amounts of *p*-benzoquinone). For example, the oxidation of 1,3-cycloheptadiene by O_2 in acetic acid (2 M on LiOAc) at 40 °C catalyzed by 5 mol % each of Co(TPP), hydroquinone, and $Pd(OAc)_2$ afforded *cis*-1,4-diacetoxy-2-cycloheptene (>92% cis) in 65% isolated yield.

The corresponding oxidation using Mn(TPP) in place of Co(TPP) also worked but was considerably slower. For example, the oxidation of 1,3-cyclohexadiene gave only a 56% yield of 1,4-diacetoxy-2-cyclohexene after 48 h, and now the trans/cis ratio was only 72/28.

The oxidation described here has similarities with biochemical processes where an oxidation becomes very mild and selective when several redox couples with falling redox potentials are interacting. In many biological systems metalloporphyrins and *p*-hydroquinones/*p*-benzoquinones play important roles as electron carriers. For example, ubiquinones are known to mediate the electron-transfer processes involved in energy production in aerobic organisms. The model system described here is to our knowledge the first example of a selective oxidation using a triple catalysis with oxygen as the ultimate oxidant.

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Registry No. Co(TPP), 14172-90-8; Pd, 7440-05-3; O_2, 7782-44-7; hydroquinone, 123-31-9; 1,3-cyclohexadiene, 592-57-4; 1,3-cycloheptadiene, 4054-38-0.

Enantioselective Ring Construction through Asymmetric Olefin-Ketene Cycloaddition. A Highly Enantiocontrolled Approach to (−)-α-Cuparenone and (+)-β-Cuparenone

Andrew E. Greene,* Florence Charbonnier, Marie-Jacqueline Luche, and Albert Moyano

Laboratoire d'Etudes Dynamiques et Structurales de la Sélectivité LEDSS Bât. 52, Université Scientifique Technologique et Médicale de Grenoble BP 68 38402 St. Martin d'Hères Cedex, France

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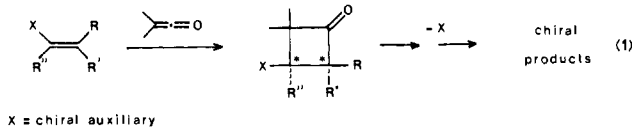
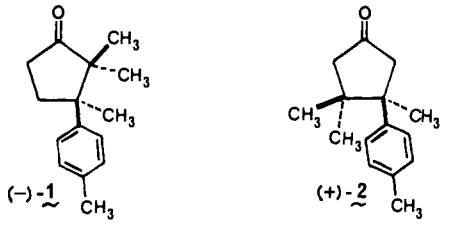
Chiral auxiliary-mediated reactions that manifest high levels of diastereoselection represent valuable sources of enantiomerically enriched synthetic intermediates.[1] The asymmetric Diels–Alder reaction has proven particularly useful for this purpose and has been effectively applied in numerous enantioselective natural product syntheses.[1,2] In surprising contrast, the potential in asymmetric synthesis of the versatile [2 + 2] cycloaddition reaction of olefins with ketenes,[3] which also offers an excellent possibility for auxiliary-directed π-face stereoselection,[4] has yet to be demonstrated. In this communication we wish to report *the first example of the use of chiral olefin–ketene diastereofacial differentiation for enantioselective natural product synthesis (eq 1).*



X = chiral auxiliary

α- and β-Cuparenones (**1** and **2**), deceptively simple sesquiterpenes from the essential oil of *Mayur pankhi* and the liverwort *Mannia fragrans*,[5] have often been synthesized in racemic form



(−)-α-Cuparenone (+)-β-Cuparenone

to illustrate new procedures for cyclopentanone construction and/or methods for juxtaposing quaternary centers.[6,7] Our enantioselective chiral olefin–dichloroketene based common approach to these model cyclopentanoid natural products will serve both to indicate the excellent level of chiral induction that can attend this cycloaddition process and to show some of the significant latent flexibility[8] that resides in the cyclobutanones so obtained.

