Hz, $J_{7a,6e}$ = 5.3 Hz), 2.53 (1 H, H-3a, dd, $J_{3a,3e}$ = 14.8 Hz, $J_{3a,2a}$ = 7.8 Hz), 2.43 (1 H, H-1a, dd, $J_{1a,1e}$ = 18.5 Hz, $J_{1a,2a}$ = 8.9 Hz), 2.35 (1 H, H-5a, ddd, $J_{5a,5e}$ = 17.1 Hz, $J_{5a,6e}$ = 5.6 Hz, $J_{5a,4}$ = 2.6 Hz), 2.16–1.98 (2 H, H-1e, H-3e, m), 1.96 (3 H, s) superimposed on 1.98–1.88 (1 H, H-2e, m), 1.61 (1 H, H-7e, dd, $J_{7e,7a}$ = 17.7 Hz, $J_{7e,6e}$ = 5.4 Hz), 1.53 (1 H, H-5e, dt, $J_{5e,5a}$ = 17.5 Hz, $J_{5e,6e}$ = $J_{5e,4}$ = 4.9 Hz), 1.39–1.13 (1 H, H-2a, m); homonuclear decoupling, irradiation at δ 5.50 collapsed the signals at δ 2.60 and 1.61 to d and at δ 2.35 and 1.53 to dd, irradiation at δ 4.76 collapsed the signals at δ 2.35 and 1.53 to dd; ^{13}C NMR (100 MHz) 170.31 (CO, s), 122.35 (C-3a, s), 96.08 (C-7a, s), 67.15 (C-4, d), 64.36 (C-6, d), 36.75 (2 C, t), 33.99 (t), 32.56 (t), 23.79 (C-2, t), 21.22 (q) ppm. Anal. Calcd for $(C_{11}H_{15}O_2PdCl)_2$: C, 41.15; H, 4.71. Found: C, 41.10; H, 4.80.

Di(μ-chloro)bis[(3a,4,7a-η)-2,3,4,5,6,7-hexahydro-6-acetoxy-1*H*-inden-4-yl]dipalladium (8, MeCN, $CuCl_2$). Similar treatment of 122 mg (1.02 mmol) of 4,7-dihydroindan, as described for 7 (MeCN, $CuCl_2$) except that the reaction was performed for 48 h, produced 143 mg of a brown oil, which after flash chromatography afforded 94 mg (0.15 mmol, 29%) of 8 as a yellow oil, which solidified to yellow crystals in a freezer (−18 °C): mp 128–134 °C (with decomposition to black particles).

Dimethyl *cis*-5-Acetoxy-2,3-dimethyl-2-cyclohexene-1-malonate (1a). To a stirred, yellow solution of 278 mg (0.45 mmol) of (η^3-cyclohexenyl)palladium complex 1 and 471 mg (1.80 mmol) of triphenylphosphine in 25 mL of anhydrous THF (freshly distilled from sodium benzophenone ketyl radical) under a N_2 atmosphere was added a solution containing 1.80 mmol of sodium dimethyl malonate in 15 mL of anhydrous THF.[13] After 19 h at 22 °C, the resulting red solution with black particles was poured into 100 mL of water and extracted twice with 100-mL portions of Et_2O. The combined organic phase was washed with 100 mL of water and dried ($MgSO_4$), and the solvent was removed at reduced pressure (water aspirator) on a rotary evaporator to afford a red-black oil, which was flash chromatographed (2.5 × 13-cm column packed and eluted with EtOAc–hexane, 2:3). Removal of solvent at reduced pressure (water aspirator) afforded 181 mg (0.61 mmol, 68%) of 1a as a yellow oil. Subsequent bulb-to-bulb distillation (220 °C, 0.4 Torr) for analytical purposes afforded 112 mg (0.38 mmol, 42%) of 1a as a colorless oil: IR (film) 2990, 2950, 2850, 1735, 1435, 1365, 1245, 1145, 1030 cm^{-1}; ^{1}H NMR (200 MHz) δ 4.88 (1 H, H-5a, tt, $J_{5a,4a}$ = $J_{5a,6a}$ = 8.8 Hz, $J_{5a,4e}$ = $J_{5a,6e}$ = 5.9 Hz), 3.85 (1 H, $CH(CO_2Me)_2$, d, J = 5.5 Hz), 3.74 (3 H, OMe, s), 3.70 (3 H, OMe, s), 3.06–2.91 (1 H, H-1, br m), 2.35–2.08 (2 H, H-4e, H-4a, complex m), 2.03 (3 H, MeCO, s), 1.96 (2 H, H-6a, H-6e, superficial t or dd, $J_{6a,1a}$ = $J_{6a,5a}$ = 8.1 Hz, $J_{6e,1a}$ = $J_{6e,5a}$ = 5.5 Hz), 1.63 (3 H, br s), 1.59 (3 H, br s); homonuclear decoupling, irradiation at δ 4.88 collapsed the signals at δ 2.35–2.08 to an apparent dd and at δ 1.96 to a d, irradiation at δ 3.85 collapsed the signal at 3.06–2.91 to an apparent t, irradiation at δ 2.99 collapsed the signals at δ 3.85 to a s and at δ 1.96 to a d, irradiation at δ 2.22 collapsed the signal at δ 4.88 to an apparent t, irradiation at δ 1.96 simplified the signals at δ 4.88 and 3.06–2.91; ^{13}C NMR (50 MHz) 170.04 (CO, s), 168.90 (CO, s), 168.02 (CO, s), 126.94 (s), 124.31 (s), 69.71 (C-5, d), 53.43 (d), 52.66 (q), 52.23 (q), 41.20 (C-1, d), 37.36 (C-4, t), 30.80 (C-6, t), 21.70 (q), 20.32 (q), 16.66 (q) ppm. Anal. Calcd for $C_{15}H_{22}O_6$: C, 60.43; H, 7.43. Found: C, 60.30; H, 7.30.

4-*exo*-Carbomethoxy-6,7-dimethyl-2-oxabicyclo[3.3.1]-non-6-en-3-one (1b). After a solution of 112 mg (0.38 mmol) of malonate 1a and 19 mg (0.04 mmol) of *p*-toluenesulfonic acid in 12 mL of methanol was refluxed for 24 h, the solvent was removed at reduced pressure (water aspirator) on a rotary evaporator and the residue was flash chromatographed (2.5 × 12-cm column packed and eluted with EtOAc–petroleum ether, 2:3). Removal of solvent at reduced pressure (water aspirator) afforded 66 mg (0.29 mmol, 78%) of 1b as a colorless oil.[1a]

Acknowledgment. We are grateful to the Swedish Natural Science Research Council, the Swedish Board for Technical Development, Hoffmann-La Roche Inc., the Rutgers University Graduate School, and the Rutgers University President's Coordinating Council on International Programs for supporting this research. We also thank the Knut and Alice Wallenberg Foundation and the Swedish Council for Planning and Coordination of Research (FRN) and the State of New Jersey (Department of Higher Education) for grants for 400-MHz NMR instruments, J. Cheng for some 100-MHz ^{13}C NMR spectra, and Johnson Matthey, Inc., for palladium dichloride (Loan Program).

