Ring Expansions of [2 + 2] Photoadducts. Potential Applications in the Synthesis of Triquinane and Taxane Skeletons

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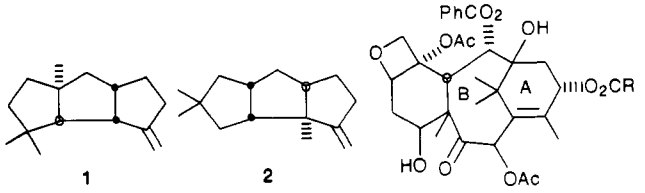
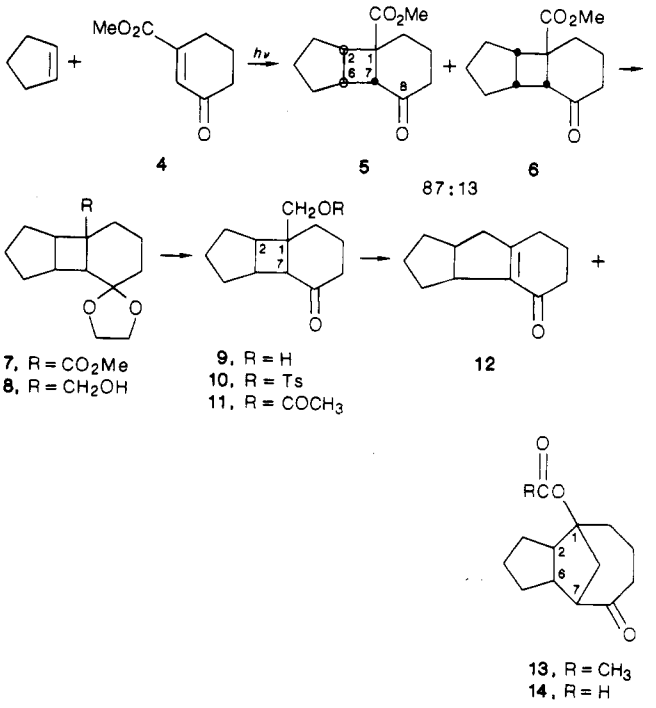
Photoadditions of enones **4** or **18** with cyclopentene gave in good yield adducts **5/6** or **20/21**, respectively, with the anti isomers predominating by a ratio of ~9:1. These adducts were converted to hydroxy ketones **9** or **24** by the following sequence: ketalization, $LiAlH_4$ reduction, and hydrolysis. The alcohol function in these ketones was converted to a good leaving group, and the resultant derivatives were solvolyzed to give ring-expanded products **12** or **28** as well as bridged products **13–14** or **29–32**, respectively. The sequence starting with the enone **18** has potential applications in the synthesis of the triquinane and the taxol carbon skeletons.

Adducts derived from [2 + 2] photoaddition reactions have been used in a variety of ways for the synthesis of natural products,[1] and a recent review has outlined the application of cyclobutane derivatives in organic synthesis.[2] In this report we describe rearrangements of the strained cyclobutane ring in suitably functionalized photoadducts that lead to the formation of a cyclopentane ring or a bridged system. The cyclopentane ring that is formed may be part of a linearly fused triquinane (tricyclo[6.3.0.$0^{2,6}$]-undecane), a skeleton that has been the target of many synthetic organic chemists.[3] A number of sesquiterpenoids (e.g. $\Delta^{9,12}$-capnellene, **1**, and hirsutene, **2**) contain this carbon skeleton, and a few of these natural products display significant levels of biological activity.[4] The bridged system that may be formed from the photoadduct is related to the A/B-ring portion of the taxol skeleton. The diterpene taxol (**3**) has been reported to possess potent antileukemic activity,[5] and although numerous approaches to the synthesis of the taxane skeleton have been reported,[6] the A/B-ring portion with a bridgehead hydroxyl group is a particularly challenging region of the molecule.[7] We report first the results of a model study, which yielded a 6–5–5 ring system (tricyclo[6.4.0.$0^{2,6}$]dodecane) and a related bridged system. That is followed by a discussion of our approach to the synthesis of a linear triquinane and a bridged system similar to that present in taxol.



Synthesis of Tricyclo[6.4.0.$0^{2,6}$]dodecane Skeleton (6–5–5 Ring System). Photoaddition of the readily available enone ester **4**[8] with excess cyclopentene in toluene gave a 91% yield of adducts **5** and **6** (Scheme I) in a ratio of 87:13, respectively. It was assumed that the fusion between the four- and the five-membered rings was cis, and since the mixture of adducts was recovered unchanged upon treatment with sodium methoxide, the 6–4 ring fusions must also be cis. Thus, the two compounds must be the cis-anti-cis and cis-syn-cis adducts. The adducts were separated by GLC, but detailed analysis of their ^1H NMR spectra did not unambiguously distinguish between them. Thus, a single-crystal X-ray analysis of the major adduct was undertaken[9] and established that it possessed the cis-anti-cis stereochemistry depicted in **5** and the minor component was then the syn adduct **6**. A comparison of the ^{13}C NMR spectra of **5** and **6** (Experimental Section) indicates a significant difference in the chemical shifts of C-3 and C-5 with these carbons being more shielded in the syn adduct **6** (27.7 vs 32.4 ppm in **5**). This γ-gauche interaction between these carbons and the cyclohexanone ring in a syn adduct has been noted previously for related adducts[10] and will be utilized again in the next section of this report.

Scheme I



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(3) For other synthetic approaches to the triquinanes, see: Kinney, W. A.; Coghlan, M. J.; Paquette, L. A. *J. Am. Chem. Soc.* **1985**, *107*, 7352 and references cited therein.

(4) Sheikh, Y. M.; Singy, G.; Kaisin, M.; Eggert, H.; Djerassi, C.; Tursch, B.; Daloze, D.; Braekman, J. C. *Tetrahedron* **1976**, *32*, 1171.

(5) Wani, M. C.; Taylor, H. L.; Wall, M. E.; Coggon, P.; McPhail, A. T. *J. Am. Chem. Soc.* **1971**, *93*, 2325.

(6) Lin, J.; Nikaido, M. M.; Clark, G. *J. Org. Chem.* **1987**, *52*, 3745, see reference (5) therein.

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(10) Williams, J. R.; Lin, C.; Chodosh, D. F. *J. Org. Chem.* **1985**, *50*, 5815.

