

- [3] a) R. V. Southwood-Jones, W. L. Earl, K. E. Newman, A. E. Merbach, *J. Chem. Phys.* **1980**, 73, 5909–5917; b) C. Cossy, L. Helm, A. E. Merbach, *Inorg. Chem.* **1988**, 27, 1973–1979.
- [4] a) S. Aime, M. Botta, M. Fasano, S. Paoletti, P. L. Anelli, F. Uggeri, M. Virtuani, *Inorg. Chem.* **1994**, 33, 4707–4711; b) G. Gonzalez, D. H. Powell, V. Tissières, A. E. Merbach, *J. Phys. Chem.* **1994**, 98, 53–59; c) S. Aime, M. Botta, M. Fasano, S. Geninatti Crich, E. Terreno, *J. Biol. Inorg. Chem.* **1997**, 2, 470–479.
- [5] (a) S. Aime, M. Botta, G. Ermondi, *Inorg. Chem.* **1992**, 31, 4291–4299; (b) S. Hoeft, K. Roth, *Chem. Ber.* **1993**, 126, 869–873.
- [6] D. H. Powell, O. M. Ni Dhubbghaill, D. Pubanz, L. Helm, Y. S. Lebedev, W. Schlaepfer, A. E. Merbach, *J. Am. Chem. Soc.* **1996**, 118, 9333–9346.
- [7] S. Aime, A. Barge, M. Botta, A. De Sousa, D. Parker, *J. Am. Chem. Soc.* **1997**, 119, 4767–4768.
- [8] S. Aime, M. Botta, E. Terreno, unpublished results.
- [9] S. Amin, J. R. Morrow, C. H. Lake, M. R. Churchill, *Angew. Chem.* **1994**, 106, 824–826; *Angew. Chem. Int. Ed. Engl.* **1994**, 33, 773–775.
- [10] P. H. Smith, K. N. Raymond, *Inorg. Chem.* **1985**, 24, 3469–3477.

A Novel Aldol Condensation with 2-Methyl-4-pentenal and Its Application to an Improved Total Synthesis of Epothilone B**

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Samuel J. Danishefsky*

Dedicated to Professor Ryoji Noyori

The recognition that the fermentation metabolites epothilones A and B (**1** and **2**, respectively) have potent in vitro antitumor properties and function through a paclitaxel-like (taxol-like) mechanism as inhibitors of microtubule disassembly has spurred a great deal of multidisciplinary research.^[1, 2] Included in the pursuits which have followed in the wake of the exciting biology of the epothilones is the goal of total synthesis. Indeed, for those research groups (such as

ours) for whom fermentation-derived epothilones are not available, chemical synthesis provides the only recourse to gain access to this series.

The total syntheses of epothilones A and B were accomplished by our group^[3] and, shortly thereafter, by groups directed by Nicolaou^[4a–c] and Schinzer.^[5] A collection of fully synthetic epothilones from our laboratory,^[6] as well as an even more extensive compendium from Nicolaou and co-workers,^[7] were used to identify the zones of the epothilones that could undergo molecular modification with maintenance of biological function, at least at the in vitro level. The mapping exercises on structure–activity relationships performed by both groups provided very similar conclusions. An interesting finding first reported by our group,^[6] and shortly thereafter by Nicolaou et al.,^[7] was that the 12,13-deoxy versions of epothilones A and B (**3** and **4**, respectively) were quite active in in vitro assays. This discovery suggested the possibility that the epoxide linkages of the epothilones, which might be detrimental from the standpoint of peripheral toxicity, may not be crucial for eventual clinical function.