Stereoselective Addition of Enol Silanes to Nitro Olefins. A Simple Synthesis of Compounds Related to the Insect Antifeedants Azadiradion and Gedunin

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Received April 25, 1989

The Lewis acid mediated aldol reactions of 1-[(trimethylsilyl)oxy]cyclohexene (2) and 2,6,6-trimethyl-1-[(trimethylsilyl)oxy]cyclohexene (6) with (*E*)-1-(3-furyl)-2-nitro-1-propene (1) was investigated (Schemes I and II and Chart II). The addition of enol silane 2 to nitro olefin 1 shows a 4:1 selectivity lk/ul; the same relative topicity observed as that of the corresponding reaction of enamines. The addition of enol silane 6 to 1 shows a synthetically useful lk selectivity (100%). This was applied to the preparation of compounds 8a and 12 related to the insect antifeedants azadiradion and gedunin (Chart I) by a short and stereocontrolled synthetic approach (Scheme II).

Introduction

Azadiradion and gedunin are two potent insect antifeedants, members of the limonoid family, isolated from the neem tree *Azadirachta indica* (A. Juss).[1] This kind of compound could be used in novel pesticides, in view of the growing interest for the industrial development on neem extracts.[2] Despite the widespread occurrence of the limonoids in nature and their interesting biological properties, there are few approaches to the limonoid[3] and re-

(1) (a) Siddiqui, S.; Mitra, C. *J. Sci. Ind. Res.* **1945**, *4*, 5. (b) Henderson, R.; McCrindle, R.; Overton, K. H. *Tetrahedron Lett.* **1964**, 3969. (c) Harris, M.; Henderson, R.; McCrindle, R.; Overton, K. H.; Turner, D. W. *Tetrahedron* **1968**, *24*, 1517. (d) Lavie, D.; Levie, E. C.; Jain, M. K. *Tetrahedron* **1971**, *27*, 3927.

(2) Kulkarni, R. A. *Pure Appl. Chem.* **1986**, *58*, 917.

(3) Corey, E. J.; Gregory, J. G.; Myers, A. G.; Hahl, R. W. *J. Am. Chem. Soc.* **1987**, *109*, 918.

0022-3263/90/1955-1349$02.50/0

Chart I

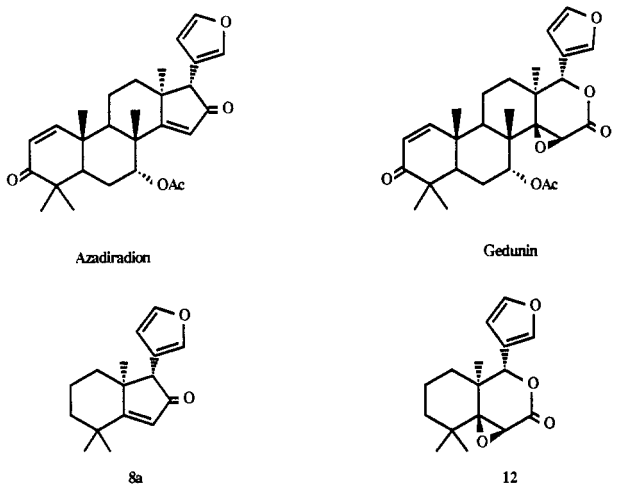


Chart II

Entry	X	R	R_1	Ar	Yield	ul/lk	Ref
1	-N O	CH_3	H	Ph	—	0/100	(7c)
2	"	H	"	"	—	0/100	(7a)
3	-N	CH_3	"	Furyl	65%	5/95	This work
4	OTMS	H	"	Ph	81%	75/25	(6a)
5	"	CH_3	"	Furyl	96%	20/80	This work
6	"	"	CH_3	"	75%	0/100	This work

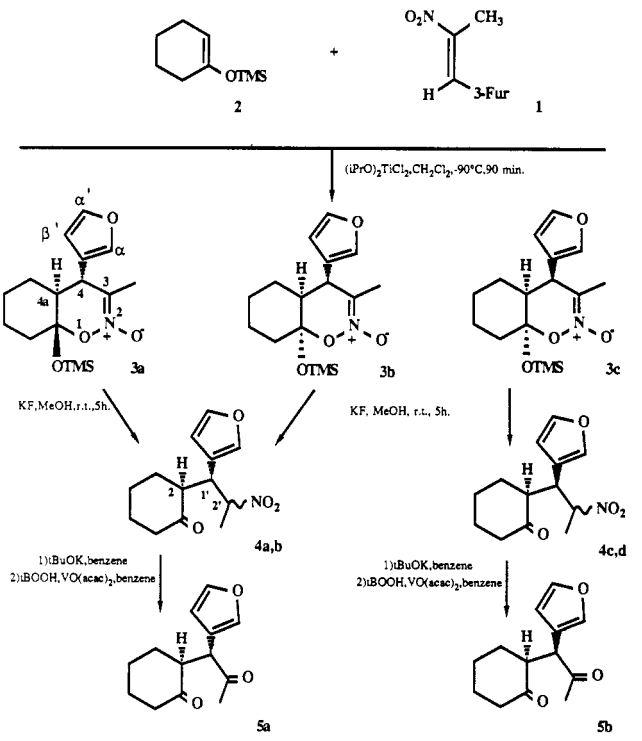
lated degraded systems.[4] Recently S. V. Ley[5] has shown that small synthetic "structural units" related to azadirachtin exhibit insect antifeedant activity comparable to the archetype compound.

We are thus prompted to develop a synthetic approach to "structural units" (Chart I) related to azadiradion and gedunin, nonetheless sufficiently versatile to provide access to other limonoids. These compounds can be used to probe structure–activity relationships. The approach is based in the stereoselective addition of the enol silane **6** to nitro olefin **1** (Chart II, entry 6 and Scheme II). This type of addition has recently been reviewed.[6]

Results and Discussion

To gain experience on the selectivity of the addition we first started with the Lewis acid mediated reaction of the enol silane **2** with the nitro olefin **1**. We found that 3 equiv of $(iPrO)_2TiCl_2$[6a] induce the stereoselective addition to give three cyclic silyl nitronates **3a–c** (96% yield)[6e] at a ratio

Scheme I



of 1:4:1, respectively (Scheme I). The structures are assigned and supported by the following arguments.

The mild nonepimerizing hydrolysis of nitronates **3a** or **3b** separately using KF in MeOH (Scheme I) gave a mixture of the γ-nitro ketones **4a,b** identical with those obtained from the hydrolysis of nitroamine, obtained as the main product of the addition[7] of 1-*N*-piperidinocyclohex-1-ene to nitro olefin **1**. Under the same conditions, the nitronate **3c** gave a mixture of γ-nitro ketones **4c** and **4d**.

The Nef reaction[8] of pairs **4a,b** and **4c,d** (Scheme I) yielded the diketones **5a** and **5b**, respectively. This supports the relative configuration of the newly formed C–C bonds.

The ^1H NMR spectrum of nitronate **3a** shows a doublet at δ 3.20 ppm (J = 10.0 Hz), while that of **3b** shows a singlet at δ 3.16 ppm ($W_{1/2h}$ = 3.4 Hz) due to proton H-4, geminal with the furan ring. Only the first coupling constant (H–H trans-diaxial) is compatible with a trans ring junction. In view of the relative configuration at the newly formed C–C bond, the ring junction of **3b** must be cis; this structure was also demonstrated by the existence of NOE between $(CH_3)_3Si$ and furyl signals (H-α′ 2%, H-α 6%, H-β′ 4%). The cis ring junction of the nitronate **3c** was tentatively assigned by the absence of NOE between $(CH_3)_4Si$ and furyl signals. The large coupling constant (J = 10.0 Hz) for the H-4 could be explained by a small dihedral angle (10–15°) for H–C_4–C_{4a}–H.