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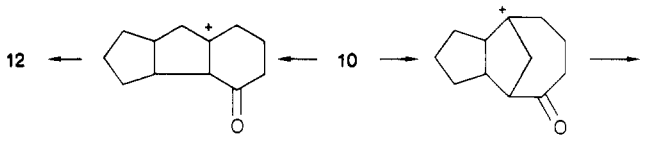
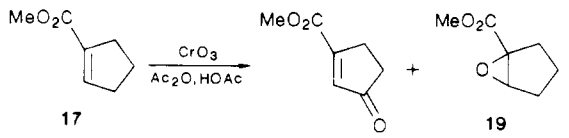
We then proceeded with the remainder of the sequence outlined in Scheme I using the mixture of adducts because of the difficulty in removing the minor component (13%). Our strategy was to convert the ester group in **5** (and **6**) to functionality with a good leaving group and then to take advantage of the strain inherent in a cyclobutane ring to expand it to a five-membered ring. Toward this end, **5**/**6** was converted to ketal **7**, the ester function was reduced with lithium aluminum hydride to yield **8**, and the ketal was hydrolyzed to give hydroxy ketone **9**. Conversion of **9** to tosylate **10** gave a substrate with a leaving group at the required position. In the crucial ring-expansion step, solvolysis of **10** in acetic acid/sodium acetate, gave a 45:55 mixture of enone [12] (the desired 6–5–5 ring system) and bridged acetate **13** while in formic acid/sodium formate the ratio of **12**:**14** was improved to 64:36. The latter solvolysis gave a 59% isolated yield of **12** from **10**. An attempted direct solvolysis of alcohol **9** in acetic acid/sulfuric acid gave simply the Fischer esterification product **11**. The spectroscopic data presented in the Experimental Section are entirely consistent with the structures proposed for the rearranged products **12**, **13**, and **14**. Thus, in these solvolysis reactions, migration of the 1,2-bond in **10** gives enone **12** via carbocation **15** whereas migration of the 1,7-bond leads to the bridged products **13** or **14** via carbocation **16**. In a study of a related bicyclo[4.2.0]octane system, Dauben[11] found that solvolysis of a 1-methyl tosylate yielded *only* a bridged product, so clearly in our system the appended cyclopentane ring and/or the carbonyl group are dramatically influencing the course of the reactions.

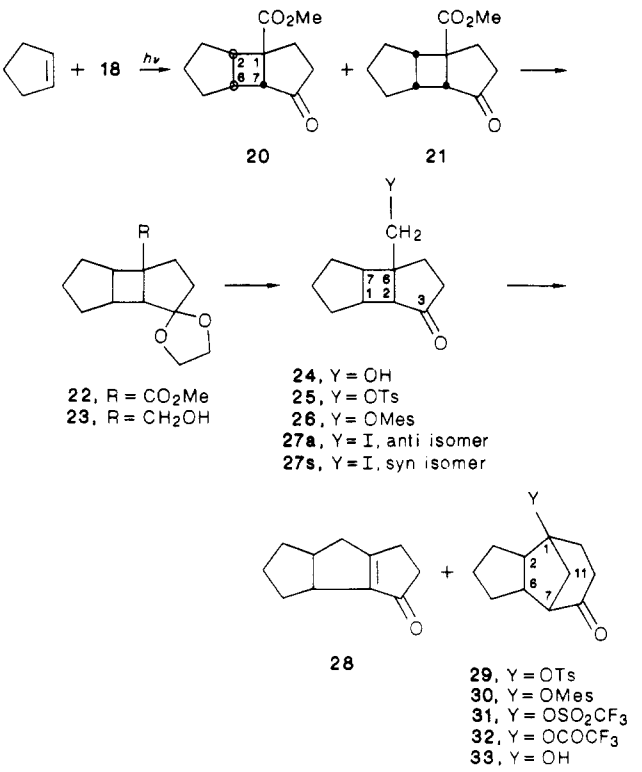


Synthesis of Tricyclo[6.3.0.0^{2,6}]undecane Skeleton (Linear Triquinane System). As our approach to the triquinane system is similar to that described above for the 6–5–5 system, it was necessary to prepare first the enone ester **18**. The unsaturated ester **17** was prepared from cyclopentanecarboxylic acid and was oxidized by a procedure similar to that described previously for the cyclohexane homologue **4**.[8] The allylic oxidation conditions gave the desired enone **18** and epoxide **19** in a ratio of 7:3 as determined by GLC. Preparation of the ethyl ester of **18** using a different procedure has been reported,[2] but the conversions were low and the reaction mixture sometimes exploded! The formation of epoxides during Cr(VI) oxidations of alkenes has been discussed.[13]



Irradiation of **18** with excess cyclopentene in toluene solution gave a 90:10 ratio of adducts **20** and **21**, respectively (Scheme II). It was assumed that all ring fusions

Scheme II



in the adducts were cis, and detailed analysis of their ^{1}H and ^{13}C NMR spectra established the proposed structures. A COSY NMR experiment on **20** in C_6D_6 assisted in the assignment of the protons in this adduct. In **20**, $J_{H_6-H_7}$ is 4.0 Hz while in **21** this coupling is 10.6 Hz. Smaller trans couplings and larger cis couplings are characteristic of vicinal protons in cyclobutane rings,[14] and similar couplings were also observed in adducts **5** and **6**, respectively. In the ^{13}C NMR spectra, C-3 and C-5 in **20** appeared at 32.8 and 32.9 ppm while in **21** these carbons were significantly shielded and resonated at 27.7 ppm (for an explanation of these differences see the discussion of adducts **5** and **6** above). These spectral data support the conclusion that **20** is the anti adduct and **21** is the syn adduct.

Continuing with our synthetic sequence, protection of the ketone in **20** (the small amount of **21** was not removed) gave ketal **22**; reduction of the ester group gave **23** and removal of the protective group gave hydroxy ketone **24** (92% from **22**). Compound **24** was converted to tosylate **25**, which upon solvolysis in formic acid/sodium formate gave enone **28**, the desired triquinane system, and tosylate **29** in a ratio of 1:2. The fact that the bridged tosylate rather than the formate was produced suggests that in the more strained system **25** (compared with **10**) an intimate ion pair reverted to **29** before there was an opportunity to form a solvent-separated ion pair and thence a formate. Solvolysis of mesylate **26** in trifluoroacetic acid/sodium acetate similarly gave a 1:2 ratio of enone **28** and bridged mesylate **30**. In contrast, treatment of alcohol **24** with triflic anhydride, $(CF_3SO_2)_2O$, in pyridine gave directly a 1:9 ratio of **28** and triflate **31**.

In an attempt to understand more clearly the solvolysis reactions, alcohol **24** was converted to iodide **27**, which was separated by flash chromatography into the anti isomer **27a** and the syn isomer **27s** in a ratio of 9:1, respectively (previous derivatives of **24** were not separable by TLC or flash chromatography). The two iodides were solvolyzed

(11) Dauben, W. G.; Chitwood, J. L. *J. Am. Chem. Soc.* **1970**, *92*, 1624.
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(14) Fleming, I.; Williams, D. H. *Tetrahedron* **1967**, *23*, 2747.

separately in trifluoroacetic acid/silver acetate with **27a**, yielding a 1:9 ratio of enone **28:32**, while **27s** gave a 9:1 ratio of **28:32**. The spectral data reported for the starting iodides and the products are entirely consistent with the structures proposed. In the ^1H NMR spectra of the bridged solvolysis products **29–32** there was a characteristic broadened doublet of doublets at about 2.85 ppm corresponding to H-7. A 2D-COSY experiment was performed at 400 MHz with several of these products to assist in the assignment of the protons. From this more detailed investigation of the solvolysis of the iodides **27** we conclude that the syn derivatives (e.g. **27s**) are transformed relatively cleanly to the triquinane **28** while the anti derivatives (e.g. **27a**) favor formation of the bridged products (**29** to **32**). Dauben[11] examined previously the related but simpler bicyclo[3.2.0]heptane system and found that solvolysis of the 1-methyl tosylate yielded *only* a bridged product. Thus, upon solvolysis, derivatives of **24** (and of **9**) lead to a mixture of enone and bridged products presumably because of the influence of the appended cyclopentane ring and/or the carbonyl group.