Our original synthesis of the epothilones, though quite long, had the feature of high stereoselectivity in each of the coupling steps.^[3] While a disadvantage in enhancing access to multicomponent libraries,^[4d,e, 7a] stereoselectivity allowed for accumulation of substantial quantities of fully synthetic key epothilones. Comparable harvesting of required amounts of material through the stereorandom olefin metathesis route, practiced by others^[4, 5] as well as ourselves,^[6a] would be virtually prohibitive. Its overall length notwithstanding, our first-generation total synthesis, which features the highly stereoselective LACDAC (Lewis acid catalyzed diene–aldehyde cyclocondensation) and *B*-alkyl Suzuki coupling steps, produced substantial quantities of epothilones. In fact, the only published in vivo data on epothilones available when this manuscript was submitted were obtained with our fully synthetic materials.^[6c] These early findings in xenograft mice identified some significant toxicity problems with the highly potent epothilone B (**2**). Remarkably, in vivo studies in the interperitoneal mode of injection demonstrate that the less potent 12,13-deoxyepothilone B (**4**) is well tolerated and is virtually curative against human mammary tumor xenografts.^[8] The lead compound **4** has many significant and clear advantages over paclitaxel in terms of efficacy against multiple drug resistant (MDR) tumors when administered intraperitoneally. We shall return to issues of bioactivity shortly.

These exciting early results^[8] underscored the need for a greatly improved total synthesis which can sustain a serious and substantial discovery research program for assaying candidate structures in rodents as well as in higher animals. We now report major progress in this regard. Our new route, which retains the advantages of high stereoselectivity throughout, is totally reworked in the treatment of the once difficult C1–C11 domain. Scheme 1 provides an overview of the problem.

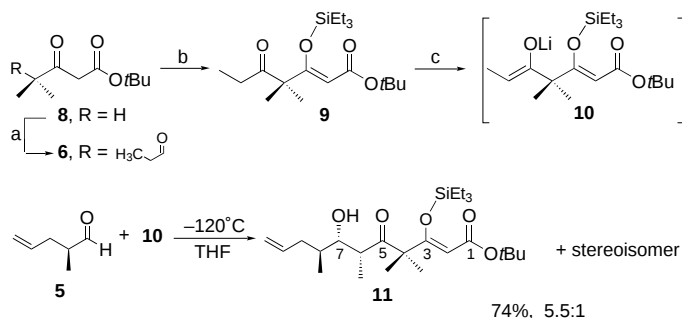
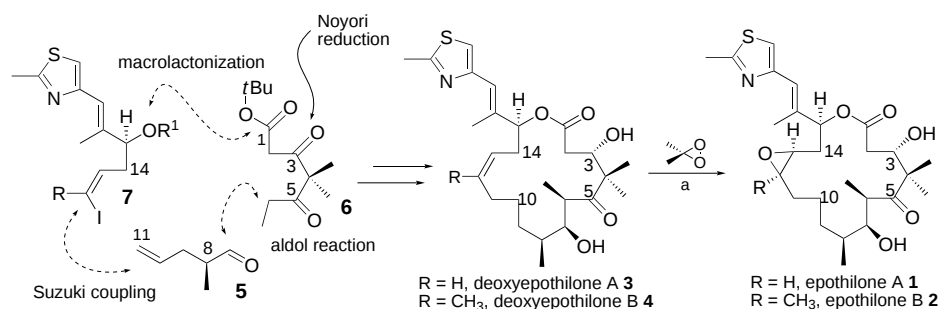
The new route is based on four findings, each of which has implications well beyond epothilone. The first is the ease of formation and the synthetic utility of the (*Z*)-lithium enolate **10**, which is readily prepared from **8** (Scheme 2). The ethyl ketone unit, from which the critical enolate is formed, is part

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[**] This research was supported by the National Institutes of Health (NIH, grants CA-28824 and CA-08748). Postdoctoral Fellowship support is gratefully acknowledged by A.B. (NIH, CA-GM 72231), C.H. (American Cancer Society, PF-98–173–001), and K.S. (NIH, GM-18248). We gratefully acknowledge Dr. George Sukenick (NMR Core Facility, Sloan-Kettering Institute) for NMR and mass spectral analyses. Professor Dr. G. Höfle of the Gesellschaft für Biotechnologische Forschung is gratefully acknowledged for providing natural epothilones A and B for comparative analysis. We also thank Professor Gunda Georg of the University of Kansas for bringing the epothilone problem to our attention. We dedicate this paper to Professor Ryoji Noyori, whose accomplishments were critical to this work.



of a β,δ -diketoester ensemble embracing carbon atoms 1–6 of the target compound (see **6**).