The addition of the enol silane **2** to nitro olefin **1** catalyzed by $(iPrO)_2TiCl_2$ shows a preference for the lk topicity (Chart II, entry 5) which is the favored diastereoselectivity in the addition of enamines to nitro olefins (entries 1–3). However, there are several reported cases of enol silanes (entry 4) with the relative ul topicity.[9] The opposite

(4) (a) Weber, W.; Spitzner, D.; Kraus, W. *J. Chem. Soc., Chem. Commun.* **1980**, 1212. (b) Weber, W.; Kraus, W.; Spitzner, D. *Chem. Ber.* **1980**, *113*, 385. (c) Fukuyama, Y.; Tokoroyama, T. *Tetrahedron Lett.* **1973**, *49*, 4869. (d) Drewes, S. E.; Grieco, P. A.; Huffman, J. C. *J. Org. Chem.* **1985**, *50*, 1309. (e) Tokoroyama, T.; Fukuyama, Y.; Kotsuji, Y. *J. Chem. Soc., Perkin Trans. 1* **1988**, 445.

(5) Ley, S. V.; Santafianos, D.; Blaney, W. M.; Simmonds, M. S. *Tetrahedron Lett.* **1987**, 221.

(6) (a) Seebach, D.; Brook, M. A. *Helv. Chim. Acta* **1985**, *68*, 319. (b) Miyashita, M.; Yanami, T.; Kumazawa, T.; Yoshikoshi, A. *J. Am. Chem. Soc.* **1984**, *106*, 2149. (c) Barret, A. G.; Graboski, G. G. *Chem. Rev.* **1986**, *86*, 751. (d) Seebach, D.; Golinski, J. *Helv. Chim. Acta* **1981**, *64*, 1413. (e) All compounds synthesized are racemic modifications although only one enantiomer is depicted.

(7) (a) Risaliti, A.; Forchiassin, M.; Valentin, E. *Tetrahedron Lett.* **1966**, 6331. (b) Colonna, F. P.; Valentin, E.; Pitacco, G.; Risaliti, A. *Tetrahedron* **1973**, *29*, 3011. (c) Daneo, S.; Pitacco, G.; Risaliti, A.; Valentin, E. *Tetrahedron* **1982**, *38*, 1499.

(8) (a) Bartlett, P. A.; Green, F. R. III; Webb, T. R. *Tetrahedron Lett.* **1977**, 331. (b) Very poor yields of **7** were obtained by other Nef reaction procedures, which damaged the furan ring.

Table I. ^{13}C Chemical Shifts for 8a–12

	8a	8b	9	10	11		12
C-1	59.87	57.54	61.15	48.71	50.88	C-1	78.96
C-2	205.74	207.01	78.91	75.50	209.75	C-3	168.06
C-3	125.13	125.34	123.75	60.31	57.57	C-4	52.86
C-3a	191.45	193.28	157.32	72.58	74.72	C-4a	69.72
C-4	35.87	36.76	33.86	33.34	33.83	C-5	34.54
C-5	40.72	41.66	40.39	33.98	33.59	C-6	32.70
C-6	18.60	18.61	18.95	18.66	18.81	C-7	17.61
C-7	39.36	36.76	40.71	38.36	39.08	C-8	38.30
C-7a	48.11	47.84	48.30	43.39	43.99	C-8a	38.95
C-α	141.42	140.65	140.12	140.19	141.59	C-α	141.18
C-β	118.89	119.69	122.40	121.53	118.64	C-β	120.43
C-α'	142.55	142.58	142.84	142.89	142.34	C-α'	142.79
C-β'	111.25	110.79	111.14	111.13	111.33	C-β'	110.15
CH_3	24.82	25.95	21.95	19.06	19.79	CH_3	16.02
	27.35	27.92	28.19	25.36	25.34		25.88
	31.07	30.97	30.92	27.45	27.03		26.11

stereochemical course of addition (entries 4 and 5) could be due to steric requirements (i.e. the larger nature of R in entry 5). Addition of the enol silane **6** to the nitro olefin **1** is even more selective, showing a total preference for the lk approach (Chart II, entry 6).

We therefore carried out the synthetic approach to the "structural units" **8a** and **12** (Scheme II).

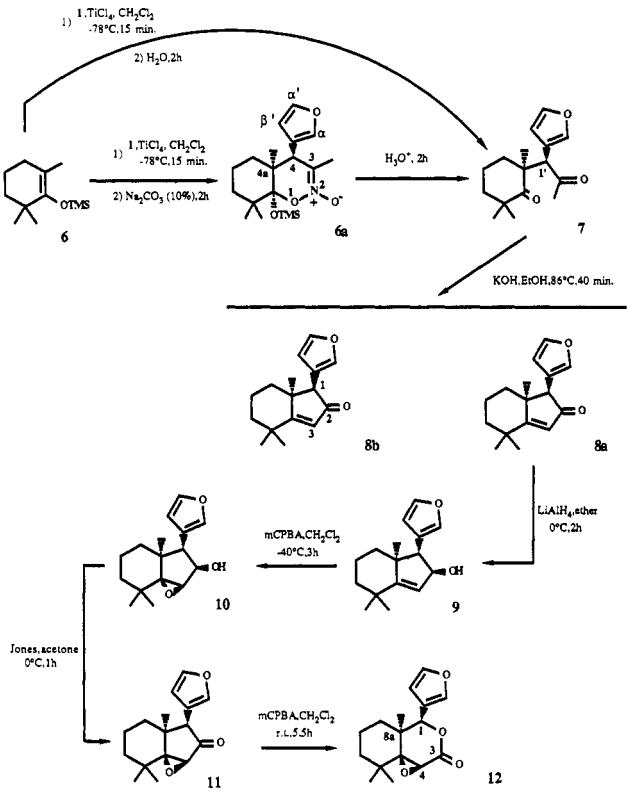
The primary product obtained from the reaction of **6** and **1**, catalyzed by $TiCl_4$,[6a,b] is the cyclic silyl nitronate **6a**, which by treatment with aqueous acid gives the diketone **7**. This product can be obtained exclusively by quenching the addition reaction with water (75% yield). The structure of **6a** is assigned and supported by the existence of NOE between $(CH_3)_3Si$ and furyl signals (H-α' 2%, H-α 5%, H-β' 3%) and by a transition state which is more favorable for the lk topicity.

Exposure of **7** to a solution of KOH (0.24 M in ethanol)[6b] at 86 °C for 40 min afforded a mixture of two cyclopentenones **8a** and **8b** (81%) in a 4:1 ratio, respectively.[10] Their structures have been assigned by their ^1H NMR spectra. The chemical shifts of the angular methyl groups attached to C-7a in **8a** and **8b** were δ 1.00 and 1.46 ppm, respectively. The diamagnetic shielding effect in the major product arises with a cis configuration for the angular methyl group and the furan ring.[11] The assignments agree with those reported in the literature[4c–e] for similar compounds whose structure has been analyzed by X-ray measurements.

Attempts at epoxidation of the cyclopentenone **8a** directly by the OH^-/H_2O_2 in MeOH gave complex mixtures of products; among them the epoxy lactone **12** was detected by TLC. To obtain this target compound, we followed a rather longer but better procedure.

