

the bond lengths of the molecule containing π electrons or its fragment.

- [12] See M. Boronat, E. Ortí, P. M. Viruela, F. Tomás, *J. Mol. Struct. Theochem* **1997**, 390, 149–156.
- [13] Gaussian 94: M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. W. Gill, B. G. Johnson, M. A. Robb, J. R. Cheeseman, T. Keith, G. A. Petersson, J. A. Montgomery, K. Raghavachari, M. A. Al-Laham, V. G. Zakrzewski, J. V. Ortiz, J. B. Foresman, J. Cioslowski, B. B. Stefanov, A. Nanayakkara, M. Challacombe, C. Y. Peng, P. Y. Ayala, W. Chen, M. W. Wong, J. L. Andres, E. S. Replogle, R. Gomperts, R. L. Martin, D. J. Fox, J. S. Binkley, D. J. Defrees, J. Baker, J. P. Stewart, M. Head-Gordon, C. Gonzalez, J. A. Pople, Gaussian, Pittsburgh, PA, **1995**.
- [14] For further calculations on the porphyrin system, see a) D. Lamoén, M. Parinello, *Chem. Phys. Lett.* **1996**, 248, 309–315 and references therein; b) P. M. Kozłowski, A. A. Jarzecki, P. Pulay, *J. Phys. Chem.* **1996**, 100, 7007–7013 and references therein.

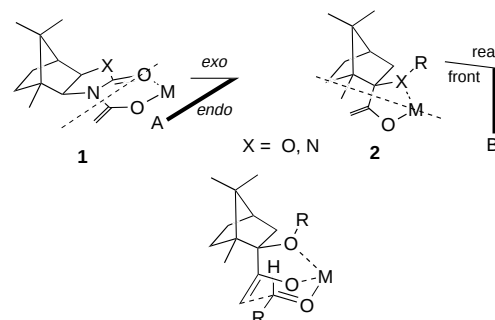
Design and Evaluation of a Practical Camphor-Based Methyl Ketone Enolate for Highly Stereoselective “Acetate” Aldol Reactions**

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Control of the configuration of newly forming stereogenic carbon atoms in aldol condensation processes has focused enormous efforts over the last two decades.^[1] Special attention has been given to the use of chiral enolates derived from carboxylic acids^[2] because of the easy final removal of the auxiliary to obtain either β -hydroxy carbonyl or 1,3-dihydroxylic compounds, which are frequently present in natural products.^[3] A conceptually different, but in practice equivalent, strategy to access to these fragments lies in the use of enolates derived from chiral α -hydroxy ketones.^[4] In this instance, the aldol products, upon oxidative cleavage of the α -ketol moiety, give the desired β -hydroxy carbonyl system.^[5] The major drawbacks associated with this strategy are the destruction of the covalently bounded chiral adjuvant at the final stage, and the insufficient stereoselectivity generally

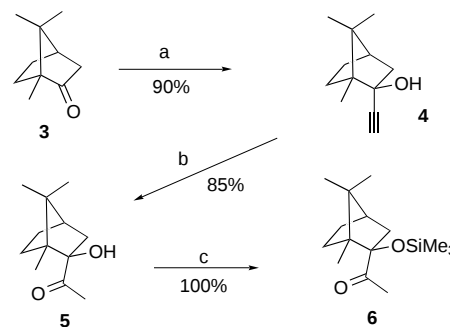
attained with α -unsubstituted enolates.^[6] Although considerable advances have been made in recent years to overcome this latter limitation by carrying out acetate aldol reactions mediated by both metal enolates bearing chiral ligands and external chiral catalysts,^[7] the problem associated with enolates of chiral acetates still remains not well resolved;^[8] in all but one case,^[4j] the lack of stereoselection in aldol reactions with methyl ketone enolates is specially dramatic.^[4b,g,h,i]

We have recently reported on the reaction of *N*-acetyl imide enolates **1** with aldehydes to give the corresponding adducts with modest levels of diastereoselectivity (Scheme 1).^[9] In an attempt to take advantage of the stereo-



Scheme 1. Design of the new chiral methyl ketone enolate **2** by moving the acetyl moiety of **1** nearer to the camphor skeleton. Also shown is the transition state accounting for the aldol reaction of **2**.