Finally, the potential applications of this methodology to natural product synthesis should be noted.[15] Photoaddition of enone **18** with appropriately substituted cyclopentenes followed by solvolysis of adduct derivatives could ultimately lead to either capnellene **1** or hirsutene **2**. Also, the formation of hydroxy ketone **33** (or its derivatives **29–32**) offers a potential solution to the bridgehead hydroxy problem in the A/B portion of taxol **3**. A number of these leads are presently under investigation in our laboratory, and the approach to the taxol skeleton appears particularly promising.

Experimental Section

^1H and ^{13}C NMR spectra were obtained on a Bruker WH-400 or a Varian EM-360 spectrometer. The interpretation of some ^1H NMR spectra was facilitated by 2D-COSY experiments. The multiplicities of ^{13}C spectra were determined by the attached proton test, which produced positive (+) quaternary C and CH_2 signals and negative (–) CH and CH_3 signals. TLC analyses were performed on silica gel GF 254 plates of 0.25 mm thickness and flash chromatography purifications were done with 230–400 mesh silica gel. Petrol is 30–60 °C petroleum ether. GLC analyses and separations were performed on a Aerograph Autoprep Model A-700 using one of the following columns: A, 8 ft × 0.25 in. column of 20% Carbowax on HP 80–100 mesh Chromosorb W; B, 5 ft × 0.25 in. column of 20% OV 210 on HP 80–100 mesh Chromosorb W.

Methyl 8-Oxotricyclo[5.4.0.0^{2,6}]undecane-1-carboxylates (5 and 6). In each of two 14-mm Pyrex tubes was placed 1.00 g (6.49 mmol) of methyl 3-oxo-1-cyclohexene-1-carboxylate (**4**),[8] 3.4 mL (39 mmol) of cyclopentene, and 7.2 mL of toluene. The solutions were degassed with N_2, and the tubes were sealed with a serum cap, placed in a water-cooled immersion well, and irradiated for 93 h in a Rayonet RPR 208 preparative reactor equipped with 350-nm lamps. The irradiation was followed by GLC (column A, 190 °C), and after 93 h all of **4** had reacted. The solutions were combined, the solvent was evaporated at reduced pressure, and the residue was distilled in a Kugelrohr short-path apparatus to yield 2.63 g (91%) of adduct as a colorless oil, bp 95–100 °C (bath temperature) (0.15 Torr). GLC analysis (column A, 210 °C) of the distillate indicated it was an 87:13 mixture of two adducts **5** and **6**, retention times 51 and 61 min, respectively. These two peaks were separated by preparative GC (210 °C) to give analytical samples.

Adduct 5: mp 39–42 °C; IR (CCl_4) 1730, 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45–2.15 (10 H, m), 2.28 (1 H, dt, J = 18, 7.2 Hz), 2.47 (1 H, dt, J = 18, 6.1 Hz), 2.63 (1 H, t, J = 7.6 Hz), 2.76 (1 H, 4-line m), 3.00 (1 H, d, J = 6.4 Hz), 3.73 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 211.9 (+, C-8), 174.4 (+, CO_2), 51.5 (–, OCH_3), 49.0 (–, C-7), 48.3 (+, C-1), 46.7 (–, C-2), 39.7 (–, C-6), 38.1 (+, C-9), 32.4 (+, C-3 and -5), 29.0 (+, C-4), 25.2 (+, C-11), 19.6 (+, C-10); MS m/z (rel intensity) 222 (M^+, 5), 194 (5), 163 (12), 156 (22), 155 (100), 127 (14), 123 (22), 95 (20). Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.21; H, 8.20.

Adduct 6: an oil; IR (CCl_4) 1730, 1703 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35 (2 H, m), 1.52 (1 H, m), 1.7–1.9 (4 H, m), 1.97 (1 H, m), 2.20 (1 H, 7-line m), 2.38 (1 H, br d, J = 18 Hz), 2.92 (1 H, t, J = 8.1 Hz), 3.16 (1 H, m), 3.53 (1 H, d, J = 11.1 Hz); ^{13}C NMR ($CDCl_3$) δ 212.1 (+, C-8), 178.0 (+, CO_2), 52.5 (–, OCH_3), 48.1 (+, C-1), 45.6 (–, C-7), 45.4 (–, C-2), 40.5 (–, C-6), 39.4 (+, C-9), 27.7 (+, C-3 and -5), 26.7 (+, C-4), 24.3 (+, C-11), 19.6 (+, C-10); MS m/z (rel intensity) 222 (M^+, 1), 163 (18), 156 (67), 155 (100), 127 (10), 123 (60), 97 (10), 95 (45), 91 (24). Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.30; H, 8.29.

Preparation of Ketal 7. A solution of 0.913 g (4.11 mmol) of **5/6**, 10.6 mL of ethylene glycol, 40 mg of *p*-toluenesulfonic acid, and 40 mL of toluene was refluxed for 4 h using a Dean–Stark trap to effect removal of the water formed. The solution was cooled and diluted with 25 mL of $NaHCO_3$ solution, and the aqueous phase was extracted three times with ether. The combined organic phase was washed once with saturated $NaHCO_3$ solution and once with brine and dried (anhydrous $MgSO_4$). Removal of the solvent and distillation of the residue in a Kugelrohr apparatus yielded 0.895 g (82%) of ketal **7**: bp 75–95 °C (bath) (0.15 Torr); IR (CCl_4) 1735, 1200, 1145, 1120, 1085, 1040 cm^{-1}; NMR ($CDCl_3$) δ 1.3–2.7 (15 H, m), 3.69 (3 H, s), 3.93 (4 H, br s); MS m/z (rel intensity) 266 (M^+, 9), 207 (5), 199 (5), 139 (6), 113 (36), 99 (100), 83 (100). Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.65; H, 8.33. Found: C, 67.86; H, 8.30.