Reduction of **8a** using $LiAlH_4$ in ether at 0 °C for 2 h afforded, stereospecifically, the allylic β-alcohol **9** (97%). The β-orientation of the hydroxy group is supported by the presence in its NMR spectrum of two doublet at δ 2.69 and 4.90 ppm (J = 8.6 Hz) assigned to H-1 and H-2, respectively; the coupling constant observed agrees with similar cases reported in the literature.[1d] In order to verify this assignment, nuclear Overhauser enhancement experiments were carried out with **9**. Irradiation of the $H_{\beta'}$-furyl resonance of **9** resulted in NOE of the H-1 (8%) and H-2 (9%) resonances; additionally, irradiation of the H-2 resonance resulted in NOE of the H-3 (7%) and the furyl hydrogens (H-α' 4%, H-α 6%, H-β' 5%), while irradiation on H-1 resonance resulted in NOE only of the furyl hydrogens (H-α' 8%, H-α 12%, H-β' 5%).

Scheme II



The allylic β-alcohol **9** was epoxidized in a stereospecific manner with *m*-chloroperoxybenzoic acid (mCPBA) in CH_2Cl_2 at −40 °C over 3 h, to give the epoxide alcohol **10** (75% yield). The epoxidation is assumed to proceed from the β-face, due to the syn effect caused by hydrogen bonding of the reactants. The assignement has been probed by the following facts: irradiation of the $H_{\beta'}$-furyl resonance of **10** resulted in NOE of the H-1 (6%) and H-2 (7%) resonance; also, irradiation of the H-2 resonance resulted in NOE of the H-3 (9%) and the furyl hydrogens (H-α' 2%, H-α 9%, H-β' 6%). When the acetate of the allylic alcohol **9** was subjected to epoxidation under the same conditions used for **9**, a very low conversion (9%) was observed, even after longer reaction periods (6 h). This result shows the great influence of the OH syn effect. As was previously observed in a series of steroids[12] and some

(9) The addition of **2** to 3-furaldehyde catalyzed by $TiCl_4$ gives only the aldol formed by the ul approach. This result is being applied to the synthesis of *epi*-pyroangolensolide and the results will appear in a forthcoming publication.

(10) A previous report of a similar cyclization shows no epimerization. Ishihara, M.; Tsuneya, T.; Shiota, H.; Shiga, M. *J. Org. Chem.* **1986**, *51*, 491.

(11) The relative cis configuration demonstrated in enone **8a** for the angular methyl group and the furan ring is the argument which supports the lk approach in the addition of enol silane **6** to nitro olefin **1**.

diterpenoids,[13] introduction of the epoxide into the unsaturated ring of **9** to obtain **10** causes the ^{13}C NMR signal for the homoallylic C-1, bearing an axial proton cis to the oxygenated function (epoxide), to shift upfield, also found in the epoxide cyclopentanone **11** with respect to the cyclopentenone **8a** (Table I).

Oxidation of **10** with the Jones reagent at 0 °C in acetone for 1 h gave the single epoxy ketone **11** (96%), that upon Baeyer–Villiger oxidation, with *m*-chloroperoxy benzoic acid in CH_2Cl_2 at 25 °C over 5.5 h, afforded the desired epoxy lactone **12** at a yield of 60%. There is good concordance among the ^{13}C NMR values reported by Kraus et al.[14] for similar compounds and our own values for the compounds **8a**, **11**, and **12** (Table I).

The synthetic approach to the "structural units" **8a** and **12** related to azadiradion and gedunin described in the present paper is short and stereocontrolled and is flexible enough to be applied to the total synthesis of archetype compounds.

Experimental Section

General Methods. Melting points were determined on a hot-stage apparatus and are not corrected. The ^1H and ^{13}C NMR spectra in $CDCl_3$ solution were recorded at 200 MHz for proton. IR spectra were obtained as thin films. The NOE difference measurements were performed by subtracting the FID (NS = 8) obtained by irradiation of a proton from other FID, off-resonance decoupling (FL = 50 Hz); irradiation time (D2) was 1 s; relaxation delay (D1) was 0.004 s; experiments were repeated to obtain a proper signal to noise ratio. Reactions requiring anhydrous conditions were performed in flame-dried glassware under a positive pressure of dry N_2. All reactions were monitored by TLC. Flash column chromatographies were carried out using silica gel 60 (0.040–0.063 mm Merck). Organic extracts were dried with anhydrous Na_2SO_4 and evaporated under reduced pressure below 40 °C.

(*E*)-1-(3-Furyl)-2-nitro-1-propene (1).[15] A solution of 3-furaldehyde (5.0 g, 52.0 mmol), freshly distilled 1-nitropropane (3.70 mL, 52.0 mmol), *n*-butylamine (0.26 mL, 3.0 mmol), and ethyl alcohol (5.20 mL) was stirred under N_2 at 85–90 °C for 5.5 h. The solution was allowed then to cool, whereupon yellow crystals precipitated. The product was filtered, washed with cold ethyl alcohol (20 mL), and dried over Na_2SO_4, yielding the nitro olefin **1** (5.6 g, 71% yield); mp 86–87 °C; IR 3010, 1665, 1520, 1500, 1320, and 1215 cm^{-1}; ^1H NMR δ 2.43 (3 H, s), 6.63 (1 H, s), 7.53 (1 H, s), 7.76 (1 H, s), and 7.92 (1 H, s). Anal. Calcd for $C_7H_7O_3N$: C, 54.90; H, 4.57; N, 9.15. Found: C, 54.88; H, 4.60; N, 9.12.

4-(3-Furyl)-3-methyl-8a-(trimethylsiloxy)-4a,5,6,7,8,8a-hexahydro-4*H*-1,2-benzoxazine *N*-Oxides (3a-c). $(i\text{-}PrO)_4Ti$ (3.74 mL, 12.65 mmol) and then $TiCl_4$ (1.38 mL, 12.65 mmol) were added to dry CH_2Cl_2 (255 mL) at room temperature with stirring under N_2. The resulting solution was cooled to −40 °C, and a solution of the nitro olefin **1** (1.29 g, 8.52 mmol) in dry CH_2Cl_2 (10 mL) was added, generating a red color. After further cooling to −90 °C, the enol silane **2**[16] (1.0 g, 10.20 mmol) was added. Stirring was continued at −90 °C for 90 min. The mixture was poured into an ether/water bilayer (680 mL, 3:1), shaken, and then neutralized with $NaHCO_3$ (5%). The organic layer was separated, and the aqueous phase was extracted twice with ether. The combined organic layers were washed with water and dried over Na_2SO_4. Evaporation of the solvent left a crude (2.39 g, 96% yield) of three different bicyclic nitronates **3a–c**, which were separated by flash chromatography.

For the first isomer **3a** (432 mg, 18.1%), hexane–ether (4:5) as the eluting solvent, its ^1H NMR spectrum shows δ 0.16 (9 H, s, OTMS), 1.77 (3 H, d, J = 1.6 Hz, N=CCH_3), 3.20 (1 H, d, J = 10.0 Hz, H-8), 6.14 (1 H, m, H-β'), 7.29 (1 H, m, H-α), and 7.34 (1 H, m, H-α').

