before being dried over sodium sulphate. The products are obtained as yellow oils by silica gel flash chromatography (eluent = pentane).

Methyl 2-Phenylethanedithioate (6a).

Methyl 4'-Methyl-2-phenylethanedithioate (6b).

Methyl 4'-Methoxy-2-phenylethanedithioate (6c).

Methyl 3-Methyl-butanedithioate (6d).

1-[2-(*tert*-Butyldithio)-2-(methylthio)ethenyl]benzene (7a). 82% yield. ^{1}H (CCl_4): 1.27 (s, 9 H, $SC(CH_3)_3$), 2.20 (s, 3 H, SCH_3), 7.00–7.63 (m, 5 H, H_{arom}), 7.47 (s, 1 H, $Ph(H)C{=}C$). ^{13}C ($CDCl_3$): 17.78, 30.07, 49.69, 127.34, 128.13, 128.9, 135.50, 135.91, 130.26. MS *m/z*: 270 ($M^{\bullet+}$, 24), (46), 181 (27), 149 (60), 134 (100), 121 (13), 91 (68), 57 (52). Sulfur analysis: calcd 35.56, found 35.76.

1-[2'-(*tert*-Butyldithio)-2'-(methylthio)ethenyl)-4-methylbenzene (7b).[26] 44% yield. ^{1}H (CCl_4): 1.40 (s, 9 H, $SC(CH_3)_3$), 2.33 (s, 3 H, SCH_3), 2.50 (s, 3 H, $C_6H_4CH_3$), 7.13 (s, 1 H, $C_6H_4(H)C{=}$), 7.28 (AB system, 4 H, d_A = 7.08, d_B = 7.48, J = 8, H_{arom}). ^{13}C ($CDCl_3$): 17.72, 21.20, 30.07, 49.57, 128.91, 129.16, 134.34, 137.20, 133.17, 130.59.

(26) Compounds **7b** and **7d** were characterized by NMR from the crude mixtures before complete conversion to the dithioesters **6** by treatment with lithium methylthiolate.

1-(*tert*-Butyldithio)-1-(methylthio)-3-methylbutene (7d).[26] 43% yield. ^{1}H (CCl_4): 0.98 (d, 6 H, J = 7, $(CH_3)_2CHC(H){=}$), 1.33 (s, 9 H, $SC(CH_3)_3$), 2.13 (s, 3 H, SCH_3), 2.73–3.33 (m, 1 H, $(CH_3)_2CHC(H){=}$), 6.10 (d, 1 H, J = 9, $(CH_3)_2CHC(H){=}$). ^{13}C ($CDCl_3$): 17.76, 22.42, 30.08, 49.59, 60.92, 130.9, 142.0.

Acknowledgment. The financial support of the French ANRS is gratefully acknowledged.

Registry No. **1a**, 55921-51-2; **1b**, 92659-86-4; **1c**, 141982-83-4; **1d**, 141982-84-5; **2a**, 141982-85-6; **2b**, 141982-86-7; **2c**, 141982-87-8; **2d**, 141982-88-9; **2e**, 141982-89-0; **2f**, 141982-90-3; **2g**, 141982-91-4; **2h**, 141982-92-5; **2i**, 141982-93-6; **2j**, 141982-94-7; **2k**, 141982-95-8; **3**, 141982-96-9; (*R**,*R**)-**4a**, 141982-97-0; (*R**,*S**)-**4a**, 141982-98-1; (*R**,*R**)-**4b**, 141982-99-2; (*R**,*S**)-**4b**, 141983-00-8; (*R**,*R**)-**4c**, 141983-01-9; (*R**,*S**)-**4c**, 141983-02-0; **5a**, 141983-03-1; **5b**, 141983-04-2; **5c**, 141983-05-3; **5d**, 141983-06-4; **5e**, 141983-07-5; **5f**, 141983-08-6; **6a**, 2168-85-6; **6b**, 68542-17-6; **6c**, 76579-50-5; **6d**, 66312-45-6; (*E*)-**7a**, 141983-09-7; (*Z*)-**7a**, 141983-10-0; **7b**, 141983-11-1; $(CH_3)_2C{=}CH(SMe)SSBu\text{-}t$, 142003-29-0; $(i\text{-}PrO)_2P(O)C(SMe(SSMe^-)\cdot Li^+$, 141983-12-2; $(CH_3)_2CHO$, 78-84-2; *t*-BuSH, 75-66-1; $CH_3(CH_2)_{11}SH$, 112-55-0; PrSH, 107-03-9; MeSH, 74-93-1; PhSH, 108-98-5; $Ph(CH_2)_2SH$, 4410-99-5; EtSH, 75-08-1; PhCHO, 100-52-7; $4\text{-}MeC_6H_4CHO$, 104-87-0; $4\text{-}MeOC_6H_4CHO$, 123-11-5.

Synthetic Studies on Furanoheliangolides. Stereocontrolled Construction of the Oxygen-Bridged Tricyclic Framework

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Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210

Received February 3, 1992

The heavily functionalized 6,9-epoxycyclodeca[*b*]furan-11-ones **34** and **37** have been prepared in 13 steps from 4-methyl-2-[(phenylmethoxy)methyl]furan. The key elements of the scheme include a high-pressure Diels–Alder cycloaddition to 1-cyanovinyl acetate, highly regioselective hydroboration, controlled stepwise oxidation to give keto aldehyde **20**, and thermal oxy-Cope rearrangement of both **32** and **36b**. The prior introduction of a phenylthio substituent provides for the accommodation of different levels of unsaturation at a more advanced stage of furanoheliangolide construction. While the present strategy is developed around a racemic model, the potential for adoption of enantioselective features is immediate. The overall stereocontrolled sequence provides a general and flexible entry into oxygen-bridged frameworks closely related to substructures occurring in many furan-type germacranolides.

Many sesquiterpenes characterized by the presence in their framework of a 6,9-epoxycyclodeca[*b*]furan structural array have been identified[2] since zexbrevin (**1**), the first member of this class to be isolated, was reported in 1970.[3] This large family of tricyclic α-methylene lactones features an enormous range of stereochemical variation and pattern of oxygenation as reflected in goyazensolide (**2**),[4] isocentratherin (**3**),[4a,5] tagitinin B (**4**),[6] and tirotundin (**5**).[6a,b,7] Additional cyclization to the ester side chain as found in eremantholide C (**6**)[4b,c,8] further enriches the variations

(1) NATO Postdoctoral Fellow of the Science and Engineering Research Council, 1990–1991.

(2) For a survey of this area of natural products, see: Brown, D. S.; Paquette, L. A. *Heterocycles* **1992**, *34*, 807.

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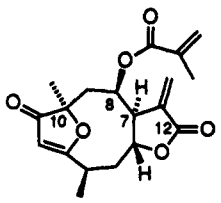
present in this class of natural products.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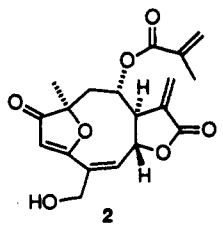
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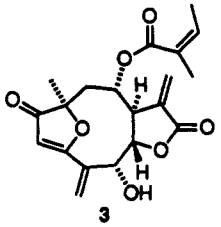
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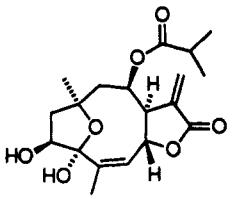
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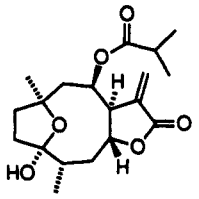
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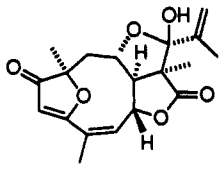
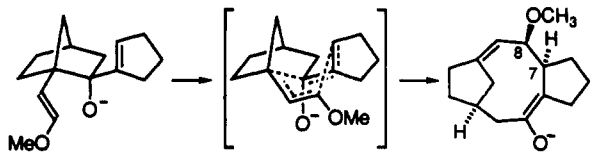

6

Despite the significant biological properties of several of the furanoheliangolides,[2] very little synthetic interest has been accorded to representative examples.[9] As part of a program directed toward construction of several of the more important targets in this series, the development of a route adequately generic to accommodate such scope was considered highly desirable.

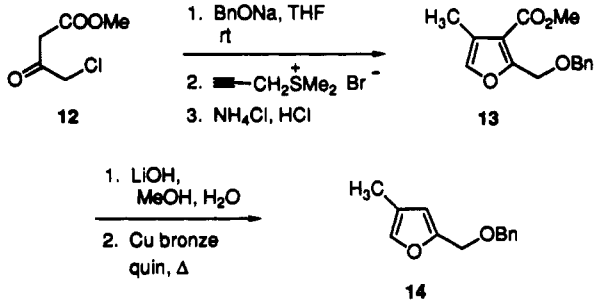
Difficult carbon–carbon bond constructions are now recognized to be reliable with exceptional stereocontrol when performed intramolecularly via an oxy-Cope rearrangement.[10] Elaboration of the requisite carbinol precursors rests simply on intermolecular 1,2-addition of a suitable vinyl organometallic to the β,γ-unsaturated ketone of choice.[11] Proper deployment of this highly convergent scheme can result in the rapid fabrication of complex polycyclic backbones closely related to the target molecules.

Our synthetic plan for construction of the linchpin oxygen-bridged tricyclic framework developed from earlier scrutiny of the manner in which endo-norbornanols such as **7** undergo isomerization.[12] These studies revealed that

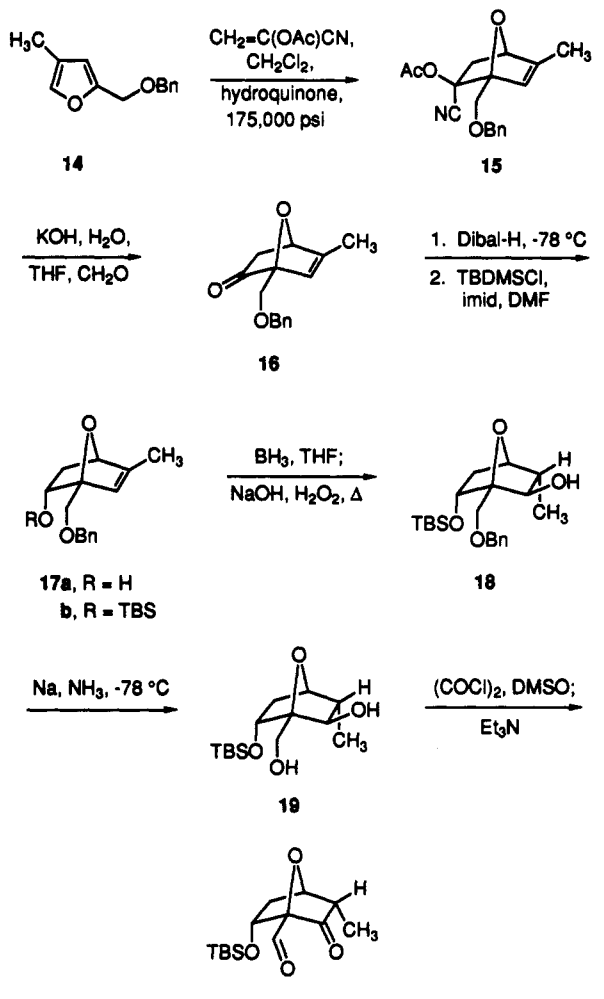

7 8 9

the [3,3]sigmatropic event occurred invariantly via an exo-boat transition state (viz. **8**) to deliver enolate anions

Scheme I

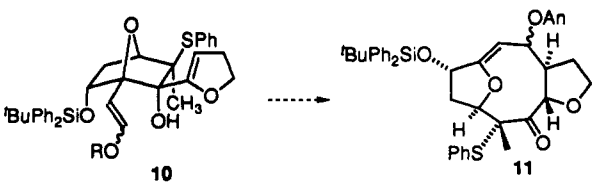

12 13 14

Scheme II


14 15 16 17a, R = H b, R = TBS 18 19 20

typified by **9** having the proper relative stereochemistry at the 7- and 8-positions.