The second and perhaps most surprising finding is that the sense of addition of enolate **10** to the readily available (*S*)-aldehyde **5**^[9] provides the desired C7–C8 *anti* relationship with good diastereoface selectivity in conjunction with the expected C6–C7 *syn* relationship (by 1k-addition)^[10] (see compound **11** and its stereoisomer).^[11] The 5.5:1 outcome for the diastereoface selectivity of this aldol reaction is counter to expectations arising from the traditional models first advanced by Cram and then by Felkin.^[12] These extensively invoked formulations, which differ widely in their underlying conformational assumptions and stereochemical treatments, usually converge in terms of their predicted outcome.

The high diastereoface selectivity arises from a peculiarity of aldehyde **5** and reflects, somehow, the relationship of its vinyl and formyl groups. It is not, to a first approximation, the result of a gross property of the novel enolate **10**. Indeed, the same enolate, upon addition of phenylpropanal (**12a**), performs in the expected fashion,^[10] yielding an 11:1 ratio of **13a** and **14a** (Table 1). Furthermore, with aldehyde **12b**, the dihydro derivative of **5**, the ratio of *syn* to *anti* diastereomers (with respect to the groups on C7 and C8; **13b**:**14b**) drops to 1:1.3. Moreover, when the distance between the vinyl and formyl groups is extended, as in **12c**, selectivity is also compromised. By contrast the phenyl and dimethylallyl analogues of **5** (**12d** and **12e**), bearing the same relationship of unsaturated groups as in **5**, exhibit good *anti* selectivity (see products **13d** and **13e** as well as **14d** and **14e**). Also, aldehyde **12f**, a substrate that on the basis of chelation control tends to

favor the *anti*-diastereoface product,^[13] performs normally with enolate **10** to afford a 1:4 ratio of **13f** and **14f**. We shall return to a consideration of these interesting data. First, we deal with the impact of the strong diastereoface selectivity (*anti* > *syn*) in the aldol reaction of **5** and **10** for achieving a dramatically improved total synthesis of epothilone B.^[11]

The rather favorable result in establishing the C7–C8 bond allowed us to explore the possibility that the C1–C7 fragment could be incorporated as an achiral block. For this hope to become a real option, it would be necessary to gain control over the eventual stereochemistry at C3. This was to be accomplished by the implementation of an asymmetric, reagent-controlled Noyori reduction (see below).^[14]

The third critical element was the finding that the key *B*-alkyl Suzuki coupling, which controls the geometry of the trisubstituted double bond, can be conducted successfully even on the elaborate substrate **15**, obtained from **11**. The cognate substrate for the Suzuki reaction was the previously described^[3b] vinyl iodide **16**. The remarkable coupling step afforded the (*Z*)-olefin **17** and thence **18** after removal of the silyl protecting group on C15 (Scheme 3). The β,δ -diketo ester

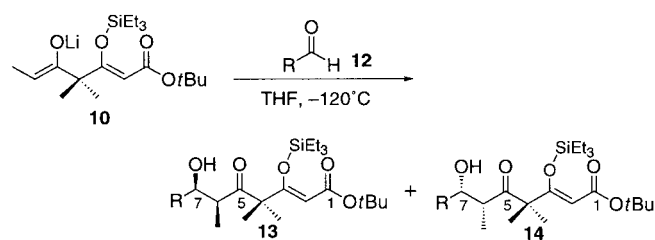
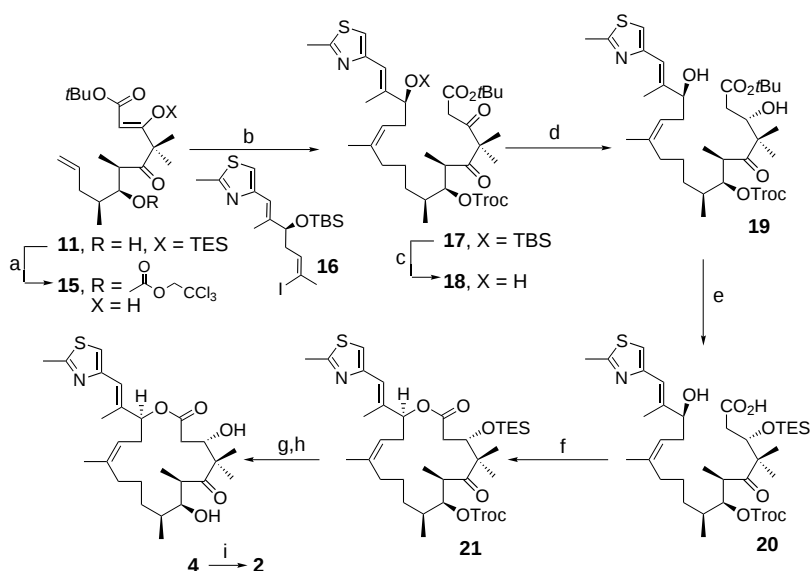


