earlier,[15] bp 41 °C (0.1 mmHg) (lit.[15] bp 75–76.5 °C (0.25 mmHg)). Magnesium turnings were purchased from Fisons, Birmingham, England. ^{13}C NMR were recorded on a Bruker AM 250 spectrometer operating at 63.86 MHz in a septum-sealed 8.4-mm tube contained in a 10-mm tube with CD_3OD in the annular space. Electron microscopy was carried out with JEOL JEM 200FX instrument in SM mode operating at 2000 KV with a spot size of 5000A.

The following procedure is typical for the synthesis of benzylic Grignard reagents. Magnesium metal turnings (16 g) were transferred to a Schlenk tube (ca. 300-mL capacity, 60 mm o.d.) together with a Teflon-coated stirrer bar (50 mm). The system was sealed with a 250-mL pressure-equalized dropping funnel and purged with purified N_2. Vigorous mechanical stirring was carried out for 2 day. After this time much of the magnesium was finely divided and dark gray in color. Sufficient Et_2O (freshly distilled off sodium benzophenone ketyl) was run in to cover the magnesium. The solution was cooled to 0 °C under a nitrogen atmosphere, and a solution of 1-chloro-1-phenylethane (**4a**) (13.2 g, 0.1 mol) in dry Et_2O (150 cm^3) was added dropwise to the center of the vortex created by the stirrer. The addition was complete after 3.5 h, and stirring was then continued at 0 °C for a further 2.5 h. The clear solution was filtered by cannula into another Schlenk tube of the same dimensions and made up to 250 cm^3. The stock solution was titrated as 0.38 M (95%, including transfer losses) against 0.1 M HCl and phenolphthalein, and stored at 0 °C prior to use. Samples prepared and stored in this was have a shelf life of at least several weeks. [NB. The activated magnesium may be pyrophoric and create a flare which is hazardous to the eyes if exposed to air. This has never occurred with our samples even when deliberately brought into contact with the air. Nevertheless, due caution should always be observed in the handling of activated magnesium.]

Acknowledgment. K. V. B. thanks SERC and ICI Organics Division for a CASE studentship. We are indebted to Professor R. J. P. Williams for arranging access to an optical microscope.

Unsymmetrical Oxidative Cleavage of Cyclic Ketones. Conversion to ω-Ethoxycarbonyl Aldoximes under Alkaline Conditions[1]

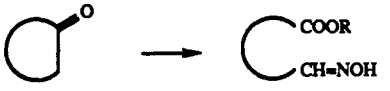
Cornelis M. Moorhoff and Leo A. Paquette*

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

Received May 30, 1990

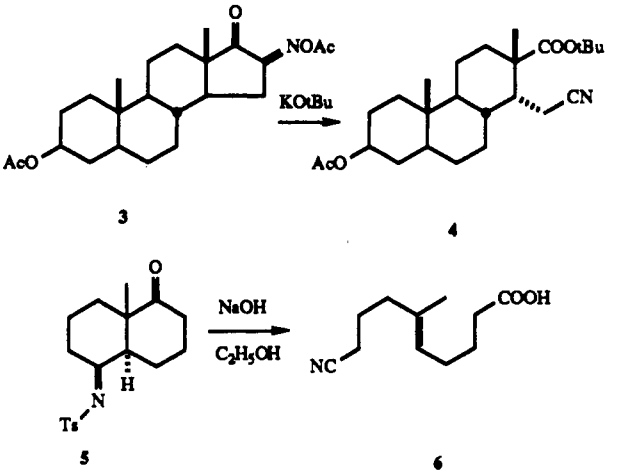
A useful procedure for effecting the direct unsymmetrical cleavage of an enolizable cyclic ketone to an oximino ester has been developed. The process begins by deprotonation with LDA and is followed by the addition of ethyl nitrite in THF at low temperature. Rapid reaction customarily ensues with resultant overall nitrosolysis. Of particular importance is the facile application of this procedure to substrate ketones that are otherwise sensitive to acidic environments. This feature is exemplified in particular in the case of *syn*- and *anti*-sesquinorbornenones **34** and **35**, access to which is described for the first time. Since the entire process is executed in a single flask, the methodology is very convenient to implement in practice.

To the extent that predictable regiochemistry results, the oxidative cleavage of ketones to oximino esters (**1** → **2**) holds considerable synthetic interest since such a process results in the simultaneous conversion of adjoining carbonyl and methylene groups into two differently oxidized terminal carbon atoms. While the Baeyer–Villiger[2] and



1 **2**

Beckmann rearrangements[3] constitute chemical operations that result in functional group transmutations of a similar type, the oxidation level of the methylene center is only nominally affected by these changes, and additional steps are required to arrive at an aldehyde or aldehyde equivalent. A few exceptions typified by the behavior of **3**[4] and **5**[5] (both reactions can be classified as Grob fragmentations[6]) are known that lead to cyano carboxylates.



3 **4**

5 **6**

In actuality, the feasibility of the transform **1** → **2** has been intensively scrutinized by Rogic and co-workers for reaction conditions that are quite acidic.[7] For example, they found that exposure of cyclohexanone to nitrosyl

(1) Part 53 of the series Isodicyclopentadiones and Related Molecules. For part 52, see: Sivik, M. R.; Rogers, R. D.; Paquette, L. A. *J. Organomet. Chem.*, in press. Part 51: Paquette, L. A.; Bauer, W., Sivik, M. R.; Buhl, M.; Feigel, M.; Schleyer, P. v. *J. Am. Chem. Soc.*, in press.

(2) (a) Hassall, C. H. *Org. React.* **1957**, *9*, 53. (b) Krow, G. R. *Tetrahedron* **1981**, *37*, 2697. (c) Bentley, P. H. *Chem. Soc. Rev.* **1973**, *2*, 29. (d) Plesnicar, B. In *Oxidation in Organic Chemistry, Part C*; Trahanovsky, W. S., Ed.; Academic Press: New York, 1978; pp 254–262.

(3) (a) Gawley, R. E. *Org. React.* **1988**, *35*, 1. (b) Krow, G. R. *Tetrahedron* **1981**, *37*, 1283.

(4) Kohen, F. *Chem. Ind. (London)* **1966**, 1378.

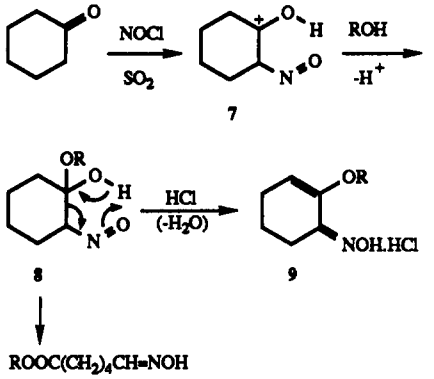
(5) (a) Eisele, W.; Grob, C. A.; Renk, E.; von Tschammer, H. *Helv. Chim. Acta* **1968**, *51*, 816. (b) Grob, C. A.; von Tschammer, H. *Ibid.* **1968**, *51*, 1082. (c) Artz, K. G.; Grob, C. A. *Ibid.* **1968**, *51*, 807.

(6) Becker, K. B.; Grob, C. A. In *Chem. Double-Bond Functional Groups*, John Wiley: Chichester, England, 1977; Vol. 2, pp 653–723.

(7) (a) Rogić, M. M.; Van Peppen, J. F.; Klein, K. P.; Demmin, T. R. *J. Org. Chem.* **1974**, *39*, 3424. (b) Rogić, M. M.; Vitrone, J.; Swerdloff, M. D. *J. Am. Chem. Soc.* **1975**, *97*, 3848. (c) Rogić, M. M.; Tetenbaum, M. T.; Swerdloff, M. D. *J. Org. Chem.* **1977**, *42*, 2748. (d) Rogić, M. M.; Vitrone, J.; Swerdloff, M. D. *J. Am. Chem. Soc.* **1977**, *99*, 1156.

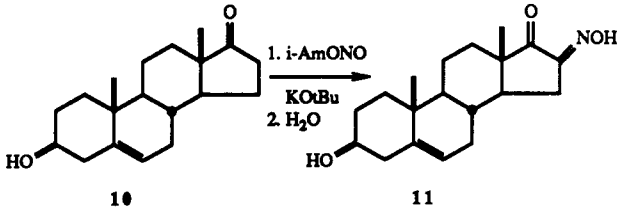
0022-3263/91/1956-0703$02.50/0

chloride in liquid sulfur dioxide containing methanol, ethanol, or isopropyl alcohol gave rise to the corresponding alkyl 6-oximinohexanoates. The cleavage process, which was also extended to other cyclic ketones, was rationalized in terms of capture of intermediate α-nitroso hydroxy carbocations (e.g., 7) by the alcohol with subsequent cleavage of the α-nitroso hemiacetal (8) so produced. This



pathway was suggested by the fact that the presence of at least 1 equiv of hydrogen chloride in the mixture presumably leads to the interception of 8 (via protonation and dehydration) to provide 2-alkoxy-3-oximinocyclohexene hydrochlorides (9) instead.