1-(Hydroxymethyl)tricyclo[5.4.0.0^{2,6}]-8-undecanone (9). To a stirred and refluxing suspension of 85 mg (2.24 mmol) of $LiAlH_4$ in 20 mL of anhydrous ether was added over 10 min 0.515 g (1.94 mmol) of ketal ester **7** in 5 mL of ether, and the refluxing was continued for an additional 2 h. The reaction was cooled, 10 mL of 2 M NaOH solution and 10 mL of water were added cautiously, and the aqueous phase was extracted with ether (three times) to give a total organic volume of 300 mL. [In one run the hydroxy ketal **8** was purified by prep TLC (R_f 0.32, 50% ethyl acetate/petrol) and examined by IR (CCl_4) (3500, 1120, 1085, 1045 cm^{-1})]. The organic phase was stirred with 30 mL of 1 M aqueous H_2SO_4 for 2 h at room temperature, the aqueous phase was extracted two times with ether, and the combined organic phases were washed with saturated $NaHCO_3$ solution (two times) and with brine (one time) and then dried (anhydrous $MgSO_4$). Removal of the solvent gave 373 mg (99%) of crude hydroxy ketone **9**. An analytical sample of **9** was obtained as an oil by prep TLC (R_f 0.22, 50% ether/petrol): IR (CCl_4) 3640, 3450, 1700, 1040 cm^{-1}; NMR ($CDCl_3$) δ 1.4–1.6 (3 H, m), 1.65–1.95 (7 H, m) 2.09 (1 H, d, J = 6.8 Hz), 2.19 (1 H, s, OH), 2.21 (1 H, m), 2.44 (1 H, t, J = 7.9 Hz), 2.54 (1 H, m), 2.72 (1 H, 4-line m), 3.47 (1 H, d, J = 11 Hz) 3.50 (1 H, d, J = 11 Hz); MS m/z (rel intensity) 194 (M^+, 3), 163 (5), 127 (100), 85 (46), 83 (70), 81 (61). Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.32; H, 9.20.

1-[[(*p*-Tolylsulfonyl)oxy]methyl]tricyclo[5.4.0.0^{2,6}]-8-undecanone (10). A solution of 163 mg (0.840 mmol) of crude keto alcohol **9** in 3 mL of dry pyridine was cooled in an ice bath, and 209 mg (1.10 mmol) of p-toluenesulfonyl chloride was added. The reaction was allowed to warm gradually to room temperature, and after 18 h, 10 mL of water was added, and this solution was extracted three times with ether. The combined organic phase was extracted with 120 mL of 10% hydrochloric acid, with saturated $NaHCO_3$ solution, and with brine and then dried ($MgSO_4$). Removal of the solvent gave 246 mg of crude tosylate, which was purified by preparative TLC (R_f 0.37, 30% ethyl acetate/petrol) to yield 179 mg (61% from **7**) of **10**: mp 94–95 °C; IR (CCl_4) 1702, 1370, 1190, 1178, 965 cm^{-1}; NMR ($CDCl_3$) δ 1.2–2.9 (15 H, m), 2.44 (3 H, s) 3.81 (2 H, s), 7.35 (2 H, d), 7.76 (2 H, d); MS m/z (rel intensity) 348 (M^+, 1), 281 (37), 176 (23), 155 (13), 110 (23), 109 (100), 81 (36). Anal. Calcd for $C_{19}H_{24}O_4S$: C, 65.52; H, 6.90. Found: C, 65.35; H, 6.97.

Solvolysis of Tosylate 10. (a) In Acetic Acid. A solution of 104 mg (0.298 mmol) of tosylate **10** and 41 mg (0.50 mmol) of

(15) For other synthetic aspects of [2 + 2] photoadditions, including subsequent Wagner-Meerwein rearrangements, see: Baldwin, S. W. In *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker: New York, 1981; Vol. 5, Chapter 2.

anhydrous sodium acetate in 3 mL of acetic acid was refluxed for 75 min under nitrogen. The reaction mixture was cooled, 10 mL of water was added, and the solution was extracted with ether (three times). The combined organic phase was extracted with saturated $NaHCO_3$ solution (four times) and with brine (one time) and dried ($MgSO_4$). Removal of the solvent gave 59 mg of a 45:55 mixture of enone **12** (t_R 0.9 min) and acetate **13** (t_R 6.9 min) by GLC analysis (column B, 230 °C). Analytical samples of **12** and **13** were prepared by preparative TLC (30% ethyl acetate/petrol).

Tricyclo[6.4.0.0^{3,7}]dodec-1(8)-en-9-one (12): IR (CCl_4) 1675, 1640 cm^{-1}; NMR ($CDCl_3$) δ 1.0–3.5 (m); UV (ethanol λ_{max} 248 nm (ϵ 11300); MS m/z (rel intensity) 176 (M^+, 74), 148 (100), 147 (64), 91 (38). Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.64; H, 9.44.

1-Acetoxytricyclo[5.4.1.0^{2,6}]-8-dodecanone (13): IR (CCl_4) 1735, 1700, 1250 cm^{-1}; NMR ($CDCl_3$) δ 1.25–1.55 (2 H, m) 1.6–1.9 (3 H, m), 1.95 (1 H, 4-line m), 2.03 (3 H, s), 2.1–2.2 (2 H, m), 2.29 (1 H, d, J = 14 Hz), 2.4–2.6 (5 H, m), 2.73 (1 H, 4-line m); MS m/z (rel intensity) 236 (M^+, 1), 193 (10), 176 (80), 166 (17), 148 (18), 126 (41), 123 (27), 120 (100), 109 (40).

(b) In Formic Acid. A solution of 168 mg (0.482 mmol) of tosylate **10**, 32 mg (0.470) of anhydrous sodium formate, and 3 mL of formic acid was refluxed under N_2 for 50 min. The reaction was worked up as described for the acetic acid solvolysis, and removal of the solvent gave 94 mg of a 64:36 mixture of enone **12** and formate **14** by GLC analysis (column B, 230 °C). The components were separated by preparative TLC (30% ethyl acetate/petrol) to give 49 mg (59%) of **12** and 20 mg of **14** (R_f 0.40): IR (CCl_4) 1730, 1700, 1180 cm^{-1}; NMR ($CDCl_3$) δ 1.0–2.8 (17 H, m) 8.03 (1 H, s).

1-(Acetoxymethyl)tricyclo[5.4.0.0^{2,6}]-8-undecanone (11). A solution of 185 mg (.954 mmol) of **9** and one drop of concentrated H_2SO_4 in 5 mL of acetic acid was refluxed for 2 h under N_2. The solution was cooled, diluted with 5 mL of water, and extracted with ether (three times). The combined phases were extracted with saturated $NaHCO_3$ solution (three times) and with brine (one time) and dried ($MgSO_4$). Removal of the solvent gave 180 mg of crude product, which was purified by preparative TLC (50% ether/petrol) to give 120 mg (53%) of acetate **11** (R_f 0.47) as an oil: IR (CCl_4) 1745, 1700, 1240 cm^{-1}; NMR ($CDCl_3$) δ 1.3–2.8 (15 H, m), 1.95 (3 H, s), 4.00 (2 H, d); MS m/z (rel intensity) 236 (M^+, 2), 169 (36), 126 (13), 109 (100). Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.13; H, 8.50.