Table 1. Aldol reaction of enolate **10** with different aldehydes **12**.

12	R	Yield. [%]	13 : 14
a		64	11:1.0
b		80	1:1.3
c		68	1:2.0
d		63	1:5.0
e		71	1:4.5
f		61	1:4.0



Scheme 3. Synthesis of deoxyepothilone B (**4**) and epothilone B (**2**) from the product of the aldol reaction (**11**). a) TrocCl, pyridine, CH₂Cl₂, 0 → 25 °C, then 0.5 N HCl in MeOH, 0 °C, 87 %; b) 9-BBN, THF, **15**, then **16**, [Pd(dppf)Cl₂], Ph₃As, Cs₂CO₃, H₂O, DMF; c) 0.4 N HCl in MeOH, 50 % (over two steps); d) [(*R*)-binap]RuCl₂, H₂ (83 bar), MeOH, HCl, 25 °C, 7 h, 88 % (d.r. > 95:5); e) TESOTf, 2,6-lutidine, CH₂Cl₂, -78 → -25 °C, then HCl/MeOH, 77 %; f) 2,4,6-trichlorobenzoyl chloride, TEA, 4-DMAP, PhCH₃, 78 %; g) SmI₂, cat. NiI₂, THF, -78 °C, 95 %; h) HF·pyridine, THF, 98 %; i) 2,2-dimethyldioxirane, CH₂Cl₂, -50 °C, 98 % (d.r. > 20:1). 9-BBN = 9-borabicyclo[3.3.1]nonane, binap = 2,2'-bis(diphenylphosphanyl)-1,1'-binaphthyl, 4-DMAP = 4-dimethylaminopyridine, dppf = 1,1'-bis(diphenylphosphanyl)ferrocene, TBS = *tert*-butyldimethylsilyl, TEA = triethylamine, Troc = trichloroethoxycarbonyl.

array in **18** responded well to asymmetric catalytic reduction under modified Noyori conditions^[14b] to give the diol **19** (88 %, *d.r.* > 95:5). The ability to maintain strict regiochemical and diastereoface control in the Noyori reduction arose only after extensive developmental studies, which will be described elsewhere.^[15] With this reduction achieved, no significant obstacles remained in the total synthesis. The conversion of **19** into deoxyepothilone B (**4**) and then epothilone B (**2**) was accomplished by methodologies worked out in our previous syntheses^[3] as well as the syntheses of Nicolaou et al.^[4]

The matter of explaining the results of the key aldol coupling of **5** and **10** is best approached through earlier arguments of Roush on the diastereoface selectivity of reactions of (*Z*)-enolates.^[16b] Roush postulated that with an enolate such as **10**, the conformer that reacts according to the Curtin–Hammett principle^[17] would be one in which the R group of the aldehyde is distanced from the methyl and the R' group of the enolate.^[16b] The methyl group of the “ α -methylaldehyde” rather than the R group is placed on the inside face of the transition state complex **22**. The aldol reaction will lead to the

anti product. Of course, if R is approximately equal to methyl with respect to the effective A value (conformation energy), the selectivity for *anti* product correspondingly must deteriorate. To rationalize why maximal *anti* selectivity was obtained from aldehyde **5** or related systems **12d** and **12e**, it can be argued that the presence of unsaturation at C4–C5 in the aldehyde moiety provides a favorable nonbonding interaction between the double bond in the aldehyde and the carbonyl group of the enolate. This interaction tends to stabilize the transition state leading to the observed stereoisomer (see **23**). The possibility of fine-tuning the structure of Curtin–Hammett conformers in C–C bond forming reactions through subtle secondary interactions has significant implications for the enhancement of stereoselectivity.

