length (1.46 Å) in *N*-methylpyridinium.[16] Although small, these bond length differences are intriguing in that the C_3–$C_{3'}$ and $C_{3'}$–Z bond length variations seem to be inversely related and associated with short β-lactam contacts. The cause of the differences could be some thermal motion of the C_3 atom or a coupling akin to the leaving group mechanism.

The concept of leaving group effect takes on added significance in light of the recently reported X-ray diffraction investigation of an exocellular DD-carboxypeptidase-transpeptidase from Streptomyces R61.[17,18] Improving resolution of the X-ray data has shown that, when an antibiotic like cephalosporin C is in the active site cleft, the hydroxyl group of the enzyme's active serine is close enough to form a covalent bond to the β-lactam carbonyl carbon. With the 7-(acylamino) side chain of the antibiotic embedded into the deepest reaches of the cleft, the 3-position side chain projects back toward the opening and lies just below the surface of the enzyme. There is a lysine residue and a threonine residue in proximity to where the 3-(acetoxymethyl) side chain of cephalosporin C would be. The present interpretation of the Fourier electron density difference map is that the 3′ leaving group (acetate) has departed.[17,18] Hence, it has been proposed that these residues may direct the side chain's orientation and/or promote its elimination. This sort of phenomenon could help explain the Gram-negative biological activity data mentioned before.

A further clue about the synchronicity of ring opening and leaving group elimination comes in kinetics experiments. For nonenzymatic hydrolysis of cephalosporins, the rate of appearance of free acetate and pyridinium leaving groups has been confirmed to be comparable to that of β-lactam ring opening.[19] This fact means that ring opening and departure of the leaving group are simultaneous or that opening of the β-lactam ring is the rate-determining step.

In order to unambiguous about **1**, it should be pointed out that the placement of arrows in a drawing such as **1** is somewhat arbitrary. The placement should not be taken to imply that a particular pair of electrons is shifted to the potential leaving group. Indeed, it is impossible to identify particular pairs of electrons in a chemical reaction. The proper way to consider the electron movement is in terms of shifts in electron density.[20]

Previous papers have discussed the correlation between Gram-negative minimum inhibitory concentration (MIC) and transition-state energy (TSE), which is a theoretical measure of the ease of nucleophilic attack on the β-lactam carbonyl carbon of cephalosporins.[3,4] Such a correlation was discoverable because all the other factors affecting biological activity, such as penetration and β-lactamase resistance, were nearly constant for the set of closely related cephalosporins that was used. Hence the differences in MIC for the compounds in the set were related to their intrinsic inhibition of the bacterial enzymes, which, in turn, was related to the predicted acylating ability. A more diverse set of β-lactams would not have worked.

A final point that should not be overlooked is that β-lactam compounds like penicillins and monobactams are able to exert their antibiotic activity without any assistance from mechanism 1. Cephalosporins with "direct" 3-position side chains like methyl can exhibit excellent activity depending on the nature of the 7-(acylamino) side chain. Thus, the leaving-group mechanism enhances, rather than being essential to, the Gram-negative activity of certain cephalosporins.

Acknowledgment. Helpful comments were provided by W. H. W. Lunn, J. M. Morin, W. Gleason, J. A. Kelly, and Professor J. R. Knox, who also kindly provided a preprint of ref 17.

Registry No. Cephalosporin, 11111-12-9.

(16) Lalancette, R. A.; Furey, W.; Constanzo, J. N.; Hemmes, P. R.; Jordan, F. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1978**, *B34*, 2950.
(17) Bartolene, J. B.; Hite, G. J.; Kelly, J. A.; Knox, J. R. Proceedings of Symposium on Recent Advances in the Chemistry of β-Lactam Antibiotics, July 2–4, 1984, Cambridge, England, Royal Society of Chemistry, U.K.
(18) Knox, J. R., University of Connecticut, personal communication, 1984.
(19) Coene, B.; Schanck, A.; Dereppe, J.-M.; Van Meerssche, M. *J. Med. Chem.* **1984**, *27*, 694.
(20) See, e.g.: Nakatsuji, H. *J. Am. Chem. Soc.* **1973**, *95*, 2084; **1974**, *96*, 30. Boyd, D. B. *J. Phys. Chem.* **1974**, *78*, 2604. Coppens, P. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 32.