For the second isomer **3b** (1.534 g, 64.2%), hexane–ether (3:5) as the eluting solvent, its ^1H NMR spectrum shows δ 0.13 (9 H, s, OTMS), 1.99 (3 H, d, J = 1.2 Hz, N=CCH_3), 3.16 (1 H, s, H-8), 6.22 (1 H, m, H-β'), 7.23 (1 H, m, H-α), and 7.23 (1 H, m, H-α').

For the third isomer **3c** (432 mg, 17.7%), hexane–ether (1:3) as the eluting solvent, its ^1H NMR spectrum shows δ 0.22 (9 H, s, OTMS), 1.89 (3 H, d, J = 1.4 Hz, N=CCH_3), 3.53 (1 H, d, J = 10 Hz, H-8), 6.30 (1 H, m, H-β'), 7.23 (1 H, m, H-α), and 7.30 (1 H, m, H-α').

2-[1′-(3-Furyl)-2′-nitropropyl]cyclohexanones (4a-c). A solution of the nitro olefin **1** (1.00 g, 6.5 mmol) in dry ether (2 mL) was added at room temperature, under N_2, to a solution of 1-*N*-piperidinocyclohex-1-ene (1.15 g, 7.0 mmol)[17] in the same solvent (18 mL). The mixture was kept in these conditions for 21 h. The solvent was evaporated in vacuo, and the residue was stirred in a mixture (1:1) of ethanol and aqueous hydrochloric acid (10%) (total volume 20 mL) for 1 h at room temperature before working up with chloroform. The combined extracts were washed with water and brine and dried over Na_2SO_4. The solvent was evaporated, and the residue (1.56 g) was flash chromatographed using hexane–ether (2:1) as the eluting solvent.

For the first isomer (294 mg, 18.0% yield), which was a crystalline product, identified as one of the diastereomers of (1′*RS*,2*SR*)-2-[1′-(3-furyl)-2′-nitropropyl]cyclohexanone (**4a**): mp 84–86 °C; IR 3125, 2930, 2850, 1710, 1545, 1390, 1360, 1015, and 865 cm^{-1}; ^1H NMR δ 1.38 (3 H, d, J = 6.6 Hz, CH_3), 2.98 (1 H, m, H-2), 3.25 (1 H, dd, J = 10.0 and 4.2 Hz, H-1′), 5.11 (1 H, dq, J_q = 6.6 and J_d = 4.2 Hz, H-2′), 6.11 (1 H, m, H-β'), 7.24 (1 H, m, H-α), and 7.34 (1 H, m, H-α'); ^{13}C NMR δ 17.05, 25.13, 28.48, 33.24, 40.06, 42.61, 50.94, 82.82, 109.73, 118.97, 141.31, 143.11, and 211.91. Anal. Calcd for $C_{13}H_{17}O_4N$: C, 60.16; H, 6.77; N, 5.58. Found: C, 60.15; H, 6.75; N, 5.59.

For the second isomer (708 mg, 43.4% yield), which was an oily product, identified as the other diastereomer of (1′*RS*,2*SR*)-2-[1′-(3-furyl)-2′-nitropropyl]cyclohexanone (**4b**): ^1H NMR δ 1.36 (3 H, d, J = 6.7 Hz, CH_3), 2.22 (1 H, m, H-2), 3.86 (1 H, dd, J = 6.5 and 8.2 Hz, H-1′), 4.98 (1 H, dq, J_q = 6.7 and J_d = 8.2 Hz, H-2′), 6.20 (1 H, m, H-β'), 7.28 (1 H, m, α-H), and 7.35 (1 H, m, H-α'); ^{13}C NMR δ 15.75, 24.36, 27.14, 30.37, 39.08, 41.74, 51.10, 83.57, 110.19, 119.14, 141.73, 142.90, and 209.98. Anal. Calcd for $C_{13}H_{17}O_4N$: C, 60.16; H, 6.77; N, 5.58. Found: C, 60.12; H, 6.78; N, 5.51.

For the third isomer (49 mg, 3.0% yield), an oily product identified as one of the diastereomers of (1′*RS*,2*RS*)-2-[1′-(3-furyl)-2′-nitropropyl]cyclohexenone (**4c**): ^1H NMR δ 1.43 (3 H, d, J = 6.7 Hz, CH_3), 2.72 (1 H, m, H-2), 3.10 (1 H, dd, J = 9.8 and 4.9 Hz, H-1′), 5.43 (1 H, dq, J_q = 6.7 and J_d = 9.8 Hz, H-2′), 6.26 (1 H, m, H-β'), 7.17 (1 H, m, H-α), and 7.22 (1 H, m, H-α'). Anal. Calcd for $C_{13}H_{17}O_4N$: C, 60.16; H, 6.77; N, 5.58. Found: C, 60.11; H, 6.79; N, 5.50.

General Procedure for the Hydrolysis of the Cyclic Silyl Nitronates to γ-Nitro Ketones. The nitronate (1.0 mmol) was dissolved in MeOH (67 mL), and KF (0.7 mmol) was added. After stirring for 5 h at room temperature, the solution was diluted with water (13 mL) and extracted with ether. The organic layers were washed with water and brine, dried over Na_2SO_4, and evaporated to give a crude (70–85% yield). ^1H NMR analysis of the mixture of the three different hydrolysis showed that (a) hydrolysis of the first nitronate **3a** afforded a mixture of the γ-nitro ketones **4a**/**4b**, ratio 1.0/2.7; (b) hydrolysis of the second nitronate **3b** afforded a mixture of the γ-nitro ketones **4a**/**4b**, ratio 1.0/7.5; (c) hydrolysis of the third nitronate **3c** afforded a mixture of the γ-nitro ketones **4c**/**4d**, ratio 1.0/1.2.

For the new γ-nitrocyclohexanone **4d** its ^1H NMR spectrum shows δ 1.35 (3 H, d, J = 6.5 Hz, CH_3), 2.48 (1 H, m, H-2), 3.02 (1 H, dd, J = 10.7 and 4.4 Hz, H-1′), 5.54 (1 H, dq, J_q = 6.5 and J_d = 10.7 Hz, H-2′), 6.39 (1 H, m, H-β'), 7.33 (1 H, m, H-α), and 7.35 (1 H, m, H-α').

General Procedure for the Oxidative Conversion of γ-Nitro Ketones to 1,4-Diketones. A mixture of the γ-nitro ketone (100 mg, 0.40 mmol) and t-BuOK (49 mg, 0.44 mmol) in dry

(12) Tori, K.; Komemo T.; Sangaré, M.; Septe, B.; Delpech, B.; Ahond, A.; Lukacs, G. *Tetrahedron Lett.* **1974**, 1157.
(13) Imamura, P.; Rúveda, E. *J. Org. Chem.* **1980**, *45*, 512.
(14) Kraus, W.; Cramer, R.; Sawitzki, G. *Phytochemistry* **1981**, *20*, 117.
(15) Gilsdorf, R. T.; Nord, F. F. *J. Org. Chem.* **1950**, *15*, 807.
(16) Cazeau, P.; Duboudin, F.; Moulines, F.; Babot, O.; Dunogues, J. *Tetrahedron* **1987**, *43*, 2075.
(17) The piperidine enamine of cyclohexanone was prepared using the procedure of Stork, G. et al. *J. Am. Chem. Soc.* **1963**, *85*, 207.

benzene (1.0 mL) was stirred for 20 min at 9 °C under N_2. A solution of t-BuOOH (0.1 mL, 0.80 mmol), $VO(acac)_2$ (1.4 mg, 0.005 mmol), and dry benzene (0.5 mL) was added dropwise to the former mixture. After 30 min, the mixture was diluted with ether, washed with water and brine, and then dried over Na_2SO_4. The solvent was evaporated, and the residue was purified by flash chromatography, yield 70–75%.