Thus, our immediate goal was to prepare carbinols such as **10** for the purpose of evaluating their conversion into tricyclic vinyl ethers functionalized as in **11**.


10 11

Results and Discussion

A building-block approach to **10** requires that an efficient synthesis of 4-methyl-2-[(phenylmethoxy)methyl]-furan (**14**) be first achieved. Several approaches to **14** were screened.[13-16] Of these, the route shown in Scheme I

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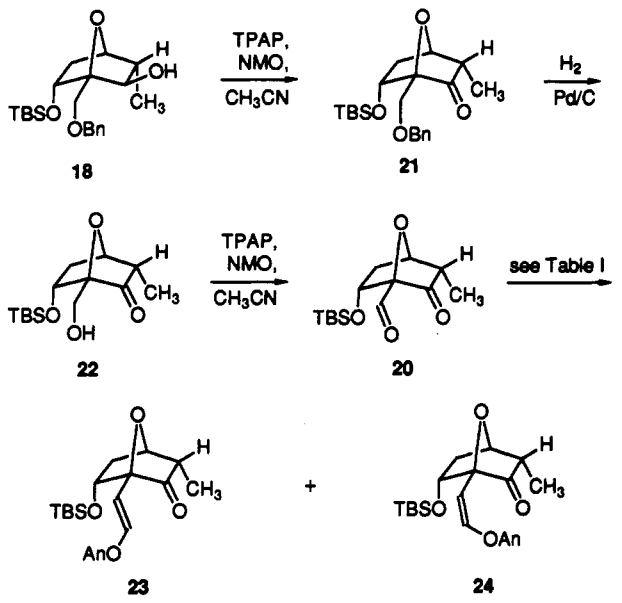
Scheme III



proved to be the most expedient and efficient. Admixture of methyl 4-chloroacetoacetate with 2 equiv of sodium phenylmethoxide in THF at room temperature and treatment of the resulting reaction mixture with dimethyl-2-propynylsulfonium bromide[17a] was found to lead directly to **13** (93%).[17b] Saponification of **13** followed by copper–bronze-promoted decarboxylation[18] then afforded the desired **14**.

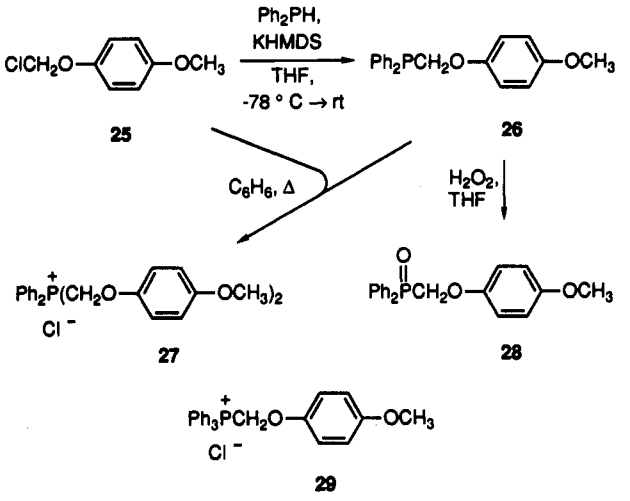
Diels–Alder cycloaddition of 1-cyanovinyl acetate[19] to **14** under high-pressure conditions[20] led to near-quantitative formation of a single diastereomeric adduct (Scheme II). This compound has been assigned the indicated stereochemistry on the strength of comparative analysis with the results of Vogel and co-workers involving related systems.[21] The hydrolysis of **15**,[22] hydride reduction of **16**, and protection of the hydroxyl group in **17a**[23] were carried out under standard conditions. The ensuing hydroboration of **17b** proved to be highly regioselective, leading exclusively to exo alcohol **18** (90%). Since comparable positional control was not observed in the desmethyl series,[24] the methyl substituent is clearly contributory to this selectivity as expected. The selective debenzylation of **18** was achieved with sodium in liquid ammonia, and the resulting diol **19** was oxidized under Swern conditions[25] to give the sensitive keto aldehyde **20**. Unfortunately, the latter reaction did not lend itself to scale

Table I. Ratios of 23:24 Produced from 20 and Phosphorus Reagents 27–29

entry	reagent	condns	23:24[a]
1	29	CH_3Li, THF, −78 °C	3:1
2	29	CH_3Li·LiBr, THF, −78 °C	3:1
3	29	CH_3Li·LiBr, THF, 0 °C	3:2[b]
4	29	CH_3Li·LiBr, THF, 35 °C	3:2
5	29	CH_3Li·LiBr, THF, TMEDA	complex mixture
6	27	CH_3Li·LiBr, THF, 0 °C (at −78, 0, and 35 °C)	1:1
7	28	(1) LDA, THF; (2) NaH, THF, 0 °C	1:1

[a] Determined by ^1H NMR at 300 MHz. [b] Entry 3 was employed for this study because it gave a higher overall yield of both **23** and **24**.

Scheme IV



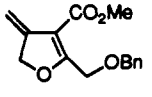
(13) An obvious approach is benzylation of the known 4-methyl-2-furanmethanol.[14] Although the original route could be shortened by reducing 4-methyl-2-furancarbonitrile to the aldehyde with diisobutylaluminum hydride and then to the alcohol with $NaBH_4$ and standard benzylation conditions gave **14** in reasonable yield, the drawback of a long, five-step synthesis of the nitrile could not be neglected. Another obvious approach was to condense methyl 4-(benzyloxy)acetoacetate with chloroacetone in the presence of ammonia as an extension of the Feist–Benary method for furan production.[15] However, only very low yields were observed.

(14) Bornowski, H. *Tetrahedron* **1971**, *27*, 4101.

(15) (a) Tsuboi, S.; Uno, T.; Takeda, A. *Chem. Lett.* **1978**, 1325. (b) Blomquist, A. T.; Stevenson, H. B. *J. Am. Chem. Soc.* **1934**, *56*, 146 and references cited therein.

(16) For other routes to 4-methylfurans see: Srikishna, A.; Krishnan, K. *Tetrahedron Lett.* **1988**, *29*, 4995. Baciocchi, E.; Ruzziconi, R. *Synth. Commun.* **1988**, *18*, 1841. Minami, I.; Yuhara, M.; Watanabe, H.; Tsuji, J. *J. Organomet. Chem.* **1987**, *334*, 225. Tsuji, J.; Watanabe, H.; Minami, I.; Shimizu, I. *J. Am. Chem. Soc.* **1985**, *107*, 2196. Knight, D. W.; Rustidge, D. C. *J. Chem. Soc., Perkin Trans. 1* **1981**, 679; Cornforth, J. W. *J. Chem. Soc.* **1958**, 1310. Miyashita, M.; Kumazawa, T.; Yoshikoshi, A. *J. Org. Chem.* **1980**, *45*, 2945. Miyashita, M.; Kumazawa, T.; Yoshikoshi, A. *J. Chem. Soc., Chem. Commun.* **1978**, 362.

(17) (a) Howes, P. D.; Stirling, C. J. M. *Org. Synth.* **1973**, *53*, 1. Batty, J. W.; Howes, P. D.; Stirling, C. J. M. *J. Chem. Soc., Perkin Trans.* **1973**, 65. Batty, J. W.; Howes, P. D.; Stirling, C. J. M. *J. Chem. Soc., Chem. Commun.* **1971**, 534. (b) An acidic workup is critical to the success of this conversion. Otherwise, **i** is produced. This olefinic isomer can, however, be cleanly isomerized to **13** upon exposure to a catalytic amount of acid or suitable transition metal catalyst.



i

(18) Rinkes, I. J. *Rec. Trav. Chim. Pays-Bas* **1931**, *50*, 1127.

(19) Due to the cost of this commercially available compound, it was prepared on a large scale from chloroacetaldehyde dimethyl acetal using a slightly modified variation of the original procedures; see: McCann, W. P.; Hall, L. M.; Nonidez, W. K. *Anal. Chem.* **1983**, *55*, 1454. Nowak, R. M. *J. Org. Chem.* **1963**, *28*, 1182. For two alternative preparations from acetyl cyanide see: Oku, A.; Nakaoji, S.; Kadono, T.; Imai, H. *Bull. Chem. Soc. Jpn.* **1972**, *52*, 2966. Oku, A.; Arita, S. *Bull Chem. Soc. Jpn.* **1979**, *52*, 3337.

(20) Kotsuki, H.; Nishizawa, H.; Ochi, M.; Matsuoka, K. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 496. Kotsuki, H.; Nishizawa, H. *Heterocycles* **1981**, *16*, 1287. For examples with 2-vinylfurans and of intramolecular high-pressure Diels–Alder reactions, see, respectively: Kotsuki, H.; Kondo, A.; Nishizawa, H.; Ochi, M.; Matsuoka, K. *J. Org. Chem.* **1981**, *46*, 5454. Harwood, L. M.; Leeming, S. A.; Issacs, N. S.; Jones, G.; Pickard, J.; Thomas, R. M.; Watkin, D. *Tetrahedron Lett.* **1988**, *29*, 5017.

(21) Vieira, E.; Vogel, P. *Helv. Chim. Acta* **1983**, *66*, 1865.

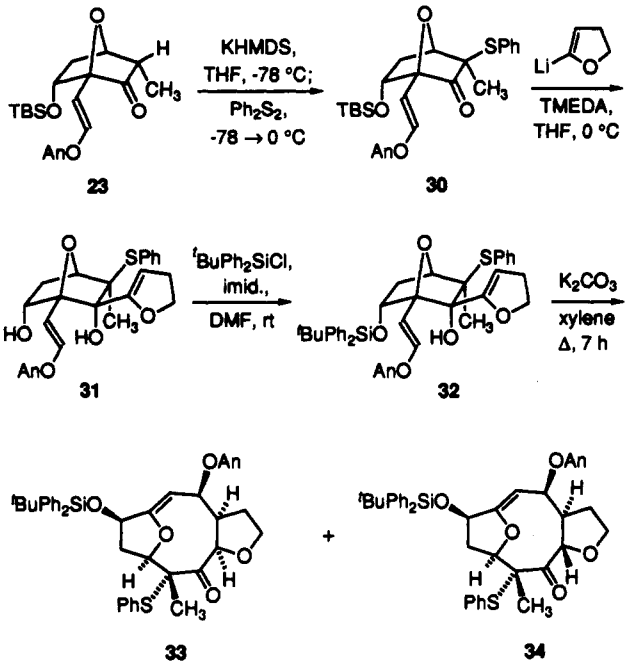
(22) Warm, A.; Vogel, P. *J. Org. Chem.* **1986**, *51*, 5348. For some other methods of hydrolysis of the 1-cyanovinyl acetate adducts see: Saf, R.; Faber, K.; Penn, G.; Griengl, H. *Tetrahedron* **1988**, *44*, 389; Le Drian, C.; Vogel, P. *Helv. Chim. Acta* **1987**, *70*, 1703. Black, K. A.; Vogel, P. *J. Org. Chem.* **1986**, *51*, 5341. Wharton, P. S.; Aw, B. T. *J. Org. Chem.* **1966**, *31*, 3787. Bartlett, P. D.; Tate, B. E. *J. Am. Chem. Soc.* **1956**, *78*, 2473.