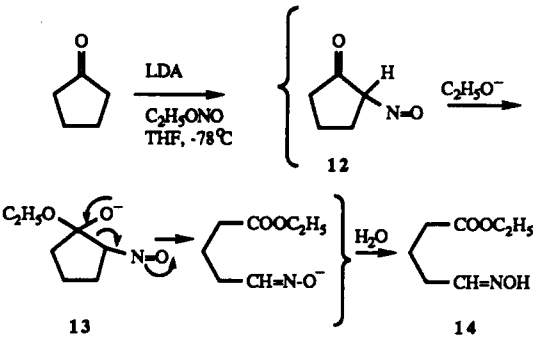
Our immediate need for a parallel unsymmetrical oxidative cleavage was for a system that was otherwise quite sensitive to acid. Consequently, recourse had to be made to the development of a base-promoted equivalent of Rogic's nitrosolysis scheme. Detailed scrutiny of the literature has succeeded in uncovering very few reports where an alkaline alternative of the desired fragmentation has been deployed.[8] Furthermore, indication that the conditions utilized earlier are not generally applicable surfaced in many locations. The simple oximation of dehydroisoandrosterone (10) to give 11 without evidence of ring cleavage constitutes an especially well-tested example.[9]



The present research was addressed at removing such limitations. Indeed, recourse to less basic and less sterically hindered alkoxides possessing greater levels of nucleophilicity has resulted in the evolution of an appealing strategy for the direct conversion of cyclic ketones to ω-oximino alkanoate esters.

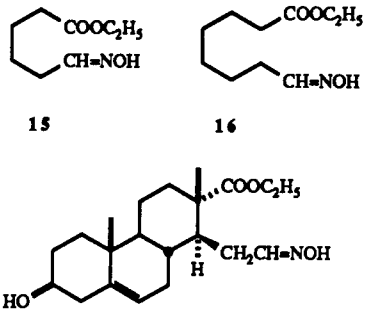
Results and Discussion

Nonbridged Cyclic Ketones. As illustrated for cyclopentanone, the general approach involves deprotonation with lithium diisopropylamide (LDA) in THF and condensation of the resulting enolate anion with ethyl nitrite at −78 °C. This simple procedure leads rapidly to an α-nitroso ketone (12) with liberation of an equivalent of ethoxide ion. Despite the fact that 12 possesses a relatively acidic proton, its irreversible abstraction by the alkoxide byproduct is of little or no consequence relative to the main reaction pathway. Rather 1,2-addition to the carbonyl group leading to 13 presumably operates, setting the stage for Beckmann-like fragmentation to give ultimately 14 on quenching. The unmaximized yield of 14 after a reaction time of 1 h was 65%.



As a consequence of our recourse to LDA as the initiating base, diisopropylnitrosamine[10] is produced concomitantly. This material, the carcinogenic activity of which has been established as weak,[11,12] is readily separated during the chromatographic purification and rendered inactive by reduction with lithium aluminum hydride.

In light of this positive early development, we proceeded to treat cyclohexanone and cyclooctanone in comparable fashion. The homologous ethoxycarbonyl aldoximes 15 and 16 were isolated in 78% and 70% yields, respectively. Despite the steric hindrance prevailing in the vicinity of the carbonyl group in dehydroisoandrosterone (10), cleavage of the ketonic ring likewise proceeds smoothly to give 17 (59%).



For most preparations, ethyl nitrite was utilized in order to take advantage of the relatively small size of the ethoxide ion made available for consumption in the second step. Yields of cleavage product fell rather precipitously when recourse was made instead to isoamyl nitrite. Use of *tert*-butyl nitrite did not work.

2-Norbornanone and 5-Norbornen-2-one. Extension of the preceding methodology to 2-norbornanone (18) in a solvent system consisting of 3:1 THF–petroleum ether gave mainly 19 (46%). Accompanying this now conventional product were the pair of aldols 20 and 21, keto oxime

(8) (a) Dieckmann, W. *Chem. Ber.* **1900**, *33*, 579. (b) Dieckmann, W.; Groenevell, A. *Ibid.* **1990**, *33*, 505. (c) Clarke, R. W. L.; Lapworth, A.; Wechsler, E. *J. Chem. Soc.* **1908**, *93*, 30. (d) Woodward, R. B.; Doering, W. E. *J. Am. Chem. Soc.* **1945**, *67*, 860. (e) Carson, M. S.; Cocker, W.; Evans, S. M.; Shannon, P. V. R. *Tetrahedron Lett.* **1968**, 6153. (f) Delgado, A.; Garcia, J. M.; Mauleon, D.; Minguillon, C.; Subirats, J. R.; Feliz, M.; Lopez, F.; Velasco, D. *Can. J. Chem.* **1988**, *66*, 517.

(9) Wheeler, T. N.; Meinwald, J. *Org. Synth.* **1972**, *52*, 53.

(10) (a) Lunazzi, L.; Cerioni, G.; Ingold, K. U. *J. Am. Chem. Soc.* **1976**, *98*, 7484. (b) Lunazzi, L.; Guerra, M.; Macciantelli, D.; Cerioni, G. *J. Chem. Soc., Perkin Trans. 2* **1982**, 1527.

(11) (a) Lee, S. Y.; Guthenplan, J. B. *Carcinogenesis* **1981**, *2*, 1339. (b) Rose, S. L.; Jurs, P. C. *J. Med. Chem.* **1982**, *25*, 769.

(12) Among the structural features deemed necessary for high mutagenic activity is a "potential unsubstituted methylating or ethylating group" attached to the nitrogen. Alkyl groups linked to the α-carbon atoms reduce the capacity for a mutagenic response.[10a]

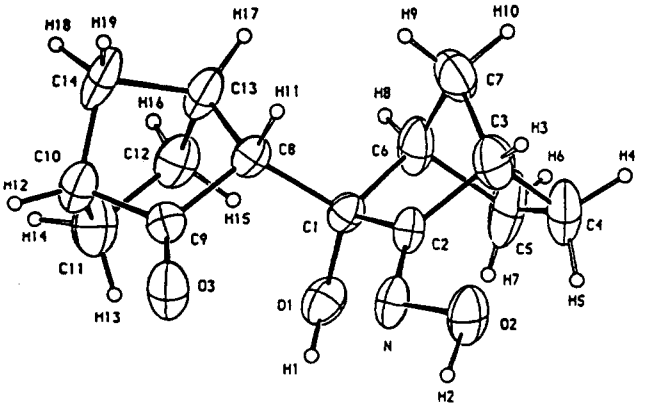
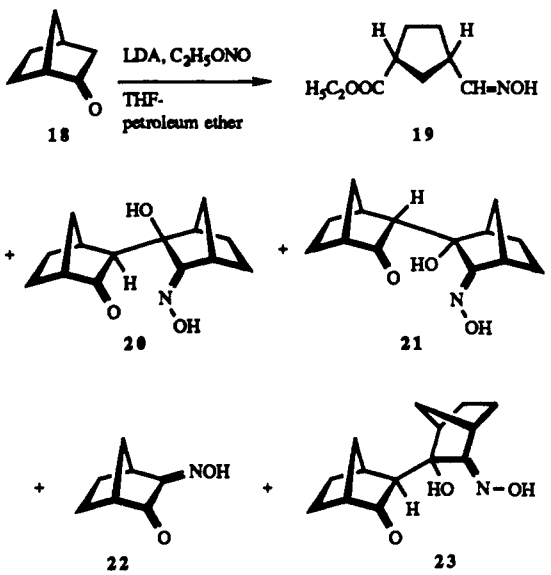


Figure 1. A computer-generated perspective view of the final X-ray model of **21**. The non-hydrogen atoms are represented by 50% probability thermal ellipsoids. The hydrogen atoms are drawn with an artificial radius.

22,[13] and a trace amount of the third "dimer" **23**. The structural assignments to **20** and **21** rest upon the lesser polarity and lesser solubility of **20** and an X-ray crystallographic analysis of **21** (Figure 1).

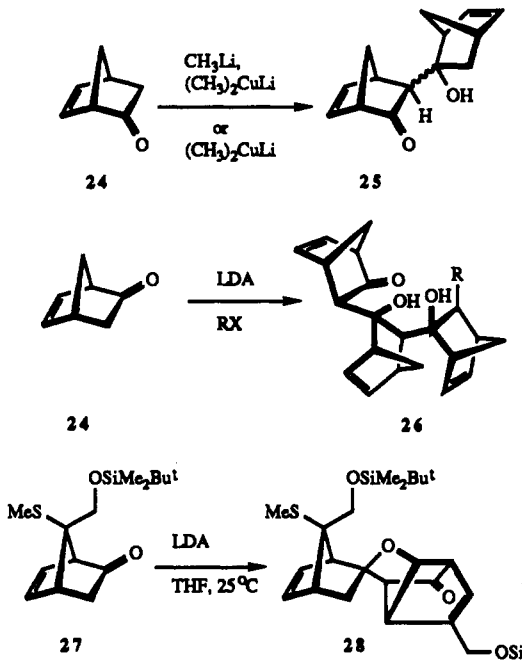


The product distribution just defined can be altered considerably by modification of the solvent polarity. For example, with a 3:5 mixture of THF and petroleum ether as the reaction medium, **18** was transformed into **19** (44%), **22** (15%), and **23** (2%) previously seen in minor amounts; no **20** or **21** was found. The structural features of **23** including stereochemical detail were rigorously established by chemical correlation as detailed subsequently.

