K.-C. *J. Am. Chem. Soc.* **1997**, *119*, 11341−11342. (b) Chen, C.-T.; Chao, S.-D.; Yen, K.-C. *Synlett* **1998**, 924−926. (c) Chen, C.-T.; Chao, S.-D. *J. Org. Chem.* **1999**, *84*, 1090−1091.

[13] The angle of inclination of the phenyl blades greatly affects hydride affinity, see ref 1f.

[14] The following citation suggests that hydride abstraction occurs via a transition state (2.6 Å) between C−H−C atoms with an angle between 160 and 170°. Ritzeler, O.; Parel, S.; Therrien, B.; Bensel, N.; Reymond, J.-L.; Schenk, K. *Eur. J. Org. Chem.* **2000**, 1365−1372.

[15] The [$SbCl_6^-$] species, unlike [BF_4^-], [PF_6^-], and [OTf^-] systems, is rarely used for hydride abstraction and we found no examples of a [Ph_3C^+ $SbCl_6^-$] species used with an organometallic substrate. This distinction might be due to the "softness" of these types of carbenium ions and the labile nature of the [Cl^-] ligands, which results in a media-dependent equilibrium between $Ph_3C{\cdot}SbCl_6$ and Ph_3CCl + $SbCl_5$.

[16] Neither the starting triarylcarbinol **10** nor the triarylmethane were among the products of these unsuccessful reactions. The products appear to correspond to some type of skeletal rearrangement. Thus, it would seem that in addition to the hydride affinity the relative stability and the reactivity of the carbenium ions of this type depend on both R1 substituents and the associated counteranion.

in 97% in 2 h, while **18** forms in 60% after 6 h. Refluxing **17** [0.1 M in ethanol-free $CHCl_3$] with $(Ph_3P)_3RhCl$ [0.1 equiv] affords a 3:1 ratio of conjugated and nonconjugated dienes. Subjecting this mixture [0.1 M in refluxing Bu_2O] to $Fe(CO)_5$ [2.1 equiv] yields the *meso* η^4 iron diene complex **1a** in 74%. In the case of **1b**, the best overall yield is obtained if $(Ph_3P)_3RhCl$ is omitted from this sequence (**18** → **1b** directly in 20% yield with $Fe(CO)_5$).

These *meso* η^4 iron dienes **1a**−**b** were then subjected to hydride abstraction with chiral cations **2**−**3**. Because [H-T] occurs opposite the metal atom, only the *exo* hydrogen atoms [H_x and $H_{x'}$] are eligible for abstraction. If **4** is optically enriched, then the chiral cation has differentiated between these atoms. The selectivity can be determined by exposing **4** to aqueous $NaHCO_3$ which yields the chiral ketone **5** that can be purified by chromatography and analyzed by chiral stationary phase HPLC using a Chiracel OF column.