differentiating power of the camphor skeleton more effectively, we designed the new camphor-derived enolate **2**. The conception of **2** has been guided by two major goals: a) to provoke the electrophilic aldehyde to follow a trajectory of approach closer to the camphor skeleton, and b) to force a facial discrimination between the rear side and the sterically more demanding front side of the camphor skeleton, depicted as the half-spaces defined by plane B in Scheme 1,^[10] instead of the more commonly used *endo/exo* discrimination across opposite sides of plane A.^[11] Accordingly, if one assumes that a chelating metal ion like lithium engages in three-point coordination, a very high diastereoselectivity should be expected through a Zimmerman–Traxler six-membered transition state.^[12] From this design the methyl ketone **5**^[13] (Scheme 2) is a primary candidate to evaluate the above



Scheme 2. Synthesis of the chiral methyl ketone reagents **5** and **6**: a) $\text{HC}\equiv\text{CLi}$, THF, $-78 \rightarrow$ room temperature (RT) (*endo:exo* 97:3); b) HgO , H_2SO_4 , Me_2CO , reflux; c) TMSO, TFOH cat., RT.

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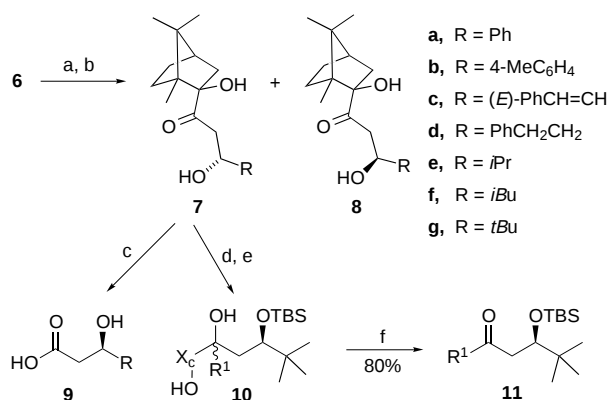
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[+] X-ray structure analysis.

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hypothesis. The crystalline **5** was prepared by addition of lithium acetylide to the commercially available (1*R*)-(+)-camphor (**3**) according to the procedure of Midland.^[14] The addition proceeded in a 97:3 *endo:exo* ratio from which **4** was isolated in 90 % yield after column chromatography. Standard hydration provided **5** [m.p.: 94–95°C, $[\alpha]_D^{25} = -65.6$ ($c = 1.0$ in CH_2Cl_2)] in 85 % yield after crystallization from hexane.^[15]

Concordant with our expectations, the corresponding aldol products obtained from the reaction of representative aldehydes with the lithium enolate of **6**, generated from **5** by silylation with *N*-trimethylsilyl-2-oxazolidinone (TMSO)^[16] and subsequent treatment with lithium diisopropylamide (LDA), were indeed formed with remarkably high diastereoselectivity (Scheme 3). The diastereomeric ratio of the



Scheme 3. Diastereoselective synthesis of α -unsubstituted β -hydroxy carboxylic acids and ketones: a) LDA (1.2 equiv), THF, -78°C , 0.5 h then RCHO, 3–7 h; b) 1M HCl, MeOH or TBAF (2 equiv), THF, RT, 5 min; c) NaIO₄, MeOH/H₂O (2/1), RT or reflux, 12–48 h; d) ClSiMe₂*t*Bu, imidazole, DMF, RT, 3 days, 86 %; e) R¹MgBr, CeCl₃, THF or Et₂O, 0°C , 2 h; f) Pb(OAc)₄ (2 equiv), C₆H₆, 5°C , 2 h.

product was unchanged after desilylation to afford the adducts **7/8** (typically 95:5, Table 1). The stereochemical assignments for the major products **7** from the reaction with benzaldehyde, isobutyraldehyde, and pivalaldehyde were made by cleavage of the acyloin moiety^[5] to afford the

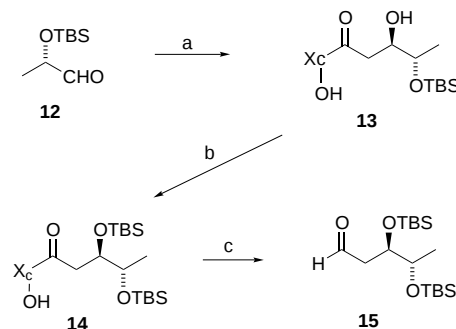
Table 1. Aldol condensation of the lithium enolate of **6** with representative aldehydes.^[a]

Aldehyde	<i>t</i> [h]	7:8 ^[b]	Yield (7) [%] ^[c]
C ₆ H ₅ CHO	6	96:4	80
4-CH ₃ C ₆ H ₄ CHO	7	96:4	67
C ₆ H ₅ CH=CHCHO	6	92:8	80
C ₆ H ₅ CH ₂ CH ₂ CHO	2	95:5	81
<i>i</i> -C ₃ H ₇ CHO	3	97:3	67
(CH ₃) ₂ CHCH ₂ CHO	6	96:4	75
(CH ₃) ₃ CCHO	6	> 98:2	70

