Perhydroindan Derivatives. 19. Opening of a Cyclopropyl Ketone That Is Part of an Indanone System[1]

Herbert O. House,* William C. McDaniel, Ronald F. Sieloff, and Don Vanderveer

School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia 30332

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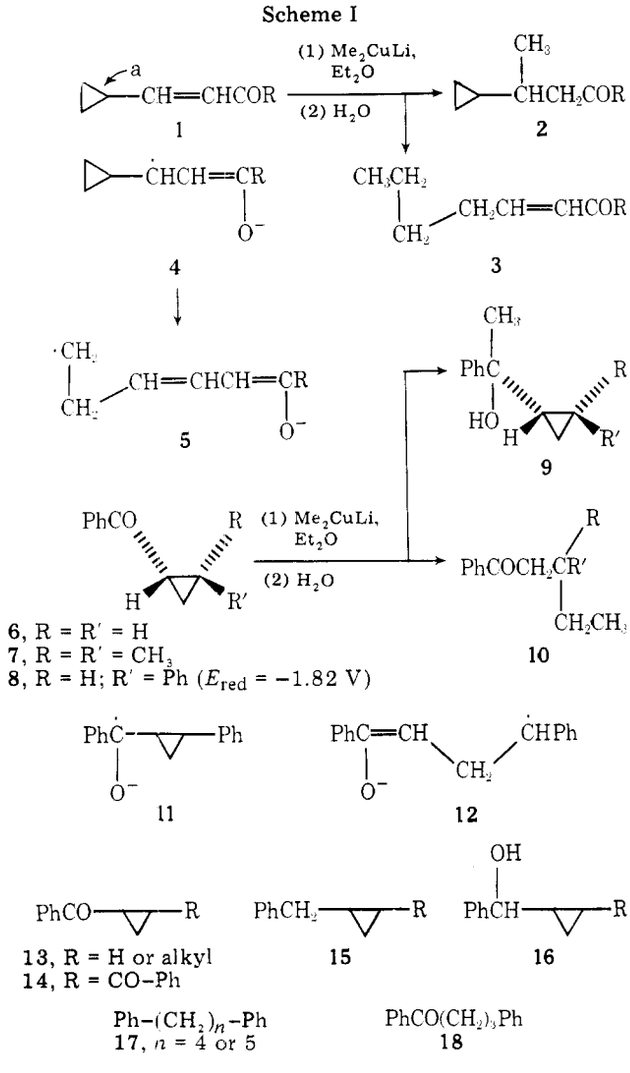
Reaction of the relatively rigid cyclopropyl ketone **19** with Me_2CuLi gives significantly more ring-opened product **30** than is found in an analogous reaction with the less rigid cyclopropyl ketone **8**. However, both the direction of ring opening and the effect of added donor solvents on the reaction **19** → **30** indicate that this reaction does not involve an initial electron transfer step. Reduction of the ketone with Li and *t*-BuOH in liquid NH_3 (a process that does involve initial electron transfer) results in the formation of products **41–43**. These products are thought to result from rearrangement of the initial anion radical **20** to the anion radical **21b** followed by further transformations to yield the products.

A number of β-cyclopropyl enones **1** (Scheme I) react normally with Me_2CuLi and other cuprate reagents to form the conjugate adducts **2**. However, when special structural features hold the cyclopropyl bond a (structure **1**) approximately perpendicular to the plane of the enone system, then an alternative reaction path involving formation of a ring-opened product **3** becomes either a significant competing reaction or the dominant reaction.[2] This ring-opening reaction **1** → **3** appears to predominate only in those cases where rearrangement of the intermediate enone anion radical **4** to the ring-opened radical **5** is relatively fast (half-life of **4** is 10^{-3} s or less); a geometry with bond a (structure **1**) perpendicular to the enone system is of course favorable to this anion radical rearrangement **4** → **5**.

Scheme I



In a related study of the reaction of Me_2CuLi with the aryl cyclopropyl ketones **6–8** (all of which have reduction potentials in the range −1.8 to −2.1 V vs. SCE),[3] the major product was invariably the 1,2-adduct **9** with only minor amounts (0.6–3.5%) of ring-opened products **10**. Electrochemical reduction[3] of the ketones **6** and **7** in an aprotic medium formed relatively stable anion radicals (half-lives 4–5 s). A much less stable anion radical **11** (half-life 0.005 s) was formed from the ketone **8** with a phenyl substituent that could stabilize the rearranged anion radical **12**. In keeping with these relative anion radical stabilities, both reduction of various cyclopropyl ketones **13** with Li or Na in NH_3[4] and electrochemical reduction of ketone **6** in aqueous EtOH[5] formed products (**15**, **16**, and the corresponding pinacol) with the cyclopropyl ring intact. In contrast, the cyclopropyl ring was opened in the electrochemical reduction of ketone **8** to form ketone **18**[5] and in the reduction of ketones **8** and **14** with Na in NH_3 to form hydrocarbons **17**.[4a] However, the structures of the ring-opened products **10** (attack at the less substituted cyclopropane carbon atom) formed in the cuprate reactions all corresponded to the result expected from an S_N2 attack by the cuprate reagent rather than rebonding to a rearranged radical anion (eg., **12**) derived from the cyclopropyl ketone (eg., **8**). To explore further the question of whether any cuprate–aryl cyclopropyl ketone reaction might involve, at least in part, an initial electron transfer step to form an anion radical (eg., **11**), we wished to examine the cuprate reaction with a cyclopropyl ketone whose anion radical underwent rearrangement faster than the ketyl **11**.