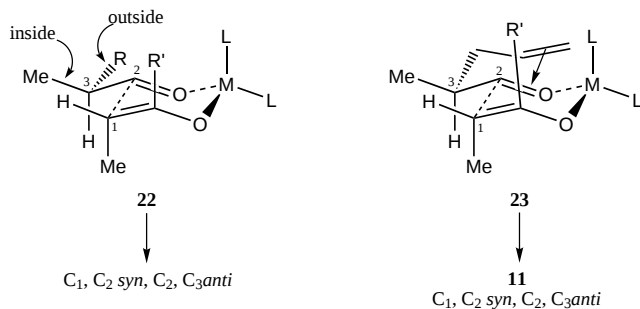
Quite aside from identifying a potentially important principle governing diastereoface selection, the total synthesis we present herein enables a serious and focused drug-discovery program in the epothilone area directed toward obtaining analogues in useful amounts for *in vivo* examination. The opportunities for preclinical biological exploration opened up by this greatly improved

access to the epothilones are being pursued in a resolute way. For instance, we have recently found using fully synthetic material that compound **4** has a far superior efficacy and a much more exploitable maximum tolerable dose (MTD) than paclitaxel, adriamycin, camptothecin, or epothilone B when administered intraperitoneally.^[8] Of course, the optimal administration of paclitaxel is intravenous. Therefore, we recently compared **4** with paclitaxel for intravenous administration in xenograft mice. Our previously reported toxicity^[8] in the intravenous administration of **4** has now been overcome by using a slow infusion protocol (over 4 h). This has allowed us to compare the therapeutic profiles of **4** and paclitaxel in the intravenous modality. Our comparisons were conducted in nude mice bearing the MX-1 xenograft. Even under the formulation conditions for paclitaxel (Cremophor–EtOH), **4** is equally effective (**4**: ca. 99 % tumor reduction for a dose of 30 mg kg⁻¹; paclitaxel: ca. 99 % tumor reduction for a dose of 24 mg kg⁻¹).

Received: June 15, 1998 [Z11982IE]

German version: *Angew. Chem.* **1998**, *110*, 2821–2824

Keywords: aldol reactions • epothilones • natural products • Suzuki coupling • total synthesis



- [1] a) D. M. Bollag, P. A. McQuency, J. Zhu, O. Hensens, L. Koupal, J. Liesch, M. Goetz, E. Lazarides, C. M. Woods, *Cancer Res.* **1995**, *55*, 2325; b) G. Höfle, N. Bedorf, H. Steinmetz, D. Schomburg, K. Gerth, H. Reichenbach, *Angew. Chem.* **1996**, *108*, 1671; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1567; c) K. Gerth, N. Bedorf, G. Höfle, H. Irschik, H. Reichenbach, *J. Antibiot.* **1996**, *49*, 560.
[2] P. B. Schiff, J. Fant, S. B. Horwitz, *Nature* **1979**, *277*, 665.