[a] Reactions were carried out at -78°C on 0.5 mmol scale by adding a precooled (-78°C) solution of the aldehyde in THF to the lithium enolate of **6** in the same solvent at -78°C . [b] Ratios were determined by both ¹³C NMR (area of CHO signals of both diastereomers at $\delta = 65$ –75) and HPLC analysis of the crude reaction mixture. Diastereomer **8** had the shorter retention time in all HPLC experiments. [c] Yields of **7** after purification of the crude product by column chromatography and separation of diastereomers by HPLC on a Merck LiChrosorb Si 60 column (7 μm) with mixtures of ethyl acetate and hexane as eluent.

corresponding carboxylic acid **9** along with the recovery of the starting camphor (85–90 %). The observed optical rotations of these β -hydroxy acids were then compared with published values.^[17] In addition, a single-crystal X-ray analysis of the aldol **7g** corroborated the assigned configuration for the adducts. From the data in Table 1 it is evident that the reaction diastereoselectivity is independent of the nature of the aldehyde, showing generality for aromatic, α,β -unsaturated, and linear as well as branched chain aliphatic aldehydes. The excellent diastereoselectivity observed in these reactions is of particular interest in that it provides, through carbonyl addition and subsequent diol cleavage, the basis for an enantioselective synthesis of α -unsubstituted β -hydroxy ketones. For example, using organocerium reagents,^[18] we could prepare the carbinols **10** [R¹ = Me, 85 %; R¹ = Ph, 90 %; R¹ = allyl, 80 %],^[19] which upon exposure to lead tetraacetate in benzene gave the α -unsubstituted β -silyoxy ketones **11** in good overall yields and essentially in optically pure form.

A further example that illustrates the efficiency of the present system is the reaction of the dianion of **5** with the α -oxy aldehyde **12** (Scheme 4), a chiral aldehyde that shows



Scheme 4. a) **5**, LDA (2.4 equiv), LiCl (6 equiv), THF, -78°C , 4 h, 75 %. b) TBDMS-Cl, imidazole, DMF, RT, overnight, 90 %. c) BH₃·THF, THF, 0°C , 7 h then Pb(OAc)₄ (2 equiv), C₆H₆, 5°C , 2 h, 70 %.

essentially no diastereoselection with either methyl acetate or α -silyloxy methyl ketone enolates.^[4b, 5b] When **12** was allowed to react with the dianion of **5** in the presence of LiCl, a mixture of diastereomeric aldols was obtained in the ratio 93:7. The major isomer **13** was isolated in 75 % yield after column chromatography. A single crystal X-ray analysis of **13** confirmed the assigned configuration for the adduct.^[20] Finally, diborane reduction of the keto group in the TBS-protected aldol **14** (TBS = *tert*-butyldimethylsilyl) followed by oxidative workup provided the α -unsubstituted β -silyloxy aldehyde **15** in 70 % yield along with the recovery of the starting camphor.

The α -hydroxy methyl ketone enolate developed here helps to fill the existing gap with regard to the usual behavior of α -unsubstituted enolates in diastereoselective aldol reactions and, in addition, enables for the first time the recovery of the starting source of chiral information.