Methyl 3-Oxo-1-cyclopentene-1-carboxylate (18). An oxidizing solution was prepared as follows: 19.1 g (0.19 mol) of CrO_3 was added slowly to 15 mL of acetic anhydride. When all of the CrO_3 was dissolved, 30 mL of glacial acetic acid was added. The oxidizing solution was added dropwise over 45 min to a stirred, cooled (11–14 °C) solution of 8.9 g (0.071 mol) of methyl 1-cyclopentene-1-carboxylate (**17**)[16] in 125 mL of CH_2Cl_2. After the addition, 98 mL of 12.5 M KOH was added cautiously to the ice-cooled solution, which was then extracted with ether (3 × 150 mL). The ether phase was washed with saturated $NaHCO_3$ solution (5 × 70 mL) and brine (1 × 50 mL) and dried over $MgSO_4$. Solvent removal left an oily residue, which contained a 7:3 mixture of **18** and epoxide **19** as determined by GLC analysis (135 °C, column A) along with a significant amount of acetic anhydride. The latter was removed by distillation, and the two products were separated by MPLC (18% ethyl acetate/petrol) to give 5.4 g (54%) of enone **18** (R_f 0.26), which crystallized on cooling, and 2.4 g (24%) of epoxide **19** (R_f 0.35).

18: mp 23–24 °C; bp 100–108 °C (10 Torr); IR (CCl_4) 1730, 1720, 1604, 1431, 1155 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.76 (1 H, t, J = 1.0 Hz), 3.88 (3 H, s), 2.87 (2 H, m), 2.55 (2 H, m); ^{13}C NMR ($CDCl_3$) δ 208.8 (+), 164.6 (+), 163.7 (+), 138.0 (–), 52.5 (–), 35.5 (+), 27.5 (+); MS m/z (rel intensity) 140 (M^+, 97), 112 (100), 109 (50), 81 (72). Anal. Calcd for $C_7H_8O_3$: C, 60.00; H, 5.83. Found: C, 60.33; H, 5.75.

Methyl 6-oxabicyclo[3.1.0]hexane-1-carboxylate (19): bp 80–95 °C (10 Torr); IR (CCl_4) 3020, 2948, 1735, 1271, 1118 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.77 (3 H, s), 3.72 (1 H, br s), 2.2–2.0 (3 H, m), 1.70 (2 H, m), 1.43 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 169.5 (+), 62.7 (+), 52.0 (–), 29.8 (–), 27.0 (+), 26.5 (+), 18.9 (+); MS m/z (rel intensity) 142 (M^+, 8), 111 (8), 83 (100).

Methyl 8-Oxotricyclo[5.3.0.0^{2,6}]decane-1-carboxylates (20/21). Solutions of 0.50 g (3.6 mmol) of **18** and 3.8 mL (43 mmol) of cyclopentene in 5 mL of toluene were prepared in two 12-mm Pyrex irradiation tubes, degassed with N_2 for 2 min and sealed with serum caps. The tubes were irradiated in a Rayonet RPR 208 reactor (350 nm) at 10 °C, and the reaction was monitored by TLC for the disappearance of **18** (complete after 60 h). The two solutions were combined, and the solvent was removed. Kugelrohr short-path distillation (bath 70–80 °C, 0.25 Torr.) gave 1.09 g (78%) of a colorless oil. GLC analysis of the distillate using column B (210 °C) revealed two peaks in a ratio of 9:1 with retention times of 22.8 and 26.4 min for adducts **20** and **21**, respectively. Analytical samples of the adducts were obtained by preparative GLC (column B, 210 °C).

Cis-anti-cis adduct 20: TLC (30% EtOAc/petrol) R_f 0.38; IR (CCl_4) 2950, 1740, 1732 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.72 (3 H, s), 2.77 (2 H, m), 2.62 (1 H, d, J = 4.0 Hz), 2.60 (1 H, m), 2.39 (1 H, m), 2.29 (2 H, m) 1.79 (3 H, m), 1.67 (1 H, m), 1.55 (2 H, m); ^{13}C NMR ($CDCl_3$) δ 218.3 (+, C-8), 174.0 (+, CO_2), 51.6 (–, OCH_3), 50.9 (–, C-7), 48.9 (+, C-1), 48.0 (–, C-2), 39.2 (–, C-6), 37.1 (+, C-9), 32.9 (+, C-5), 32.8 (+, C-3), 29.9 (+, C-4), 25.0 (+, C-10); MS m/z (rel intensity) 208 (M^+, 7), 180 (11), 149 (13), 142 (21), 141 (100), 68 (38). Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.32; H, 8.01.

Cis-syn-cis adduct 21: TLC (30% EtOAc/petrol) R_f 0.38; IR (CCl_4) 2940, 1732 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.77 (3 H, s), 3.22 (1 H, m), 3.09 (2 H, m), 2.48 (2 H, m), 2.18 (2 H, m), 1.82 (2 H, m), 1.76 (1 H, m), 1.58 (1 H, m), 1.40 (1 H, m), 1.27 (1 H, m); ^{1}H NMR (C_6D_6) (partial spectrum) δ 3.33 (3 H, s), 3.03 (1 H, dd, J = 8.5, 8.5 Hz, H-2), 2.97 (1 H, d, J = 10.6 Hz, H-7), 2.76 (1 H, m, H-6); ^{13}C NMR ($CDCl_3$) δ 219.0 (+, C-8), 177.5 (+, CO_2), 52.4 (–, OCH_3), 48.6 (+, C-1), 48.4 (–, C-7), 44.0 (–, C-2), 40.0 (–, C-6) 38.6 (+, C-9), 27.7 (+, C-3 and C-5), 26.8 (+, C-4), 22.6 (+, C-10); MS m/z (rel intensity) 208 (M^+, 11), 180 (18); exact mass calcd for $C_{12}H_{16}O_3$ 208.1099, found 208.1094.

Preparation of Ketal 22. A mixture of 65 mg (3.1 mmol) of adducts **20/21**, 10 mL of ethylene glycol, 40 mL of toluene, and 35 mg of *p*-toluenesulfonic acid was refluxed with stirring for 4.5 h with a Dean–Stark water separator. The reaction mixture was cooled and poured into 25 mL of saturated $NaHCO_3$ solution, and the aqueous phase was extracted with ether (3 × 50 mL). The combined organic phase was washed with saturated $NaHCO_3$ solution and with brine and dried over anhydrous $MgSO_4$. Removal of the solvent gave a crude product, which was shown by GLC (column B, 205 °C) to be a 9:1 mixture of ketals, but on TLC the two compounds were inseparable. The crude product was purified by flash chromatography (20% EtOAc/petrol) to give 70 mg (90%) of ketal **22**: IR (CCl_4) 2940, 1737, 1266, 1192, 1175, 1070, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.92 (4 H, m), 3.68 (3 H, s), 2.53 (1 H, dd, J = 8.3, 8.3 Hz), 2.46 (1 H, m), 2.29 (2 H, m), 1.88 (3 H, m), 1.72 (4 H, m), 1.50 (2 H, m); MS m/z (rel intensity) 252 (M^+, 3), 185 (15), 99 (100), 74 (26), 73 (41). Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99. Found: C, 66.36; H, 8.05.