The extent to which aldolization occurs is seen to be quite dependent on solvent polarity. When the hydrocarbon environment is enhanced and the tetrahydrofuran concentration is reduced to 37%, neither **20** nor **21** are seen. Instead, a small amount (2%) of **23** was isolated. The reasons underlying these observations are undoubtedly complex and likely linked to the proclivity for aldol formation as well as to the feasibility for retro-fragmentation of these same aldols.

Noteworthy is the fact that the aldolization process involves highly selective bonding between molecules of the same absolute configuration. The structural differences that separate **20**, **21**, and **23** do *not* arise from stereochemically mixed combinations. Rather, these are constant throughout the triad, their mutual distinction resting instead on the directionality (exo or endo) of the C–C coupling. In **23**, the interconnective bond is exo to both norbornyl residues. Its slight predominance can be understood on simple steric grounds. The two possible exo,endo combinations are found in **20** and **21**. The possible source of this obviously significant diastereomeric selectivity is to be discussed elsewhere in a more general context.

The remarkable ease with which 5-norbornen-2-ones undergo base-promoted dimerization is now well established.[14-17] Exposure of parent ketone **24** to organocuprates leads to a mixture of two aldol products (**25**, 60% combined yield), indicating a strong tendency for enolization under these conditions.[14] No definitive structural assignments to **25** were undertaken in the course of this investigation. Attempted alkylation of the lithium enolate of **24** in THF with alkyl halides is recognized to deliver a single trimeric oligomer (**26**) that contains but one alkyl group.[15,17] The presence of a 7-anti substituent on the bicyclic framework arrested this condensation process and permitted isolation of 3-alkylnorbornenones in satisfactory yield. The deprotonation of **27** with LDA in THF at room temperature resulted in exclusive attack of its enolate anion on a second enone molecule of the identical absolute configuration with ultimate ejection of CH_3S^- to furnish **28**.[16]



As a consequence of the foregoing, we were attracted to examine the response of **24** to the standardized cleavage conditions. Despite the obvious proclivity of this ketone for base-catalyzed self-condensation, oximino ester **29** was formed to the extent of 33%. The other pertinent endproducts were keto oxime **30** (12%), the aldol pair **25** (13%), and the aldol oxime **31** (8%). Since **31** was found

(13) Balsamo, A.; Breschi, M. C.; Lapucci, A.; Macchia, B.; Macchia, F.; Martinotti, E.; Nencetti, S.; Nieri, P.; Orlandini, E. *J. Med. Chem.* **1989**, *32*, 856.

(14) Arjona, O.; Fernández de la Pradilla, R.; Mallo, A.; Pérez, S.; Plumet, J. *J. Org. Chem.* **1989**, *54*, 4158.

(15) Homer, J. H.; Vera, M.; Grutzner, J. B. *J. Org. Chem.* **1986**, *51*, 4212.

(16) Paquette, L. A.; Romine, J.; Barth, W.; Hsu, L.-Y. *Tetrahedron Lett.* **1985**, *26*, 567.

(17) Turecek, F.; Brabec, L.; Korvola, J. *J. Am. Chem. Soc.* **1988**, *110*, 7984. These workers show that the methylation of 5-norbornen-2-one can be uncomplicated.

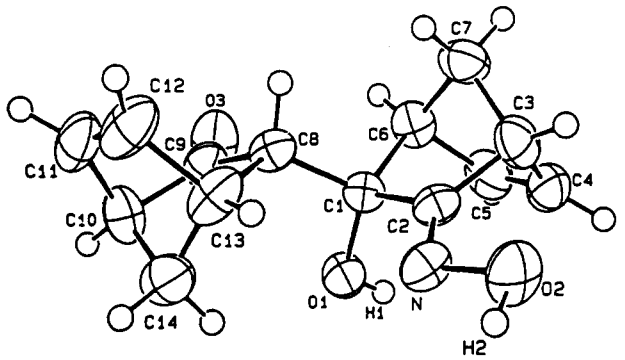
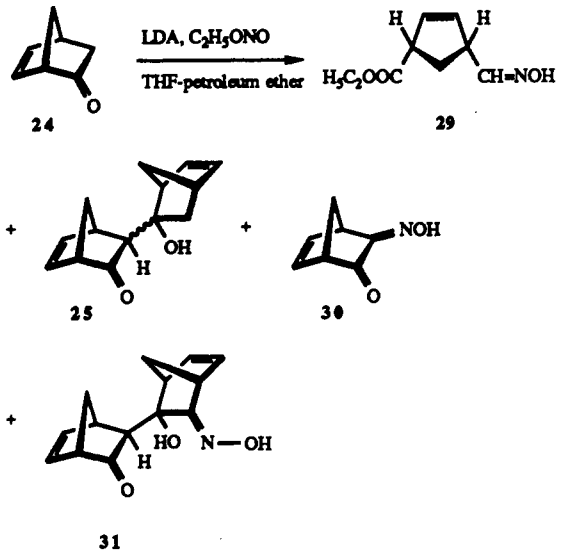


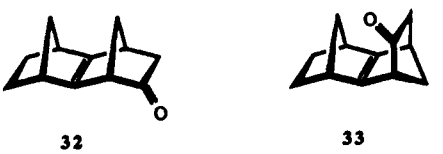
Figure 2. A computer-generated perspective view of the final X-ray model of **31**. The non-hydrogen atoms are represented by 50% probability thermal ellipsoids. The hydrogen atoms are drawn with an artificial radius.

by ^1H and ^{13}C NMR spectroscopy to be a single isomer and because its recrystallization from ether–petroleum ether afforded white crystals suitable for study by X-ray diffraction, its three-dimensional stereochemistry was established in this fashion (Figure 2). Additionally, the catalytic hydrogenation of **31** led to **23**, thereby confirming that both compounds reside in the same diastereomeric series.



It is noteworthy that all of the ω-ethoxycarbonyl aldoximes were isolated as *E*/*Z* mixtures stereoisomeric about the C–N double bond. When stored below 0 °C for short periods of time, **29** crystallized so as to give a single compound exhibiting an oxime olefinic proton resonance in C_6D_6 at δ 6.71. Equilibration with the second isomer is rapid at room temperature however. When this solution was allowed to stand at 25 °C for 5 and 10 min, the isomer ratios were noted by ^1H NMR to drop to 66:34 and 51:49, respectively. Complete equilibration showed the *E* isomer (δ 7.35) to be ultimately dominant (43:57).[18]

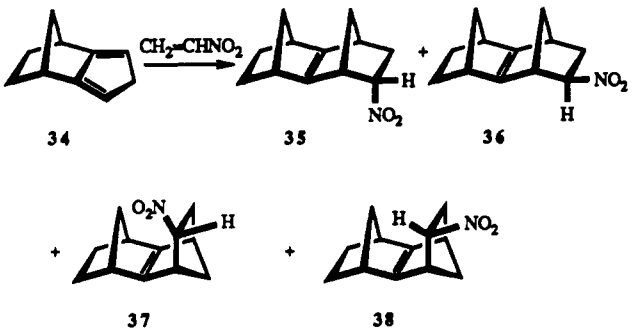
***syn*- and *anti*-Sesquinorbornen-4-one.** At this point, it was clear that the alkaline cleavage reaction exhibits characteristics that render it applicable in cases where acid sensitivity would otherwise preclude protic or Lewis acid catalysis. The structural features inherent in tetracyclic ketones **32** and **33** constitute an especially stringent test



32 **33**

of the feasibility of this working hypothesis. Thus, *syn*-sesquinorbornenes possess a highly folded central double bond[19,20] that is especially reactive toward electrophilic reagents.[21] Although the susceptibility of these systems to nucleophilic attack had not been given prior scrutiny, we were of the opinion that similar heightened reactivity would not be manifested in a basic environment.

Two approaches to **32** and **33** were therefore examined. The first was designed to take advantage of the Nef reaction[22] as well as the proclivity of isodicyclopentadiene (**34**) for dienophile capture predominantly from the below-plane direction.[23] To this end, **34** was admixed with nitroethylene[24] at −78 °C in the absence of solvent but with hydroquinone present. The high reactivity of nitroethylene made possible Diels–Alder condensation in the temperature range −78 → +25 °C. Such conditions do not normally promote the competitive formation of angular adducts.[25] Direct examination of the reaction mixture after removal of the hydroquinone indicated the four linear adducts **34**–**38** to be formed in a relative ratio of 29:42:26:3, respectively.



The three principal adducts were secured in pure condition by careful chromatography and identified on the basis of their ^1H NMR spectra. A key facet of this analysis is the substantive shielding recognized to be experienced by the endo ethano bridge protons in *syn*-sesquinor-

(18) The general rule of thumb for oximes is that the formyl proton syn to the oxygen always resonantes downfield from the corresponding anti proton: Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, 2nd ed.; Pergamon Press: Oxford, 1969; p 226.

(19) (a) Watson, W. H.; Galloy, J.; Bartlett, P. D.; Proof, A. A. M. *J. Am. Chem. Soc.* **1981**, *103*, 2022. (b) Bartlett, P. D.; Combs, G. L., Jr. *J. Org. Chem.* **1984**, *49*, 625. (c) Watson, W. H.; Galloy, J.; Grossie, D. A.; Bartlett, P. D.; Combs, G. L., Jr. *Acta Crystallogr.* **1984**, *C40*, 1050. (d) Hagenbuch, J.-P.; Vogel, P.; Pinkerton, A. A.; Schwarzenbach, D. *Helv. Chim. Acta* **1981**, *64*, 1818.