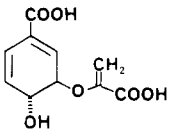
(–)-Methyl 4,5-*O*-Benzylidene-4-*epi*-shikimate: An Intermediate for the Synthesis of (–)-Chorismic Acid and Analogues

Dominique Lesuisse and Glenn A. Berchtold*

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

Received August 8, 1984

(–)-Chorismic acid (**1**) is the last common intermediate in the biosynthesis of aromatic substances through the



1

shikimate pathway in bacteria, fungi, and higher plants.[1] Previously we published the first synthesis of racemic **1**.[2] Shortly thereafter a synthesis was reported from Ganem's laboratory,[3] and more recently an improved synthesis was published from our laboratory.[4]

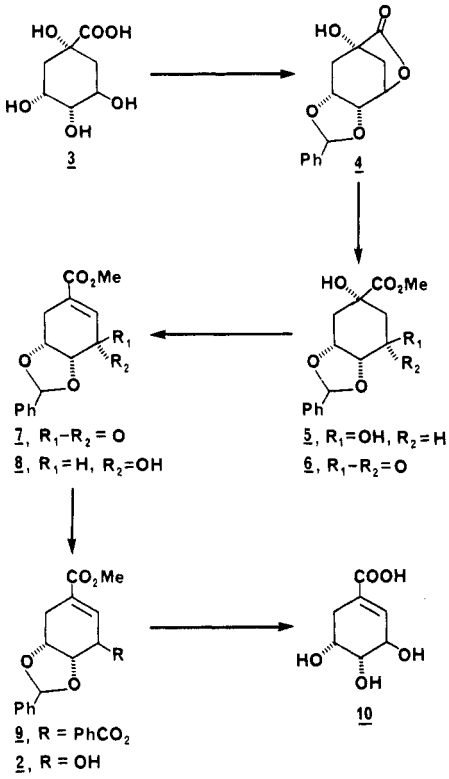
In view of our continuing interest in **1** and analogues for enzymatic studies, we desired a synthetic route to an enantiomerically pure intermediate for further transformation to (–)-**1** or analogues of (–)-**1** in which the enolpyruvyl side chain has been modified. The target intermediate selected was (–)-**2** since (±)-**2** is a convenient intermediate for the synthesis of (±)-**1**.[2] Described below is the synthesis of (–)-**2** from commercially available (–)-quinic acid (**3**).

Acid-catalyzed reaction of **3** and benzaldehyde with removal of H_2O gave **4**[5] as a ~3:1 mixture of diastereomers (75% yield) from which the major isomer could be obtained in crystalline form and, on the basis of steric arguments is assigned the *S* configuration at the acetal

(1) For detailed reviews, see: (a) Weiss, U.; Edwards, J. M. "The Biosynthesis of Aromatic Compounds"; Wiley: New York, 1980. (b) Haslam, E. "The Shikimate Pathway"; Halstead Press, Wiley: New York, 1974.
(2) McGowan, D. A.; Berchtold, G. A. *J. Am. Chem. Soc.* **1982**, *104*, 1153–1154, 7036–7041.
(3) Ganem, B.; Ikota, N.; Muralidharan, V. B.; Wade, W. S.; Young, S. D.; Yukimoto, Y. *J. Am. Chem. Soc.* **1982**, *104*, 6787–6788.
(4) Hoare, J. H.; Policastro, P. P.; Berchtold, G. A. *J. Am. Chem. Soc.* **1983**, *105*, 6264–6267.
(5) The isopropylidene[6] and cyclohexylidene[7] ketals corresponding to **4** have been prepared under similar conditions.
(6) Fischer, H. O. L. *Chem. Ber.* **1921**, *54*, 775–785. Fischer, H. O. L.; Dangschat, G. *Chem. Ber.* **1932**, *65*, 1009–1031.
(7) Mercier, D.; Leboul, J.; Cléophax, J.; Gero, S. D. *Carbohydr. Res.* **1971**, *20*, 299–304.