6-(Hydroxymethyl)tricyclo[5.3.0.0^{2,6}]-3-decanone (24). A solution of 520 mg (2.1 mmol) of ketal **22** in 2 mL of anhydrous ether was added dropwise to a stirred suspension of 93 mg (2.4 mmol) of $LiAlH_4$ in 20 mL of anhydrous ether, and the mixture was reluxed for 2 h. To the cooled reaction mixture was added cautiously 10 mL of 1 M NaOH solution followed by 10 mL of water, and the aqueous phase was extracted with ether (3 × 70 mL). The combined ether phase containing the crude hydroxy ketal **23** was stirred with 30 mL of 1 M H_2SO_4 for 2 h at room temperature. The ether layer was separated, the aqueous layer was extracted once with ether, and the combined ether phase was washed with saturated $NaHCO_3$ solution and with brine and dried over anhydrous $MgSO_4$. After removal of the solvent the crude product was purified by flash chromatography (50% ether/petrol) to give 350 mg (92%) of hydroxy ketone **24**: IR (CCl_4) 3640, 3460, 1737, 1200, 1150, 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.56 (1 H, d, J = 10.9 Hz), 3.48 (1 H, d, J = 10.9 Hz), 2.62 (3 H, m), 2.56 (1 H, d, J = 8.7 Hz), 2.28 (2 H, m), 1.97 (2 H, m), 1.87 (2 H, m), 1.74 (1 H, m), 1.56 (1 H, m), 1.49 (2 H, m); ^{13}C NMR ($CDCl_3$) δ 221.1, 64.0, 51.5, 45.7, 44.1, 39.7, 38.0, 32.7 (2 C's), 28.1, 26.3; MS m/z (rel intensity) 180 (M^+, 15), 149 (14), 113 (100), 107 (26), 95 (30).

(16) Prepared in high yield from cyclopentane carboxylic acid using the same procedures as described for preparation of the cyclohexene homologue.[8]

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.22; H, 8.87.

6-[[(*p*-Tolylsulfonyl)oxy]methyl]tricyclo[5.3.0.0^{2,6}]-3-decanone (25). A solution of 110 mg (0.611 mmol) of hydroxy ketone **24** and 3 mL of dry pyridine was cooled in an ice bath, 140 mg (0.728 mmol) of *p*-toluenesulfonyl chloride was added, and the solution was allowed to warm gradually to room temperature. After the mixture was stirred for 18 h, 10 mL of water was added, and the solution was extracted with ether (3 × 20 mL). The combined organic phase was washed with 1 M HCl (1 × 30 mL), saturated $NaHCO_3$ solution (1 × 20 mL), and brine (1 × 20 mL) and dried over $MgSO_4$. Removal of the solvent and purification by preparative TLC (30% ethyl acetate/petrol, R_f 0.35) gave 118 mg (58%) of tosylate **25** as an oil: IR (CCl_4) 3020, 2940, 1737, 1375, 1192, 965 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.78 (2 H, d, J = 8.2 Hz), 7.37 (2 H, d, J = 8.2 Hz), 4.02 (1 H, d, J = 9.7 Hz), 3.88 (1 H, d, J = 9.7 Hz), 2.62 (2 H, m), 2.54 (1 H, m), 2.46 (3 H, s), 2.33 (1 H, m), 2.08 (1 H, m), 2.01 (1 H, m), 1.90 (1 H, d, J = 4.2 Hz), 1.82 (1 H, s), 1.70 (2 H, m), 1.47 (3 H, m); ^{13}C NMR ($CDCl_3$) δ 219.1, 145.1, 132.6, 130.0, 129.8, 128.0, 127.3, 71.1, 51.0, 45,6, 41.8, 37.7, 32.7, 32.5, 28.0, 25.9, 21.8; MS m/z (rel intensity) 334 (M$^+$, 2), 243 (17), 163 (80).

6-[[(Methylsulfonyl)oxy]methyl]tricyclo[5.3.0.0^{2,6}]-3-decanone (26). To a solution of 200 mg (1.11 mmol) of hydroxy ketone **24** and 170 mg (1.67 mmol) of triethylamine in 3 mL of dry methylene chloride at 0 °C was added 140 mg (1.22 mmol) of methanesulfonyl chloride. The mixture was stirred for 5 h at 0 °C and then allowed to warm to room temperature. Chloroform (50 mL) was added, and the organic phase was washed with water (2 × 10 mL), 2 M HCl solution (2 × 10 mL), saturated $NaHCO_3$ solution (1 × 10 mL), and brine (1 × 10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was purified by flash chromatography (40% EtOAc/petrol, R_f 0.22) to give 237 mg (83%) of a pale yellow crystalline mesylate (**26**): mp 41–45 °C; IR (CCl_4) 1738, 1365, 1348, 1178, 950 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.10 (AB doublets, J = 9.9 Hz), 2.96 (3 H, s), 2.62 (1 H, m), 2.55 (1 H, dd, J = 6.2, 6.2 Hz), 2.36 (1 H, m), 2.15 (1 H, m), 2.0 (2 H, m), 1.8–1.5 (6 H, m), 1.3 (1 H, dt, J = 16, 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 218.6 (+), 70.3 (+), 51.5 (–), 45.8 (–), 42.0 (+), 39.9 (–), 37.7 (+), 37.6 (–), 32.8 (+), 32.6 (+), 28.1 (+), 26.1 (+); MS m/z (rel intensity) 258 (M$^+$, 5), 243 (3), 163 (20); CIMS m/z (rel intensity) 259 (M + 1, 57), 163 (100).