The allylic chloride **3**[9] was transformed with readily available, optically pure (1*S*,2*R*)-(+)-2-phenylcyclohexanol[10] (0.6 equiv, 1.2 equiv of NaH, THF, 90%) to the chiral allylic ether (+)-**4**[11] (Scheme I), which on contact with 1.6 equiv of sublimed potassium *tert*-butoxide in dimethyl sulfoxide[12] at 65 °C afforded in 75% yield and with essentially complete stereoselectivity the *E* enol ether (−)-**5**.[11]

Our expectation that (−)-**5** would enter into reaction with dichloroketene through a favorable π-face discriminating transition-state conformation was based on steric considerations. For steric reasons, (−)-**5** was expected to adopt the s-trans (or nearly s-trans) conformation depicted,[13] which would effectively bare

(1) For excellent reviews in this area, see: ApSimon, J. W.; Collier, T. L. *Tetrahedron* **1986**, *42*, 5157–5254. *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2 and Vol. 3.

(2) For reviews of the asymmetric Diels–Alder reaction in organic synthesis, see: Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 876–889. Helmchen, G.; Karge, R.; Weetman, J. In *Modern Synthetic Methods*; Scheffold, R., Ed.; Springer-Verlag: Berlin, 1986; Vol. 4, pp 261–306.

(3) See: Brady, W. T. In *The Chemistry of Ketenes, Allenes, and Related Compounds*; Patai, S., Ed.; John Wiley and Sons: New York, 1980; Chapter 8. Brady, W. T. *Tetrahedron* **1981**, *37*, 2949–2966, and references cited therein.

(4) Greene, A. E.; Charbonnier, F. *Tetrahedron Lett.* **1985**, *26*, 5525–5528. See, also: Wynberg, H.; Staring, E. G. J. *J. Am. Chem. Soc.* **1982**, *104*, 166–168. Houge, C.; Frisque-Hesbain, A. M.; Mockel, A.; Ghosez, L.; Declercq, J. P.; Germain, G.; Van Meerssche, M. *J. Am. Chem. Soc.* **1982**, *104*, 2920–2921.

(5) (a) Chetty, G. L.; Dev, S. *Tetrahedron Lett.* **1964**, 73–77. (b) Irie, T.; Suzuki, T.; Itô, S.; Kurosawa, E. *Ibid.* **1967**, 3187–3189. (c) Benesova, V. *Collect. Czech. Chem. Commun.* **1976**, *41*, 3812–3814.

(6) For syntheses of racemic α-cuparenone, see: (a) Martin, S. F.; Phillips, F. W.; Puckette, T. A.; Colapret, J. A. *J. Am. Chem. Soc.* **1980**, *102*, 5866–5872. (b) Halazy, S.; Zutterman, F.; Krief, A. *Tetrahedron Lett.* **1982**, *23*, 4385–4388, and references cited therein. (c) Gadwood, R. C. *J. Org. Chem.* **1983**, *48*, 2098–2101. (d) Greene, A. E.; Lansard, J. P.; Luche, J. L.; Petrier, C. *Ibid.* **1983**, *48*, 4763–4764. (e) Eilbracht, P.; Balss, E.; Acker, M. *Chem. Ber.* **1985**, *118*, 825–839. For enantioselective approaches to natural α-cuparenone, see: (f) Posner, G. H.; Kogan, T. P.; Hulce, M. *Tetrahedron Lett.* **1984**, *25*, 383–386. (g) Taber, D. F.; Petty, E. H.; Raman, K. *J. Am. Chem. Soc.* **1985**, *107*, 196–199. (h) Kametani, T.; Kawamura, K.; Tsubuki, M.; Honda, T. *Chem. Pharm. Bull.* **1985**, *33*, 4821–4828. (i) Meyers, A. I.; Lefker, B. A. *J. Org. Chem.* **1986**, *51*, 1541–1544.