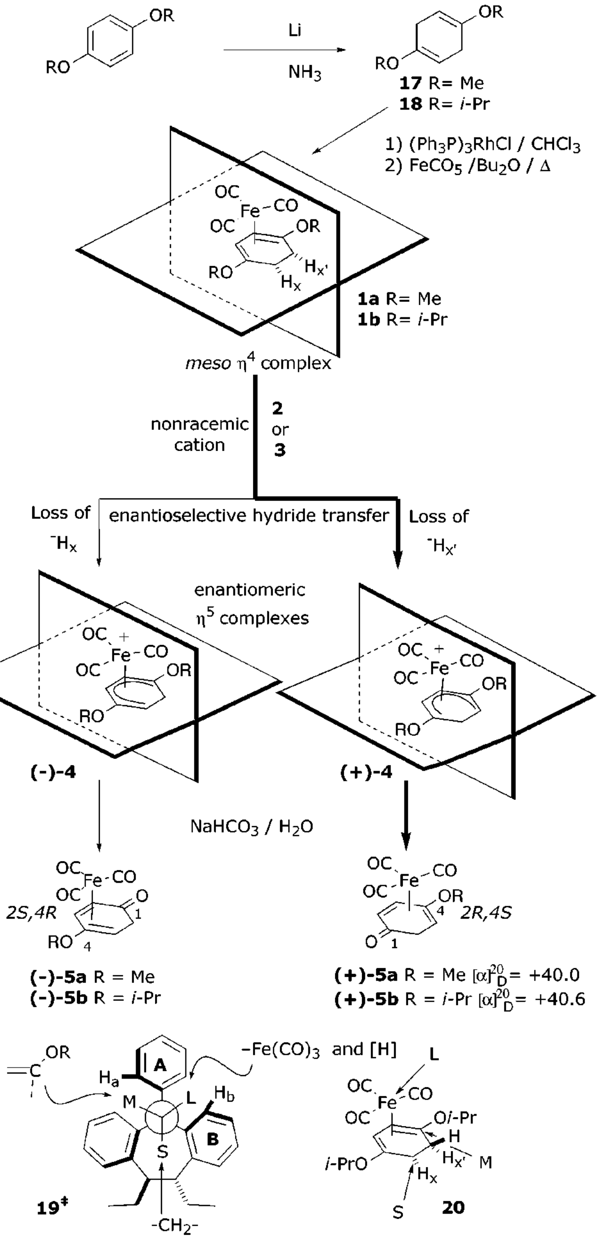
The enantiomeric excesses obtained in this stoichiometric procedure are shown in Table 1. These reactions led to **5a**−**b** in comparable yield [60−70%] and enantioselectivity [43−53%]. Increasing the size of the ether substituent caused a slight increase in *enantiomeric excess*, but the conversion proceeded in a lower overall yield. *To the best of our knowledge, these results are the first report of an enantioselective hydride abstraction.* This selectivity supports the idea that [H-T] in tricarbonyliron complexes proceeds through an ion transfer rather than an [SET] pathway.[17] Circular dichroism spectra were recorded for the η^4 iron dienes **5a** and **5b**. A positive value of $\Delta\epsilon$ at $\lambda = 354$ nm empirically establishes the absolute configuration of products afforded from *(R,R)* carbenium cations **2**−**3** to be predominately in the *2R,4S* configuration.[18]

Table 1. ee Afforded for **1a** and **1b**

entry	substrate	cation	product	yield, %	ee, %
1	**1a**	**2**	2*R*,4*S*-**5a**	62	43
2	**1a**	**3**	2*R*,4*S*-**5a**	71	46
3	**1b**	**3**	2*R*,4*S*-**5b**	65	53

We speculate that the difference in the angle of inclination for the **A** and **B** aryl rings regulates the *enantiomeric excess* accumulating from the essentially linear transition state **19**‡.[14] The three groups adjacent to the C-H donor atom [cf. **20**] align with the chiral cation so as to minimize nonbonded interactions. The outcome observed results when the largest group adjacent to the hydride donor atom, the *endo* H and more importantly the tricarbonyliron moiety in **1**, overlaps with [H_b] of the cation. The medium sized vinyl ether residue of **1**, in turn, extends over [H_a] of the cation, while the methylene, the smallest group adjacent to the CH donor atom, is directed toward the seven-membered ring (Scheme 2).

Scheme 2



We believe that our efforts may have revealed a useful asymmetric transformation. In due course higher enantioselectivities should be achievable with **1** as well as other types of *meso* substrates using less than a stoichiometric equivalent of the chiral carbenium ion.

Acknowledgment. Support from the Petroleum Research Fund, administered by the American Chemical Society (ACS-PRF# 34986-G), is appreciated.

Supporting Information Available: Experimental details, full spectral characterization for **18**, **1b**, **(+)-5b**, and the corresponding [*Ar_3CH], and all relevant HPLC data. This material is available free of charge via the Internet at http://pubs.acs.org.

OL006963K

---

[17] Mandon, D.; Astruc, D. *Organometallics* **1989**, *8*, 2372−2377.

[18] Stephenson, G. R.; Howard, P. W. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2873−2880.