- [3] a) A. Balog, D. Meng, T. Kamenecka, P. Bertinato, D.-S. Su, E. J. Sorensen, S. J. Danishefsky, *Angew. Chem.* **1996**, *108*, 2976; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2801; b) D.-S. Su, D. Meng, P. Bertinato, A. Balog, E. J. Sorensen, S. J. Danishefsky, Y.-H. Zheng, T.-C. Chou, L. He, S. B. Horwitz, *Angew. Chem.* **1997**, *109*, 775; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 757; c) D. Meng, P. Bertinato, A. Balog, D.-S. Su, T. Kamenecka, E. J. Sorensen, S. J. Danishefsky, *J. Am. Chem. Soc.* **1997**, *119*, 10073.
- [4] a) Z. Yang, Y. He, D. Vourloumis, H. Vallberg, K. C. Nicolaou, *Angew. Chem.* **1997**, *109*, 170; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 166; b) K. C. Nicolaou, F. Sarabia, S. Ninkovic, Z. Yang, *Angew. Chem.* **1997**, *109*, 539; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 525; c) K. C. Nicolaou, N. Winssinger, J. A. Pastor, S. Ninkovic, F. Sarabia, Y. He, D. Vourloumis, Z. Yang, T. Li, P. Giannakakou, E. Hamel, *Nature* **1997**, *387*, 268; d) K. C. Nicolaou, Y. He, D. Vourloumis, H. Vallberg, F. Roschangar, F. Sarabia, S. Ninkovic, Z. Yang, J. I. Trujillo, *J. Am. Chem. Soc.* **1997**, *119*, 7960; e) K. C. Nicolaou, S. Ninkovic, F. Sarabia, D. Vourloumis, Y. He, H. Vallberg, M. R. V. Finlay, Z. Yang, *J. Am. Chem. Soc.* **1997**, *119*, 7974; f) K. C. Nicolaou, Y. He, D. Vourloumis, H. Vallberg, Z. Yang, *Angew. Chem.* **1996**, *108*, 2554; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2399.
- [5] D. Schinzer, A. Limberg, A. Bauer, O. M. Böhm, M. Cordes, *Angew. Chem.* **1997**, *109*, 543; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 523.
- [6] a) D. Meng, D.-S. Su, A. Balog, P. Bertinato, E. J. Sorensen, S. J. Danishefsky, Y.-H. Zheng, T.-C. Chou, L. He, S. B. Horwitz, *J. Am. Chem. Soc.* **1997**, *119*, 2733; b) A. Balog, P. Bertinato, D.-S. Su, D. Meng, S. J. Danishefsky, Y.-H. Zheng, T.-C. Chou, L. He, S. B. Horwitz, *Tetrahedron Lett.* **1997**, *38*, 4529; c) D.-S. Su, A. Balog, D. Meng, P. Bertinato, S. J. Danishefsky, Y.-H. Zheng, T.-C. Chou, L. He, S. B. Horwitz, *Angew. Chem.* **1997**, *109*, 2178; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2093.
- [7] a) K. C. Nicolaou, D. Vourloumis, T. Li, J. Pastor, N. Winssinger, Y. He, S. Ninkovic, F. Sarabia, H. Vallberg, F. Roschangar, N. P. King, M. R. V. Finlay, P. Giannakakou, P. V. Pinard, E. Hamel, *Angew. Chem.* **1997**, *109*, 2181; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2097; b) K. C. Nicolaou, F. Sarabia, S. Ninkovic, M. R. V. Finlay, C. N. C. Boddy, *Angew. Chem.* **1998**, *110*, 85; *Angew. Chem. Int. Ed.* **1998**, *37*, 81; c) K. C. Nicolaou, S. Ninkovic, M. R. V. Finlay, F. Sarabia, T. Li, *Chem. Commun.* **1997**, 2343; d) K. C. Nicolaou, H. Vallberg, N. P. King, F. Roschangar, Y. He, D. Vourloumis, C. G. Nicolaou, *Chem. Eur. J.* **1997**, *3*, 1957; e) K. C. Nicolaou, M. R. V. Finlay, S. Ninkovic, N. P. King, D. Vourloumis, Y. He, *Chem. Eur. J.* **1997**, *3*, 1971.
- [8] T.-C. Chou, Z.-G. Zhang, A. Balog, D.-S. Su, D. Meng, K. Savin, J. R. Bertino, S. J. Danishefsky, *Proc. Natl. Acad. Sci. USA* **1998**, *95*, 9642.
- [9] The aldehyde **5** was readily available by the preparation given in N.-H. Lin, L. E. Overman, M. H. Rabinowitz, L. A. Robinson, M. J. Sharp, J. Zablocki *J. Am. Chem. Soc.* **1996**, *118*, 9062. The alcohol precursor to this aldehyde could also be accessed by yeast reduction of the corresponding allylic alcohol, thereby shortening the synthetic pathway (24 steps) by three steps.
- [10] C. H. Heathcock in *Asymmetric Synthesis*, Vol. 3 (Ed.: J. D. Morrison), Academic Press, New York, **1984**, p. 111.