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- [1] Reviews on the asymmetric aldol condensation: a) D. A. Evans, J. V. Nelson, T. R. Taber, *Top. Stereochem.* **1982**, 13, 1; b) S. Masamune, W. Choy, J. S. Petersen, L. R. Sita, *Angew. Chem.* **1985**, 97, 1; *Angew. Chem. Int. Ed. Engl.* **1985**, 24, 1; c) *Comprehensive Organic Chemistry*, Vol. 2 (Eds.: B. M. Trost, I. Fleming, C. H. Heathcock), Pergamon, Oxford, **1991**; d) C. H. Heathcock in ref. [1c], p. 133; e) M. Kim, S. F. Williams, S. Masamune, in ref. [1c], p. 239; f) I. Paterson, in ref. [1c], p. 301; g) A. S. Franklin, I. Paterson, *Contemp. Org. Synth.* **1994**, 1, 317; h) M. Braun in *Stereoselective Synthesis*. (Houben-Weyl), Vol. E21/3 (Eds.: G. Helmchen, R. W. Hoffmann, J. Mulzer, E. Schaumann), Thieme, Stuttgart, **1996**, p. 1603.
- [2] Extensive list of chiral auxiliaries: a) A.-ur Rahman, Z. Shah, *Stereoselective Synthesis in Organic Chemistry*, Springer, Berlin, **1993**; b) J. Seyden-Penne, *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*, Wiley, New York, **1995**; c) D. J. Ager, I. Prakash, D. R. Schaad, *Chem. Rev.* **1996**, 96, 835.
- [3] S. Hanessian, *Total Synthesis of Natural Products: The Chiron Approach*, Pergamon, Oxford, **1983**.
- [4] a) C. H. Heathcock; M. C. Pirrung, C. T. Buse, J. P. Hagen, S. D. Young, J. E. Sohn, *J. Am. Chem. Soc.* **1979**, 101, 7077; b) C. H. Heathcock, M. C. Pirrung, J. Lampe, C. T. Buse, S. D. Young, *J. Org. Chem.* **1981**, 46, 2290; c) N. A. Van Draanen, S. Arseniyadis, M. T. Crimmins, C. H. Heathcock, *ibid.* **1991**, 56, 2499; d) S. Masamune, S. K. A. Ali, D. L. Snitman, D. S. Garvey, *Angew. Chem.* **1980**, 92, 573; *Angew. Chem. Int. Ed. Engl.* **1980**, 19, 557; e) S. Masamune, W. Choy, F. A. L. Kerdesky, B. Imperiali, *J. Am. Chem. Soc.* **1981**, 103, 1566; f) C. Siegel, E. R. Thornton, *ibid.* **1989**, 111, 5722; g) B. M. Trost, H. Urabe, *J. Org. Chem.* **1990**, 55, 3982; h) C. H. Heathcock, C. T. White, J. J. Morrison, D. VanDerveer, *ibid.* **1981**, 46, 1296; i) D. A. Evans, J. V. Nelson, E. Vogel, T. R. Taber, *J. Am. Chem. Soc.* **1981**, 103, 3099; j) B. R. Lagu, H. M. Crane, D. C. Liotta, *J. Org. Chem.* **1993**, 58, 4191; k) S. Figueras, R. Martín, P. Romea, F. Urpí, J. Vilarrasa, *Tetrahedron Lett.* **1997**, 38, 1637.
- [5] a) C. H. Heathcock, C. T. Buse, W. A. Kleschick, M. C. Pirrung, J. E. Sohn, J. Lampe, *J. Org. Chem.* **1980**, 45, 1066; b) C. H. Heathcock, S. D. Young, J. P. Hagen, M. C. Pirrung, C. T. White, D. Vanderveer, *ibid.* **1980**, 45, 3846.
- [6] For a detailed information on this topic, see: a) M. Braun, *Angew. Chem.* **1987**, 99, 24; *Angew. Chem. Int. Ed. Engl.* **1987**, 26, 24; b) M. Braun in *Advances in Carbanion Chemistry*, Vol. 1 (Ed.: V. Snieckus), Jai, London, **1992**, p. 177.
- [7] Aldol reactions of achiral methyl ketones with achiral aldehydes on use of chiral boron reagents: a) I. Paterson, J. M. Goodman, *Tetrahedron Lett.* **1989**, 30, 997; b) P. V. Ramachandran, W. Xu, H. C. Brown, *Tetrahedron Lett.* **1996**, 37, 4911; c) A. Bernardi, C. Gennari, J. M. Goodman, I. Paterson, *Tetrahedron Asymmetry* **1995**, 6, 2613; on use of chiral titanium reagents: d) R. O. Duthaler, P. Herold, W. Lottenbach, K. Oertle; M. Riediker, *Angew. Chem.* **1989**, 101, 490; *Angew. Chem. Int. Ed. Engl.* **1989**, 28, 495; on use of chiral palladium(II) reagents: e) M. Sodeoka, R. Tokunoh, F. Miyazaki, E. Hagiwara, M. Shibasaki, *Synlett* **1997**, 463; on use of external chiral catalysts: f) K. J. Hale, S. Manaviazar in *Advanced Asymmetric Synthesis*, Vol. 2 (Ed.: G.-R. Stephenson), Chapman and Hall, London, **1996**, p. 27; g) T. Mukaiyama, *Aldrichimica Acta* **1996**, 29, 59.