0022-3263/85/1950-0888$01.50/0

carbon. In further transformations the major acetal di-



astereomer was utilized.[8] Cleavage of the lactone functionality of **4** with NaOMe/MeOH provided methyl ester **5** (97% yield).[9] On the basis of reported dehydration studies in similar systems,[10] dehydration of the tertiary alcohol moiety of **5** was expected to give a mixture of olefin isomers. Consequently, the secondary alcohol group of **5** was oxidized (Swern oxidation) to give **6** (45% yield).

Ketone **6** was dehydrated ($POCl_3$/pyridine) to give enone **7** which was reduced with $NaBH_4$ to afford the benzylidene acetal of methyl 5-*epi*-shikimate[11] (**8**) in 68% yield from **6**. Inversion of stereochemistry at the carbon atom bearing the secondary hydroxyl group was effected by Mitsunobu reaction[15-17] to give benzoate **9** (91% yield) and subsequent ester interchange (NaOMe/MeOH) to provide the benzylidene acetal of (−)-methyl 4-*epi*-shikimate (**2**) in 92% yield. The IR, 250-MHz ^1H NMR, and 67.9-MHz ^{13}C NMR of (−)-**2** were identical with the corresponding spectra of the major acetal diastereomer of (±)-**2** prepared previously.[2]

Base-catalyzed cleavage of the ester group of **2** followed by acid-catalyzed cleavage of the benzylidene acetal gave (−)-4-*epi*-shikimic acid (**10**) in 96% yield. The ^1H NMR spectrum of (−)-**10** agreed with the spectral data of **10** reported by Snyder and Rapoport.[10]

Since (±)-**2** has been converted to (±)-**1** in our previous work,[2] the synthesis of (−)-**2** from (−)-quinic acid (seven steps; 18% overall yield), in principle, provides an intermediate for the synthesis of (−)-chorismic acid. Additionally, hydrolysis of (−)-**2** provides an alternative route (17% overall yield) to the Snyder and Rapoport[10] synthesis of (−)-4-*epi*-shikimic acid from (−)-quinic acid.

Experimental Section[18]

(1*S*,3*R*,5*RS*,7*R*,8*R*)-5-Phenyl-10-oxo-4,6,9-trioxatricyclo-[6.2.1^{1,8}.0^{3,7}]undecan-1-ol (4). A mixture of (−)-**3**[19] (49.4 g, 0.257 mol), benzaldehyde (39.2 mL, 0.386 mol), and *p*-toluenesulfonic acid monohydrate (2.44 g, 13 mmol) in C_6H_6 (500 mL) was refluxed for 12 h in a flask equipped with a Dean–Stark trap (8 mL of H_2O collected). The reaction mixture was concentrated under reduced pressure. The major diastereomer of **4** (19.2 g, 30%) crystallized upon addition of ether. Flash chromatography[20] of the ether filtrate on silica gel (1:1 ethyl acetate–petroleum ether) gave a 3:2 mixture of the diastereomers of **4** (30.1 g, 45%) as an oil that solidified on standing. **4** (major diastereomer): mp 95 °C; $[\alpha]^{20}_D$ +4.7° (*c* 2.62, $CHCl_3$); IR ($CHCl_3$) 3560, 1795 cm^{-1}; ^1H NMR δ 7.40–7.52 (m, 5 H), 5.77 (s, 1 H), 4.81–4.84 (m, 1 H), 4.52–4.58 (m, 1 H), 4.37–4.41 (m, 1 H), 2.79 (d, *J* = 11.8 Hz, 1 H), 2.31–2.51 (m, 3 H); ^{13}C NMR δ 179.0, 135.6, 129.8, 128.5, 126.7, 103.7, 75.4, 72.9, 72.7, 71.5, 37.5, 34.3; MS (EI), *m/e* (relative intensity) 262 (M^+, 34), 261 (76); high-resolution mass spectrum, calcd for $C_{14}H_{14}O_5$ 262.0841, found 262.0827.