6-(Iodomethyl)tricyclo[5.3.0.0^{2,6}]-3-decanone (27). A solution of 75 mg (0.42 mmol) of **24** (9:1 mixture of anti and syn stereoisomers), 132 mg (0.50 mmol) of triphenylphosphine, 34 mg (0.50 mmol) of imidazole, and 127 mg (0.50 mmol) of iodine in 3 mL of dry toluene was stirred at room temperature for 3 h.[17] The reaction was diluted with ether and filtered through a short pad of silica gel (230–400 mesh), and the solvent was removed to yield 76 mg (67%) of a 9:1 mixture of iodides **27**. The anti (**27a**) and syn iodides (**27s**) were separated by flash chromatography (5% EtOAc/petrol, R_f's 0.21 and 0.24, respectively to afford the pure isomers. **27a**: mp 53–56 °C; IR (CCl_4) 2940, 1735, 1445, 1180, 910 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.23 (2 H, AB doublets, J = 9.8 Hz), 2.70 (1 H, quint, J = 9.0 Hz), 2.60 (1 H, m), 2.54 (1 H, d, J = 6.4 Hz), 2.41 (1 H, m), 2.1 (4 H, m), 1.87 (1 H, m), 1.77 (1 H, m), 1.6 (3 H, m); ^{13}C NMR ($CDCl_3$) δ 219.2 (+), 55.1 (–), 46.3 (–), 42.7 (+), 38.0 (–), 37.7 (+), 37.1 (+), 32.4 (+), 27.8 (+) 26.1 (+), 14.4 (+); MS m/z (rel intensity) 290 (M$^+$, 1), 233 (38), 163 (100), 135 (47), 96 (78); exact mass calcd for $C_{11}H_{15}O^+$ 163.1122, found 163.1122. **27s**: an oil; IR (CCl_4) 2940, 1735, 1445, 1180, 910 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.50 (2 H, AB doublets, J = 2.0 Hz), 2.97 (1 H, dd, J = 9.4, 8.1 Hz), 2.63 (1 H, dd, J = 9.1, 8.0 Hz), 2.5 (1 H, m), 2.4 (2 H, m), 2.1 (1 H, m), 1.8 (2 H, m), 1.7 (2 H, m), 1.6 (1 H, m), 1.4 (1 H, m), 1.25 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 220.3 (+), 50.5 (–), 46.9 (–), 45.5 (+), 40.9 (+), 36.3 (–), 28.2 (+), 27.4 (+), 26.8 (+), 26.5 (+), 23.5 (+); MS m/z (rel intensity) 290 (M$^+$, 1), 223 (88), 163 (97), 135 (51), 96 (100); exact mass calcd for $C_{11}H_{15}IO$ 290.0169, found 290.0169.

Solvolysis of 25 in Formic Acid. A solution of 124 mg (0.37 mmol) of **25** and 48 mg (0.70 mmol) of anhydrous sodium formate in 3 mL of formic acid was refluxed for 3 h under nitrogen. To the cooled reaction mixture was added 20 mL of water, and the aqueous phase was extracted with ether (3 × 30 mL). The combined organic phase was washed with saturated $NaHCO_3$ solution (2 × 20 mL) and brine (1 × 10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was purified by flash chromatography (30% EtOAc/petrol) to yield 17 mg (28%) of **28** and 73 mg (59%) of **29**.

Tricyclo[6.3.0.0^{2,6}]-2(6)-undecen-3-one (28): TLC (30% EtOAc/petrol) R_f 0.37; IR (CCl_4) 2950, 1703, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.21 (2 H, br s), 2.80 (1 H, dd, J = 16, 9.1 Hz), 2.71 (2 H, t, J = 4.3 Hz), 2.47 (2 H, br s), 2.16 (1 H, br d, J = 16 Hz), 1.73 (2 H, m), 1.63 (2 H, m), 1.43 (2 H, m); UV (EtOH) λ_{max} 238 (9500), 328 nm (100); MS m/z (rel intensity) 162 (M$^+$, 68), 112 (90), 82 (100).

1-[(*p*-Tolylsulfonyl)oxy]tricyclo[5.3.1.0^{2,6}]-8-undecanone (29): IR (CCl_4) 3020, 2940, 1725, 1368, 1348, 1215, 1188, 1175 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.79 (2 H, d, J = 8.6 Hz), 7.33 (2 H, d, J = 8.6 Hz), 2.79 (1 H, dd, J = 7.5, 7.0 Hz), 2.45 (3 H, s), 2.38 (7 H, m), 2.10 (3 H, m), 1.77 (1 H, m), 1.55 (1 H, m), 1.36 (1 H, m), 1.15 (1 H, m); MS m/z (rel intensity) 334 (M$^+$, not observed), 277 (67), 179 (72), 162 (83), 155 (100).

Solvolysis of 26 in Trifluoroacetic Acid. A solution of 117 mg (0.45 mmol) of **26** and 66 mg (0.80 mmol) of anhydrous NaOAc in 3 mL of trifluoroacetic acid was refluxed (72 °C) under nitrogen for 2.5 h. To the cooled, dark red reaction mixture was added 20 mL of water, and this aqueous phase was extracted with ether (3 × 30 mL). The combined ether phase was washed with saturated $NaHCO_3$ solution (2 × 20 mL) and brine (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was purified by flash chromatography (30% EtOAc/petrol) to give 18 mg (25%) of **28** and 66 mg (57%) of 1-[(methylsulfonyl)oxy]tricyclo[5.3.1.0^{2,6}]-8-undecanone, **30**: TLC (30% EtOAc/petrol) R_f 0.23; IR (CCl_4) 1725, 1365, 1350, 1178, 950, 935 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.05 (3 H, s), 2.80 (1 H, dd, J = 7.8, 7.0 Hz), 2.35–2.55 (7 H, m), 2.10 (3 H, m), 1.84 (1 H, m), 1.58 (1 H, m), 1.37 (1 H, m), 1.21 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 209.5 (+), 93.9 (+), 53.9 (–), 50.2 (–), 44.7 (–), 40.3 (–), 36.4 (+), 34.7 (+), 34.1 (+), 34.0 (+), 31.1 (+), 27.2 (+). Anal. Calcd for $C_{12}H_{18}O_4S$: C, 55.87; H, 7.02. Found: C, 56.21; H, 7.14.

Reaction of 24 with Triflic Anhydride. A solution of 71 mg (0.39 mmol) of **24** and 47 mg (0.59 mmol) of pyridine in 1.0 mL of dry CH_2Cl_2 was added dropwise over 0.5 h to a stirred solution of 0.12 mL (0.43 mmol) of triflic anhydride in 5 mL of CH_2Cl_2 at 0 °C under nitrogen. After an additional 15 min of stirring, the reaction was diluted with 25 mL of CH_2Cl_2, and this organic phase was extracted with 1 M HCl solution (2 × 20 mL), water (10 mL), and brine (10 mL) and dried over anhydrous $MgSO_4$. The solvent was evaporated, and the residue was purified by flash chromatography (15% EtOAc/petrol) to yield 5 mg (8%) of **28** and 103 mg (85%) of 1-[[(trifluoromethyl)sulfonyl]oxy]-tricyclo[5.3.1.0^{2,6}]-8-undecanone, **31**: TLC (15% EtOAc/petrol) R_f 0.35; IR (CCl_4) 2950, 1722, 1390, 1200, 1135, 908 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.86 (1 H, q, J = 8.9 Hz, H-1), 2.55 (2 H, m, H-9α and -10α), 2.47 (3 H, m, H-5β, -9β, and -11-endo), 2.25 (1 H, br d, J = 12 Hz, H-10β), 2.15 (2 H, m, H-5α and -11-exo), 1.90 (1 H, q, J = 6.0 Hz, H-2), 1.62 (2 H, m, H-3α and -6), 1.44 (1 H, m, H-4α), 1.25 (2 H, m, H-3β and -4β) (COSY experiment used in making assignments); ^{13}C NMR ($CDCl_3$) δ 209.5 (+, C-8), 198.2 (+, CF_3), 101.7 (+, C-1), 53.6 (–, C-7), 50.2 (–, C-6), 44.6 (–, C-2), 36.3 (+, C-9), 34.6 (+, C-11), 34.0 (+, C-3 and -5), 31.1 (+, C-10), 27.2 (+, C-4); MS m/z (rel intensity) 312 (M$^+$, 10), 255 (5), 179 (22), 163 (16), 134 (25), 120 (100), 107 (36).