(23) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.

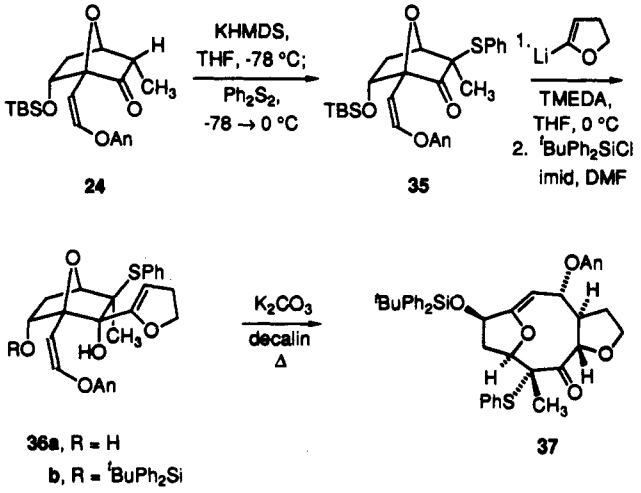
(24) Brown, D. S. Unpublished results.

(25) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651. For a recent review on the oxidation of alcohols by activated DMSO and related reactions see: Tidwell, T. T. *Synthesis* **1990**, 857; *Org. React. (N.Y.)* **1990**, *39*, 297.

Scheme V



Scheme VI



up, and no alternative oxidant[26] was found that provided respectable yields. In every instance, the primary alcohol was transformed quite rapidly into the carboxaldehyde, at which point the secondary carbinol responded much more slowly, presumably because of the sterically hindered setting of its associated geminal hydrogen atom. The instability of the intermediate hydroxy aldehyde is simply not compatible with the requisite long reaction times. Consequently, the order in which these groups are oxidized had to be reversed.

To this end, **18** was subjected to perruthenate oxidation,[27] and ketone **21** (93%) was debenzylated by catalytic hydrogenolysis[28] (92%, Scheme III). The ability of **22** to function as a serviceable intermediate was revealed upon its efficient oxidation with TPAP to deliver **20** in useful amounts.

The next phase of this investigation was to probe the response of **20** to Wittig reaction conditions.[29] For this purpose, phosphonium salt **27** and phosphine oxide **28** were obtained from the common phosphine **26**, which was prepared by alkylation of chloride **25**[30] with potassium diphenylphosphide (Scheme IV).[31] As seen in Table I, considerable variation in the trans–cis vinyl ether ratio was noted. The following generalizations were gleaned from those experiments involving phosphonium salts **27** and **29**:[32] (a) no change in the 3:1 product distribution was observed when methyllithium was replaced by the lithium bromide complex (entries 1 and 2); (b) an increase in the reaction temperature from −78 to 0 °C decreased the trans–cis ratio, but only to 60:40 (entry 3); (c) a further increase in temperature had little additional effect on product distribution (entry 4); (d) the use of TMEDA as cosolvent at several temperatures gave complex mixtures containing very little of the desired enol ethers (entry 5); and (e) a change to the less hindered Wittig salt **27** produced a closely balanced ratio of 1:1 (entry 6). The same isomer distribution could be realized via a Horner–Wittig reaction involving phosphine oxide **28** (entry 7).[33] However, this process was rather inefficient. Consequently, preparative-scale experiments were conducted according to entry 3 and the readily separable ketones **23** and **24** were obtained in a combined yield of 42%.

Phenylsulfenation of these ketones held the prospect of addressing the need for accommodating diverse levels of unsaturation later in the synthetic scheme. Accordingly, the enolate anions of **23** and **24** were individually generated at −78 °C and condensed with diphenyl disulfide (Schemes V and VI). Once **30** and **35** were in hand, their condensation with 4,5-dihydro-2-furanyllithium, a prototypical synthon for the lactone subunit, proceeded smoothly and delivered **31** and **36a**. Competitive desilylation, a feature common to endo silyl ethers of this general structural type,[24] was remedied by direct reprotection.

Rapid loss of the bulky silyl group was again observed during attempts to isomerize **32** and **36b** under conventional anionic oxy-Cope conditions. In light of these developments, recourse was made to thermal activation for accomplishing the desired ring expansion. As anticipated, the exo-boat transition state was adhered to in both series, thereby setting the proper stereochemical relationship at the 7- and 8-positions. For **32**, the [3,3]sigmatropic shift took place quite rapidly to produce mixtures of the cis and trans diastereomers **33** (19%) and **34** (43%). These isomers were distinguished on the basis of NOE studies, the proper proton and carbon assignment having been previously recognized by decoupling and $^1H/^{13}C$ correlation

(26) For example: (a) Parikh, J. R.; Doering, W. von E. *J. Am. Chem. Soc.* **1967**, *89*, 5505. (b) Corey, E. J.; Kim, C. U.; Misco, P. F. *Organic Syntheses*; Wiley: New York, 1988; Collect. Vol. VI, p 220. Corey, E. J.; Kim, C. U. *J. Org. Chem.* **1973**, *38*, 1233. Corey, E. J.; Kim, C. U. *J. Am. Chem. Soc.* **1972**, *94*, 7586. (c) Ma, Z.; Bobbitt, J. M. *J. Org. Chem.* **1991**, *56*, 6110. (d) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1988**, *48*, 4155. (e) Poos, G. I.; Arth, G. E.; Beyler, R. E.; Sarett, L. H. *J. Am. Chem. Soc.* **1953**, *75*, 422. (f) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647. (g) Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, *20*, 399. (h) Bowers, A.; Halsall, T. G.; Jones, E. R. H.; Lemin, A. J. *J. Chem. Soc.* **1953**, 2548. Bowden, K.; Heilbron, I. M.; Jones, E. R. H.; Weedon, B. C. L. *J. Chem. Soc.* **1946**, 39. (i) Brown, H. C.; Garg, C. P.; Liu, K.-T. *J. Org. Chem.* **1971**, *36*, 387. (j) Corey, E. J.; Fleet, G. W. *J. Tetrahedron Lett.* **1973**, 4499.

(27) Griffith, W. P.; Ley, S. V. *Aldrichimica Acta* **1990**, *23*, 13. Griffith, W. P.; Ley, S. V.; Whitcombe, G. P.; White, A. D. *J. Chem. Soc., Chem. Commun.* **1987**, 1625.

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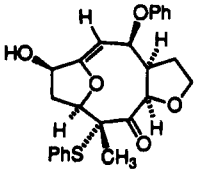
(33) (a) Earnshaw, C.; Wallis, C. J.; Warren, S. *J. Chem. Soc., Chem. Commun.* **1977**, 314. (b) Earnshaw, C.; Wallis, C. J.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1979**, 3099.

Table II. Product Ratios from Thermal Oxy-Cope Rearrangement of 32 (K_2CO_3 Present)

solvent	condns	33:34
decalin	reflux, 20 min	55:45
xylene	reflux, 45 min	45:55
toluene	reflux, 5 h	30:70

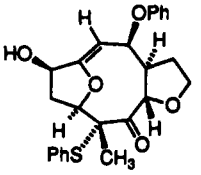
experiments. The most relevant NOE results are illustrated in Figure 1. Especially diagnostic of the cis,syn relationship of H-6α, H-7α, and H-8α in **33** is the magnitude of the mutual integral enhancements. The alternative cis-fused arrangement with both H-6 and H-7 β-oriented was discounted due to the lack of an NOE contribution from the 4-methyl substituent to H-6. This effect is intense in trans isomer **34**. This product features obviously close proximity between H-8 and H-7. As before, the NOE data also confirm the relative stereochemistry of the anisyloxy substituent. Thus, **33** and **34** are epimeric only at C-6. This distinction is consistent with their common origin for the uniquely stereodefined enol formed via an exo-boat transition state.[12]

Comparable heating of **36b** led uniquely to **37** (61%), the stereochemical features of which were elucidated in an entirely comparable manner (Figure 1). The evolution of trans networks as in **34** and **37** stems from the greater stabilities of these epimers. Somewhat simplified versions of all four possible products were minimized using the MODEL program (version KS 2.96).[34] Following a multiconformer run performed on each stereoisomer with simultaneous rotation about the C–O–Ph and C–S–Ph bonds, over 425 conformers were generated and minimized to ensure discovery of the global minimum. Final optimization was accomplished by making recourse to MMX. The strain and total energy terms for A–D are given above;



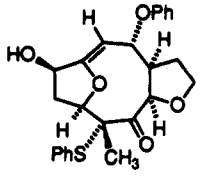
A

E_{Strain} = 50.4 kcal/mol
E_{Total} = 66.1 kcal/mol



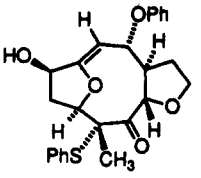
B

E_{Strain} = 46.4 kcal/mol
E_{Total} = 62.2 kcal/mol



C

E_{Strain} = 49.6 kcal/mol
E_{Total} = 65.4 kcal/mol

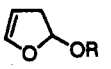


D

E_{Strain} = 46.8 kcal/mol
E_{Total} = 62.5 kcal/mol

the associated conformations appear in Figure 2. The biases in favor of B and D seem unequivocal. The variations in product distribution that appear in Table II are not equilibrium values, since heterogeneous conditions were used to effect the rearrangement.

In summary, an interesting, stereoselective 13-step route has been developed that links furan **14** to either **34** or **37**. The practicality of the scheme further exemplifies the applications that can be realized when facial selectivity of 1,2 vinyl anion addition to a carbonyl group and topological selectivity in the sigmatropic rearrangement are well coordinated. The present advance requires further refinement prior to its ultimate adoption as a serviceable route to furanoheliangolides. The first involves introduction of an angular methyl group at C-10. The existing bridgehead double bond is expected to play a vital role in facilitating this modest structural modification. Clearly, C-12 must also eventuate in a more highly oxidized state. We hope to address this issue by utilizing the anions of dihydrofurans such as **38**[35] and **39**[36] early in the synthesis. For the



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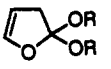

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moment, all that is known is that these seemingly labile compounds are considerably more robust than expected at first glance. Finally, future work will also be engineered so as to provide an enantioselective entry into this class of natural products by taking advantage of the recognized ability of (+)- and (−)-1-cyanovinyl camphanate to deliver optically pure 7-oxabicyclo[2.2.1]hept-5-en-2-ones.[37]

Experimental Section

All flash chromatographic separations were carried out on Merck silica gel 60 (60–200 mesh). All reactions were routinely performed under a nitrogen atmosphere. Solvents were reagent grade and dried prior to use. The purity of all compounds was chosen to be ≥95% by TLC and high-field ^1H NMR analyses.