- [8] Recent examples from chiral acetate imide enolates: a) K. Otsuka, T. Ishizuka, K. Kimura, T. Kunieda, *Chem. Pharm. Bull.* **1994**, 42, 748; b) T.-H. Yan, A.-W. Hung, H.-C. Lee, C. S. Chang, W.-H. Liu, *J. Org. Chem.* **1995**, 60, 3301; c) T. H. Yan, A.-W. Hung, H.-C. Lee, C. S. Chang, *ibid.* **1994**, 59, 8187; from chiral *N*-acetyl sultam enolates: d) W. O. Oppolzer, C. Starkemmann, *Tetrahedron Lett.* **1992**, 33, 2139; from Fisher carbene enolates: e) T. S. Powers, Y. Shi, K. J. Wilson, W. D. Wolff, *J. Org. Chem.* **1994**, 59, 6882.
- [9] a) C. Palomo, M. Oiarbide, A. Gonzalez, J. M. García, F. Berree, A. Linden, *Tetrahedron Lett.* **1996**, 37, 6931; b) C. Palomo, F. Berree, A. Linden, J. M. Villagordo, *J. Chem. Soc. Chem. Commun.* **1994**, 1961.
- [10] For an earlier camphor-based ester acetate aldol approach exploiting this concept in another way, see G. Helmchen, U. Leikauf, I. Tauferknöpfel, *Angew. Chem.* **1985**, 97, 874; *Angew. Chem. Int. Ed. Engl.* **1985**, 24, 874.
- [11] Review on camphor-based chiral auxiliaries: W. Oppolzer, *Tetrahedron* **1987**, 43, 1969.
- [12] H. E. Zimmerman, M. D. Traxler, *J. Am. Chem. Soc.* **1957**, 79, 1920.
- [13] M. Kagawa, *Chem. Pharm. Bull.* **1959**, 7, 306.
- [14] a) M. M. Midland, *J. Org. Chem.* **1975**, 40, 2250; b) M. M. Midland, J. I. McLoughlin, R. T. Werley, Jr., *Org. Synth. Coll.* **1993**, Vol 8, p 391.
- [15] The addition of lithium acetylide to (1*R*)-(+)-camphor has been previously reported to give the *endo* adduct: a) M.-L. Capmau, W. Chodkiewicz, P. Cadot, *Bull. Soc. Chim. Fr.* **1968**, 3233. Other authors, however, suggest that the *exo* adduct was produced instead: b) C. D. Johnson, S. Lane, P. N. Edwards, P. J. Taylor, *J. Org. Chem.* **1988**, 53, 5130; c) P. Bovonsombat, E. McNelis, *Tetrahedron Lett.* **1993**, 34, 4277. In our hands the procedure of Midland^[14] gives reproducible results. Product **5** can also be obtained by direct hydration of the crude *endo:exo* mixture of **4** followed by a single crystallization from hexane (yield, 90 %).^[20]
- [16] J. M. Aizpurua, C. Palomo, A. L. Palomo, *Can. J. Chem.* **1984**, 62, 336.
- [17] Observed values **9a**: +15.5 (*c* = 0.9 in EtOH) [Published value: +17.9 (*c* = 2.3 in EtOH 95 %)^[10]]; **9e**: +41.7 (*c* = 1.0 in CHCl₃) [Published value: +40.5 (*c* = 0.6 in CHCl₃)^[10]]; **9g**: +53.0 (*c* = 1.0 in CHCl₃) [Published value: +53.2 (*c* = 1.0 in CHCl₃)^[7a]].
- [18] T. Imamoto, N. Takiyama, K. Nakamura, T. Hatajima, Y. Kamiya, *J. Am. Chem. Soc.* **1989**, 111, 4392.
- [19] Every attempt at attacking the carbonyl group of the corresponding aldols with both lithium and Grignard reagents led to unsatisfactory results.
- [20] Crystallographic data (excluding structure factors) for the structures **5**, **7g**, and **13** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-100315. Copies of the data can be obtained free of charge on application to: CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: int. code + (44) 1223-336033; e-mail: deposit@chemcrs.cam.ac.uk).

[{Pt(CN)(C₁₀H₂₁N₄)₆]: A Luminescent Hexanuclear Platinum(II) Macrocycle Containing Chelating Dicarbene and Bridging Cyanide Ligands**

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Transition metal mediated self-assembly reactions are a versatile strategy for generating supermolecules with appealing structural and spectroscopic properties.^[1–6] In this context we are interested in luminescent molecular hosts^[7] composed of square-planar platinum(II) complexes as building blocks, since such materials could have applications in host–guest photochemistry and as novel luminescent sensors. Fujita et al.^[1] and Stang et al.^[5a, b] reported the preparation of tetranuclear platinum(II) compounds with pyridine-based ligands. Here we describe the crystal structure of a novel luminescent hexanuclear platinum(II) macrocycle bearing cyclic dicarbene and bridging cyanide ligands.

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