(a) The γ-nitro ketones **4a** and **4b** afforded[18] the same crystalline 1,4-diketone **5a**: mp 75–78 °C; IR 3000–2850, 1716, 1692, 1518, and 1008 cm^{-1}; ^1H NMR δ 2.24 (3 H, s, CH_3), 2.38 (2 H, m, H-6), 3.15 (1 H, m, H-2), 3.80 (1 H, d, J = 10.1 Hz, H-1′), 6.23 (1 H, m, H-β′), 7.31 (1 H, m, H-α), and 7.38 (1 H, m, H-α′). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.91; H, 7.27. Found: C, 70.83; H, 7.25. (b) The γ-nitro ketones **4c** and **4d** afforded the same oily 1,4-diketone **5b**: IR 3000–2860, 1715, 1688, 1520, and 1012 cm^{-1}; ^1H NMR δ 2.17 (3 H, s, CH_3), 2.38 (2 H, m, H-6), 2.97 (1 H, m, H-2), 3.38 (1 H, d, J = 6.0 Hz, H-1′), 6.30 (1 H, m, H-β′), 7.29 (1 H, m, H-α), and 7.36 (1 H, m, H-α′). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.91; H, 7.27. Found: C, 70.86; H, 7.26.

2,2,6-Trimethylcyclohexanone was prepared as reported[19] from ethyl 2-oxocyclohexanecarboxylate (42.5 g, 1.25 mol) to obtain a liquid (27.0 g, 77% yield), bp 176.5–178 °C.

(4*RS*,4a*SR*)-4-(3-Furyl)-3,4a,8,8-tetramethyl-8a-(trimethylsiloxy)-4a,5,6,7,8,8a-hexahydro-4*H*-1,2-benzoxazine *N*-Oxide (6a) and (1′*RS*,2*SR*)-2,6,6-Trimethyl-2-[1′-(3-furyl)-2-oxopropyl]cyclohexanone (7). A solution of the enol silane **6** (267 mg, 1.26 mmol)[20] in dry CH_2Cl_2 (3.5 mL) was added rapidly, under N_2 at −78 °C, to a solution of the nitro olefin **1** (190 mg, 1.26 mmol) in the same solvent (3.5 mL). Then, $TiCl_4$ (0.17 mL, 1.56 mmol) was added dropwise over 2 min, and the resulting red mixture was stirred at −78 °C for an additional 15 min. An aqueous solution of Na_2CO_3 (5 mL, 10%) was added, and the resulting heterogeneous mixture was stirred and gradually warmed to room temperature (2 h). The organic layer was separated, and the aqueous phase was extracted twice with CH_2Cl_2. The combined extracts were washed with water and brine and then dried over Na_2SO_4. Evaporation of the solvent left a crude (453 mg) of two different compounds which were separated by flash chromatography.

The first one eluted (188 mg, 57%), hexane–ether (7:3) as the eluting solvent, was a crystalline product identified as the diketone **7**: mp 119–120 °C; IR 3000–2860, 1715, 1690, 1520, 1390, and 1010 cm^{-1}; ^1H NMR δ 0.98 (3 H, s), 1.14 (3 H, s), 1.17 (3 H, s), 1.98 (3 H, s, $COCH_3$), 4.31 (1 H, s, H-1′), 6.19 (1 H, m, H-β′), 7.32 (1 H, m, H-α), and 7.40 (1 H, m, H-α′); ^{13}C NMR δ 17.81, 25.30, 27.73, 28.00, 28.93, 33.81, 38.24, 44.33, 47.90, 58.35, 111.80, 118.50, 141.96, 143.14, 207.66, and 221.14; MS m/e (relative intensity) 262 (14, M^+), 235 (8), 219 (7), 191 (15), 149 (18), 135 (28), 121 (38), 109 (60), 95 (62), 69 (100), and 55 (74). Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.28; H, 8.40. Found: C, 73.29; H, 8.40.

The second compound (69 mg, 15%), hexane–ether (1:1) as the eluting solvent, was an unstable crystalline solid identified as the cyclic silyl nitronate **6a**; IR 3000–2860, 1630, 1470, and 1010 cm^{-1}; ^1H NMR δ 0.23 (9 H, s), 1.02 (3 H, s), 1.06 (3 H, s), 1.10 (3 H, s), 1.82 (3 H, d, J = 1.76 Hz, N=CCH_3), 3.46 (1 H, m, H-4), 6.17 (1 H, m, H-β′), 7.28 (1 H, m, H-α), and 7.37 (1 H, m, H-α′); ^{13}C NMR δ 3.27, 17.55, 17.79, 20.45, 24.50, 26.81, 31.02, 36.73, 39.47, 40.67, 44.71, 109.79, 112.04, 119.79, 121.13, 142.13, and 142.96. Anal. Calcd for $C_{19}H_{31}O_4NSi$: C, 62.47; H, 8.49; N, 3.84; Si, 7.67. Found: C, 62.38; H, 8.43; N, 3.83; Si, 7.69.

When the red mixture was quenched with water (5 mL) and then worked up, only the diketone **7** was obtained (75% yield).

The cyclic silyl nitronate **6a** (1 mmol) readily afforded the diketone **7** when mixed with an aqueous solution of $TiCl_3$ (1 mmol) in THF (5 mL) and was stirred at room temperature for 10 h.

(1*RS*,7a*SR*)-1-(3-Furyl)-4,4,7a-trimethyl-1,4,5,6,7,7a-hexahydro-2*H*-inden-2-one (8a). A mixture of the diketone **7** (1.0 g, 3.89 mmol) and potasium hydroxide (0.43 g, 7.62 mmol) in ethanol (32 mL) was stirred at reflux for 40 min[21] under N_2. The cooled reaction mixture was poured into water and extracted with ether. The ether extract was washed with water and brine and dried over Na_2SO_4. Evaporation of the solvent left a crude (920 mg). The product mixture was separated by flash chromatography using hexane–ether (1:1) as the eluting solvent. The first fraction (166 mg) was the starting material **7**.

The second fraction (608 mg, 64% yield) was the crystalline cyclopentenone **8a**: mp 86–87 °C; IR 3000–2900, 1700, 1605, 1460, 1380, 1160, 1020, and 870 cm^{-1}; ^1H NMR δ 1.00 (3 H, s, CH_3-7a), 1.23 (3 H, s), 1.26 (3 H, s), 3.42 (1 H, s, H-1), 5.96 (1 H, s, H-3), 6.22 (1 H, m, H-β′), 7.39 (1 H, m, H-α), and 7.40 (1 H, m, H-α′). Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.69; H, 8.20. Found: C, 78.68; H, 8.21. The third fraction (161 mg, 17% yield) was an oil identified as (1*RS*,7a*RS*)-1-(3-furyl)-4,4,7a-trimethyl-1,4,5,6,7,7a-hexahydro-2*H*-inden-2-one (**8b**): IR 3000–2900, 1700, 1610, 1370, and 870 cm^{-1}; ^1H NMR δ 1.23 (3 H, s), 1.28 (3 H, s), 1.46 (3 H, s, CH_3-7a), 3.34 (1 H, s, H-1), 5.96 (1 H, s, H-3), 6.13 (1 H, m, H-β′), 7.24 (1 H, m, H-α), and 7.36 (1 H, m, H-α′). Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.69; H, 8.20. Found: C, 78.68; H, 8.23.