(1*S*,2*R*,4*R*,6*R*,8*S*)-4-(Methoxycarbonyl)-8-phenyl-7,9-dioxabicyclo[4.3.0]nonane-2,4-diol (5). A solution of **4** (4.59 g, 17.5 mmol) and NaOMe (946 mg, 17.5 mmol) in MeOH (100 mL) was stirred at room temperature for 1 h. Acetic acid (1 mL) was added dropwise, and the mixture was stirred for 5 min. Saturated aqueous NH_4Cl (100 mL) was added, and the mixture was extracted with CH_2Cl_2 (200 mL). The organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure to afford **5** (4.96 g, 97%) as a white foam. **5**: $[\alpha]^{20}_D$ −12.6° (*c* 8.08, $CHCl_3$); IR ($CHCl_3$) 3600, 3540, 1740 cm^{-1}; ^1H NMR δ 7.37–7.54 (m, 5 H), 5.87 (s, 1 H), 4.47–4.53 (m, 1 H), 4.06–4.22 (m, 2 H), 3.82 (s, 3 H), 3.29 (br s, 1 H), 2.6 (br s, 1 H), 2.34 (d, *J* = 4.1 Hz, 1 H), 2.07 (dd, *J* = 13.7, 3.5 Hz, 1 H), 1.91 (dd, *J* = 13.7, 10.5 Hz, 1 H); ^{13}C NMR δ 175.7, 137.2, 129.5, 128.5, 126.8, 104.1, 79.9, 75.6, 73.7, 68.4, 53.0, 38.8, 34.8; MS (EI), *m/e* (relative intensity) 294 (M^+, 8), 293 (10); high-resolution mass spectrum, calcd for $C_{15}H_{18}O_6$ 294.1103, found 294.1128.

(1*R*,4*S*,6*R*,8*S*)-4-(Methoxycarbonyl)-2-oxo-8-phenyl-7,9-dioxabicyclo[4.3.0]nonan-4-ol (6). The general procedure of Mancuso, Huang, and Swern[21] was utilized for oxidation of **5** (4.96 g, 18.8 mmol) with dimethyl sulfoxide (2.68 mL, 2.25 equiv), oxalyl chloride (1.62 mL, 1.1 equiv), and triethylamine (12.9 mL, 5.5 equiv) in CH_2Cl_2 (220 mL). After the reaction was complete,[21] 10% aqueous $NaHCO_3$ (100 mL) was added. The organic layer was washed with brine and dried ($MgSO_4$). Flash chromatography[20] (ethyl acetate–petroleum ether, 1.5:3.5, 1:1, then 2:1) gave pure **6** (2.19 g, 45% along with a less pure fraction (720 mg, 15%). **6**: $[\alpha]^{20}_D$ +3.1° (*c* 5.35, $CHCl_3$); IR (CH_2Cl_2) 3540, 1740 cm^{-1}; ^1H NMR δ 7.47–7.51 (m, 2 H), 7.27–7.40 (m, 3 H), 5.86 (s, 1 H), 4.75–4.81 (m, 1 H), 4.54 (d, *J* = 6.5 Hz, 1 H), 3.82 (s, 3 H), 3.45 (s, 1 H), 2.94 (d, *J* = 14.2 Hz, 1 H), 2.78 (dd, *J* = 14.2, 1.5 Hz, 1 H), 2.52–2.72 (m, 2 H); ^{13}C NMR δ 203.0, 173.3, 136.2, 129.8, 128.4, 127.4, 105.0, 77.9, 76.2, 68.0, 53.2, 48.2, 34.9.

(1*S*,2*S*,6*R*,8*S*)-4-(Methoxycarbonyl)-8-phenyl-7,9-dioxabicyclo[4.3.0]non-3-en-2-ol (8). Phosphorus oxychloride (freshly

(8) Both acetal diastereomers of (±)-**2** were utilized in the synthesis of (±)-**1**.[2].

(9) Compounds **4** and **5** were first prepared in our laboratory by Dr. Donald A. McGowan.