Methyl 4-Methyl-2-[(phenylmethoxy)methyl]-3-furancarboxylate (13). Benzyl alcohol (16.4 g, 152 mmol) was added dropwise to a stirred suspension of 97% NaH (3.76 g, 152 mmol) in dry THF (300 mL) at 25 °C under N_2. After the mixture had stirred for 1 h, a solution of methyl 4-chloroacetoacetate (10.84 g, 72 mmol) in dry THF (30 mL) was added dropwise over 45 min and the mixture was transferred 3 h later via a large bore cannula to a stirred suspension of dimethyl-2-propynylsulfonium bromide[17a] (14.5 g, 80 mmol) in dry THF (300 mL) at rt under nitrogen. The resulting mixture was stirred at rt for 20 h under a dry atmosphere (drying tube, dimethyl sulfide evolved), quenched with saturated NH_4Cl solution (150 mL) and 2 M HCl (50 mL), and extracted 1 h later with ether. The combined organic fractions were washed with brine, dried, and concentrated in vacuo. The residue was purified by silica gel chromatography (elution with 5–10% ether in petroleum ether) to give **13** (17.5 g, 93%) as a colorless liquid: bp 150–153 °C (1 Torr); IR (neat, cm^{-1}) 1715, 1607; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37–7.25 (m, 5 H), 7.19 (s, 1 H), 4.80 (s, 2 H), 4.59 (s, 2 H), 3.80 (s, 3 H), 2.17 (s, 3 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) ppm 164.2, 157.7, 139.7, 137.8, 128.3 (2C), 127.8 (2C), 127.6, 121.3, 116.1, 72.5, 63.1, 51.1, 9.7; MS m/z (M^+) calcd 260.1049, obsd 260.1055.

Anal. Calcd for $C_{15}H_{16}O_4$: C, 69.22; H, 6.20. Found: C, 68.95; H, 6.21.

4-Methyl-2-[(phenylmethoxy)methyl]furan (14). Method A. A mixture of **13** (16.9 g, 65 mmol), $LiOH·H_2O$ (5.45 g, 130 mmol), and water (13 mL) in methanol (130 mL) was stirred at rt for 3 days. The mixture was concentrated in vacuo to remove the methanol, and the residue was acidified with 2 M HCl (70 mL) and extracted with CH_2Cl_2. The combined organic fractions were dried and concentrated to give crude carboxylic acid. A mixture of this acid and copper–bronze (0.98 g) in quinoline (25.2

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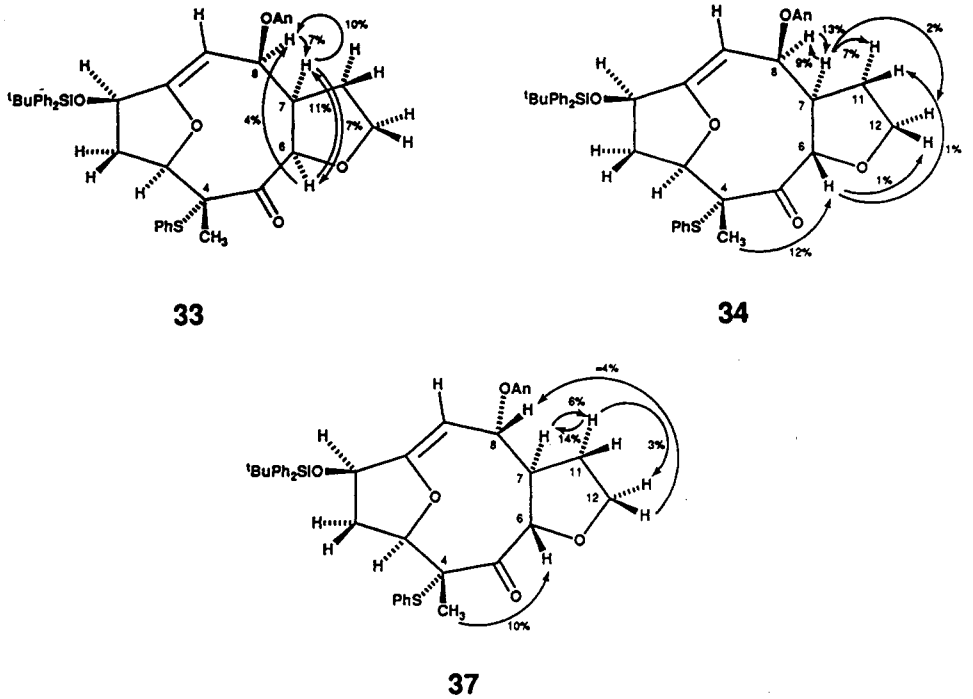

Figure 1. Key NOE results for **33**, **34**, and **37**.

g, 195 mmol) was heated at gentle reflux for 1 h, cooled, poured into ice-cold 1 M H_2SO_4 (200 mL), and extracted with ether. The combined organic fractions were washed with water, dried, concentrated, filtered through a silica gel pad (elution with 5% ether in petroleum ether), and distilled (125–130 °C (4 Torr)) to give **14** (7.09 g, 54%) as a colorless liquid: IR (neat, cm^{-1}) 1543, 1494, 1452, 1354, 1147, 1125, 1074; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.18 (m, 6 H), 6.19 (s, 1 H), 4.55 (s, 2 H), 4.44 (s, 2 H), 2.02 (d, J = 1.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 151.8, 139.4, 138.0, 128.4 (2 C), 127.9 (2 C), 127.6, 120.6, 112.0, 71.9, 64.0, 9.7; MS m/z (M^+) calcd 202.0994, obsd 202.0998.

Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.17; H, 6.97.

Method B (Large-Scale Procedure). Benzyl alcohol (227 g, 2.1 mol) was added dropwise over 1 h to a stirred suspension of NaH (84 g 60% dispersion in oil, 2.1 mol) in dry THF (2 L) at 25 °C under nitrogen. After 1 h, a solution of methyl 4-chloroacetoacetate (151 g, 1.0 mol) in dry THF (200 mL) was added dropwise over 1.5 h. After 3 h, the mixture was transferred via a large bore cannula over 40 min to a stirred suspension of dimethyl-2-propynylsulfonium bromide (199 g, 1.1 mol) in dry THF (1 L) at rt under N_2, stirred at rt for 18 h under a dry atmosphere, and quenched with saturated NH_4Cl solution (1 L) and 2 M HCl (500 mL). The above workup gave the crude ester which was taken up in 5 M aqueous NaOH (300 mL) in THF (750 mL), stirred at rt for 10 days, and concentrated in vacuo to remove the THF. The residue was diluted with water and washed with ether. The aqueous fraction was cooled and slowly acidified with 6 M HCl prior to ether extraction. The combined ether extracts were dried and concentrated in vacuo to give crude carboxylic acid as a light yellow solid (ca. 250 g). A mixture of this acid and copper–bronze (15 g) in quinoline (387 g, 3 mol) was heated at gentle reflux (210–220 °C) for 4 h, cooled, filtered, and purified by distillation (125–130 °C (4 Torr)) to give **14** (80 g, 39% over three steps) as a colorless liquid, identical with the previous sample by NMR, IR, and MS.

***endo*-2-Acetoxy-5-methyl-1-[(phenylmethoxy)methyl]-7-oxabicyclo[2.2.1]hept-5-ene-2-carbonitrile (15).** A mixture of **14** (7.08 g, 35 mmol), 1-cyanovinyl acetate (4.67 g, 42 mmol), hydroquinone (116 mg, 1.05 mmol), and dry CH_2Cl_2 (8.75 mL) in a glass-stoppered Teflon tube was placed in a high-pressure reactor at 175 000 psi for 13 days. The reaction mixture was concentrated, and the residue was purified by silica gel chromatography (elution with 10–40% ether in petroleum ether) to give **15** (10.7 g, 98%) as a colorless oil: IR (neat, cm^{-1}) 2217, 1752, 1635; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37–7.27 (m, 5 H), 5.89 (d, J = 1.6 Hz, 1 H), 4.80 (d, J 4.6 Hz, 1 H), 4.73 (d, J = 12.1 Hz, 1 H), 4.61 (d, J = 12.1 Hz, 1 H), 4.17 (d, J = 11.3 Hz, 1 H), 4.09 (d, J = 11.3 Hz, 1 H), 2.93 (dd, J = 13.2, 4.7 Hz, 1 H), 2.04 (s, 3 H), 1.91 (d, J = 1.7 hz, 3 H), 1.72 (d, J = 13.2 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 169.1, 151.0, 137.6, 128.4 (2 C), 127.74, 127.70 (2 C), 125.1, 117.6, 92.1, 81.8, 75.1, 73.8, 67.2, 43.7, 20.6, 12.9; MS m/z (M^+) calcd 313.1314, obsd 313.1269.

Anal. Calcd for $C_{18}H_{19}NO_4$: C, 69.00; H, 6.11. Found: C, 69.20; H, 6.17.

5-Methyl-1-[(phenylmethoxy)methyl]-7-oxabicyclo-[2.2.1]hept-5-en-2-one (16). Aqueous 1 M KOH (100 mL) was added at rt to a stirred solution of **15** (10.3 g, 33 mmol) in a mixture of THF (100 mL) and water (50 mL). After 45 min, 37% aqueous formaldehyde (120 mL) was added and the dark mixture stirred for a further 20 min prior to extraction with CH_2Cl_2. The combined extracts were dried, concentrated in vacuo, and purified by silica gel chromatography (elution with 10–25% ether in petroleum ether) to give **16** (7.3 g, 91%) as a colorless oil: IR (neat, cm^{-1}) 1749, 1622; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37–7.25 (m, 5 H), 5.83 (br s, 1 H), 4.95 (d, J = 4.3 Hz, 1 H), 4.67 (d, J = 12.3 Hz, 1 H), 4.58 (d, J = 12.3 Hz, 1 H), 3.98 (d, J = 11.8 Hz, 1 H), 3.80 (d, J = 11.8 Hz, 1 H), 2.32 (ddd, J = 15.8, 4.3, 0.4 Hz, 1 H), 1.91 (d, J = 15.8 Hz, 1 H), 1.89 (d, J = 1.7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 206.1, 154.1, 137.7, 128.3 (2 C), 127.7 (2 C), 127.6, 123.1, 91.3, 80.5, 73.6, 65.0, 34.7, 13.9; MS m/z (M^+ – CH_2=C=O) calcd 202.0993, obsd 202.1020.

Anal. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.76; H, 6.62.