(7) For syntheses of racemic β-cuparenone, see: (a) Lansbury, P. T.; Hilfiker, F. R. *J. Chem. Soc., Chem. Commun.* **1969**, 619–620. (b) Mane, R. B.; Rao, G. S. K. *J. Chem. Soc., Perkin Trans 1* **1973**, 1806–1808. (c) Leriverend, P. *Bull. Soc. Chim. Fr.* **1973**, 3498–3499. (d) Casares, A.; Maldonado, L. A. *Synth. Commun.* **1976**, *6*, 11–16. (e) Paquette, L. A.; Fristad, W. E.; Dime, D. S.; Bailey, T. R. *J. Org. Chem.* **1980**, *45*, 3017–3028. (f) Jung, M. E.; Radcliffe, C. D. *Tetrahedron Lett.* **1980**, *21*, 4397–4000. (g) Halazy, S.; Zutterman, F.; Krief, A. *Ibid.* **1982**, *23*, 4385–4388. (h) Greene, A. E.; Lansard, J. P.; Luche, J. L.; Petrier, C. *J. Org. Chem.* **1984**, *49*, 931–932.

(8) Greene, A. E.; Deprês, J. P. *J. Am. Chem. Soc.* **1979**, *101*, 4003–4005. Deprês, J. P.; Greene, A. E. *J. Org. Chem.* **1980**, *45*, 2036–2037.

(9) Prepared with NaOCl by the method of Wolinsky: Hegde, S. G.; Vogel, M. K.; Saddler, J.; Hrinyo, T.; Rockwell, N.; Haynes, R.; Oliver, M.; Wolinsky, J. *Tetrahedron Lett.* **1980**, *21*, 441–444.

(10) $[\alpha]^{23}_D$ +58.9° (*c* 10, CH_3OH). See: Verbit, L.; Price, H. C. *J. Am. Chem. Soc.* **1972**, *94*, 5143–5152. Whitesell, J. K.; Chen, H. H.; Lawrence, R. M. *J. Org. Chem.* **1985**, *50*, 4663–4664. Whitesell, J. K.; Lawrence, R. M. *Chimia* **1986**, *40*, 318–321.

(11) (+)-**4**: mp 72–74 °C, $[\alpha]^{21}_D$ +32° (*c* 1.0, $CHCl_3$); (−)-**5**: mp 60–61 °C, $[\alpha]^{21}_D$ −80° (*c* 1.1, acetone); (−)-**6a**: mp 89–90 °C, $[\alpha]^{21}_D$ −57° (*c* 1.1, $CHCl_3$); (+)-**7**: mp 42–44 °C, $[\alpha]^{20}_D$ +71° (*c* 1.7, $CHCl_3$); (−)-**8**: mp 57–60 °C, $[\alpha]^{20}_D$ −66° (*c* 1.7, $CHCl_3$); (+)-**9**: $[\alpha]^{20}_D$ +253° (*c* 1.7, $CHCl_3$); (−)-**1**: mp 50–51 °C (lit.[5a] mp 52–53 °C), $[\alpha]^{21}_D$ −170° (*c* 0.2, $CHCl_3$); (+)-**2**: $[\alpha]^{29}_D$ +45° (*c* 1.4, $CHCl_3$).

(12) Price, C. C.; Snyder, W. H. *J. Am. Chem. Soc.* **1961**, *83*, 1773.

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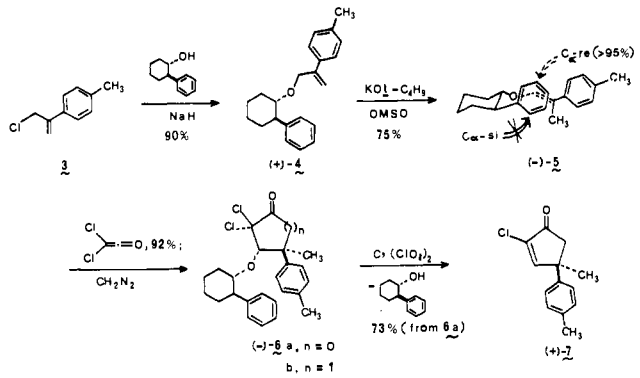
Scheme I