For this purpose we elected to study the fused cyclopropyl ketone **19** (Scheme II) since this molecule is held in a rigid conformation with one cyclopropyl bond (bond a in structure **19**) approximately perpendicular to the plane of the carbonyl group. Our selection of this substrate was also influenced by the possibility of an efficient conversion of ketone **19** via the intermediates **20** and **21a** to indanone derivatives of interest in other synthetic work.[6] Known procedures[7] were used to convert the styrenes **22** and **23** to the esters **24** and **25** (mixtures of stereoisomers) and the acids **26** and **27** (mixtures of stereoisomers). Reaction of the acid **26** (a mixture of stereoisomers) with polyphosphoric acid[7d] or, preferably, with $SOCl_2$ to form **28** followed by reaction with $AlCl_3$[8] produced the desired ketone **19**. In at least the latter procedure, where the ketone **19** was obtained in 61% yield, trans → cis epimerization is believed[8b] to occur during the cyclization of the acid chloride **28**. Our efforts to effect the same cyclization with the methoxy acid **27** led to complex mixtures even when we employed reaction conditions that are satisfactory[6a] for the formation of the methoxyindanone **49** from the corresponding acid chlo-

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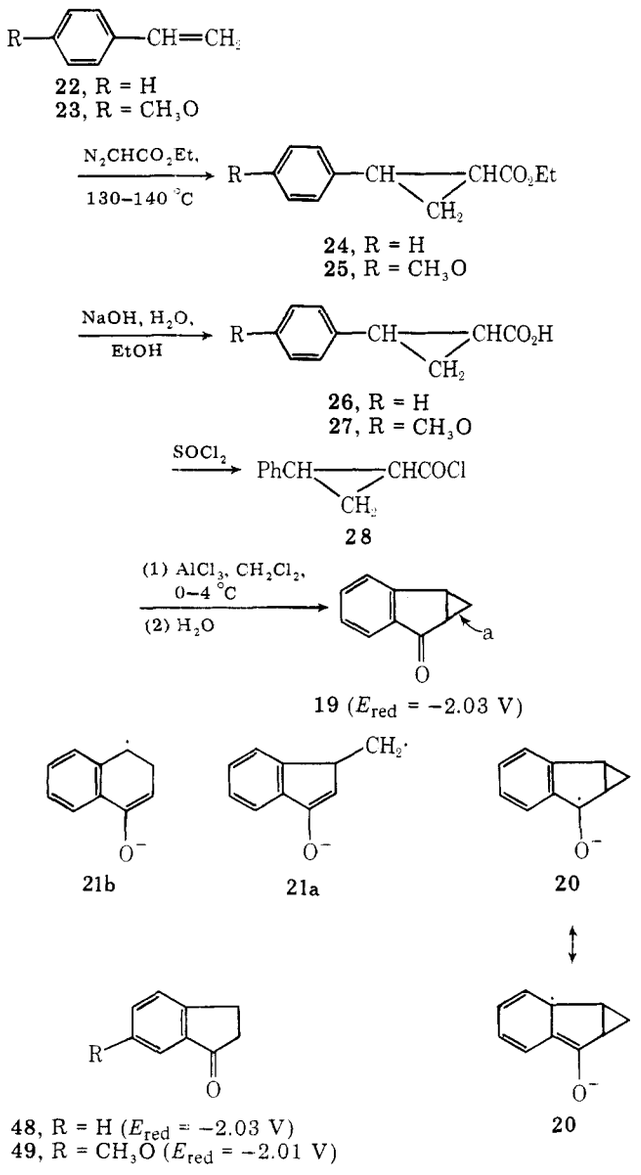
Scheme II