(1*RS*,2*RS*,7a*SR*)-1-(3-Furyl)-4,4,7a-trimethyl-1,4,5,6,7,7a-hexahydro-2*H*-inden-2-ol (9). $LiAlH_4$ (29 mg, 0.76 mmol) was added to a solution of cyclopentenone **8a** (534 mg, 2.19 mmol) in dry ether (15 mL) at 0 °C. The solution was stirred under N_2 at this temperature for 3 h and quenched by the addition of $Na_2SO_4 \cdot 10H_2O$ (29 mg). The mixture was then stirred for 1 h at 25 °C and filtered. Removal of solvent afforded a crude product, which was crystallized from hexane (520 mg, 97% yield) and identified as the unsaturated alcohol **9**: mp 73–74 °C; IR 3600–3100, 3060, 3000–2840, 1640, 1460, and 870 cm^{-1}; ^1H NMR δ 0.88 (3 H, s), 1.10 (3 H, s), 1.14 (3 H, s), 2.69 (1 H, d, J = 8.6 Hz, H-1), 4.90 (1 H, d, J = 8.6 Hz, H-2), 5.47 (1 H, d, J = 1.1 Hz, H-3), 6.31 (1 H, m, H-β′), 7.34 (1 H, m, H-α), and 7.40 (1 H, m, H-α′); MS m/e (relative intensity) 246 (100, M^+), 231 (29), 213 (12), 175 (14), 161 (15), 147 (20), 123 (68), 108 (61), 91 (33), 81 (52) and 69 (22). Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.05; H, 8.94. Found: C, 78.04; H, 8.93.

(1*RS*,2*RS*,7a*SR*)-2-Acetoxy-1-(3-furyl)-4,7,7a-trimethyl-1,4,5,6,7,7a-hexahydro-2*H*-indene (9a). The unsaturated alcohol **9** (137 mg, 0.56 mmol) was treated with acetic anhydride (1 mL) and pyridine (1 mL) at room temperature for 3 h. After the usual workup the acetate **9a** (148 mg, 93% yield) was obtained: mp 82–85 °C; IR 3000–2840, 1720, 1365, and 1015 cm^{-1}; ^1H NMR δ 0.89 (3 H, s), 1.11 (3 H, s), 1.14 (3 H, s), 2.02 (3 H, s, $COCH_3$), 2.98 (1 H, d, J = 9.0 Hz, H-1), 5.45 (1 H, s, H-3), 5.90 (1 H, d, J = 9.0 Hz, H-2), 6.29 (1 H, m, H-β′), 7,29 (1 H, m, H-α), and 7.38 (1 H, m, H-α′).

(1*RS*,2*RS*,3*RS*,3a*SR*,7a*SR*)-2-Acetoxy-1-(3-furyl)-4,4,7a-trimethyl-3,3a-epoxyhexahydroindan (10a). A solution of *m*-chloroperbenzoic acid (156 mg, 0.91 mmol) in dry CH_2Cl_2 (2.5 mL) was added dropwise at −40 °C to a solution of the allylic acetate **9a** (140 mg, 0.49 mmol) in dry CH_2Cl_2 (1.5 mL), and the resulting mixture was stirred at this temperature for an additional 6 h. After the usual workup the crude was flash chromatographed using hexane–ether (9:1) as the eluting solvent.

The first fraction (56 mg, 40%) was the allylic acetate **9a**.

The second fraction (13 mg, 9% yield) was identified as the epoxide acetate **10a**: IR 3000–2830, 1720, 1360, and 1025 cm^{-1}; ^1H NMR δ 0.81 (3 H, s), 0.86 (3 H, s), 1.17 (3 H, s), 2.05 (3 H, s, $COCH_3$), 2.89 (1 H, d, J = 9.5 Hz, H-1), 3.70 (1 H, s, H-3), 5.31 (1 H, d, J = 9.5 Hz, H-2), 6.17 (1 H, m, H-β′), 7.26 (1 H, m, H-α), and 7.36 (1 H, m, H-α′). Anal. Calcd for $C_{18}H_{24}O_4$: C, 71.05; H, 7.89. Found: C, 70.98; H, 7.82.

(1*RS*,2*RS*,3*RS*,3a*SR*,7a*SR*)-1-(3-Furyl)-4,4,7a-trimethyl-3,3a-epoxyhexahydroindan-2-ol (10). A solution of *m*-chloroperbenzoic acid (314 mg, 1.83 mmol) in dry CH_2Cl_2 (4 mL) was added dropwise at −40 °C[22] to a solution of the allylic alcohol **9** (150 mg, 0.61 mmol) in dry CH_2Cl_2 (2 mL), and the resulting mixture was stirred at this temperature for an additional 3 h. A solution of $NaHSO_3$ (10%) was added, and the resulting

(18) Reaction of the γ-nitro ketone **4a** with NaOH/EtOH and then with HCl (2 N) afforded a mixture of the **5a**/**5b** (3/1 ratio) owing to the epimerization conditions.

(19) Stevens, C. L.; Weinheimer, A. J. *J. Am. Chem. Soc.* **1958**, *80*, 4072.

(20) 1-[(Trimethylsil)oxy]cyclohexene (**2**) and 2,6,6-trimethyl-1-(trimethylsiloxy)cyclohexene (**6**) were prepared as reported[16] from the correspondent cyclohexanone. To complete the reaction 4 h were required to enol silane **6** and only 15 min to enol silane **2**.

(21) More time left less starting material but yield was reduced.

(22) Other temperatures (25, −25, and −78 °C) afforded a poorer yield in epoxide product. Epoxidation by the Sharpless reaction did not afford epoxide product.

heterogeneous mixture was stirred and gradually warmed to room temperature (30 min). The organic layer was separated, and the aqueous phase was extracted twice with ether. The combined extracts were washed with aqueous sodium hydroxide (0.5 N), water, and brine and then dried over Na_2SO_4 and filtered. Removal of the solvent afforded a residue, which was flash chromatographed using hexane–ether (1:2) as the eluting solvent, to give the epoxide alcohol **10** (120 mg, 75% yield). Crystallization from hexane/drops of ether afforded a material with mp 121–122 °C: IR 3580–3200, 3110, 3000–2800, 1600, 1450, and 860 cm^{-1}; ^1H NMR δ 0.80 (3 H, s), 0.82 (3 H, s), 1.14 (3 H, s), 2.57 (1 H, d, J = 9.3 Hz, H-1), 3.55 (1 H, s, H-3), 4.19 (1 H, d, J = 9.3 Hz, H-2), 6.20 (1 H, m, H-β'), 7.23 (1 H, m, H-α), and 7.36 (1 H, m, H-α'). Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.28; H, 8.40. Found: C, 73.28; H, 8.39.