***endo*-5-Methyl-1-[(phenylmethoxy)methyl]-7-oxabicyclo[2.2.1]hept-5-en-2-ol (17a).** Diisobutylaluminum hydride (92 mL of 1 M in hexanes, 92 mmol) was added dropwise to a stirred solution of **16** (11.2 g, 46 mmol) in dry THF (230 mL) at −78 °C under N_2. The mixture was stirred at −78 °C for 1.5 h, quenched by dropwise addition of methanol (14 mL), allowed to warm to 0 °C, diluted with saturated potassium sodium tartrate solution (460 mL), stirred vigorously for 15 min, and extracted with ether. The combined extracts were washed with brine, dried, and concentrated. The residue was purified by silica gel chromatography (elution with 0.5% methanol and 25% ether in petroleum ether up to 1.2% methanol and 60% ether in petroleum ether) to give **17a** (10.7 g, 95%) as a colorless oil: IR ($CHCl_3$, cm^{-1}) 3578 (br), 1629; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38–7.25 (m, 5 H), 5.87 (br d, J = 1.6 Hz, 1 H), 4.66 (d, J = 12.2 Hz, 1 H), 4.61 (d, J = 12.2 Hz, 1 H), 4.61 (d, J = 5.0 Hz, 1 H), 4.33–4.25 (m, 1 H), 3.92 (d, J = 10.6 Hz, 1 H), 3.86 (d, J = 10.6 Hz, 1 H), 2.37 (ddd, J = 12.0, 8.0, 4.7 Hz, 1 H), 1.91 (d, J = 1.7 Hz, 3 H), 1.69 (d, J = 6.8 Hz,

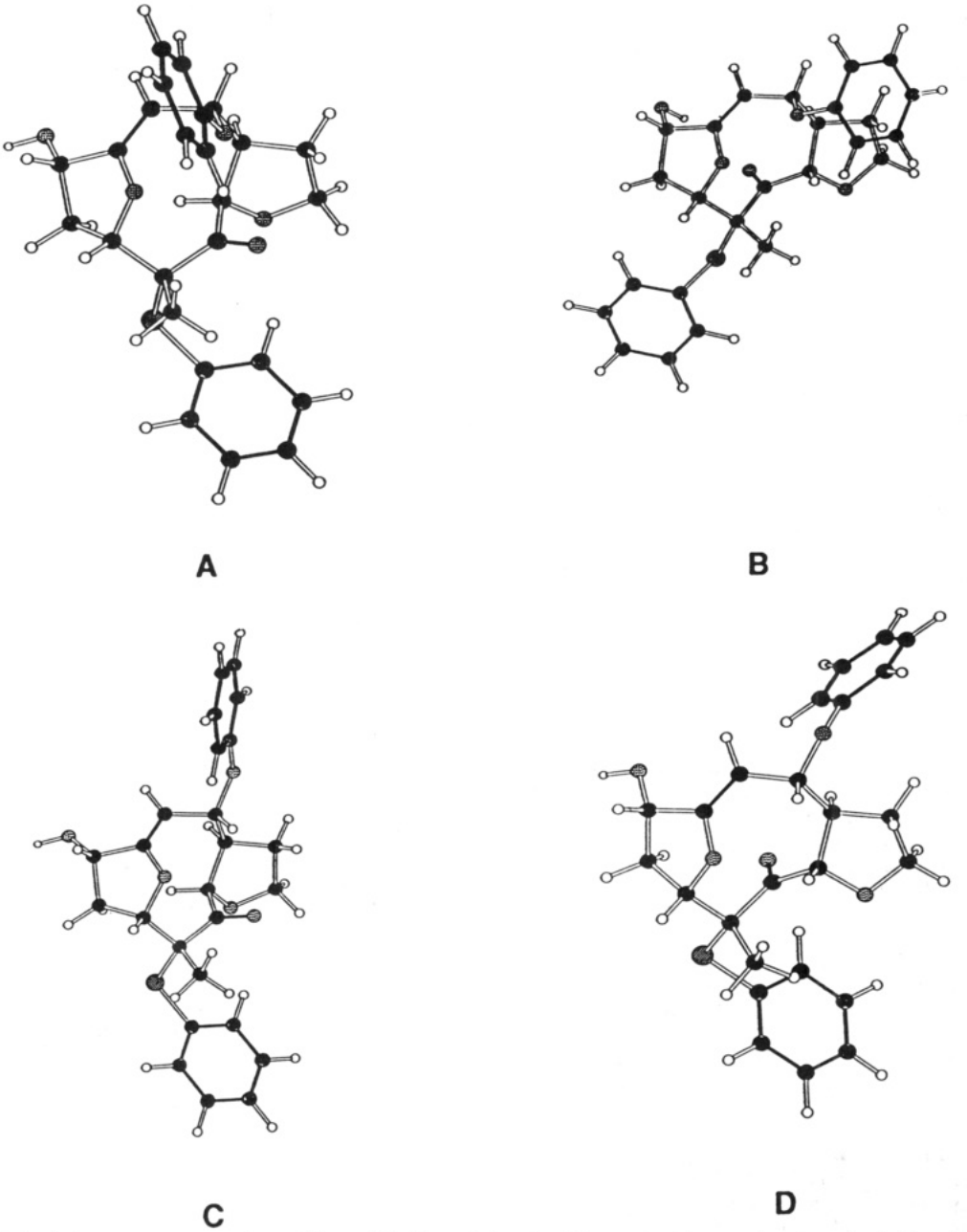

Figure 2. Global minimum energy conformations of A–D as determined by molecular mechanics calculations (3-D output).

1 H), 1.04 (dd, J = 11.9, 2.5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 150.2, 137.9, 128.4 (2 C), 127.74 (2 C), 127.71, 125.1, 89.3, 82.5, 73.7, 72.4, 68.7, 37.2, 13.0; MS m/z (M^+) calcd 246.1256, obsd 246.1248.

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.04; H, 7.42.

***endo*-6-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-3-methyl-1[(phenylmethoxy)methyl]-7-oxabicyclo[2.2.1]-hept-2-ene (17b).** *tert*-Butyldimethylsilyl chloride (9.72 g, 64.5 mmol) was added in one portion to a stirred solution of **17a** (10.6 g, 43 mmol) and imidazole (4.39 g, 64.5 mmol) in dry DMF (14.3 mL) at rt. The mixture was stirred under N_2 for 16 h, poured into water, and extracted with ether. The combined extracts were washed with brine, dried, and concentrated. The residue was purified by silica gel chromatography (elution with 5–15% ether in petroleum ether) to give **17b** (14.9 g, 96%) as a colorless oil: IR (neat, cm^{-1}) 1632; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38–7.25 (m, 5 H), 5.71 (br d, J = 1.6 Hz, 1 H), 4.65 (d, J = 12.3 Hz, 1 H), 4.60 (d, J = 12.3 Hz, 1 H), 4.60 (d, J = 4.8 Hz, 1 H), 4.30 (dd, J = 7.7, 2.3 Hz, 1 H), 3.90 (d, J = 11.3 Hz, 1 H), 3.78 (d, J = 11.3 Hz, 1 H), 2.24 (ddd, J = 11.3, 7.7, 4.8 Hz, 1 H), 1.87 (d, J = 1.6 Hz, 3 H), 0.99 (dd, J = 11.3, 2.4 Hz, 1 H), 0.92 (s, 9 H), 0.00 (s, 3 H), –0.01 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 147.6, 138.2, 128.3 (2 C), 127.8 (2 C), 127.5, 126.1, 90.4, 82.7, 73.5, 71.2, 67.8, 37.5, 25.6 (3 C), 17.8, 12.7, –4.7, –5.0; MS m/z (M^+) calcd 360.2120, obsd 360.2141.

Anal. Calcd for $C_{21}H_{32}O_3Si$: C, 69.95; H, 8.95. Found: C, 70.01; H, 8.92.

(2-*exo*,3-*endo*,6-*endo*)-6-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-3-methyl-1-[(phenylmethoxy)methyl]-7-oxabicyclo[2.2.1]heptan-2-ol (18). Borane·THF complex (60 mL of 1 M in THF, 60 mmol) was added to a stirred solution of **17b** (10.8 g, 30 mmol) in dry THF (120 mL) at 0 °C under N_2. The solution was stirred at 0 °C for 1 h, allowed to warm to rt, stirred for a further 1 h, carefully quenched by dropwise addition of water (15 mL), basified with 5 M NaOH (9 mL), and heated to reflux prior to the portionwise addition of 30% H_2O_2 (9 mL). The mixture was heated at reflux for 30 min, cooled, carefully quenched with saturated $NaHSO_3$ solution (90 mL), and extracted with ether. The combined extracts were washed with brine, dried, and concentrated. The residue was purified by silica gel chromatography (elution with 0.5% methanol and 25% ether in petroleum ether up to 0.9% methanol and 45% ether in petroleum ether) to give **18** (10.2 g, 90%) as a white solid: mp 81–82 °C; IR ($CHCl_3$, cm^{-1}) 3579, 3480 (br); ^{1}H NMR (300 Mhz, $CDCl_3$) δ 7.35–7.25 (m, 5 H), 4.62 (d, J = 12.0 Hz, 1 H), 4.57 (d, J = 12.0 Hz, 1 H), 4.30 (t, J

= 5.6 Hz, 1 H), 4.27 (dd, J = 9.7, 2.6 Hz, 1 H), 4.11 (dd, J = 8.4, 3.3 Hz, 1 H), 3.90 (d, J = 11.2 Hz, 1 H), 3.78 (d, J = 11.2 Hz, 1 H), 2.24 (d, J = 8.4 Hz, 1 H), 2.07–1.93 (m, 2 H), 1.46 (dd, J = 12.7, 2.6 Hz, 1 H), 1.13 (d, J = 7.2 Hz, 3 H), 0.87 (s, 9 H), 0.03 (s, 3 H), 0.01 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 137.7, 128.3 (2 C), 127.9 (2 C), 127.7, 89.5, 80.7, 77.6, 73.9, 71.1, 67.9, 49.9, 33.8, 25.7 (3 C), 17.8, 12.0, –4.9, –5.3; MS m/z (M^+ – ^{t}Bu) calcd 321.1522, obsd 321.1534.

Anal. Calcd for $C_{21}H_{34}O_4Si$: C, 66.62; H, 9.05. Found: C, 66.56; H, 9.03.

(2-*exo*,3-*endo*,6-*endo*)-6-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-2-hydroxy-3-methyl-7-oxabicyclo[2.2.1]heptane-1-methanol (19). A solution of **18** (883 mg, 2.2 mmol) in dry ether (35 mL) was added over 15 min to a stirred solution of sodium (1.01 g, 44 mmol) in liquid NH_3 (88 mL) at –78 °C under a dry atmosphere. The solution was stirred at –78 °C for 6 h, quenched with finely ground solid NH_4Cl (4.7 g, 88 mmol), and allowed to warm to rt overnight. The residue was triturated with ether, filtered (ether rinse), and concentrated. Purification by silica gel chromatography (elution with 2% methanol in ether) gave **19** (630 mg, 99%) as a white solid: mp 104–105.5 °C; IR ($CHCl_3$, cm^{-1}) 3579, 3415 (br); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.29 (t, J = 5.5 Hz, 1 H), 4.17–4.07 (m, 3 H), 3.85 (dd, J = 12.5, 7.0 Hz, 1 H), 2.78 (br s, 2 H), 2.13–2.00 (m, 1 H), 1.96 (dddd, J = 12.8, 9.7, 5.6, 1.4 Hz, 1 H), 1.46 (dd, J = 12.8, 2.7 Hz, 1 H), 1.13 (d, J = 7.2 Hz, 3 H), 0.87 (s, 9 H), 0.05 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 89.8, 80.5, 77.6, 74.6, 61.4, 50.0, 34.0, 25.7 (3 C), 17.8, 12.0, –4.9, –5.3; MS m/z (M^+ – ^{t}Bu) calcd 231.1053, obsd 231.1105.

Anal. Calcd for $C_{14}H_{28}O_4Si$: C, 58.29; H, 9.78. Found: C, 58.53; H, 9.78.