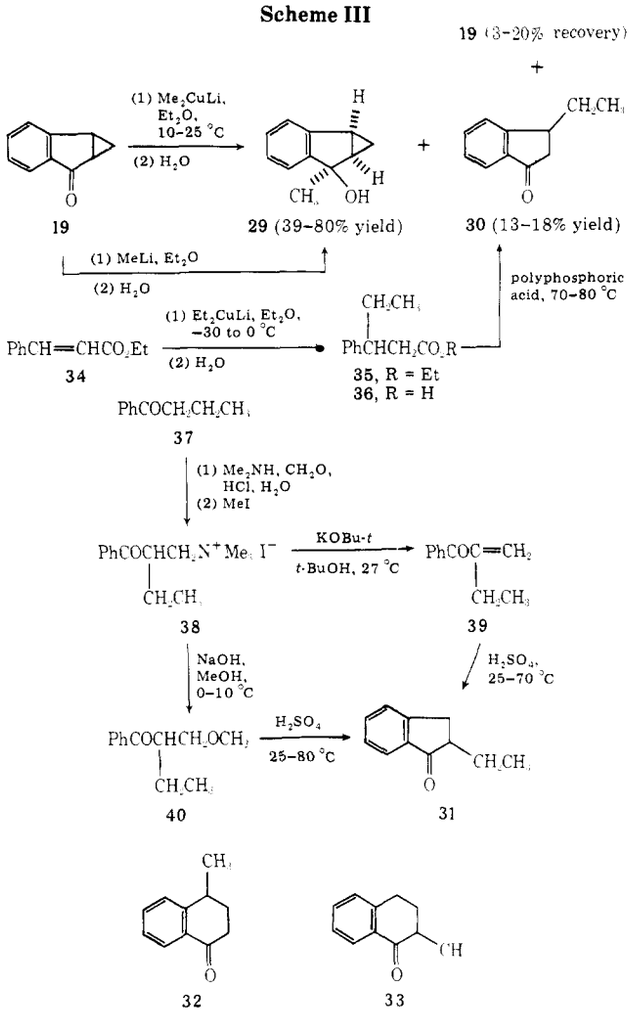


ride. In view of our subsequently described results obtained with the indanone **19**, other possible synthetic routes to the 6-methoxy derivative of indanone **19** were not investigated.

The reduction potentials of the cyclopropyl ketone **19** (E_{red} = −2.03 V vs. SCE) and the analogous indanone **48** (E_{red} = −2.03 V vs. SCE) were the same and were in a range where one-electron reduction by Me_2CuLi to form the ketyl **20** was reasonable.[9] As we had hoped, the anion radical **20** was less stable than its open chain analogue **11** and had a half-life (0.001 s) sufficiently short enough that a significant amount of rearrangement could occur during a cuprate reaction. In fact, reaction of the ketone **19** (Scheme III) with ethereal Me_2CuLi produced a mixture of the 1,2-adduct **29** (75–82% of the product) and a substantial amount of the ring-opened product **30** (18–25% of the product). Only the 1,2-adduct **29** was isolated from the reaction of the cyclopropyl ketone **19** with MeLi. Consequently, in the cuprate reaction the proportion of ring-opened product **30** (or **10**; R = H, R′ = Ph) was enhanced at least 20-fold by changing the substrate from the flexible ketone **8** to the rigid system **19**.

One could imagine that any one of the three cyclopropane C–C bonds in ketone **19** might be cleaved during the cuprate reaction so that any or all of the ketone products **30–33** might be formed. To insure that our ring-opened product was in fact the ketone **30**, we obtained authentic samples of the ketones

Scheme III

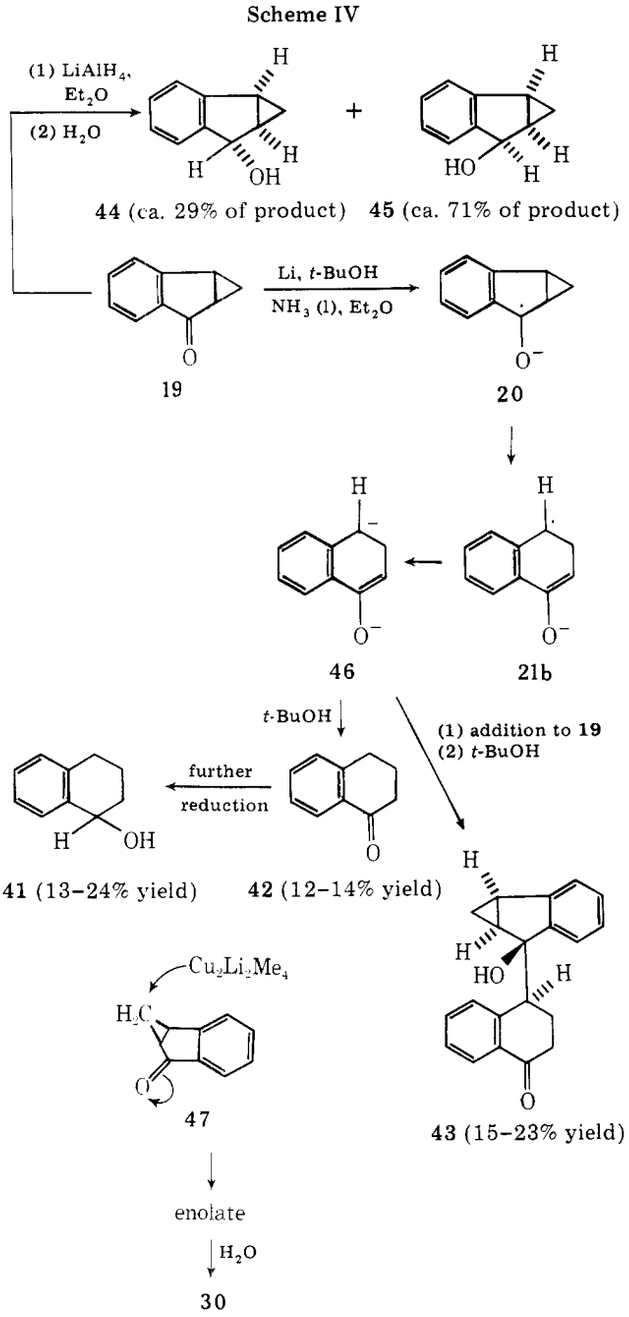


30–33 and demonstrated that our product **30** contained less than 5% (if any) of the isomeric ketones **31–33**. Authentic samples of ketones **30** and **31** were prepared by the routes indicated in Scheme III.