Solvolysis of 27a or 27s in Trifluoroacetic Acid/AgOAc. To a solution of n mmol of iodide **27a** or **27s** in 20n mL of trifluoroacetic acid was added 1.5n mmol of AgOAc with stirring. An immediate yellow precipitate was observed, and disappearance of the starting iodide was realized within 10 min as judged by TLC. Water was added to the reaction mixture, and the aqueous phase was extracted with ether (3×). The combined organic phase was washed with saturated $NaHCO_3$ solution (2×) and with brine and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was analyzed by TLC (30% EtOAc/petrol). Solvolysis of **27a** yielded a 1:9 ratio of **28**:**32** while **27s** gave a 9:1 ratio of **28**:**32**. 1-(Trifluoroacetoxy)tricyclo[5.3.1.0^{2,6}]-8-undecanone, **32**: TLC (30% EtOAc/petrol) R_f 0.62; IR (CCl_4) 1776, 1720, 1360, 1218, 1150 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.02 (1 H, dd, J = 17, 10 Hz),

(17) Wattanasin, S.; Kathawala, F. G.; Boeckman, R. K. *J. Org. Chem.* **1985**, *50*, 3810.

2.7–2.3 (5 H, m), 2.1 (3 H, m), 1.85 (2 H, m), 1.40 (2 H, m), 1.20 (2 H, m).

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Registry No. (±)-**1**, 81370-78-7; (±)-**2**, 59433-37-3; (±)-**3**, 119323-97-6; **4**, 54396-74-6; (±)-**5**, 90382-33-5; (±)-**6**, 102045-26-1; (±)-**7a**, 119323-98-7; (±)-**7s**, 119245-05-5; (±)-**8a**, 119323-99-8; (±)-**8s**, 119245-06-6; (±)-**9a**, 119324-07-1; (±)-**9s**, 119245-07-7; (±)-**10a**, 119324-08-2; (±)-**10s**, 119245-08-8; (±)-**11a**, 119324-09-3; (±)-**11s**, 119245-09-9; (±)-**12**, 119245-10-2; (±)-**13**, 119245-11-3; (±)-**14**, 119245-12-4; **17**, 25662-28-6; **18**, 108384-35-6; (±)-**19**, 119245-13-5; (±)-**20**, 119245-14-6; (±)-**21**, 119324-00-4; (±)-**22a**, 119324-05-9; (±)-**22s**, 119245-15-7; (±)-**23a**, 119324-06-0; (±)-**23s**, 119245-16-8; (±)-**24a**, 119245-17-9; (±)-**24s**, 119324-01-5; (±)-**25a**, 119324-02-6; (±)-**25s**, 119245-18-0; (±)-**26a**, 119324-03-7; (±)-**26s**, 119245-19-1; (±)-**27a**, 119245-20-4; (±)-**27s**, 119324-04-8; (±)-**28**, 119245-21-5; (±)-**29**, 119245-22-6; (±)-**30**, 119245-23-7; (±)-**31**, 119245-24-8; (±)-**32**, 119245-25-9; (±)-**33**, 119245-26-0; cyclopentene, 142-29-0.

Decarboxylation of 1-Aminocyclopropanecarboxylic Acid and Its Derivatives

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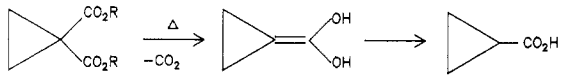
The question of whether the title compounds could be decarboxylated to cyclopropanone derivatives was answered in the affirmative by the following observations. (1) Compound **11a** was decarboxylated by 1,2,3-indantrione in acetonitrile, benzene, or methanol. The initially formed intermediate could be trapped by *N*-phenylmaleimide (to form **3**), by diethyl azodicarboxylate (to form an unstable adduct), by ninhydrin itself (to form **5**) or by a proton (in methanol, to form **8**). (2) Compound **11d** was decarboxylated by phenylbis(trifluoroacetato-*O*)iodine to yield carbinolamine **12d**. *cis*-2,3-Dideuterio-**11d** yielded *cis*-2,3-dideuterio-**12d** under the same conditions. (3) ACC was decarboxylated by phenanthroquinone to yield oxazole **9**, probably by way of oxazoline **10**.

Can cyclopropanecarboxylic acids be decarboxylated in solution under conditions that permit survival of the cyclopropane ring? We are unaware of any examples of such a reaction in the literature. One reported attempt at decarb*alkoxyl*ation in solution was unsuccessful: under conditions that effected the decarbmethoxylation of other substituted malonic esters (KCN, DMF, reflux for 12 h), the cyclopropane analogue **1c** did not decarbalkoxylate.[1] In the absence of solvent, **1a** was decarboxylated at about 200 °C.[2-5] Strained enol **2** is probably an intermediate.

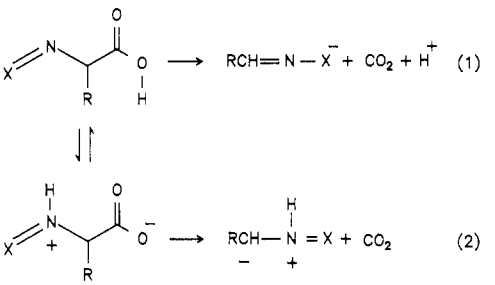


1a R = H
1b R = SiMe3
1c R = CH3

2

The intermediacy of an enol like **2** was demonstrated in the case of **1b**.[6] The observation that **1a** underwent decarboxylation in 98% sulfuric acid at 180 °C faster than did the corresponding cyclobutane- and cyclopentanedicarboxylic acids was at first unexpected.[7] Later it was found that **1a** did not decarboxylate until after it had

Scheme I



isomerized to a five-membered lactone.[8,9]

Amino acids in general are readily decarboxylated by a variety of reagents (the Strecker degradation).[10] For some time the accepted mechanism for this reaction has been the concerted mechanism outlined in eq 1 of Scheme I.[11] Its application to 1-aminocyclopropanecarboxylic acid (ACC) involves the same kind of strained intermediate that apparently inhibited the thermal decarboxylation of **1a**. Recently, however, Grigg has proposed that the decarboxylation of α-imino carboxylic acids (formed from amino acids and carbonyl compounds) involves the formation of a 1,3-dipole from a tautomer of the starting imine (eq 2 of Scheme I).[11] The 1,3-dipole formed by the application of this mechanism to ACC might have a pyramidal structure, its negative site stabilized by the inductive effect of the positive iminium ion. In that event decarboxylation

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