(10) Snyder, C. D.; Rapoport, H. *J. Am. Chem. Soc.* **1973**, *95*, 7821–7828.

(11) Synthesis of racemic 5-*epi*-shikimic acid,[12] methyl 5-*epi*-shikimate,[13,14] and the isopropylidene ketal of methyl 5-*epi*-shimimate[12,13] have been reported.

(12) Rajapaksa, D.; Keay, B. A.; Rodrigo, R. *Can. J. Chem.* **1984**, *62*, 826–827.

(13) (a) Campbell, M. M.; Kaye, A. D.; Sainsbury, M.; Yavarzadeh, R. *Tetrahedron* **1984**, *40*, 2461–2470. (b) Campbell, M. M.; Kaye, A. D.; Sainsbury, M. *Tetrahedron Lett.* **1983**, *24*, 4745–4746.

(14) Grewe, R.; Kersten, S. *Chem. Ber.* **1967**, *100*, 2546–2553.

(15) Mitsunobu, O.; Eguchi, M. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 3427–3430.

(16) Bose, A. K.; Lal, B.; Hoffman, W. A.; Manhas, M. S. *Tetrahedron Lett.* **1973**, 1619–1622.

(17) The 3,4-isopropylidene ketal of methyl 5-*epi*-shikimate undergoes dehydration under Mitsunobu conditions.[13]

(18) High-resolution mass spectra were provided by the facility supported by National Institutes of Health Grant RR00317 (principal investigator Professor K. Biemann) from the Biotechnology Resources Branch, Division of Research Resources. ^1H NMR spectra were obtained in $CDCl_3$ at 250 MHz. ^{13}C NMR spectra were obtained in $CDCl_3$ at 67.9 MHz.

(19) Aldrich Chemical Co., Milwaukee, WI.

(20) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

(21) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480–2482.

distilled, 0.142 mL, 2.2 equiv) was added via syringe to a stirring solution of **6** (208 mg, 0.71 mmol) in pyridine (1.2 mL), and the mixture was stirred for 2 h at room temperature. Methanol (10 mL) was added and sodium borohydride (300 mg) was added immediately in one portion.[22] After the exothermic reaction was complete (~5 min), saturated aqueous NH_4Cl (10 mL) was added; and the mixture was extracted with $CHCl_3$ (3 × 15 mL). The organic layer was dried ($MgSO_4$), and solvent was removed under reduced pressure. Flash chromatography[20] (1:1 ethyl acetate–petroleum ether) of the residue afforded **8** (134 mg, 68%) as an oil. **8**: $[\alpha]^{20}_D$ +71.2° (*c* 2.67, $CHCl_3$); IR (CH_2Cl_2) 3580, 1720 cm^{-1}; ^1H NMR δ 7.28–7.36 (m, 5 H), 6.98 (br s, 1 H), 5.66 (s, 1 H), 4.49–4.60 (m, 2 H), 4.11 (br s, 1 H), 3.76 (s, 3 H), 3.19 (d, *J* = 10.4 Hz, 1 H), 3.14 (d, *J* = 16.7 Hz, 1 H), 1.94 (dm, *J* = 16.3 Hz, 1 H); ^{13}C NMR δ 166.1, 142.7, 136.1, 129.9, 128.6, 128.4, 127.1, 103.4, 77.2, 73.6, 68.1, 52.0, 26.4; MS (EI), *m/e* (relative intensity) 276 (M^+, 2.5), 275 (4), 170 (100); high-resolution mass spectrum, calcd for $C_{15}H_{16}O_5$ 276.0998, found 276.1002.