(20) (a) Paquette, L. A.; Charumilind, P.; Böhm, M. C.: Gleiter, R.; Bass, L. S.; Clardy, J. *J. Am. Chem. Soc.* **1983**, *105*, 3136. (b) Paquette, L. A.; Hayes, P. C.; Charumilind, P.; Böhm, M. C.; Gletier, R.; Blount, J. F. *Ibid.* **1983**, *105*, 3148. (c) Paquette, L. A.; Green, K. E.; Gleiter, R.; Schäfer, W.; Gallucci, J. C. *Ibid.* **1984**, *106*, 8232. (d) Paquette, L. A.; Shen, C.-C.; Krause, J. A. *Ibid.* **1989**, *111*, 2351. (e) Paquette, L. A.; Shen, C.-C. *Ibid.* **1990**, *112*, 1159. (f) Irngartinger, H.; Deuter, J.; Charumilind, P.: Paquette, L. A. *Ibid.* **1989**, *111*, 9236.

(21) See, for example: Paquette, L. A.; DeLucca, G.; Ohkata, K.; Gallucci, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 1015.

(22) Pinnick, H. W. *Org. React.* **1990**, *38*, 655.

(23) (a) Paquette, L. A. In *Stereochemistry and Reactivity of Pi Systems*; Watson, W. H., Ed.; Verlag Chemie International: Deerfield Beach, FL, 1983; pp 41–73. (b) Gleiter, R.; Paquette, L. A. *Acc. Chem. Res.* **1983**, *16*, 328.

(24) (a) Buckley, G. D.; Scaife, C. W. *J. Chem. Soc.* **1947**, 1471. (b) Ranganathan, S.; Ranganathan, D.; Mehrotra, A. K. *J. Am. Chem. Soc.* **1974**, *96*, 5261. (c) Ranganathan, D.; Rao, C. B.; Ranganathan, S.; Mehrotra, A. K.; Iyengar, R. *J. Org. Chem.* **1980**, *45*, 1185.

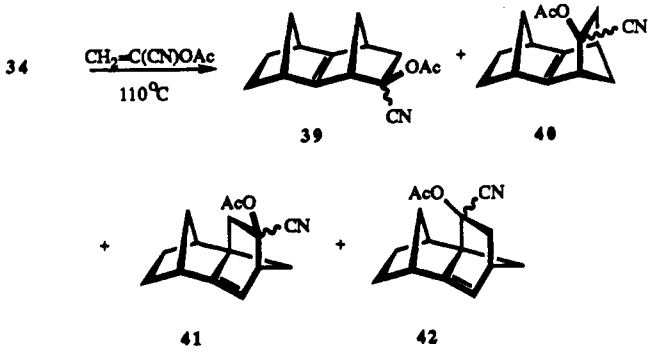
(25) (a) Paquette, L. A.; Williams, R. V.; Carr, R. V. C.; Charumilind, P.; Blount, J. F. *J. Org. Chem.* **1982**, *47*, 4566. (b) Subramanyam, R.; Bartlett, P. D.; Iglesias, G. Y. M.; Watson, W. H.; Galloy, J. *Ibid.* **1982**, *47*, 4491. (c) Bartlett, P. D.; Wu, C. *J. Am. Chem. Soc.* **1983**, *105*, 100. (d) *J. Org. Chem.* **1984**, *49*, 1880. (e) *Ibid.* **1985**, *50*, 4087.

bornenes relative to those in their anti counterparts.[20b,c,26] This distinction is especially diagnostic when the substituent(s) on the second ethano bridge are exo-oriented[20b] or linked to a site of unsaturated.[26b] On this basis, the substantive upfield shift associated with these protons in **36** (δ 0.82–0.77) and their appearance as downfield as δ 1.16 in **37** serve as reliable indicators that these are syn and anti isomers, respectively. The endo disposition of the nitro group in **37** is revealed by the near identity of its α-proton chemical shift (δ 5.10) and multiplicity relative to the data for *endo*-2-nitro-5-norbornene.[24c] The $HCNO_2$ proton in **35** is also seen as a doublet of doublet of doublets, thereby requiring the nitro group to be endo oriented as well in this isomer.[27] The shift to higher field of the proton signal in this instance (δ 4.55) stems from the *syn*-sesquinorbornene effect alluded to earlier.

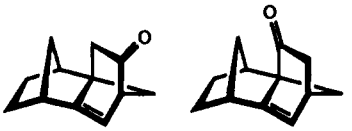
An especially interesting spectral feature is the appearance of the exo α-nitro proton in **36** at δ 4.21–4.17 instead of the usual δ 5.0 region.[24c] This we attribute to an anisotropy effect linked to the downfield buttressing against the nitro group with the resultant projection of the geminal proton into closer proximity of the methano bridge.

Unfortunately, the submission of one or more of these adducts to a myriad of the Nef conditions did not result in the formation of the desired sesquinorbornenone or its oxime. The reagents included alkaline potassium permanganate,[28] alkaline sodium chlorite,[29] unbuffered aqueous titanium trichloride,[30] $TiCl_3$ buffered with NH_4OAc,[31] and triethylamine in carbon disulfide.[32]

As a consequence, recourse was made instead to cycloaddition chemistry involving the less reactive α-acetoxyacrylonitrile.[33,34] Heating **34** with an excess of this dienophile in the absence of solvent at 110 °C resulted in the total consumption of diene after 12 h. The four diastereomers (42:16:31:11, respectively) were produced with 72% efficiency. At lower temperatures, **39** and **40** were formed exclusively, albeit in reduced yield. While the linear adducts **39** and **40** could be separated from those with angular frameworks (**41** and **42**), their further separation proved quite difficult. Since the four derived ketones were more well behaved, the acetoxy nitrile mixture was routinely saponified without extensive purification.

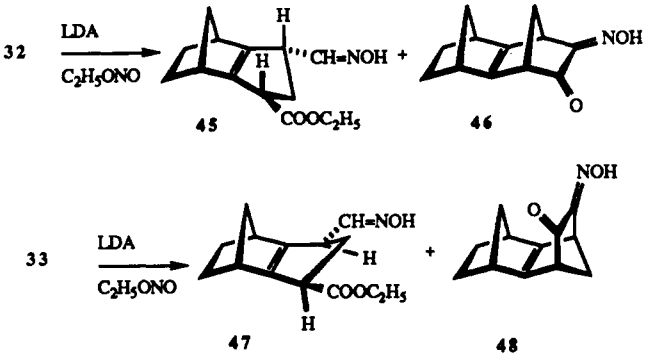


Suitable distinction between **32** and **33** was made following exo addition of *tert*-butyllithium to their carbonyl groups. When allowed to stand in the atmosphere for some time, the *syn*-sesquinorbornenyl alcohol was transformed into its epoxide, which shows the expected shielding of the methano bridge carbons.[35] This distinctive π-bond susceptibility to air oxidation is a characteristic property of this diastereomeric structural class.[36] The angular ketones **43** and **44** are easily distinguished by the downfield position of the quaternary carbon in **44** (73.80 ppm) relative to that in **43** (60.05 ppm).



43 44

Satisfyingly, the desired cleavage of **32** took place smoothly to give **45** in good yield (62%) alongside a modest amount of **46** (9%). Comparably efficient bond breaking occurred when the *anti*-sesquinorbornenone **33** was similarly treated. In parallel with an earlier example, the *E* isomer of **47** (δ 7.76) could be obtained in pure condition and its equilibration to an isomer *E*/*Z* mixture monitored by ^1H NMR during 12 h.



That the formation of ω-ethoxycarbonyl aldoximes proceeds with high stereoselectivity is clearly established by the homogeneity of these products (oxime *E*/*Z* isomerization aside). No evidence for postequilibration α to the carbethoxy group has been uncovered. Of course, the oxime functionality is initially generated in the form of its conjugate base. This negative charge, which persists until workup conditions are applied, may prove to be a source of deactivation adequate to deter dianionic character from readily materializing.

In conclusion, the methodology described herein gives every indication of fulfilling the requirements of a satisfactory base-promoted nitrosolysis. It has been demonstrated that enolate anions respond readily to the action of ethyl nitrite to give oximino esters in a single step. The **1** → **2** conversion offers a new opportunity for developing synthetic strategies built around the unsymmetrical oxidative cleavage of enolizable ketones that could hold broad applicability.

Experimental Section

Melting points are uncorrected. ^1H NMR spectra were recorded at 300 MHz, and the ^{13}C NMR data were obtained at either 75 or 20 MHz as indicated. All MPLC separations were conducted on Merck Lobar columns (Lichroprep Si-60) with the help of a

(26) (a) Paquette, L. A.; Kravetz, T. M.; Hsu, L.-Y. *J. Am. Chem. Soc.* **1985**, *107*, 6598. (b) Paquette, L. A.; Gugelchuk, M.; Hsu, L.-Y. *J. Org. Chem.* **1986**, *51*, 3864.

(27) Marchand, A. P. *Stereochemical Applications of NMR Studies in Rigid Bicyclic Systems*; Verlag Chemie International: Deerfield Beach, FL, 1982.

(28) Steliou, K.; Poupart, M.-A. *J. Org. Chem.* **1985**, *50*, 4971.