The foregoing results might be interpreted as reaction of the ketone **19** with Me_2CuLi to form the ketyl **20** followed by partial rearrangement to **21a** and rebonding to form **29** and **30**. However, such a conclusion would be warranted only if the ketyl **20** actually rearranges to the anion radical **21a** (favored by the geometry of the system) rather than some other anion radical such as **21b** (which allows stabilization of the radical by the adjacent phenyl ring). A clear indication that this second possibility might be correct was provided by an earlier study[10] of the reduction of ketone **19** with Li in an NH_3–Et_2O mixture. The reported products were an unidentified solid (mp 160–185 °C), tetralin, and tetralone.

We have repeated this reduction of ketone **19** (Scheme IV) employing a solution containing 2 equiv of Li and 1 equiv of *t*-BuOH in an NH_3–Et_2O mixture. The products were tetralol (**41**), tetralone (**42**), and the dihydro dimer **43** (mp 188–189.9 °C). Authentic samples of the alternative reduction products, the known[11] alcohols **44** and **45**, were prepared to demonstrate their absence among the reduction products. Consideration of the products (**41–43**) formed in this metal–NH_3 reduction leaves little doubt that the initially formed ketyl **20** rearranges to form anion radical **21b** and not **21a**. Further reduction of anion radical **21b** to the dianion **46** readily accounts for all of the isolated products **41–43**. In view of this, we conclude that reaction of the ketone **19** with Me_2CuLi to form ketone **30** does not involve the intermediate ketyl **20** since this latter intermediate should have rearranged to **21b** and then formed ketone **32**. Instead, the reaction with the cuprate to form ketone

Scheme IV



30 must again be an example of an S_N2 ring opening (see structure 47) in which the geometry of the substrate is especially favorable for attack at the cyclopropyl CH_2 group to displace an enolate anion. In agreement with this conclusion, the yield of ketone 30 from reaction of Me_2CuLi with ketone 19 was increased (see Table III) by the addition of good donor solvents (DME or THF). In reactions of cuprates with ketones where an initial electron transfer step is involved, the presence of good donor solvents normally retards or inhibits the reaction.[12]

The structure of the dihydro dimer 43, determined by a single crystal X-ray diffraction study, is shown in Figure 1. The bond lengths and bond angles obtained from this structural determination are listed in Table I.

Experimental Section[13]

Preparation of the Acid Derivatives 24, 26, and 28. A cold (0 °C) solution of 28.53 g (0.25 mol) of N_2CHCO_2Et[14] in 26.04 g (0.25 mol) of styrene (22) was added dropwise with stirring during 15 min to 13.02 g (0.125 mol) of styrene (22) that was maintained at 130–140 °C under

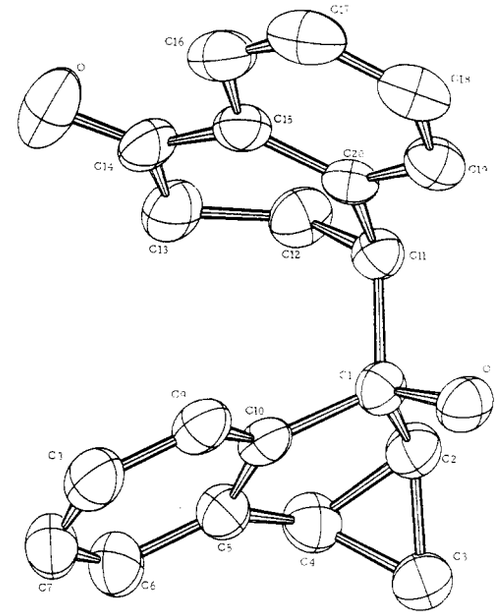


Figure 1. A perspective view of the molecular structure of the dihydro dimer 43.

an N_2 atmosphere. The resulting mixture was stirred at 130–135 °C for 24 h and then distilled to separate 4.89 g of forerun (mainly $PhCH{=}CH_2$) followed by 36.93 g of the crude ester 24 as a pale yellow liquid: bp 80–90 °C (0.15 mm); n^{25}_D 1.5182. Redistillation afforded 34.28 g (72%) of the ester 24 (a mixture of stereoisomers) as a colorless liquid: bp 80.5–82 °C (0.14 mm); n^{25}_D 1.5182 [lit. bp 103–105 °C (0.5–0.7 mm),[7a] n^{20}_D 1.518[7d]]; IR (CCl_4) 1725 cm^{-1} (ester C=O); UV (95% EtOH) intense end absorption with a series of weak maxima (ε 251–472) in the region 253–273 nm; NMR (CCl_4) δ 6.8–7.4 (5 H, m, aryl CH), 4.10 and 3.81 (2 H, overlapping quartets, J = 7 Hz, CH_2O), and 0.7–2.7 (7 H, m, ethoxyl CH_3 and cyclopropyl CH and CH_2); mass spectrum, m/e (relative intensity) 190 (M^+, 29), 145 (21), 144 (18), 117 (100), 116 (23), 115 (50), and 91 (22).

Saponification of 32.64 g (172 mmol) of the ester 24 with a refluxing solution of 10.35 g (259 mmol) of NaOH and 15 mL of H_2O in 100 mL of EtOH for 24 h followed by the usual isolation procedure yielded the crude acid 26 (a mixture of stereoisomers) as a cream-colored solid, mp 68–73 °C (lit.[7c] mp 55–63 °C). Recrystallization from H_2O afforded a mixture of stereoisomeric acids 26 in 57% yield as colorless crystals, mp 62.5–101 °C [lit.[7a] mp 93 (trans isomer) and 106–107 °C (cis isomer)].