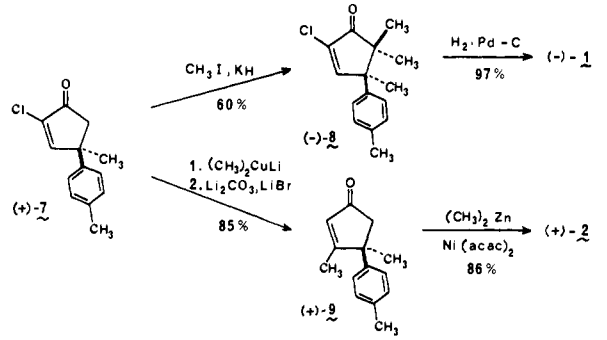


the C_α-re face of the enol ether to dichloroketene attack, while positioning the C_α-si face so as to be sterically shielded by the adjacent phenyl group. In reality, treatment of (−)-**5** with dichloroketene (3 equiv of CCl_3COCl, 5 equiv of Zn–Cu)[14] in ether at 20 °C produced in excellent yield the nicely crystalline cyclobutanone (−)-**6a**. Most pleasingly, an examination of the crude product by ^1H NMR (300 MHz) indicated that *a minimum level of induction of 95:5 had been achieved in this cycloaddition reaction.*[15] A single recrystallization of this material (pentane, −30 °C) efficiently provided pure (−)-**6a**.[11]

Ring expansion of cyclobutanone (−)-**6a** with excess diazomethane in 97:3 ether–methanol at room temperature proceeded, as expected,[8] highly regioselectively to generate the desired dichlorocyclopentanone, which on exposure to 3 equiv of chromous perchlorate in aqueous acetone[16] at 0 °C then cleanly furnished the key, optically pure[17] intermediate, α-chloroenone (+)-**7**[11] (73% from (−)-**6a**, $[\alpha]^{20}_D$ +71°).[18,19]

From this versatile α-chloroenone, both cuparenones could readily be secured by geminal dimethylation procedures (Scheme II). In the presence of excess methyl iodide and potassium hydride in tetrahydrofuran, (+)-**7** suffered α′, α′-dimethylation to give (−)-**8**[11] (60%), which on hydrogenation in ethyl acetate in the presence of sodium acetate, provided in 97% yield optically pure (−)-α-cuparenone[11] ($[\alpha]^{21}_D$ −170°, lit.[5c] $[\alpha]^{20}_D$ −170°). β,β-Dimethylation of (+)-**7** could easily be accomplished through sequential conjugate addition (1.5 equiv of $(CH_3)_2CuLi$, ether, −78 °C), dehydrochlorination (excess Li_2CO_3, LiBr, DMF, 80 °C → (+)-**9**,[11] 85% from (+)-**7**), and conjugate addition (5 equiv of $(CH_3)_2Zn$, catalytic $Ni(acac)_2$, ether, room temperature, 86%)[20]

Scheme II



to furnish for the first time synthetically derived (+)-β-cuparenone[11] ($[\alpha]^{29}_D$ +45°, lit.[5a] $[\alpha]^{30}_D$ +48°).[21]

The successful realization of this approach demonstrates the feasibility of an entirely new, powerful stategy for enantioselective natural product synthesis. While this work is obviously most relevant to chiral cyclopentanone synthesis, there is also relevance to chiral lactam and lactone synthesis. These areas are currently being developed in our laboratory, and their potential will be demonstrated in forthcoming papers.

Acknowledgment. We thank Dr. J. L. Luche for his interest in our work, Professors J. K. Whitesell and C. Triantaphylides for helpful information, and the CNRS (UA 332) for financial support. A.M. is grateful to NATO for a postdoctoral fellowship.

Supplementary Material Available: Analytical data for compounds **1**, **2**, and **4**–**9** (2 pages). Ordering information is given on any current masthead page.

(13) *cis*-Alkenyl ethers adopt an s-trans or nearly s-trans conformation, see: Fischer, P. In *Chemistry of Ethers, Crown Ethers, Hydroxyl Groups, and Their Sulphur Analogues*; Patai, S., Ed.; John Wiley and Sons: New York, 1980; Vol. 2, Chapter 17. In addition to steric effects, π–π interaction may be important, see: Whitesell, J. K.; Lawrence, R. M.; Chen, H. H. *J. Org. Chem.* **1986**, *51*, 4779–4784.

(14) Krepski, L. R.; Hassner, A. *J. Org. Chem.* **1978**, *43*, 3173–3179.

(15) That the cycloaddition had, in fact, occurred as expected on the C_α-re face of enol ether **5** was confirmed by the obtention of (−)-α-cuparenone, the absolute configuration of which is known to be R.[5b,c] (The S designation given in references 6h,i for the absolute stereochemistry of the levo isomer is incorrect.)