(29) Ballini, R.; Petrini, M. *Tetrahedron Lett.* **1989**, *30*, 5329.

(30) McMurry, J. E.; Melton, J. *J. Am. Chem. Soc.* **1971**, *93*, 5309.

(31) McMurry, J. E.; Melton, J. *J. Org. Chem.* **1973**, *38*, 4367.

(32) Barton, D. H. R.; Fernandez, I.; Richard, C. S.; Zard, S. Z. *Tetrahedron* **1987**, *43*, 551.

(33) Nowak, R. M. *J. Org. Chem.* **1963**, *28*, 1182.

(34) McCann, W. P.; Hall, L. M.; Nonider, W. K. *Anal. Chem.* **1983**, *55*, 1455.

(35) Moorhoff, C. Unpublished results.

(36) (a) Paquette, L. A.; Carr, R. V. C. *J. Am. Chem. Soc.* **1980**, *102*, 7553. (b) Paquette, L. A.; Kravetz, T. M.; Böhm, M. C.; Gleiter, R. *J. Org. Chem.* **1983**, *48*, 1250.

Fluid Metering INC pump and a Waters Associates Model R403 differential refractometer detector. All reactions were performed under an inert atmosphere (nitrogen or argon) unless otherwise indicated. Solvents were reagent grade and dried prior to use.

Prototypical Oxidative Cleavage Procedure. A. Cyclopentanone. A solution of *n*-butyllithium in hexanes (4.5 mL of 1.5 M, 6.75 mmol) was added to dry diisopropylamine (710 mg, 7.01 mmol) in anhydrous tetrahydrofuran (THF, 5 mL) at −78 °C, and the reaction mixture was allowed to warm to room temperature for 30 min. After returning to −78 °C for 5 min, a solution of cyclopentanone (600 mg, 7.13 mmol) in THF (2 mL) was introduced at a rate of 1 drop/s, and stirring was maintained for 60 min at this temperature. Dry ethyl nitrite (650 mg, 8.66 mmol) in THF (2 mL) was added during 1 min, resulting in an immediate color change to yellow. After 1 h, the cold mixture was quenched with saturated brine, brought to room temperature, and extracted with ether. The combined ethereal layers were dried and concentrated. The residue was subjected to silica gel chromatography (elution with ether–petroleum ether, 1:9 and 3:7) to give diisopropylnitrosamine (60 mg), a colorless solid, mp 42 °C,[6] and a *Z*/*E* mixture of **14** (738 mg, 65%):[7a] IR ($CHCl_3$, cm^{-1}) 3580, 3300, 2980, 2870, 1725, 915; ^1H NMR (300 MHz, $CDCl_3$) δ 8.60 and 8.13 (2 br m, total 1 H), 7.40 (t, *J* = 5.9 Hz) and 6.71 (t, *J* = 5.5 Hz, total 1 H), 4.13 and 4.12 (2 q, *J* = 7.1 Hz, total 2 H), 2.35 and 2.34 (2 t, *J* = 7.5 Hz, total 2 H), 2.24 (q, *J* = 7.4 Hz, 2 H), 1.83 (quintuplet, *J* = 7.4 Hz, 2 H), 1.24 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm (major isomer) 172.76, 150.29, 59.90, 33.19, 28.23, 21.32, 13.60.

B. Cyclohexanone. Treatment of 650 mg (6.62 mmol) of cyclohexanone in the predescribed manner gave a yellow residue that was chromatographed on silica gel (elution as above). There was isolated in addition to diisopropylnitrosamine an *E*/*Z* mixture of **15** (890 mg, 78%)[7a] as a colorless oil, bp 65–70 °C (0.5 Torr), that crystallizes in the cold: IR ($CHCl_3$, cm^{-1}) 3580, 3300, 2980, 2860, 1730, 915; ^1H NMR (300 MHz, $CDCl_3$) δ 9.20 and 8.80 (2 br s, total 1 H), 7.37 (dt, *J* = 4.9, 1.2 Hz) and 6.68 (t, *J* = 5.3 Hz, total 1 H), 4.094 and 4.091 (2 q, *J* = 7.1 Hz, total 2 H), 2.36 (q, *J* = 5.6 Hz) and 2.19 (q, *J* = 6.3 Hz, total 2 H), 2.30 and 2.28 (2 t, *J* = 7.4 Hz, total 2 H), 1.69–1.45 (series of m, 4 H), 1.215 and 1.213 (2 t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm (major isomer) 173.20, 150.94, 59.95, 33.55, 25.71, 24.26, 23.99, 13.83.

C. Cyclooctanone. Submission of cyclooctanone (2.00 g, 15.9 mmol) to the same conditions gave a residual oil that was comparably purified by silica gel chromatography to give 2.23 g (70%) of **16**[7] as a colorless liquid, bp 75 °C at 0.3 Torr, that crystallized in the cold: IR ($CHCl_3$, cm^{-1}) 3580, 3300, 2980, 2940, 2860, 1730, 910; ^1H NMR (300 MHz, $CDCl_3$) δ 9.5 (br s, 1 H), 7.37 (dt, *J* = 6.1, 1.1 Hz) and 6.66 (dt, *J* = 5.5, 1.1 Hz, total 1 H), 4.09 (q, *J* = 7.1 Hz, 2 H), 2.34 (dq, *J* = 6.5, 0.8 Hz) and 2.15 (q, *J* = 7.3 Hz, total 2 H), 2.25 (t, *J* = 7.4 Hz, 2 H), 1.60–1.29 (series of m, 8 H), 1.212 (t, *J* = 7.1 Hz) and 1.209 (t, *J* = 7.1 Hz, total 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm (major isomer) 173.39, 151.14, 59.75, 33.75, 28.87, 28.27, 25.97, 24.44, 24.33, 13.74.

D. Dehydroisoandrosterone. Treatment of **10** (500 mg, 1.73 mmol) in analogous fashion followed by brine quench of the reaction mixture was followed by extraction with ether (3 × 20 mL) and drying. The aqueous phase was acidified and extracted with CH_2Cl_3 (3 × 20 mL). The combined CH_2Cl_2 layers were dried and evaporated to give 20 mg (4%) of **11**, mp 245–247 °C dec.[9] The ethereal solution was concentrated and the residue so obtained was chromatographed on silica gel (elution with 100% ether) to give **17** as a colorless solid (370 mg, 59%): mp 165–172 °C (from 1:1 ether–petroleum ether); IR ($CHCl_3$, cm^{-1}) 3600, 3300, 3005, 2980, 2940, 2910, 2860, 1715; ^1H NMR (300 MHz, $CDCl_3$) δ 8.5 (br s, 1 H), 7.32 (t, *J* = 6.5 Hz) and 6.70 (dd, *J* = 6.3, 4.3 Hz, total 1 H), 5.30 (m, 1 H), 4.11 and 4.10 (2 q, *J* = 7.1 Hz, total 2 H), 3.55–3.45 (m, 1 H), 2.51 (dt, *J* = 17.2, 6.4 Hz, 1 H), 2.35–1.30 (series of m, 15 H), 1.23 and 1.22 (2 t, *J* = 7.1 Hz, total 3 H), 1.14 and 1.13 (2 s, total 3 H), 1.2–1.0 (m, 2 H), 0.972 and 0.967 (2 s, total 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm (major isomer) 178.07, 151.93, 140.07, 120.96, 71.40, 60.57, 49.08, 47.04, 45.54, 41.72, 36.92, 36.57, (2C), 33.91, 32.17, 31.46, 31.18, 19.53, 19.13, 14.94, 14.06; MS *m*/*z* (M^+) calcd 363.2410, obsd 363.2373.

Anal. Calcd for $C_{21}H_{33}NO_4$: C, 69.39; H, 9.15. Found: C, 69.08; H, 9.12.

Cleavage of 2-Norbornanone. A. Tetrahydrofuran–Petroleum Ether (3:1) Solvent System. A solution of *n*-butyllithium in hexanes (8 mL of 1.5 M, 12.0 mmol) was added to dry diisopropylamine (1.00 g, 9.88 mmol) in anhydrous THF (15 mL) at −78 °C, stirred for 15 min at room temperature, and returned to −78 °C. 2-Norbornanone (1.00 g, 9.08 mmol) in THF (5 mL) was introduced, and the reaction mixture was stirred for 30 min at −78 °C and for 20 min at 0 °C before again being returned to −78 °C. Ethyl nitrite (950 mg, 12.6 mmol) dissolved in THF (5 mL) was slowly added, stirring was maintained for 30 min at −78 °C, and the mixture was allowed to warm to 0 °C. After 30 min, the reaction was quenched with saturated brine and the products were extracted into ether (3 × 30 mL). The aqueous phase was carefully acidified and extracted with CH_2Cl_2 (2 × 40 mL). All of the organic phases were combined, dried, and concentrated. The resulting residue was chromatographed on silica gel (sequential elution with ether–petroleum ether 1:9, 3:7, and 1:1) gave diisopropylnitrosamine, **19** (120 mg, 46%), and the two dimeric diasteromeric oximes **20** (120 mg, 11%) and **21** (90 mg, 8%).