This crude acid (8.11 g, 50 mmol) was dissolved in 17.85 g (150 mmol) of warm $SOCl_2$ and then stirred at 25 °C for 24 h, concentrated, and distilled. The acid chloride 28 (a mixture of stereoisomers) was collected as 8.69 g (96%) of pale yellow liquid: bp 126–128 °C (24 mm) [lit. bp 108–110 (2.1 mm)[7a] and 130 °C (10 mm)[7c]; n^{25}_D 1.5548–1.5551; IR (CCl_4) 1780 cm^{-1} (C=O); NMR (CCl_4) δ 6.7–7.6 (5 H, m, aryl CH) and 1.2–3.0 (4 H, m, CH and CH_2); mass spectrum, m/e (relative intensity) 182 (M^+, <1), 180 (M^+, 3), 145 (79), 127 (48), 125 (48), 117 (89), 116 (70), 115 (99), 91 (58), 55 (100), and 39 (37).

Preparation of the Ketone 19. A solution of 24.33 g (150 mmol) of the acid chloride 28 in 40 mL of CH_2Cl_2 was added dropwise and with stirring during 1 h to a cold (0–3 °C) mixture of 26.0 g (195 mmol) of anhydrous $AlCl_3$ and 40 mL of CH_2Cl_2. After the resulting mixture had been stirred at 0–4 °C for 24 h, it was poured into ice water, acidified with HCl, and extracted with CH_2Cl_2. The organic layer was stirred for 24 h with aqueous Na_2CO_3 and then separated, dried, and concentrated. Distillation of the residual brown liquid (23.5 g) afforded 13.28 g (61%) of the ketone 19 as a colorless liquid: bp 77–85 °C (0.15–0.20 mm) [lit.[15] bp 80 °C (0.4 mm)]; n^{25}_D 1.5850–1.5855; IR (CCl_4) 1720 cm^{-1} (C=O); UV max (95% EtOH) 255 nm (ε 6450) and 298 (1530), with a shoulder at 305 nm (ε 1360); NMR (CCl_4) δ 6.8–7.5 (4 H, m, aryl CH), 2.1–3.0 (2 H, m, cyclopropyl CH), and 1.0–1.7 (2 H, m, cyclopropyl CH_2); mass spectrum, m/e (relative intensity) 144 (M^+, 68), 117 (13), 116 (72), 115 (100), 89 (14), and 63 (15).

In an alternative preparation, a mixture of 27.83 g (146 mmol) of the acid 26 (a mixture of stereoisomers) and 300 g of polyphosphoric acid was stirred at 40–65 °C for 1.5 h and then poured into ice water and extracted with Et_2O. After the ethereal extract had been dried and concentrated, distillation of the residual amber liquid (13.7 g)

Table I. Molecular Geometry of the Dihydro Dimer 43 [a]

A. Bond Lengths

atoms	distance, Å	atoms	distance, Å
C1–O1	1.437 (3)	C11–C1	1.557 (4)
C1–C2	1.520 (3)	C11–C12	1.538 (4)
C2–C3	1.497 (4)	C11–C20	1.514 (4)
C2–C4	1.506 (4)	C12–C13	1.525 (4)
C3–C4	1.511 (4)	C13–C14	1.492 (4)
C4–C5	1.493 (4)	C14–O2	1.232 (3)
C5–C6	1.381 (4)	C14–C15	1.478 (4)
C5–C10	1.394 (3)	C15–C16	1.401 (4)
C6–C7	1.391 (4)	C16–C17	1.374 (4)
C7–C8	1.382 (4)	C17–C18	1.392 (4)
C8–C9	1.388 (4)	C18–C19	1.380 (4)
C9–C10	1.387 (3)	C19–C20	1.391 (3)
C10–C1	1.516 (3)	C20–C15	1.405 (4)

B. Bond Angles

atoms	angle, deg	atoms	angle, deg
O1–C1–C2	113.1 (2)	C9–C10–C1	128.2 (2)
O1–C1–C10	111.7 (2)	C10–C1–C2	103.4 (2)
O1–C1–C11	105.1 (2)	C11–C1–C10	114.7 (2)
C1–C2–C3	119.0 (2)	C11–C12–C13	113.9 (2)
C1–C2–C4	108.8 (2)	C11–C20–C19	120.1 (2)
C2–C3–C4	60.1 (2)	C12–C11–C1	114.2 (2)
C2–C4–C3	59.5 (2)	C12–C13–C14	113.8 (2)
C2–C4–C5	105.6 (2)	C13–C14–C15	118.4 (2)
C2–C1–C11	109.1 (2)	C13–C14–O2	120.9 (3)
C3–C2–C4	60.4 (2)	C14–C15–C16	118.4 (2)
C3–C4–C5	113.4 (2)	C15–C14–O2	120.8 (3)
C4–C5–C6	129.3 (2)	C15–C16–C17	120.8 (3)
C4–C5–C10	110.1 (2)	C15–C20–C11	121.6 (2)
C5–C6–C7	118.6 (3)	C15–C20–C19	118.2 (2)
C5–C10–C1	111.2 (2)	C16–C17–C18	119.5 (2)
C5–C10–C9	120.5 (2)	C19–C18–C17	120.2 (3)
C6–C5–C10	120.5 (2)	C20–C11–C1	114.4 (2)
C6–C7–C8	121.0 (2)	C20–C11–C12	110.3 (2)
C7–C8–C9	120.5 (2)	C20–C15–C14	121.6 (2)
C8–C9–C10	118.8 (2)	C20–C15–C16	119.9 (2)
		C20–C19–C18	121.4 (2)

[a] Numbers in parentheses indicate estimated standard deviations in the least significant digit.

afforded 4.79 g (23%) of the ketone **19**: bp 74–78 °C (0.1 mm); n^{25}_D 1.5841–1.5847.