(1*R*,2*R*,6*R*,8*S*)-2-(Benzoyloxy)-4-(methoxycarbonyl)-8-phenyl-7,9-dioxabicyclo[4.3.0]non-3-ene (9). The reaction of **8** (19.6 mg, 0.071 mmol) with triphenylphosphine (36 mg, 0.137 mmol), diisopropyl diazocarboxylate (15.6 mg, 0.077 mmol), and benzoic acid (8.67 mg, 0.077 mmol) in THF was carried out according to the procedure of Mitsunobu[15] and Bose.[16] The mixture was stirred for 3 h at room temperature, and the solvent was removed under reduced pressure. Flash chromatography[20] (ethyl acetate–petroleum ether, 1:9, 1.5:3.5, then 1:1) afforded **9** (25 mg, 91%) as an oil. **9**: IR ($CHCl_3$) 1724 cm^{-1}; ^1H NMR δ 8.04 (m, 2 H), 7.55–7.61 (m, 1 H), 7.36–7.48 (m, 7 H), 7.08 (d, *J* = 3.8 Hz, 1 H), 5.83 (s, 1 H), 5.68–5.72 (m, 1 H), 4.53–4.65 (m, 2 H), 3.78 (s, 3 H), 3.07 (dd, *J* = 16.9, 5.8 Hz, 1 H), 2.76 (dm, *J* = 16.9 Hz, 1 H); ^{13}C NMR δ 165.8, 165.6, 136.4, 136.2, 133.4, 131.4, 129.8, 129.6, 128.5, 128.4, 126.9, 126.2, 103.7, 77.1, 73.4, 71.3, 52.1, 27.3; MS (EI), *m/e* (relative intensity) 380 (M^+, 15), 379 (8), 274 (86); high-resolution mass spectrum, calcd for $C_{22}H_{20}O_6$ 380.1260, found 380.1222.

(–)-Methyl 4,5-*O*-Benzylidene-4-*epi*-shikimate (2). A solution of **9** (270 mg, 0.71 mmol) and NaOMe (42.2 mg, 1.1 equiv) in MeOH (20 mL) was stirred at room temperature for 1 h. Saturated aqueous NH_4Cl (20 mL) was added, and the mixture was extracted with $CHCl_3$ (3 × 20 mL). The organic layer was dried and concentrated under reduced pressure. Flash chromatography[20] (ethyl acetate–petroleum ether, 1.5:3.5, then 1:1) gave **2** (179 mg, 92%) as a colorless oil. **2**: $[\alpha]^{20}_D$ –18.0° (*c* 2.40, $CHCl_3$); the IR, ^1H NMR, and ^{13}C NMR spectra were identical with the corresponding spectra of the major acetal diastereomer of (±)-**2** prepared previously;[2] high-resolution mass spectrum, calcd for $C_{15}H_{16}O_5$ 276.0998, found 276.1012.

(–)-4-*epi*-Shikimic Acid (10). Alcohol **2** (111 mg, 0.40 mmol) was dissolved in THF (4 mL), and an aqueous solution of KOH (24.6 mg, 1.1 equiv in 1 mL of H_2O) was added. The mixture was stirred for 1 h at room temperature. A solution of aqueous acetic acid (80%, 5 mL) was added, and the mixture was stirred for 12 h at room temperature. Solvents were removed under reduced pressure. Methanol (1 mL) and excess diethylamine (1 mL) were added to the residue, and the mixture was concentrated under reduced pressure. The residue was loaded on a 10-cm ion-exchange resin column (Amberlite IR-120, H^+ form) and 50 mL of eluent were collected. Evaporation of the water under reduced pressure gave 67 mg (96%) of pure **10**. Sublimation (150–180 °C, 10^{-3} mm) gave **10** as an extremely hygroscopic, amorphous solid.[10] **10**: $[\alpha]^{22}_D$ –80.6° (*c* 1.03, H_2O) (lit.[10] $[\alpha]^{22}_D$ –93° (*c* 0.9, H_2O)); the ^1H NMR spectrum of **10** was in agreement with the literature spectral data.[10]

Acknowledgment. We are grateful to the National Institutes of Health, Grant GM 31958, for financial support.

Registry No. (–)-**2**, 94903-41-0; (–)-**3**, 77-95-2; **4** (isomer 1), 32384-44-4; **4** (isomer 2), 94903-42-1; **5**, 94843-95-5; **6**, 94843-96-6; **8**, 94903-43-2; **9**, 94843-97-7; (–)-**10**, 94903-44-3; chorismic acid, 617-12-9.