For **19**: colorless liquid, bp 75–80 °C at 0.7 Torr; IR ($CHCl_3$, cm^{-1}) 3575, 3300, 3010, 2970, 2900, 2870, 1720, 910; ^1H NMR (300 MHz, $CDCl_3$) δ 8.75 (br s, 1 H), 7.35 (d, *J* = 7.2 Hz) and 6.68 (d, *J* = 6.9 Hz, total 1 H), 4.10 (q, *J* = 7.1 Hz, 2 H), 3.43–3.28 and 2.80 (2 pentuplet, *J* = 8.0 Hz, total 2 H), 2.75–2.65 (m, 1 H), 2.22 (dt, *J* = 13.0, 7.8 Hz) and 2.12 (dt, *J* = 12.9, 7.7 Hz, total 2 H), 1.97–1.86 (m) and 1.76–1.58 (m, total 3 H), 1.22 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm (major isomer) 175.52, 153.79, 60.11, 43.23, 39.73, 33.99, 29.58, 28.66, 13.74; MS *m*/*z* (M^+ + 1) calcd 186.1130, obsd 186.1170.

Anal. Calcd for $C_9H_{15}NO_3$: C, 58.36; H, 8.16. Found: C, 58.24; H, 8.22.

For **20**: colorless solid, mp 188–190 °C (from ether–petroleum ether); IR ($CDCl_3$, cm^{-1}) 3560, 3300, 3005, 2960, 1730; ^1H NMR (300 MHz, $CDCl_3$) δ 7.53 (br s, 1 H), 3.97 (s, 1 H), 3.46 (d, *J* = 3.1 Hz, 1 H), 2.78 (m, 1 H), 2.67 (m, 2 H), 2.40 (d, *J* = 3.9 Hz, 1 H), 2.13–2.05 (m, 1 H), 1.98–1.51 (m, 11 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 218.78, 167.74, 79.27, 60.80, 51.08, 46.90, 39.43, 38.51, 37.42, 33.86, 26.62, 24.18, 23.48, 20.85; MS *m*/*z* (M^+) calcd 249.1365, obsd 249.1350.

For **21**: colorless crystals, mp 177–179 °C (from $CHCl_3$–petroleum ether); IR ($CHCl_3$, cm^{-1}) 3570, 3350, 2970, 2875, 1735; ^1H NMR (300 MHz, $CDCl_3$) δ 9.5 (br s, 1 H), 3.54 (s, 1 H), 3.17 (s, 1 H), 2.79 (s, 1 H), 2.69–2.68 (m, 1 H), 2.54–2.49 (m, 2 H), 2.13–1.88 (m, 2 H), 1.84–1.40 (series of m, 10 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 218.21, 168.97, 78.16, 58.98, 51.74, 44.76, 38.46, 38.11, 36.44, 33.76, 27.00, 25.76, 22.36, 20.76; MS *m*/*z* (M^+) calcd 249.1365, obsd 249.1381.

B. Petroleum Ether–Tetrahydrofuran (5:3) Solvent System. A solution of *n*-butyllithium in hexanes (20.0 mL of 1.5 M, 30.0 mmol) was added via syringe to a solution of dry diisoproplamine (3.70 g, 36.6 mmol) in anhydrous THF (20 mL) at −78 °C and warmed and cooled as in A. A solution of 2-norbornanone (3.00 g, 27.2 mmol) in petroleum ether (20 mL) was introduced, and reaction was allowed to proceed as before, including the addition of ethyl nitrite (2.50 g, 33.3 mmol). the analogous workup was applied except that the ether and CH_2Cl_2 extracts were handled separately. Chromatography of the residue from the ethereal solution provided 760 mg of diisopropylnitrosamine, 2.22 g (44%) of **19**, and 50 mg (2%) of the third dimer **23**. The CH_2Cl_2 solution yielded 580 mg (15%) of the known 2,3-dione nomoxime **22**.[13]

For **23**: colorless crystals, mp 159–164 °C (from $CHCl_3$–petroleum ether); ^1H NMR (300 MHz, $CDCl_3$) δ 7.50 (br s, 1 H), 3.41 (d, *J* = 2.9 Hz, 1 H), 3.16 (s, 1 H), 3.05 (s, 1 H), 2.57 (s, 1 H), 2.35 (d, *J* = 10.2 Hz, 1 H), 1.98–1.25 (series of m, 13 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 218.06, 169.58, 81.44, 57.10, 50.13, 45.10, 38.79, 37.13, 35.95, 34.56, 29.29, 27.26, 24.22, 20.67; MS *m*/*z* (M^+) calcd 249.1365, obsd 249.1327.

Cleavage of 5-Norbornen-2-one. A solution of *n*-butyllithium in hexanes (2.2 mL of 1.5 M, 3.30 mmol) was added to dry diisopropylamine (350 mg, 3.46 mmol) in dry THF (2 mL), followed as before with 5-norbornen-2-one (350 mg, 3.24 mmol) in petroleum ether (2 mL) and finally ethyl nitrite (280 mg, 3.73 mmol) in the same solvent (2 mL). The customary workup and MPLC on silica gel (sequential elution with ether–petroleum ether (1:9, 1:4, and 6:4) then 100% ether) gave diisopropylnitrosamine (27

mg), the two aldol dimers **25** (47 mg, 13%), **29** (196 mg, 33%), **30** (55 mg, 12%), and **31** (31 mg, 8%).

For **25**: white crystals, mp 111–115 °C (from ether–petroleum ether); IR ($CHCl_3$, cm^{-1}) 3570, 3060, 3000, 2980, 1735; ^1H NMR (300 MHz, $CDCl_3$) δ (major isomer) 6.64 (dd, J = 2.7, 5.3 Hz, 1 H), 6.44 (dd, J = 3.0, 5.6 Hz, 1 H), 6.20 (dd, J = 3.3, 8.3 Hz, 1 H), 6.13 (dd, J = 3.2, 5.6 Hz, 1 H), 3.70 (m, 1 H), 3.22 (s, 1 H), 2.96 (s, 1 H), 2.84 (d, J = 5.5 Hz, 1 H), 2.83 (s, 1 H), 2.03 (d, J = 2.9 Hz, 1 H), 1.94 (dd, J = 3.8, 12.6 Hz, 2 H), 1.62–1.58 (m, 1 H), 1.43 (s, 1 H), 1.41 (d, J = 10.1 Hz, 1 H), 1.17 (dd, J = 3.5, 12.6 Hz, 1 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm (major isomer) 215.27, 145.02, 140.66, 133.09, 132.92, 82.24, 55.99, 51.52, 50.14, 48.71, 47.57, 44.32, 43.54, 42.59; MS m/z (M^+) calcd 216.1150, obsd 216.1151.

Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.72; H, 7.42.

For **29**: colorless liquid, bp 75 °C at 0.7 Torr; IR ($CHCl_3$, cm^{-1}) 3580, 3300, 3010, 2980, 1730, 1185; ^1H NMR (300 MHz, $CDCl_3$) δ 8.7 and 8.3 (2 br s, total 1 H), 7.35 (d, J = 7.5 Hz) and 6.71 (d, J = 6.6 Hz, total 1 H), 5.92–5.87 (m, 1 H), 5.78–5.75 (m, 1 H), 4.16 (q, J = 7.1 Hz, 2 H), 3.63–3.55 (m, 2 H), 2.53–2.38 (m, 1 H) 2.14–2.01 (m, 1 H), 1.27 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm (major isomer) 173.76, 153.47, 132.93, 131.35, 60.78, 50.54, 45.57, 30.92, 14.08; MS m/z (M^+) calcd 183.0980, obsd 183.0930.

Anal. Calcd for $C_9H_{13}NO_3$: C, 59.00; H, 7.15. Found: C, 59.26; H, 7.18.

For **30**: pale yellow oil; IR ($CHCl_3$, cm^{-1}) 3550, 3300, 3005, 2930, 1750, 910; ^1H NMR (300 MHz, $CDCl_3$) δ 9.86 (br s, 1 H), 6.56 (dd, J = 5.4, 2.9 Hz, 1 H), 6.36 (dd, J = 3.2, 5.4 Hz, 1 H, 4.15 (br s, 1 H), 4.23 (dd, J = 1.6, 3.2 Hz, 1 H), 2.46 (dt, J = 9.9, 1.6 Hz, 1 H), 2.15 (dd, J = 9.9, 0.4 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm (major isomer) 199.61, 154.46, 139.71, 135.99, 54.08, 47.57, 41.31; MS m/z (M^+) calcd 137.0476, obsd 137.0488.

Anal. Calcd for $C_7H_7NO_2$: C, 61.32; H, 5.15. Found: C, 61.48; H, 5.65.

For **31**: white crystals, mp 159–161 °C (from ether); IR ($CHCl_3$, cm^{-1}) 3580, 3000, 2980, 2870, 1740; ^1H NMR (300 MHz, $CDCl_3$) δ 7.94 (br s, 1 H), 6.63 (dd, J = 3.0, 5.5 Hz, 1 H), 6.39 (m, 2 H), 6.21 (dd, J = 3.2, 5.5 Hz, 1 H), 4.02 (s, 1 H), 3.84 (s, 1 H), 3.68 (s, 1 H), 3.02 (m, 1 H), 2.79 (d, J = 9.2 Hz, 1 H), 2.20 (dd, J = 10.7, 2.7 Hz, 2 H), 2.16 (d, J = 1.3 Hz, 1 H), 2.01 (dd, J = 3.2, 9.2 Hz, 1 H), 1.91 (dd, J = 1.7, 10.0 Hz, 1 H), 1.71 (d, J = 10.0 Hz, 1 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 214.68, 167.40, 145.28, 138.23, 135.27, 133.42, 80.29, 55.86, 49.48, 48.95, 47.63, 44.99, 44.01, 43.36; MS m/z (M^+) calcd 245.1052, obsd 245.1030.

Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.56; H, 6.16. Found: C, 68.38; H, 6.18.

Catalytic Hydrogenation of 31. A solution of **31** (11 mg, 0.45 mmol) in ethyl acetate (1 mL) was hydrogenated at atmospheric pressure over 5% Pd/C (1 mg) for 17 h, filtered through Celite, and evaporated. There was obtained 11 mg (100%) of **23** identical by IR, ^1H NMR, and ^{13}C NMR with the sample characterized earlier.

Diels–Alder Addition of Nitroethylene to Isodicyclopentadiene. Freshly distilled nitroethylene (590 mg, 8.08 mmol) was added via syringe at −78 °C under nitrogen to **34** (750 mg, 5.67 mmol) containing hydroquinone (80 mg, 0.73 mmol). The mixture was stirred in the cold for 4 h in the absence of solvent, slowly brought to room temperature, and stirred for another 3 h. Excess nitroethylene was removed in vacuo, and the residue was triturated with ether to leave behind much of the hydroquinone. Filtration through a short column of silica gel and solvent evaporation afforded 650 mg (56%) of a 29:42:26:3 mixture of adducts **35–38**, respectively (300 MHz ^1H NMR analysis). MPLC purification (silica gel, elution with 5% ether in petroleum ether) resulted in facile separation of the pairs of syn and anti stereoisomers. Separation of **35** from **36** ultimately proved possible.

For **35**: pale yellow oil, bp 95 °C at 0.3 Torr; IR ($CHCl_3$, cm^{-1}) 2980, 2870, 1545, 1365; ^1H NMR (300 MHz, $CDCl_3$) δ 4.55 (ddd, J = 7.8, 3.4, 1.0 Hz, 1 H), 3.35 (s, 1 H), 2.94 (m, 2 H), 2.32 (dt, J = 12.7, 3.6 Hz, 1 H), 2.08 (dd, J = 7.7, 1.1 Hz, 1 H), 2.00 (ddd, J = 12.6, 8.1, 2.8 Hz, 1 H), 1.75–1.74 (m, 1 H), 1.72–1.71 (m, 1 H), 1.69–1.60 (m, 1 H), 1.33–1.31 (m, 2 H), 1.09 (dd, J = 7.3, 2.2 Hz, 2 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 160.52, 151.43, 86.77, 53.99, 53.21, 48.58, 41.68, 40.96, 40.64, 35.67, 26.45, 26.07; MS m/z (M^+) calcd 205.1102, obsd 205.1116.

Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37. Found: C, 70.21; H, 7.39.

For **36**: pale yellow oil, bp 85–95 °C at 0.3 Torr; IR ($CHCl_3$, cm^{-1}) 2950, 2865, 1530, 1360; ^1H NMR (300 MHz, $CDCl_3$) δ 4.21–4.17 (ddd, J = 5.8, 3.5, 1.7 Hz, 1 H), 3.47 (s, 1 H), 3.09 (s, 1 H), 3.03 (d, J = 5.9 Hz, 2 H), 2.25 (dt, J = 12.0, 3.4 Hz, 1 H), 1.85 (dm, J = 8.6 Hz, 1 H), 1.66–1.59 (m, 4 H), 1.39 (dm, J = 8.3 Hz, 1 H), 1.10 (dt, J = 8.2, 1.3 Hz, 1 H), 0.82–0.77 (m, 2 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 158.29, 148.88, 85.46, 60.58, 50.31, 47.53, 42.86, 42.56, 41.94, 33.69, 25.40, 24.90; MS m/z (M^+) calcd 205.1102, obsd 205.1124.

Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37. Found: C, 70.29; H, 7.40.

For **37**: pale yellow oil that crystallized in the cold, bp 85 °C at 0.07 Torr; IR ($CHCl_3$, cm^{-1}) 2955, 2850, 1535, 1480, 1370; ^1H NMR (300 MHz, $CDCl_3$) δ (major isomer) 5.10 (ddd, J = 8.7, 3.5, 3.5 Hz, 1 H), 3.56 (m, 1 H), 2.97 (s, 1 H), 2.93 (s, 1 H), 2.82 (s, 1 H), 2.24 (ddd, J = 12.7, 8.6, 3.7 Hz, 1 H), 2.02 (dt, J = 12.8, 3.1 Hz, 1 H), 1.78–1.68 (m, 2 H), 1.64–1.55 (m, 2 H), 1.38 (dm, J = 8.0 Hz, 1 H), 1.26 (d, J = 8.0 Hz, 1 H), 1.16–1.06 (m, 2 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 157.82, 149.22, 86.44, 55.17, 54.25, 47.80, 41.93, 41.68 (2C), 33.12, 26.65, 26.43; MS m/z (M^+) calcd 205.1103, obsd 205.1123.

Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37. Found: C, 70.31; H, 7.37.

Diels–Alder Addition of α-Acetoxyacrylonitrile to Isodicyclopentadiene. α-Acetoxyacrylonitrile (0.5 mL, 4.5 mmol) was added via syringe to freshly distilled **34** (470 mg, 3.56 mmol) containing hydroquinone (100 mg, 0.91 mmol) at room temperature. This mixture was heated for 12 h without solvent at 110 °C under a nitrogen atmosphere. The excess dienophile was removed in vacuo, and the residue was triturated with ether to precipitate hydroquinone. Filtration through a short column of silica gel gave 620 mg (72%) of a 42:16:31:11 mixture of diastereomers. The sesquinorbornenes **39** and **40** could be separated from the angular adducts **41** and **42**, but further separation proved difficult.

For **39** and **40**: colorless oil, bp 125–130 °C at 0.3 Torr; IR ($CDCl_3$, cm^{-1}) 2960, 2940, 2855, 2220, 1745; ^1H NMR (300 MHz, $CDCl_3$) δ 3.78 (s, 1 H), 3.02 (d, J = 3.4 Hz, 1 H), 2.89 (s, 1 H), 2.76 (s, 1 H), 2.63–2.57 (m, 1 H), 2.00 (s, 3 H), 1.89–1.14 (series of m, 9 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm (isomer A) 169.14, 158.34, 149.07, 120.68, 76.18, 55.45, 52.54 (2 C), 44.27, 41.53 (2 C), 41.35, 26.58, 26.26, 20.65; (isomer B) 169.02, 158.58, 148.14, 120.95, 76.58, 54.26, 52.28, 50.63, 42.80 (2C), 42.60, 41.53, 24.79, 24.56, 21.13; MS m/z (M^+) calcd 243.1259, obsd 243.1245.

Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04. Found: C, 74.10; H, 7.22.

For **41** and **42**: colorless liquid, bp 120–125 °C at 0.3 Torr; IR ($CHCl_3$, cm^{-1}) 2955, 2860, 2220, 1745; ^1H NMR (300 MHz, $CDCl_3$) δ (isomer A) 5.20 (d, J = 2.9 Hz, 1 H), 3.64 (m, 1 H), 2.86 (d, J = 3.8 Hz, 1 H), 2.44 (d, J = 12.9 Hz, 1 H), 2.31 (d, J = 3.9 Hz, 1 H), 2.04 (s, 3 H), 1.89 (d, J = 10.2 Hz, 1 H), 1.85–1.75 (m, 1 H), 1.69–1.63 (m, 3 H), 1.54 (d, J = 10.2 Hz, 1 H), 1.34–1.24 (m, 2 H), 0.89–0.81 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm (isomer B) 169.24, 160.06, 121.27, 119.67, 69.41, 50.54, 44.63, 44.19, 42.34, 38.65, 38.19, 32.53, 25.95, 24.95, 21.22; (isomer A) 169.35, 166.84, 121.20, 110.87, 61.75, 56.44, 47.54, 43.41, 42.26, 39.02, 38.72, 31.28, 24.23 (2C), 20.79; MS m/z (M^+) calcd 243.1259, obsd 243.1259.

Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04. Found: C, 74.08; H, 7.09.

***syn*- and *anti*-Sesquinorbornen-4-ones (32 and 33).** A mixture of the adducts **39–42** (420 mg, 1.73 mmol) was added to a solution of sodium hydroxide (1.0 g, 25 mmol) in distilled water (10 mL) and heated at 90 °C with stirring under nitrogen for 2 h. After cooling, water (20 mL) was introduced and the products were extracted into dichloromethane (3 × 20 mL). The combined organic layers were washed with water (2 × 50 mL), 1 N hydrochloric acid (50 mL), and saturated sodium bicarbonate solution (20 mL) prior to drying and solvent evaporation. Bulb-to-bulb distillation of the ketonic mixture gave a semicrystalline distillate (210 mg, 69%) from which it was possible to separate **32** as a white solid, mp 89 °C (from petroleum ether), upon addition of hot petroleum ether followed by cooling: IR ($CHCl_3$, cm^{-1}) 2960, 2860, 1725; ^1H NMR (300 MHz, $CDCl_3$) δ 3.08 (s, 1 H), 2.94–2.93 (m,

2 H), 2.15 (m, 2 H), 2.09–1.91 (m, 3 H), 1.80–1.70 (m, 2 H), 1.46 (dm, J = 8.0 Hz, 1 H), 1.31 (d, J = 8.0 Hz, 1 H), 1.22–1.08 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 214.72, 162.89, 148.55, 56.56, 54.40, 54.14, 42.07, 41.89, 39.23, 39.13, 26.59, 26.54; MS m/z (M^+) calcd 174.1045, obsd 174.1048.

Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.66; H, 8.11.

The mother liquor from above was concentrated, and the residue was subjected to MPLC on silica gel (elution with 5% ether in petroleum ether) to give in turn **44**, **33**, and **43**.

For **33**: a colorless oil, bp 70–75 °C at 0.7 Torr; IR ($CHCl_3$, cm^{-1}) 2980, 2930, 2880, 1735; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.15 (s, 1 H), 3.09 (s, 2 H), 3.00 (s, 1 H), 2.15 (s, 1 H), 1.95 (d, J = 8.9 Hz, 1 H), 1.85 (dd, J = 16.6, 2.8 Hz, 1 H), 1.67–1.50 (m, 3 H), 1.40 (d, J = 6.9 Hz, 1 H), 1.14 (d, J = 8.2 Hz, 1 H), 0.94–0.85 (m, 1 H), 0.71–0.63 (m, 1 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 213.52, 158.68, 146.30, 55.04, 50.37, 49.25, 43.10, 42.53, 39.64, 34.96, 24.78, 24.02; MS m/z (M^+) calcd 174.1045, obsd 174.1038.

Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.77; H, 8.11.

For **43**: colorless liquid, bp 70 °C at 0.5 Torr; IR ($CHCl_3$, cm^{-1}) 3010, 2970, 2935, 2915, 2885, 2870, 1740; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.39 (d, J = 3.1 Hz, 1 H), 3.01 (d, J = 3.1 Hz, 1 H), 2.84 (d, J = 3.7 Hz, 1 H), 2.35 (s, 1 H), 2.16–2.12 (m, 1 H), 2.03–1.95 (m, 3 H), 1.82 (dm, J = 9.5 Hz, 1 H), 1.89–1.79 (m, 1 H), 1.76–1.70 (m, 2 H), 1.61 (d, J = 10.2 Hz, 1 H), 1.39–1.34 (m, 1 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 216.95, 169.35, 112.46, 60.51, 60.05, 60.78, 41.48, 30.50, 38.98, 28.71, 31.40, 23.50; MS m/z (M^+) calcd 174.1045, obsd 174.1064.

For **44**: colorless liquid, bp 70 °C at 0.5 Torr; IR ($CHCl_3$, cm^{-1}) 2970, 2930, 2870, 1730; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.79 (d, J = 2.0 Hz, 1 H), 3.15 (s, 1 H), 2.75 (d, J = 2.9 Hz, 1 H), 2.56 (d, J = 4.0 Hz, 1 H), 2.18 (dm, J = 8.7 Hz, 1 H), 2.04–2.00 (m, 3 H), 1.80 (d, J = 8.6 Hz, 1 H), 1.81–1.70 (m, 1 H), 1.76–1.59 (m, 1 H), 1.52 (d, J = 9.9 Hz, 1 H), 1.45–1.27 (m, 2 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 215.30, 159.46, 122.07, 73.80, 52.15, 42.86, 42.01, 39.77, 38.32, 35.76, 31.81, 23.96; MS m/z (M^+) calcd 174.1045, obsd 174.1064.

Cleavage of *syn*-Sesquinorbornen-4-one. Ketone **32** (500 mg, 2.87 mmol) in dry tetrahydrofuran (2 mL) was added to freshly prepared LDA at −78 °C as above. Ethyl nitrite (220 mg, 2.93 mmol) was later introduced. After quenching of the reaction mixture with brine, the products were extracted into chloroform and subjected to chromatography on silica gel (sequential elution with 2:8, 2:7, and 7:3 ether–petroleum ether) gave in order 130 mg (26%) of recovered **32**, 440 mg (62%) of **45**, and 50 mg (9%) of **46**.

For **45**: colorless oil; IR ($CHCl_3$, cm^{-1}) 3580, 3300, 3005, 2970, 2875, 1730; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (br s, 1 H), 7.39 (d, J = 7.5 Hz) and 6.74 (d, J = 6.7 Hz tota 1 H), 4.19 and 4.18 (2 q, J = 7.1 Hz, total 2 H), 3.90–3.7 and 3.25–3.15 (m, 2 H), 2.95 (d, J = 1.2 Hz, 1 H), 2.84 (d, J = 1.2 Hz, 1 H), 2.72–2.53 (m, 1 H), 2.40–2.21 (m, 1 H), 1.71 (AB q, J = 12.6 Hz, 2 H), 1.59 (dm, J = 8.2 Hz, 1 H), 1.4–1.1 (m, 1 H), 1.29 (t, J = 7.1 Hz, 3 H), 0.99–0.92 (m, 2 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm (major isomer) 173.82, 153.54, 151.13, 149.63, 60.49, 49.60, 45.63, 41.24, 41.11, 40.45, 35.69, 25.23, 22.40, 14.09; MS m/z (M^+) calcd 249.1365, obsd 249.1373.

Anal. Calcd for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68. Found: C. 67.65; H, 7.68.

For **46**: yellow crystals, mp 127 °C dec (from ether–petroleum ether); IR ($CHCl_3$, cm^{-1}) 3570, 3300, 3010, 2970, 2920, 2870, 1745, 1655, 915; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.5 (br s, 1 H), 4.13 (s, 1 H), 3.23 (d, J = 0.8 Hz, 1 H), 3.05 (s, 1 H), 2.99 (s, 1 H), 2.37 (AB q, J = 9.5 Hz, 2 H), 1.91–1.84 (m, 2 H), 1.66 (d, J = 8.2 Hz, 1 H), 1.44 (d, J = 8.2 Hz, 1 H), 1.33–1.19 (m, 2 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 198.05, 160.39, 155.32, 155.12, 55.64, 52.56, 51.93, 42.20, 42.07, 40.23, 26.54, 26.40; MS m/z (M^+) calcd 203.0946, obsd 203.0976.

Anal. Calcd for $C_{12}H_{1N}O_2$: C, 70.92; H, 6.45. Found: C, 70.78; H, 6.57.

Cleavage of *anti*-Sesquinorbornen-4-one. Analogous treatment of **33** (570 mg, 3.27 mmol) afforded 430 mg (53%) of **47** in addition to 90 mg of impure keto oxime. For **47**: colorless oil; IR ($CHCl_3$, cm^{-1}) 3580, 3300, 2970, 2870, 1725, 1190; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major isomer) 7.76 (br s, 1 H), 7.29 (d, J = 8.4 Hz, 1 H), 4.12 (dq, J = 7.2, 1.5 Hz, 2 H), 3.64–3.58 (m, 2 H), 2.92 (s, 1 H), 2.84 (s, 1 H), 2.62 (dt, J = 13.9, 5.3 Hz, 1 H), 2.37 (dt, J = 13.9, 2.8 Hz, 1 H), 1.73–1.65 (m, 4 H), 1.27 (t, J = 7.2 Hz, 3 H), 1.00 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm (major isomer) 173.42, 153.73, 151.86, 149.33, 60.61, 51.78, 47.34, 42.89, 41.73, 41.09, 36.05, 26.40, 26.00, 14.16; MS m/z (M^+) calcd 249.1365, obsd 249. 1361.

Anal. Calcd for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68. Found: C, 67.53; H, 7.66.

Acknowledgment. We thank the National Institute of Health (Grant CA-12115) for financial support and Dr. Judith Gallucci, Haibing Deng, and Anthony Blackburn (The Ohio State University) for the X-ray crystallographic analyses.

Supplementary Material Available: X-ray data for **21** and **31**; ^{1}H NMR, ^{13}C NMR, and mass spectra of **20**, **21**, **23**, **43**, **44**, and **45**; and tables of final positional parameters anisotropic thermal parameters, bond lengths, bond angles, intramolecular distance, and torsion angles for **21** and **31** (38 pages). Ordering information is given on any current masthead page.

Crystal and Molecular Structure of *cis*-1,4,9,10-Tetramethyl-9,10-dihydroanthracene-9,10-diol

Stuart Rosenfeld* and Sarah VanDyke

Department of Chemistry, Smith College, Northampton, Massachusetts 01063

Jerry P. Jasinski and Ernest S. Paight

Department of Chemistry, Keene State College, Keene, New Hampshire 03431

Received July 23, 1990

The title compound (*cis*-**2**) was found to crystallize independently from a mixture of the three possible stereoisomers. An X-ray structure determination showed that individual molecules of *cis*-**2** have a shallow boat geometry; the dihedral angle between the least-squares planes of the aromatic rings is 165.3°. The molecules of *cis*-**2** exist in infinite hydrogen-bonded chains with a stepped sheet structure and a short hydrogen bond distance of ca. 1.7 Å.

Much effort has been devoted to establishing the preferred geometries of 9,10-dihydroanthracenes (DHA's) in solution and in the solid state.[1] In general, X-ray crystallographic analyses have demonstrated that 9-substituted

0022-3263/91/1956-0710$02.50/0