Preparation of the Alcohol 29. To a cold (0 °C) solution of 1.442 g (10.0 mmol) of the ketone **19** in 50 mL of Et_2O was added dropwise and with stirring during 5 min 12 mL of an Et_2O solution containing 12 mmol of MeLi. After the resulting solution had been stirred at 25 °C for 10 min, it was partitioned between H_2O and Et_2O. The organic layer was dried and concentrated to leave 1.52 g (95%) of the crude alcohol **29** as a colorless liquid that solidified on standing, mp 47.9–52.6 °C. One recrystallization from pentane sharpened the melting point to 50–52.4 °C, and an additional recrystallization gave 384 mg of the pure alcohol **29** as colorless plates: mp 53.8–54.2 °C; IR (CCl_4) 3590 and 3460 cm^{-1} (OH); UV max (95% EtOH) 264 nm (ϵ 682), 270 (891), 277.5 (800), 296 (136), and 307 (109); NMR ($CDCl_3$) δ 6.9–7.4 (4 H, m, aryl CH), 1.3–2.5 (6 H, m, cyclopropyl CH, OH, and a CH_3 singlet at δ 1.52), and 0.2–1.1 (2 H, m, cyclopropyl CH_2); mass spectrum, *m/e* (relative intensity) 160 (M^+, 14), 146 (24), 145 (99), 141 (24), 128 (31), 127 (45), 118 (28), 117 (100), 116 (45), 115 (59), and 91 (24).

Anal. Calcd for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.49; H, 7.59.

Reaction of the Ketone 19 with Me_2CuLi. A solution of 434 mg (3.00 mmol) of the ketone **19** in 2 mL of Et_2O was added dropwise and with stirring during 2 min to a cold (0 °C) solution of Me_2CuLi from 926 mg (4.5 mmol) of Me_2SCuBr, 9.0 mmol of MeLi (halide-free), 9 mL of Me_2S, and 21 mL of Et_2O. As the resulting orange solution was slowly warmed from 0 °C, a yellow precipitate began to separate at about 10 °C. The mixture was stirred at 10 °C for 15 min and at 25 °C for 1 h and then partitioned between Et_2O and an aqueous solution of NH_4Cl and NH_3. After the organic solution had been dried and concentrated, the residual green liquid (470 mg) was subjected to a preparative TLC separation on silica gel with an Et_2O–hexane mixture (1:5 v/v) as eluent. The components separated were 61 mg (13%) of the ketone **30** (R_f 0.49), 72 mg (17%) of the starting ketone **19** (R_f 0.36), and 188 mg (39%) of the alcohol **29** (R_f 0.17). The alcohol **29** and the ketone **19** were identified with previously described samples by comparison of NMR and IR spectra and TLC R_f values. The crude ketone **30** was distilled in a short-path still (ca. 100 °C at 0.15 mm) to separate 42 mg of the pure ketone **30** as a colorless liquid, n^{25}_D 1.5477, that was identified with a subsequently described sample by comparison of GLC retention times and IR, NMR, and mass spectra.

Table II. GLC Retention Times for Various Possible Components in the Mixture from the Reaction of Ketone 19 with Me_2CuLi

compd	GLC retention time, min: silicone SE-52, 176 °C	silicone QF-1, 150 °C	UCON 50-HB, 217 °C
ketone **19**	8.3	21.0	
ketone **30**	9.8[a]	23.9[b]	62.7
ketone **32**	10.6[a]	23.8[b]	68.2
ketone **31**		18.0[c]	
ketone **33**	9.6[a]	18.3[c]	
alcohol **29**	5.1[d]	5.2–11.0 (broad)	
$PhCH_2CH_2Ph$	14.0	13.5	

[a] Ketones **30**, **32**, and **33** are not resolved. [b] Ketones **30** and **32** are not resolved. [c] Ketones **31** and **33** are not resolved. [d] This peak contains one or more dehydration products from the alcohol **29**.