(3-*endo*,6-*endo*)-6-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-3-methyl-1-[(phenylmethoxy)methyl]-7-oxabicyclo[2.2.1]heptan-2-one (21). A mixture of tetra-*n*-propylammonium perruthenate (0.35 g, 1 mmol), *N*-methylmorpholine *N*-oxide (8.8 g, 75 mmol), **18** (18.9 g, 50 mmol), and freshly activated 3-Å molecular sieves (25 g) in dry acetonitrile (150 mL) was stirred at rt under N_2 for 20 h. The mixture was concentrated in vacuo to remove most of the acetonitrile, transferred to a silica gel column with a little CH_2Cl_2, and eluted (5–20% ether in petroleum ether) to give **21** (16.8 g, 89%) as a colorless oil: IR (neat, cm^{-1}) 1768; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.25 (m, 5 H), 4.67 (t, J = 5.4 Hz, 1 H), 4.62 (d, J = 12.1 Hz, 1 H), 4.55 (d, J = 12.1 Hz, 1 H), 4.46 (d, J = 8.9 Hz, 1 H), 3.87 (d, J = 11.7 Hz, 1 H), 3.76 (d, J = 11.7 Hz, 1 H), 2.62–2.60 (m, 1 H), 2.29 (dddd, J = 13.1, 9.0, 5.5, 1.3 Hz, 1 H), 1.66 (dd, J = 13.0, 2.1 Hz, 1 H), 1.09, (d, J = 7.3 Hz, 3 H), 0.83 (s, 9 H), 0.02 (s, 3 H), 0.00 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 209.8, 137.7, 128.3 (2 C), 127.9 (2 C), 127.6, 90.1, 78.5, 73.8, 69.9, 64.6, 47.5, 34.4, 25.5 (3 C), 17.7, 10.3, –5.0, –5.4; MS m/z (M^+ – ^{t}Bu) calcd 319.1366, obsd 319.1392.

Anal. Calcd for $C_{21}H_{32}O_4Si$: C, 66.98; H, 8.57. Found: C, 66.95; H, 8.60.

(3-*endo*,6-*endo*)-6-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-(hydroxymethyl)-3-methyl-7-oxabicyclo[2.2.1]heptan-2-one (22). A mixture of 10% Pd on C (245 mg) and **21** (2.45 g, 6.5 mmol) in ethanol (39 mL) was stirred for 6 h under an atmosphere of H_2. The mixture was then filtered through Celite, concentrated, and purified by silica gel chromatography (elution with 0.5% methanol and 25% ether in petroleum ether up to 1% methanol and 50% ether in petroleum ether) to give **22** (1.71 g, 92%) as a colorless semisolid: IR (neat, cm^{-1}) 3420 (br); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.69 (t, J = 5.6 Hz, 1 H), 4.29 (d, J = 8.9 Hz, 1 H), 4.05 (dd, J = 12.8, 5.1 Hz, 1 H), 3.91 (dd, J = 12.8, 7.7 Hz, 1 H), 2.68 (quintet, J = 7.0 Hz, 1 H), 2.28 (dddd, J = 13.1, 8.9, 5.5, 1.3 Hz, 1 H), 1.79 (dd, J = 7.7, 5.2 Hz, 1 H), 1.70 (dd, J = 13.1, 2.1 Hz, 1 H), 1.10 (d, J = 7.3 Hz, 3 H), 0.55 (s, 9 H), 0.05 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 210.7, 90.5, 78.7, 70.7, 58.6, 47.9, 34.8, 25.5 (3 C), 17.8, 10.3, –5.0, –5.3; MS m/z (M^+ – ^{t}Bu) calcd 229.0896, obsd 229.0896.

Anal. Calcd for $C_{14}H_{26}O_4Si$: C, 58.70; H, 9.15. Found: C, 58.93; H, 9.04.

(3-*endo*,6-*endo*)-6-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-3-methyl-2-oxo-7-oxabicyclo[2.2.1]heptane-2-carboxaldehyde (20). A mixture of tetra-*n*-propylammonium perruthenate (141 mg, 0.4 mmol), *N*-methylmorpholine *N*-oxide (0.94 g, 8 mmol), **22** (1.15 g, 4 mmol), and freshly activated 3-Å molecular sieves (2 g) in dry CH_2Cl_2 (20 mL) was stirred at rt under N_2 for 1 h. The total reaction mixture was then transferred to a Florisil column and eluted with ether to give **20** as a colorless oil. This keto aldehyde was utilized directly without further purification.

[(4-Methoxyphenoxy)methyl]diphenylphosphine (26). Potassium hexamethyldisilazide (66 mL of 0.5 M in toluene, 33 mmol) was added dropwise over 15 min to a stirred at –78 °C for 30 min, allowed to warm to rt, stirred for a further 16 h, quenched with saturated NH_4Cl solution, and extracted with ether. The combined extracts were dried, concentrated, and purified by silica gel chromatography (elution with 5–10% ether in petroleum ether) to give **26** (7.96 g, 82%) as a white solid: mp 78–78.5 °C; IR ($CHCl_3$, cm^{-1}) 1581, 1500, 1478, 1463, 1432, 1220; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55–7.50 (m, 4 H), 7.40–7.35 (m, 6 H), 6.95–6.83 (m, 4 H), 4.67 (d, $^2J_{C,P}$ = 4.9 Hz, 2 H), 3.78 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 154.2, 153.6 (d, $^3J_{C,P}$ = 6 Hz), 136.0 (d, $^1J_{C,P}$ = 11 Hz, 2 C), 133.1 (dd, $^2J_{C,P}$ = 18 Hz, 4 C), 128.9 (2 C), 128.5 (dd, $^3J_{C,P}$ = 7 Hz, 4 C), 115.9 (2 C), 114.6 (2 C), 69.6 (dt, $^1J_{C,P}$ = 9 Hz), 55.7; MS m/z (M^+) calcd 322.1122, obsd 322.1141.

Anal. Calcd for $C_{20}H_{19}O_2P$: C, 74.52; H, 5.94. Found: C, 74.52; H, 5.96.

Bis[(4-methoxyphenoxy)methyl]diphenylphosphonium Chloride (27). A mixture of **26** (1.13 g, 3.5 mmol) and **25** (1.38 g, 7 mmol, containing ~15 mol % of 1,4-dimethoxybenzene) in dry benzene (14 mL) was heated at reflux for 4 days under N_2. The reaction mixture was concentrated in vacuo, triturated with dry ether, and filtered to give **27** (1.47 g, 74%) as a white solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13–8.03 (m, 4 H), 7.75–7.67 (m, 2 H), 7.63–7.55 (m, 4 H), 6.97 (d, J = 9.1 Hz, 4 H), 6.67 (d, J = 9.1 Hz, 4 H), 6.27 (d, $^2J_{C,P}$ = 4.5 Hz, 4 H), 3.64 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 155.0 (2 C), 151.4 (d, $^3J_{C,P}$ = 11 Hz, 2 C), 135.0 (dd, $^4J_{C,P}$ = 2 Hz, 2 C), 134.1 (dd, $^3J_{C,P}$ = 10 Hz, 4 C), 129.8 (dd, $^2J_{C,P}$ = 13 Hz, 4 C), 116.4 (4 C), 114.5 (4 C), 114.4 (d, $^1J_{C,P}$ = 83 Hz, 2 C), 61.5 (dt, $^1J_{C,P}$ = 62 Hz, 2 C), 55.4 (q, 2 C).

[(4-Methoxyphenyl)methyl]diphenylphosphine Oxide (28). Hydrogen peroxide (2.4 mL of 30%) was added portionwise during a 15 min to a solution of **26** (3.87 g, 12 mmol) in THF (36 mL) at 20 °C. After 30 min at rt, the reaction mixture was carefully quenched with saturated $NaHSO_3$ solution (20 mL) and extracted with ether. The combined ethereal extracts were dried and concentrated to give **28** (4.0 g, 98%) as a white solid: mp 79.5–81 °C; IR ($CHCl_3$, cm^{-1}) 1587, 1500, 1462, 1436, 1210, 1175; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90–7.83 (m, 4 H), 7.58–7.43 (m, 6 H) 6.85–6.77 (m, 4 H), 4.68 (d, $^2J_{C,P}$ = 7.7 Hz, 2 H), 3.73 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 154.7, 152.8 (d, $^3J_{C,P}$ = 12 Hz), 132.2 (dd, $^4J_{C,P}$ = 3 Hz, 2 C), 131.5 (dd, $^3J_{C,P}$ = 10 Hz, 4 C), 130.8 (d, $^1J_{C,P}$ = 101 Hz, 2 C), 128.5 (dd, $^2J_{C,P}$ = 12 Hz, 4 C), 115.5 (2 C), 114.7 (2 C), 66.9 (dt, $^1J_{C,P}$ = 88 Hz), 55.6; MS m/z (M^+) calcd 338.1072, obsd 338.1114.

Anal. Calcd for $C_{20}H_{19}O_3P$: C, 71.00; H, 5.66. Found: C, 70.75; H, 5.66.

(1*E*,3-*endo*,6-*endo*)-6-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-[2-(4-methoxyphenoxy)ethenyl]-3-methyl-7-oxabicyclo[2.2.1]heptan-2-one (23) and Its 1*Z*-Isomer 24. Methyllithium–lithium bromide complex (5.9 mL, 1.5 M in ether, 8.8 mmol) was added to a stirred suspension of **29** (3.83 g, 8.8 mmol) in dry THF (21 mL) at –78 °C under N_2. The mixture was stirred at –78 °C for 10 min and at 0 °C for 10 min before addition of aldehyde **20** (4 mmol unpurified) as a solution in dry THF (32 mL). The reaction mixture was stirred at 0 °C for 3 h, quenched with water, and extracted with ether. The combined extracts were dried, concentrated in vacuo, filtered through a short pad of silica gel (elution with ether), and purified by flash silica gel chromatography (elution with 5–10% ethyl acetate in petroleum ether) to give **23** (338 mg, 21%). Further elution with 10–20% ethyl acetate in petroleum ether furnished 346 mg (21%) of **24**.

For **23**: pale yellow oil: IR (neat, cm^{-1}) 1766, 1675; ^{1}H NMR (300 MHz, C_6D_6) δ 7.43 (d, J = 12.5 Hz, 1 H), 6.97–6.90 (m, 2 H), 6.62–6.55 (m, 2 H), 5.73 (d, J = 12.5 Hz, 1 H), 4.15 (t, J = 5.5 Hz, 1 H), 3.97 (br d, J = 8.9 Hz, 1 H), 3.22 (s, 3 H), 2.40 (quintet, J = 7.0 Hz, 1 H), 1.97–1.87 (m, 1 H), 1.40 (dd, J = 12.9, 2.3 Hz, 1 H), 0.90 (d, J = 8.6 Hz, 3 H), 0.88 (s, 9 H), 0.00 (s, 3 H), –0.08 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 209.0, 156.3, 151.2, 148.6, 118.9 (2 C), 115.1 (2 C), 103.2, 88.0, 78.0, 77.4, 55.0, 48.0, 35.1, 25.7 (3 C), 18.0, 10.5, –4.88, –4.91; MS m/z (M^+) calcd 404.2019, obsd 404.2010.

For **24**: pale yellow oil; IR (neat, cm^{-1}) 1763, 1669; ^1H NMR (300 MHz, C_6D_6) δ 6.87–6.82 (m, 2 H), 6.62–6.55 (m, 2 H), 6.32 (d, J = 6.6 Hz, 1 H), 5.17 (d, J = 6.6 Hz, 1 H), 4.75 (br d, J = 8.8 Hz, 1 H), 4.23 (t, J = 5.8 Hz, 1 H), 3.22 (s, 3 H), 2.45 (quintet, J = 7.2 Hz, 1 H), 2.13–2.03 (m, 1 H), 1.46 (dd, J = 12.9, 2.0 Hz, 1 H), 0.95 (d, J = 5.9 Hz, 3 H), 0.94 (s, 9 H), 0.11 (s, 3 H), –0.01 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 208.9, 156.4, 151.8, 148.4, 118.7 (2 C), 115.0 (2 C), 101.5, 87.4, 78.2, 75.3, 55.1, 46.9, 35.3, 25.8 (3 C), 18.1, 10.7, –4.7, –4.9; MS m/z (M^+) calcd 404.2019, obsd 404.2003.