- [11] The stereochemistry of the minor diastereomer with respect to the groups on C7 and C8 was presumed to be *syn*, but was not rigorously proven. This was based on precedent,^[16a] assuming that this isomer arises from facial selectivity in the aldol reaction and not as a consequence of the *E* configuration of the enolate group of **10**. Similarly, the stereochemistry assigned as the *syn, syn* products **14** was not proven in each case. Those assignments also rely to varying extents on the examples given in ref. [16a].
- [12] For transition state models for diastereomeric additions on carbonyl groups, see a) D. J. Cram, F. A. Elhfez, *J. Am. Chem. Soc.* **1952**, *74*, 5828; b) D. J. Cram, K. R. Kopecky, *J. Am. Chem. Soc.* **1959**, *81*, 2748; c) J. W. Cornforth, R. H. Cornforth, K. K. Mathew, *J. Am. Chem. Soc.* **1959**, *81*, 112; d) G. J. Karabatsos, *J. Am. Chem. Soc.* **1967**, *89*, 1367; e) M. Cherest, H. Felkin, N. Prudent, *Tetrahedron Lett.* **1968**, 2199; f) N. T. Ahn, O. Eisenstein, *Nouv. J. Chem.* **1977**, *1*, 61; g) A. S. Cieplak, *J. Am. Chem. Soc.* **1981**, *103*, 4540; h) E. P. Lodge, C. H. Heathcock, *J. Am. Chem. Soc.* **1987**, *109*, 2819.
- [13] M. T. Reetz, *Angew. Chem.* **1984**, *96*, 542; *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 556.
- [14] a) R. Noyori, T. Ohkuma, M. Kitamura, *J. Am. Chem. Soc.* **1987**, *109*, 5856; b) D. F. Taber, L. J. Silverberg, *Tetrahedron Lett.* **1991**, *32*, 4227; c) review: D. J. Ager, S. A. Laneman, *Tetrahedron Asymmetry* **1997**, *8*, 3327.
- [15] The Noyori reduction of various diketo esters was very dependent on the amount of acid in the reaction mixture. Without the presence of stoichiometric acid, the rate of reduction and the selectivity dropped in the reduction. At higher pressures, the chemoselectivity of the reduction was poor resulting in reduction of both of the alkene groups. Furthermore, the carbonyl group at C5 was never reduced under these conditions, but was absolutely necessary for the reduction of the carbonyl group at C3. When an alcohol functionality was at C5, no reduction was seen. A. Balog, unpublished results.
- [16] a) I. Mori, K. Ishihara, C. H. Heathcock, *J. Org. Chem.* **1990**, *55*, 1114; b) W. R. Roush, *J. Org. Chem.* **1991**, *56*, 4151.
- [17] For a statement of the Curtin–Hammett principle in predicting and rationalizing stereoselection, see E. Eliel, S. H. Wilen, *Stereochemistry of Organic Compounds*, Wiley, New York, **1994**, p. 649.

Structures of Solvent-Free, Monomeric LiCCH, NaCCH, and KCCH**

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Organoalkali metal compounds are important reagents for introducing organic groups into organic and organometallic compounds in substitution or addition reactions.^[1] For example, active ingredients in widely used oral contraceptives contain alkynyl groups that are introduced by the addition of alkali metal acetylides to steroidal ketones.^[2] Organoalkali metal compounds show a pronounced tendency toward aggregation,^[3] and alkali metal acetylides are no exception.^[4,5] The organic portion and co-ligand(s) (including solvent) influence reactivity and structure of the organoalkali metal compound dramatically, both in solution and in the solid state. An example of the structural changes induced by subtle variation of coligands is that whereas the crystallization of PhCCLi in the presence of tetramethylpropylenediamine gives dimeric units,^[5c] similar treatment with the homologous tetramethylhexylenediamine gives tetrameric units.^[5d] Such aggregated structures have provided the only experimental information about alkynyl–alkali metal bond lengths to date, but with one recent exception,^[4d] the alkali metal acetylides

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[**] This research was supported by the U.S. National Science Foundation grants CHE 9531244 (to D.B.G. and L.M.Z.), AST 95-03274, and NASA grant NAGW 2989 (to L.M.Z.).

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