The following experiment was performed to demonstrate the absence of ketones **31**, **32**, and **33** in the reaction product. To a cold (−5–0 °C) solution of Me_2CuLi, from 1.26 g (6.13 mmol) of Me_2SCuBr, 12.0 mmol of MeLi, 6 mL of Et_2O, and 15 mL of THF, was added a solution of 428 mg (2.97 mmol) of the ketone **19** in 2.0 mL of THF. After the mixture had been stirred for 1 h at −5–0 °C and for 5 h at 25 °C, the previously described isolation procedure separated 431 mg of crude liquid product. One-half of this product was mixed with 147 mg of $PhCH_2CH_2Ph$ (an internal standard) and subjected to GLC analysis (silicone SE-52 on Chromosorb P; apparatus was calibrated with known mixtures). The calculated yields were 24% of ketone **19**, 31% of alcohol **29**, and 19% of ketone **30**. The GLC retention times for the various possible components on three different GLC columns are summarized in Table II. Under these GLC conditions, samples of the alcohol **29** gave a single broad GLC peak as indicated in Table II. However, samples of this peak collected from the GLC apparatus had IR [1645 cm^{-1} (C=C)] and mass spectra (M^+ at *m/e* 142) corresponding to one or more dehydration products from the alcohol **29**. Since the GLC response factor for this peak was relatively constant, this peak was used to estimate the yield of the alcohol **29** formed with the realization that some uncertainty in the yield of alcohol **29** may result from this analytical procedure. The second half of the crude reaction product was subjected to GLC analysis (silicone QF-1 on Chromosorb P) to demonstrate the absence of ketones **31** and **33**. When authentic samples of these ketones **31** and **33** were added to aliquots of the crude product in amounts corresponding to 5% of the amount of ketone **30** present, each ketone **31** or **33** was easily detected. The GLC peak (silicone QF-1 on Chromosorb P) corresponding in retention time to either ketone **30** or ketone **32** was collected; after short-path distillation, one portion of this collected sample was identified with an authentic sample of ketone **30** by comparison of IR spectra. A second portion of the collected sample was analyzed on a third GLC column (UCON 50-HB on Chromosorb P) to demonstrate the absence of ketone **32**. When a synthetic mixture of 5% of ketone **32** and 95% of ketone **30** was subjected to this same analytical procedure, the minor constituent, ketone **32**, was readily detected. Thus, we have found no evidence indicating the presence of any of the ketones **31**, **32**, or **33** in the crude product and can conclude that more than 95% of the ketonic product formed in this reaction is 3-ethylindanone (**30**).

In an additional series of experiments, colorless solutions of Me_2CuLi [containing a very small amount of yellow $(MeCu)_n$ precipitate to ensure the absence of excess MeLi], prepared from 6.0 mmol of Me_2SCuBr, 12 mmol of MeLi (halide-free), and 6 mL of Et_2O, were diluted with the solvents indicated in Table III, and then 3.0 mmol of the ketone **19** was added dropwise and with stirring during 1–5 min at the initial reaction temperature indicated in Table III. After the reaction mixtures had been stirred and allowed to warm to

Table III. Reaction of Ketone 19 with Me_2CuLi in Various Solvents

solvents (mL)	initial reaction temp, °C	reaction time, h	yields, % ketone 19	ketone 30	alcohol 29
Et_2O (14) + Me_2S (9)	5–15	1	3–20	17–18	62–80
Et_2O (5–7) + pentane (17–22)	5–15	1.5–17	1–6	6–7	87–92
Et_2O (6) + THF (17)	5	18	13	27	60
Et_2O (6) + DME (17–27)	5–15	17–18	28–36	18–21	40–47

25 °C during the times indicated in Table III, they were siphoned into an aqueous solution of NH_4Cl and NH_3 and then extracted with Et_2O. The ethereal extracts were mixed with a known weight of $PhCH_2CH_2Ph$, dried, and subjected to GLC analysis (silicone SE-52 on Chromosorb P at 176 °C; apparatus was calibrated with known mixtures). The yields of the various products **19, 29,** and **30** are summarized in Table III.

Sources of Ketones 48, 49, 31–33, 39, and 40. The preparation and properties of indanones **48** and **49** are described elsewhere,[6c] and authentic samples of tetralones **32** and **33** were obtained from Aldrich Chemical Co., Inc. A sample of the tetralone **32,** purified by short-path distillation, was obtained as a colorless liquid: n^{25}_D 1.5597 [lit.[16] bp 133–134 °C (12 mm), n^{19}_D 1.5620]; IR (CCl_4) 1691 cm^{-1} (C=O); UV max (95% EtOH) 212 nm (ϵ 9840), 249 (10 200), and 293 (1700); NMR (CCl_4) δ 6.6–7.9 (4 H, m, aryl CH) and 0.9–3.3 (8 H, m, aliphatic CH including a CH_3 doublet, J = 6.5 Hz, at δ 1.28); mass spectrum, *m/e* (relative intensity) 160 (M^+, 100), 145 (67), 132 (66), 118 (64), 117 (32), 115 (23), 104 (58), 77 (21), and 51 (22).

Purification by short-path distillation afforded a sample of the tetralone **33** as a colorless liquid: n^{25}_D 1.5523 [lit.[17] bp 136–138 °C (16 mm), n^{25}_D 1.5538]; IR (CCl_4) 1692 cm^{-1} (C=O); UV max (95% EtOH) 210 nm (ϵ 14 200), 247.5 (11 400), and 292 (1540); NMR (CCl_4) δ 7.0–8.2 (4 H, m, aryl CH), 1.4–3.2 (5 H, m, aliphatic CH), and 1.17 (3 H, d, J = 6 Hz, CH_3); mass spectrum, *m/e* (relative intensity) 161 (39), 160 (M^+, 92), 145 (76), 142 (39), 141 (33), 132 (42), 131 (65), 119 (49), 118 (100), 117 (36), 115 (37), 91 (37), 90 (68), 89 (42), and 77 (34).