(1*E*,3-*exo*,6-*endo*)-6-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-[2-(4-methoxyphenoxy)ethenyl]-3-methyl-3-(phenylthio)-7-oxabicyclo[2.2.1]heptan-2-one (30). Potassium hexamethyldisilazide (3.6 mL of 0.5 M in toluene, 1.8 mmol) was added to a stirred solution of **23** (607 mg, 1.5 mmol) in dry THF (7.5 mL) at –78 °C under N_2, stirred for 5 min, and treated with a solution of diphenyl disulfide (459 mg, 2.1 mmol) in dry THF (7.5 mL). Stirring was continued for 30 min at –78 °C and at 0 °C for 1.5 h prior to quenching with water and extraction with ether. The combined organic extracts were washed with brine, dried, concentrated, and purified by silica gel chromatography (elution with 5–10% ether in petroleum ether) to give **30** (542 mg, 70%) as a light yellow gum: IR (neat, cm^{-1}) 1754, 1661; ^1H NMR (300 MHz, C_6D_6) δ 7.67–7.60 (m, 2 H), 7.27 (d, J = 12.5 Hz, 1 H), 7.03–6.87 (m, 5 H), 6.65–6.57 (m, 2 H), 5.66 (d, J = 12.5 Hz, 1 H), 4.36 (d, J = 5.5 Hz, 1 H), 3.93 (dd, J = 7.2, 1.1 Hz, 1 H), 3.24 (s, 3 H), 1.94 (ddd, J = 13.3, 9.0, 5.8 Hz, 1 H), 1.44 (dd, J = 13.3, 2.1 Hz, 1 H), 1.28 (s, 3 H), 0.83 (s, 9 H), –0.04 (s, 3 H), –0.13 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 205.3, 156.4, 151.0, 149.0, 137.8 (2 C), 131.5, 129.3, 128.8 (2 C), 119.0 (2 C), 115.1 (2 C), 102.8, 88.5, 83.3, 77.3, 58.3, 55.1, 36.8, 25.7 (3 C), 18.6, 18.0, –4.9, –5.0; MS m/z (M^+ – ^{t}Bu) calcd 455.1348, obsd 455.1358.

(1*E*,2-*endo*,3-*exo*,6-*endo*)-2-(4,5-Dihydro-2-furanyl)-1-[2-(4-methoxyphenoxy)ethenyl]-3-methyl-3-(phenylthio)-7-oxabicyclo[2.2.1]heptane-2,6-diol (31). *tert*-Butyllithium (5.9 mL of 1.7 M, 10 mmol) was added dropwise to a stirred solution of freshly distilled 2,3-dihydrofuran (1.40 g, 20 mmol) in dry THF (0.41 mL, 361 mg, 5 mmol) at –78 °C under N_2. The reaction mixture was stirred for 20 min at –78 °C and at 0 °C for 20 min. The resulting suspension was dissolved in a mixture of dry THF (5 mL) and dry TMEDA (10 mL), and after 5 min a solution of **30** (1.28 g, 2.5 mmol) in dry THF (5 mL) was introduced at 0 °C. The reaction mixture was stirred at this temperature for 2 h, quenched with water, and extracted with ether. The combined organic phases were washed with water, dried, concentrated, and purified by silica gel chromatography (elution with 0.5% methanol and 25% ether in petroleum ether up to 1.5% methanol and 75% ether in petroleum ether) to give **31** (844 mg, 72%) as a light yellow gum: IR ($CHCl_3$, cm^{-1}) 3490 (br), 1665; ^1H NMR (300 MHz, C_6D_6) δ 7.60–7.53 (m, 2 H), 7.30 (d, J = 12.5 Hz, 1 H), 7.03–6.95 (m, 5 H), 6.70–6.63 (m, 2 H), 6.10 (d, J = 12.5 Hz, 1 H), 5.36 (t, J = 2.5 Hz, 1 H), 4.63 (br s, 1 H), 4.52 (d, J = 6.2 Hz, 1 H), 4.40–4.35 (m, 1 H), 4.13–3.90 (m, 3 H), 3.27 (s, 3 H), 2.50–2.25 (m, 2 H), 2.07 (ddd, J = 13.4, 10.6, 6.4 Hz, 1 H), 1.55 (dd, J = 13.4, 4.2 Hz, 1 H), 1.37 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 156.1, 151.5, 145.7, 138.0 (2 C), 134.8, 129.2, 129.1, 128.9 (2 C), 118.5 (2 C), 115.1 (2 C), 109.1, 100.8, 87.9, 84.6, 84.5, 82.5, 69.1, 63.9, 55.1, 35.6, 30.6, 21.3; MS m/z (M^+) calcd 468.1607, obsd 468.1625.

(1*E*,2-*endo*,3-*exo*,6-*endo*)-6-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-2-(4,5-dihydro-2-furanyl)-1-[2-(4-methoxyphenoxy)ethenyl]-3-methyl-3-(phenylthio)-7-oxabicyclo[2.2.1]heptan-2-ol (32). *tert*-Butylchlorodiphenylsilane (110 mg, 0.4 mmol) was added in one portion to a stirred solution of **31** (94 mg, 0.2 mmol) and imidazole (34 mg, 0.5 mmol) in dry DMF (0.08 mL) at rt. The mixture was stirred under N_2 for 20 h, poured into water, and extracted with ether. The combined organic layers were washed with brine, dried, concentrated, and purified by silica gel chromatography (elution with 0.25% methanol and 12% ether in petroleum ether up to 0.5% methanol and 25% ether in petroleum ether) to give **32** (75 mg, 53%) as a colorless oil: IR ($CHCl_3$, cm^{-1}) 3380 (br); ^1H NMR (300 MHz, C_6D_6) δ 7.73–7.65 (m, 2 H), 7.63–7.55 (m, 4 H), 7.23–7.07 (m, 7 H), 7.03–6.95 (m, 3 H), 6.95–6.90 (m, 2 H), 6.67–6.60 (m, 2 H), 6.45 (s, 1 H), 6.02 (d, J = 12.4 Hz, 1 H), 5.63 (t, J = 2.5 Hz, 1 H), 4.56 (d, J = 5.9 Hz, 1 H), 4.43–4.33 (m, 2 H), 4.26 (q, J = 8.7 Hz, 1 H), 3.28 (s, 3 H), 2.44 (td, J = 9.9, 2.2 Hz, 2 H), 1.65–1.55 (m, 1 H), 1.51 (s, 3 H), 1.42 (dd, J = 13.5, 3.6 Hz, 1 H), 1.07 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 159.3, 155.9, 151.6, 145.9, 138.1 (2 C), 136.3 (2 C), 136.2 (2 C), 135.1, 132.4, 131.6, 130.63, 130.57, 128.7 (2 C), 128.6, 128.2 (2 C), 128.2 (2 C), 118.4 (2 C), 115.0 (2C), 108.0, 99.5, 88.3, 85.4, 84.6, 84.0, 69.8, 64.0, 55.1, 36.1, 29.7, 26.9 (3 C), 22.4, 19.1; MS m/z (M^+) calcd 706.2784, obsd 706.2791.

(3α,4β,7β,9α,10α,11aα)-7-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-2,3,3a,4,7,8,9,10,11,11a-decahydro-4-(4-methoxyphenoxy)-10-methyl-10-(phenylthio)-6,9-epoxycyclodeca[*b*]furan-11-one (33) and (3aα,4β,7β,9α,10α,11aβ)-7-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-2,3,3a,4,7,8,9,10,11,11a-decahydro-4-(4-methoxyphenoxy)-10-methyl-10-(phenylthio)-6,9-epoxycyclodeca[*b*]furan-11-one (34). A stirred mixture of **32** (21 mg, 0.03 mmol) and anhydrous K_2CO_3 (25 mg, 0.18 mmol) in degassed anhydrous toluene (0.6 mL) was heated at gentle reflux under N_2 for 5 h. The total reaction mixture was purified by alumina chromatography (activity III, elution with 5–70% ether in petroleum ether) to give pure **33** (4 mg, 19%) and **34** (9 mg, 43%).

For **33**: colorless gum; IR (neat, cm^{-1}) 1703; ^1H NMR (300 MHz, C_6D_6 at 350 K) δ 7.75–7.65 (m, 4 H), 7.53–7.49 (m, 2 H), 7.25–7.13 (m, 6 H), 7.07–6.95 (m, 3 H), 6.80–6.67 (m, 4 H), 6.17 (d, J = 7.0 Hz, 1 H), 5.90 (dd, J = 7.7, 3.2 Hz, 1 H), 5.19 (dd, J = 7.7, 1.6 Hz, 1 H), 4.52–4.45 (m, 2 H), 4.18 (dd, J = 8.1, 6.2 Hz, 1 H), 3.91 (q, J = 7.7 Hz, 1 H), 3.42 (s, 3 H), 3.01 (dtd, J = 12.5, 6.8, 3.4 Hz, 1 H), 2.57–2.45 (m, 1 H), 2.45 (ddd, J = 12.6, 8.1, 6.4 Hz, 1 H), 2.25–2.15 (m, 1 H), 1.76 (ddd, J = 12.5, 9.1, 8.4 Hz, 1 H), 1.13 (s, 3 H), 1.12 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 213.2, 156.0, 154.0, 152.4, 136.1 (2 C), 135.9 (2 C), 134.0, 133.4, 132.3, 130.2 (2 C), 129.3 (2 C), 129.0, 128.8, 128.3 (2 C), 128.1 (2 C), 128.0, 117.5 (2 C), 115.0 (2 C), 102.6, 84.7, 71.5, 70.3, 70.1, 68.7, 55.2, 33.5, 27.0 (3 C), 24.2, 21.0, 19.3 (2 aliphatic C not observed); MS m/z (M^+) calcd 706.2784, obsd 706.2786.

For **34**: colorless gum; IR (neat, cm^{-1}) 1716; ^1H NMR (300 MHz, C_6D_6) δ 7.63–7.55 (m, 6 H), 7.25–7.10 (m, 6 H), 7.00–6.95 (m, 3 H), 6.80–6.70 (m, 4 H), 5.22 (t, J = 1.5 Hz, 1 H), 5.18 (d, J = 7.5 Hz, 1 H), 4.88 (ddd, J = 3.0, 2.5, 1.5 Hz, 1 H), 4.68 (br dddd, J = 9.5, 8.5, 7.5, 3.0 Hz, 1 H), 4.47 (dddd, J = 9.5, 7.0, 2.5, 1.5 Hz, 1 H), 4.32 (dd, J = 8.0, 5.0 Hz, 1 H), 4.29 (ddd, J = 9.0, 8.0, 6.5 Hz, 1 H), 4.01 (td, J = 8.0, 4.0 Hz, 1 H), 3.34 (s, 3 H), 2.16 (dddd, J = 11.5, 9.0, 8.5, 8.0 Hz, 1 H), 1.86 (dddd, J = 11.5, 9.5, 6.5, 4.0 Hz, 1 H), 1.85 (ddd, J = 13.5, 7.0, 5.0 Hz, 1 H), 1.70 (ddd, J = 13.5, 9.0, 8.0 Hz, 1 H), 1.36 (s, 3 H), 1.01 (s, 9 H), ^{13}C NMR (75 MHz, $CDCl_3$) ppm 207.1, 155.4, 154.8, 152.3, 137.0 (2 C), 136.1 (2 C), 136.0 (2 C), 133.8, 133.4, 131.6, 130.2 (2 C), 129.0 (2 C), 128.9, 128.09 (2 C), 128.07 (2 C), 117.7 (2 C), 115.1 (2 C), 102.4, 83.3, 83.1, 75.3, 70.9, 69.5, 64.7, 55.2, 45.8, 33.1, 29.4, 26.9 (3 C), 21.5, 19.2; MS m/z (M^+) calcd 706.2784, obsd 706.2781.