(16) Kochi, J. K.; Singleton, D. M. *J. Am. Chem. Soc.* **1968**, *90*, 1582–1589. Wade, R. S.; Castro, C. E. *Org. Synth.* **1972**, *52*, 62–66.

(17) An optical purity of >99% was established for (+)-**7** through comparison of the ^{13}C NMR (75.4 MHz) spectra of the acetals of (±)-**7** and (+)-**7** formed with (*R*,*R*)-(−)-2,3-butanediol. (See: Hiemstra, H.; Wynberg, H. *Tetrahedron Lett.* **1977**, 2183–2186.) The presence of 0.5% of the diastereomeric acetal would readily have been detected by this technique.

(18) The ejected chiral auxiliary is easily recovered in high yield at this stage.

(19) For recent alternative methods of preparing stereogenic quaternary carbon centers, see: Cram, D. J.; Sogah, G. D. Y. *J. Chem. Soc., Chem. Commun.* **1981**, 625–628. Kogen, H.; Tomioka, K.; Hashimoto, S.; Koga, K. *Tetrahedron* **1981**, *37*, 3951–3956. Dolling, U. H.; Davis, P.; Grabowski, E. J. J. *J. Am. Chem. Soc.* **1984**, *106*, 446–447. Meyers, A. I.; Harre, M.; Garland, R. *J. Am. Chem. Soc.* **1984**, *106*, 1146–1148. Tomioka, K.; Ando, K.; Takemasa, Y.; Koga, K. *J. Am. Chem. Soc.* **1984**, *106*, 2718–2719. Pfau, M.; Revial, G.; Guingant, A.; d'Angelo, J. *J. Am. Chem. Soc.* **1985**, *107*, 273–274. Meyers, A. I.; Wanner, K. Th. *Tetrahedron Lett.* **1985**, *26*, 2047–2050. Fuji, K.; Node, M.; Nagasawa, H.; Naniwa, Y.; Terada, S. *J. Am. Chem. Soc.* **1986**, *108*, 3855–3856. See, also: ref 6f-i.

(20) Petrier, C.; Barbosa, J. C. S.; Dupuy, C.; Luche, J. L. *J. Org. Chem.* **1985**, *50*, 5761–5765.

(21) ^{13}C NMR (75.4 MHz) analysis of the acetals of (±)-**2** and (+)-**2** formed with (*R*,*R*)-(−)-2,3-butanediol (quantitative yield) clearly indicated (+)-**2** to be, as expected,[17] >99% optically pure. We have no explanation for the (slight) discrepancy in the optical rotations.

Intramolecular Carbametalations. A [2 + 2 + 2] Cycloaddition as Evidence for a Palladacyclopentene Intermediate

Barry M. Trost* and Gerald J. Tanoury

McElvain Laboratories of Organic Chemistry
Department of Chemistry, University of Wisconsin
Madison, Wisconsin 53706

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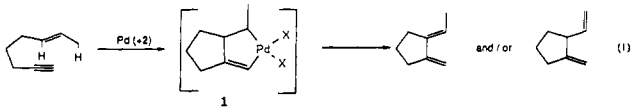
In our examination of the Pd^{2+}-catalyzed cyclization of 1,6-enynes according to eq 1, we suggested the feasibility of a palladacyclopentene intermediate such as **1**.[1] Attempts to intercept



such an intermediate utilizing our palladium acetate derived catalysts failed. Suspecting that the electron deficiency of the Pd in **1** with X being acetoxy made its rate of hydrogen shift so fast that we could not intercept **1**, we searched for a less electron deficient Pd^{2+} catalyst. We wish to report that tetracarbomethoxypalladacyclopentadiene (**2**, TCPC)[2] is a catalyst that effects the intramolecular carbametalation according to eq 1 that it also

(1) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1985**, *107*, 1781. Trost, B. M.; Lautens, M. *Tetrahedron Lett.* **1985**, *26*, 4887.

(2) Moseley, K.; Maitlis, P. M. *J Chem. Soc., Dalton Trans.* **1974**, 169.

0002-7863/87/1509-4753$01.50/0