(22) In large-scale preparations enone **7** was isolated prior to borohydride reduction to **8**.

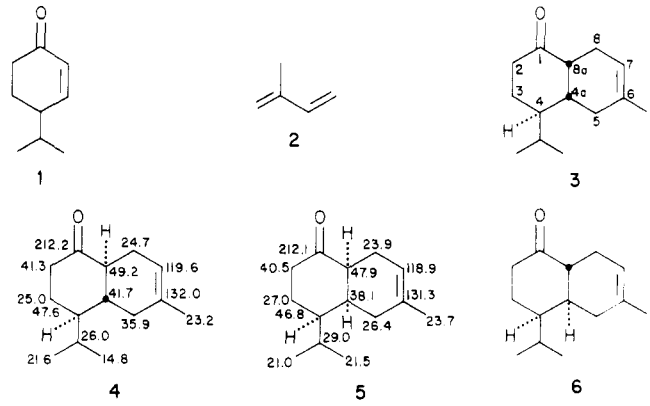
Diels–Alder Reactions of Cycloalkenones. 4. Short Syntheses of Some Cadinenes[1]

Francesco Fringuelli,*[2a] Ferdinando Pizzo,[2a] Aldo Taticchi,*[2a] Vitor F. Ferreira,[2b] Enrique L. Michelotti,[2b] Barry Porter,[2b] and Ernest Wenkert*[2b]

Dipartimento di Chimica, Università degli Studi, 06100 Perugia, Italy, and Department of Chemistry (D-006), University of California—San Diego, La Jolla, California 92093

Received August 20, 1984

As part of a general study of the Lewis acid catalyzed Diels–Alder reaction of cycloalkenones with dienes, 4-isopropyl-2-cyclohexenone (**1**)[3] was allowed to react with isoprene (**2**) in toluene solution under the influence of



anhydrous aluminum chloride, leading in 75% yield to a 9:1 mixture of octalones **4** and **5** as well as a trace of isomer **3**. Whereas the latter substance was not isolated and its presence in the product mixture recognized only by GC analysis, its structure **3** is based on the observation of the compound being formed on treatment of ketone **4** with base. The equilibrium constants (by GC analysis) of the trans/cis octalone pairs **4**/**3** and **6**/**5** are ca. 200 and 10^{-2}, respectively.[1]

The structures of the Diels–Alder reaction products were determined by ^{13}C NMR spectroscopy on the basis of previously described octalone models.[1] The carbon shifts are shown on formulas **4** and **5**.[4] *cis*-Octalones **3** and **5** are the primary Diels–Alder products. However, in analogy with the behavior of other *cis*-octalones,[1] ketone **3** had undergone acid-induced isomerization into the more stable *trans*-octalone **4**. The low tendency for the isomerization of *cis*-octalone **5** into its trans isomer **6** is due presumably to the fact of the latter carrying its isopropyl group in an axial orientation. The product structures reveal that the cycloaddition leading to the *cis*-octalones had occurred by

(1) For previous papers, see: Fringuelli, F.; Pizzo, F.; Taticchi, A.; Wenkert, E. *Synth. Commun.* **1979**, *9*, 391. Fringuelli, F.; Pizzo, F.; Taticchi, A.; Halls, T. D. J.; Wenkert, E. *J. Org. Chem.* **1982**, *47*, 5056. Fringuelli, F.; Minuti, L.; Pizzo, F.; Taticchi, A.; Halls, T. D. J.; Wenkert, E. *J. Org. Chem.* **1983**, *48*, 2802.

(2) (a) Università di Perugia. (b) University of California.

(3) (3) Soffer, M. D.; Jevnik, M. A. *J. Am. Chem. Soc.* **1955**, *77*, 1003. Stork, G.; Brizzolara, A.; Landesman, H.; Szmuszkovicz, J.; Terrell, R. *J. Am. Chem. Soc.* **1963**, *85*, 207.

(4) The δ values of the isopropyl methyl groups of ketones **4** and **5** indicate rotamer preferences i and ii for the two compounds, respectively.