(1*Z*,3-*exo*,6-*endo*)-6-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-[2-(4-methoxyphenoxy)ethenyl]-3-methyl-3-(phenylthio)-7-oxabicyclo[2.2.1]heptan-2-one (35). Potassium hexamethyldisilazide (12 mL of 0.5 M in toluene, 6 mmol) was added to a stirred solution of **34** (2.02 g, 5 mmol) in dry THF (25 mL) at –78 °C under N_2. The solution was stirred for 5 min and treated with a solution of diphenyl disulfide (1.53 g, 7 mmol) in dry THF (25 mL). Stirring was continued for 1 h at –78 °C and at 0 °C for 2 h prior to quenching with water and extraction with ether. The combined extracts were washed with brine, dried, concentrated, and purified by silica gel chromatography (elution with 5–25% ether in petroleum ether) to give **35** (2.04 g, 80%) as a light yellow gum: IR (neat, cm^{-1}) 1756, 1658; ^1H NMR (300 MHz, C_6D_6) δ 7.70–7.63 (m, 2 H), 7.03–6.95 (m, 3 H), 6.90–6.83 (m, 2 H), 6.63–6.57 (m, 2 H), 6.31 (d, J = 6.6 Hz, 1 H), 5.14 (d, J = 6.6 Hz, 1 H), 4.77 (dt, J = 8.7, 1.5 Hz, 1 H), 4.39 (dd, J = 5.6, 0.9 Hz, 1 H), 3.23 (s, 3 H), 2.09 (ddd, J = 13.3, 9.0, 5.8 Hz, 1 H), 1.49 (dd, J = 13.2, 1.9 Hz, 1 H), 1.34 (s, 3 H), 0.89 (s, 9 H), 0.09 (s, 3 H), –0.04 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 205.6, 156.4, 151.7, 148.5, 137.8 (2 C), 131.8, 129.2, 128.8 (2 C), 118.7 (2 C), 115.0 (2 C), 101.2, 88.1, 83.2, 75.1, 57.4, 55.1, 37.0, 25.8 (3 C), 19.0, 18.1, –4.8, –5.0; MS m/z (M^+) calcd 512.2053, obsd 512.2063.

(1*Z*,2-*endo*,3-*exo*,6-*endo*)-2-(4,5-Dihydro-2-furanyl)-1-[2-(4-methoxyphenoxy)ethenyl]-3-methyl-3-(phenylthio)-7-oxabicyclo[2.2.1]heptane-2,6-diol (36a). *tert*-Butyllithium (9.4 mL of 1.7 M, 16 mmol) was added dropwise to a stirred solution of freshly distilled 2,3-dihydrofuran (2.42 mL, 2.24 g, 32 mmol) in dry THF (0.65 mL, 577 mg, 8 mmol) at –78 °C under N_2. The

reaction mixture was stirred for 20 min at −78 °C and at 0 °C for 20 min. The resulting suspension was dissolved in a mixture of dry THF (8 mL) and dry TMEDA (16 mL) and after 5 min a solution of **35** (2.04 g, 4 mmol) in dry THF (8 mL) was added at 0 °C. The reaction mixture was stirred at this temperature for 3 h, quenched with water, and extracted with ether. The combined extracts were washed with water, dried, concentrated, and purified by silica gel chromatography (elution with 0.5% methanol and 25% ether in petroleum ether up to 2% methanol in ether) to give **36a** (1.15 g, 62%) as a light yellow gum: IR (neat, cm^{-1}) 3417 (br), 1660; ^1H NMR (300 MHz, C_6D_6) δ 7.67–7.60 (m, 2 H), 7.03–6.95 (m, 3 H), 6.73–6.65 (m, 2 H), 6.60–6.55 (m, 2 H), 6.30 (d, J = 6.9 Hz, 1 H), 5.58 (br s, 1 H), 5.51 (d, J = 6.9 Hz, 1 H), 5.47 (t, J = 2.5 Hz, 1 H), 4.65 (br d, J = 11.0 Hz, 1 H), 4.60 (d, J = 6.2 Hz, 1 H), 4.35 (br s, 1 H), 4.20 (t, J = 9.3 Hz, 2 H), 3.24 (s, 3 H), 2.55–2.33 (m, 2 H), 2.08 (ddd, J = 13.5, 10.9, 6.2 Hz, 1 H), 1.67 (dd, J = 13.5, 3.9 Hz, 1 H), 1.46 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 156.5, 151.0, 143.3, 138.1 (2 C), 135.0, 128.9, 128.8 (2 C), 128.7, 118.4 (2 C), 115.0 (2 C), 109.6, 99.3, 88.6, 85.7, 84.8, 80.5, 69.6, 64.3, 55.1, 35.0, 30.2, 21.7; MS m/z (M^+) calcd 468.1607, obsd 468.1607.

(1*Z*,2-*endo*,3-*exo*,6-*endo*)-6-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-2-(4,5-dihydro-2-furanyl)-1-[2-(4-methoxyphenoxy)ethenyl]-3-methyl-3-(phenylthio)-7-oxabicyclo[2.2.1]heptan-2-ol (36b). ***tert*-Butylchlorodiphenylsilane** (1.10 g, 4 mmol) was added in one portion to a stirred solution of **36a** (0.94 g, 2 mmol) and imidazole (340 mg, 5 mmol) in dry DMF (1.0 mL) at rt. The mixture was stirred under N_2 for 16 h, poured into water, and extracted with ether. The combined extracts were washed with brine, dried, concentrated, and purified by silica gel chromatography (elution with 0.25% methanol and 12% ether in petroleum ether up to 1% methanol and 50% ether in petroleum ether) to give **36b** (0.42 g, 30%) as a colorless oil; IR (neat, cm^{-1}) 3390 (br), 1670; ^1H NMR (300 MHz, C_6D_6) δ 7.77–7.67 (m, 2 H), 7.65–7.60 (m, 4 H), 7.20–7.05 (m, 6 H), 7.03–6.95 (m, 3 H), 6.65–6.55 (m, 4 H), 6.34 (s, 1 H), 6.20 (d, J = 6.9 Hz, 1 H), 5.60 (t, J = 2.4 Hz, 1 H), 5.34 (d, J = 6.9 Hz, 1 H), 5.04 (dd, J = 10.2, 3.5 Hz, 1 H), 4.50 (d, J = 5.9 Hz, 1 H), 4.45–4.27 (m, 2 H), 3.25 (s, 3 H), 2.53–2.45 (m, 2 H), 1.67–1.57 (m, 1 H), 1.57 (s, 3 H), 1.39 (dd, J = 13.0, 3.9 Hz, 1 H), 1.09 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 159.5, 156.0, 151.9, 144.5, 138.1 (2 C), 136.6 (2 C), 136.4 (2 C), 135.4, 132.7, 132.6, 130.39, 130.37, 129.8 (2 C), 128.5, 128.1 (4 C), 118.4 (2 C), 114.8 (2 C), 107.5, 99.3, 88.5, 85.2, 84.8, 81.6, 69.6, 63.9, 55.1, 36.0, 30.0, 27.0 (3 C), 22.2, 19.1; MS m/z (M^+) calcd 706.2784, obsd 706.2775.

(3a*α*,4*α*,7*β*,9*α*,10*α*,11a*β*)-7-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-2,3,3a,4,7,8,9,10,11,11a-decahydro-4-(4-methoxyphenoxy)-10-methyl-10-(phenylthio)-6,9-epoxycyclodeca[*b*]furan-11-one (37). A stirred mixture of **36b** (184 mg, 0.26 mmol) and anhydrous K_2CO_3 (180 mg, 1.3 mmol) in degassed anhydrous decalin (5.2 mL) was heated at gentle reflux under N_2 for 1 h. The total reaction mixture was purified by alumina chromatography (activity III, elution with 5–80% ether in petroleum ether) to give **37** (113 mg, 61%) as a colorless gum: IR ($CHCl_3$, cm^{-1}) 1716; ^1H NMR (300 MHz, C_6D_6) δ 7.62–7.58 (m, 4 H), 7.55–7.53 (m, 2 H), 7.23–7.10 (m, 6 H), 7.00–6.95 (m, 3 H), 6.90–6.85 (m, 2 H), 6.80–6.73 (m, 2 H), 5.42 (dd, J = 6.6, 1.6 Hz, 1 H), 4.93 (quintet, J = 8.6 Hz, 1 H), 4.47 (d, J = 7.9 Hz, 1 H), 4.33 (ddd, J = 9.3, 7.6, 1.7 Hz, 1 H), 4.30–4.21 (m, 2 H), 4.20 (dd, J = 7.8, 5.9 Hz, 1 H), 3.87 (td, J = 8.0, 2.7 Hz, 1 H), 3.37 (s, 3 H), 2.44 (dddd, J = 12.0, 7.6, 6.0, 2.6 Hz, 1 H), 1.70 (ddd, J = 13.1, 7.3, 5.9 Hz, 1 H), 1.69–1.59 (m, 1 H), 1.55 (ddd, J = 12.9, 9.3, 8.0 Hz, 1 H), 1.25 (s, 3 H), 1.09 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 205.9, 160.0, 154.8, 152.7, 137.3 (2 C), 136.0 (2 C), 135.8 (2 C), 133.6, 133.3, 131.3, 130.3 (2 C), 129.1 (2 C), 129.0, 128.2 (2 C), 128.1 (2 C), 118.4 (2 C), 114.9 (2 C), 99.7, 86.2, 83.2, 78.8, 71.0, 69.4, 64.1, 55.2, 47.3, 33.8, 33.0, 27.0 (3 C), 21.2, 19.3; MS m/z (M^+) calcd 706.2784, obsd 706.2771.

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Supplementary Material Available: 300-MHz ^1H NMR spectra of **23**, **24**, **27**, and **30–37**, as well as the final calculated (MM3) atomic coordinates for A–D as they appear in Figure 2 (16 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Tertiary Carbinamines by Addition of Organocerium Reagents to Nitriles and Ketimines

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Organocerium reagents, prepared by reaction of aromatic and primary and secondary alkyllithium reagents with anhydrous cerium chloride, add to nitriles twice to give tertiary carbinamines in often excellent yields. Addition of *n*-$BuCeCl_2$ to acetophenone is about 4 times faster than addition to benzonitrile. Only 1,2-diaddition is observed in the reaction of $MeCeCl_2$ with cinnamonitrile. The species formed in the double addition of organocerium reagents to nitriles are sufficiently basic to generate a benzyne intermediate by abstraction of an aromatic proton and nucleophilic enough to undergo an intramolecular Chichibabin reaction. Reaction of N-unsubstituted ketimines or their lithium salts with organocerium reagents permits the synthesis of tertiary carbinamines with three different groups on the tertiary carbon center.

Introduction

Tertiary carbinamines (amines in which one bond from nitrogen is to a tertiary carbon atom) are usually prepared by addition of carbocations to nitriles (the Ritter reaction[1]). This reaction requires strongly acidic conditions which may cause skeletal rearrangements and which may not be compatible with other groups present in the substrate. Hydrolysis of the initially formed acyl derivatives of tertiary carbinamines is often difficult, necessitating strongly acidic or basic conditions. Another route to these amines is the reduction of tertiary nitro compounds.[2] Treatment

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