(1*RS*,3*SR*,3a*SR*,7a*SR*)-1-(3-Furyl)-4,4a,7a-trimethyl-3,3a-epoxyhexahydroindan-2-one (11). Jones reagent (0.5 mL) was added dropwise with stirring to a solution of the epoxide-alcohol **10** (56 mg, 0.21 mmol) in acetone (6 mL) at 0 °C. The resulting mixture was stirred at 0 °C for an additional 1 h. 2-Propanol was added in small portions to discharge a brown color in the upper layer. The mixture was concentrated in vacuo to afford a residue, which was dissolved with water and extracted with ether. The organic layers were washed with water and brine, dried over Na_2SO_4, and filtered. Evaporation of the solvent left a crude which was crystallized from hexane (53 mg, 96% yield) and identified as the epoxide–cyclopentanone **11**: mp 152–154 °C; IR 3100, 3000–2800, 1750, 1460, and 890 cm^{-1}; ^1H NMR δ 0.85 (3 H, s), 0.90 (3 H, s), 1.23 (3 H, s), 3.44 (1 H, s, H-3), 3.88 (1 H, s, H-1), 6.22 (1 H, M, H-β'), 7.39 (1 H, m, H-α), and 7.44 (1 H, m, H-α'); MS m/e (relative intensity) 260 (35, M^+), 242 (13), 217 (18), 178 (21), 156 (30), 139 (32), 123 (72), 108 (90), 91 (80), 81 (100), 77 (91), 69 (64), 55 (99), and 53 (80). Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.85; H, 7.69. found: C, 73.84; H, 7.68.

(1*RS*,4*SR*,4a*SR*,8a*SR*)-1-(3-Furyl)-5,5,8a-trimethyl-4,4a-epoxyoctahydro-2-benzopyran-3-one (12). A solution of *m*-chloroperbenzoic acid (52 mg, 0.30 mmol) in dry CH_2Cl_2 (1 mL) was added at room temperature to a heterogeneous solution of epoxy ketone **11** (52 mg, 0.20 mmol) in dry CH_2Cl_2 (1 mL) and $NaHCO_3$ (20 mg). The mixture was kept in the dark for 5.5 h and then diluted with ether and washed with successive solutions of $NaHSO_3$ (10%), water and brine. The organic extract was dried over Na_2SO_4, filtered, and concentrated in vacuo to afford a solid, which was flash chromatographed using hexane–ether (4:1) as the eluting solvent, to give the epoxy lactone **12** (31 mg, 60% yield). Crystallization from hexane afforded a material with mp 121–122 °C: IR 3115, 3000–2840, 1735, 1600, 1300, 1270, and 1160 cm^{-1}; ^1H NMR δ 0.81 (3 H, s), 1.09 (3 H, s), 1.21 (3 H, s), 3.64 (1 H, s, H-3), 5.58 (1 H, s, H-1), 6.33 (1 H, m, H-β'), 7.38 (1 H, m, H-α), and 7.39 (1 H, m, H-α'); MS m/e (relative intensity) 276 (19, M^+), 248 (11), 219 (40), 181 (11), 153 (100), 137 (54), 123 (100), 109 (47), 95 (52), 81 (53), 69 (40), and 55 (55). Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.56; H, 7.25. Found: C, 69.54; H, 7.25.

Registry No. **1**, 124070-88-8; **2**, 6651-36-1; (±)-**3a**, 124070-89-9; (±)-**3b**, 124151-17-3; (±)-**3c**, 124151-18-4; (±)-**4a** (isomer 1), 124070-90-2; (±)-**4a** (isomer 2), 124151-19-5; (±)-**4c** (ismer 1), 124151-20-8; (±)-**4c** (isomer 2), 124151-21-9; (±)-**5a**, 124070-91-3; (±)-**5b**, 124070-92-4; **6**, 83999-44-4; **6** ketone, 2408-37-9; (±)-**6a**, 124070-93-5; (±)-**7**, 124070-94-6; (±)-**8a**, 124070-95-7; (±)-**8b**, 124070-96-8; (±)-**9**, 124098-16-4; (±)-**9a**, 124098-15-3; (±)-**10**, 124070-97-9; (±)-**10a**, 124070-98-0; (±)-**11**, 124070-99-1; (±)-**12**, 124071-00-7; 3-Fur-CHO, 498-60-2; *n*-$C_3H_7NO_2$, 108-03-2; ethyl 2-oxocyclohexanecarboxylate, 1655-07-8.

Notes

Reduction of α-Diketones and α-Keto Esters with HI in Acetic Anhydride–Acetic Acid

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Received March 30, 1989

Introduction

The reduction of α-keto-substituted carbonyl compounds by aqueous HI–acetic acid solutions has been known for a long time.[1-4] With the notable exception of the reduction of benzil derivatives, which cleanly generate benzoins upon reduction, the reaction has been reported to result in the net deoxygenation of the reduced carbonyl according to eq 1. α-Hydroxy ketones are rarely observed as minor byproducts, and the reaction has seen limited application.

$$RC(=O)C(=O)R' + 4HI \rightarrow RCH_2C(=O)R' + 2I_2 \quad (1)$$

We recently had cause to reexamine this rather interesting reduction of α-keto-substituted ketones and esters with HI. However, unlike the previous examinations, we were operating our system under anhydrous conditions using a solution of acetic anhydride–acetic acid in place of aqueous acetic acid. We found that the reaction provided an efficient reduction of the α-keto-substituted carbonyl compound to α-acetoxy ketones without any significant deoxygenation as reported in the earlier reports. The α-acetoxy ketones and esters obtained by this process are useful as flavoring and fragrance components of a variety of foods and beverages,[5] and we would like to discuss the details of this investigation in the remainder of this report.

Results

We would like to begin this discussion by focusing on the simplest α-diketone, 2,3-butanedione (commonly referred to as biacetyl). When we added biacetyl to a solution of HI in acetic anhydride–acetic acid at room temperature, we received a rapid, exothermic reduction of the biacetyl to acetoin acetate in quantitative yield with the

(1) Fuson, R. C.; Hoch, P. E. *J. Am. Chem. Soc.* **1949**, *71*, 1585.
(2) (a) Reusch, W.; LeMahieu, R. *J. Am. Chem. Soc.* **1964**, *86*, 3068, and references therein. (b) Reusch, W.; LeMahieu, R. *J. Am. Chem. Soc.* **1963**, *85*, 1669.
(3) (a) Nakai, T.; Mimura, T. *J. Synth. Chem. Jpn.* **1977**, *35*, 964. (b) Talapatra, S. K.; Pradhan, D. K.; Takapatra, B. *Ind. J. Chem., Sect. B* **1978**,16, 361. (c) Duddeck, H.; Wiskamp, V.; Rosenbaum, D. *J. Org. Chem.* **1981**, *46*, 5332. (d) Osman, S. M.; Ahmad, M. *Fette, Seifen, Anstrichm.* **1970**, *72*, 454 (Chem. Abstr. 73:44844q). (e) Rakhit, S.; Gut, M. *J. Org. Chem.* **1968**, *33*, 1196.
(4) Reports of the corresponding reduction of α-keto esters and acids have been limited to the reduction of pyruvic acid to propionic acid in concentrated aqueous HI solutions. See: (a) Kaplan, L. *J. Org. Chem.* **1982**, *47*, 5422. (b) Wislicenus, W. *Justus Liebigs Ann. Chem.* **1863**, *126*, 229.
(5) See, for the example: (a) Oser, B. L.; Ford, R. A. *Food Technol. (Chicago)* **1978**, *32*(2), 60. See also: (b) Schreier, P. *J. Agric. Food Chem.* **1980**, *28*, 926, and references therein.

0022-3263/90/1955-1354$02.50/0