A previously described procedure[18] was used to convert $PhCOCH_2CH_2CH_3$ to the methiodide **38** of its Mannich base. A solution of KOBu-*t*, from 0.49 g (12.5 mg-atom) of K and 25 mL of *t*-BuOH, was added dropwise and with stirring during 5 min to a suspension of 4.34 g (12.5 mmol) of the ammonium salt **38** in 25 mL of *t*-BuOH. The resulting solution was stirred at 25–27 °C for 10 min and then partitioned between H_2O and Et_2O. After the ethereal layer had dried and concentrated, distillation of the residual liquid separated 1.13 g (56%) of the pure (GLC analyses) unsaturated ketone **39** (bp 58–60 °C (0.15 mm); n^{25}_D 1.5294–1.5299) accompanied by 267 mg of less pure ketone **39** (bp 64–67 °C (0.15 mm); n^{25}_D 1.5275 [lit.[18] bp 49–50 °C (0.15 mm), n^{25}_D 1.5300]): IR (CCl_4) 1660 (C=O), 1625 (C=C), and 930 (C=CH_2) cm^{-1}; UV max (95% EtOH) 246 nm (ϵ 9510) and 335.5 (93); NMR (CCl_4) δ 6.9–7.6 (5 H, m, aryl CH), 5.5–5.6 (1 H, m, vinyl CH), 5.2–5.4 (1 H, m, vinyl CH), 2.38 (2 H, q, J = 7 Hz, CH_2), and 1.06 (3 H, t, J = 7 Hz, CH_3); mass spectrum, *m/e* (relative intensity) 160 (M^+, 20), 145 (15), 105 (100), 77 (52), and 51 (17).

A previously described[19] cyclization was effected by adding 974 mg (6.1 mmol) of the unsaturated ketone **39** dropwise and with stirring during 1 min to 4.0 mL of concentrated H_2SO_4. The resulting solution, whose temperature initially rose to 70 °C, was stirred, allowed to cool for 90 min, and then poured onto ice and partitioned between H_2O and Et_2O. The Et_2O solution was washed with aqueous $NaHCO_3$, dried, and concentrated to leave a crude yellow liquid product containing (GLC, silicone SE-30 on Chromosorb P) the indanone **31** (retention time 24.6 min) but lacking peaks corresponding to the enone **39** (15.9 min) or the subsequently described methoxy ketone **40** (29.1 min). Distillation afforded 866 mg (89%) of the indanone **31** as a colorless liquid: bp 65–66 °C (0.05 mm); n^{25}_D 1.5452–1.5456 [lit.[19] bp 143 °C (18 mm), n^{31}_D 1.5420]; IR (CCl_4) 1718 cm^{-1} (C=O); UV max (95% EtOH) 245 nm (ϵ 12 100) and 291.5 (2170); NMR (CCl_4) δ 6.7–7.5 (4 H, m, aryl CH), 1.1–3.5 (5 H, m, CH and CH_2), and 0.91 (3, H, t, J = 7 Hz, CH_3); mass spectrum, *m/e* (relative intensity) 160 (M^+, 4), 133 (19), 132 (100), 131 (50), and 103 (15).

In an alternative procedure, 94 mL of aqueous 6 M NaOH (564 mmol) was added dropwise with stirring and cooling during 30 min to a cold (−1 to −4 °C) suspension of 50.3 g (171 mmol) of the methiodide **38** in 500 mL of MeOH. After the resulting mixture had been stirred at 0 °C for 1 h and at 10 °C for 2 h, it was partitioned between H_2O and Et_2O. After the Et_2O solution had been dried and concentrated, distillation of the residual liquid (20.92 g) afforded 19.9 g of fractions (bp 90–95 °C (0.14 mm); n^{25}_D 1.5111–1.5145) containing (GLC) various mixtures of the enone **39** and the methoxy ketone **40.** Fractions rich in the methoxy ketone **40** were redistilled to separate 3.86 g of the higher boiling pure (GLC) methoxy ketone **40:** bp 114–116 °C (6 mm); n^{25}_D 1.5114; IR (CCl_4) 1685 cm^{-1} (C=O); UV max (95% EtOH) 244 nm (ϵ 12 500), 279 (1060), and 320 (80); NMR (CCl_4) δ 7.2–8.1 (5 H, m, aryl CH), 3.3–3.8 (3 H, m, CH and CH_2O), 3.17 (3 H, s, OCH_3), 1.3–1.9 (2 H, m, CH_2), and 0.83 (3 H, t, J = 7 Hz, CH_3); mass spectrum, *m/e* (relative intensity) 192 (M^+, 2), 163 (64), 160 (50), 137 (55), 136 (34), 106 (28), 105 (100), 77 (66), 51 (28), and 45 (45).

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.00; H, 8.42.

The methoxy ketone **40** (1.92 g, 10 mmol) was added dropwise and with stirring during 1 min to 4.0 mL of concentrated H_2SO_4. The resulting solution was warmed to 80 °C for 2 h and then cooled, poured onto ice, and partitioned between H_2O and Et_2O. After the Et_2O solution had been washed with aqueous $NaHCO_3$, dried, and concentrated, the residual liquid was distilled to separate 1.34 g (84%) of the indanone **31:** bp 73–74 °C (0.13 mm); n^{25}_D 1.5456.

Preparation of an Authentic Sample of the Indanone 30. A solution of 11.5 mmol of EtLi in 14 mL of PhH and 15 mL of Et_2O was added dropwise with stirring and cooling to a cold (−50 °C) mixture of 1.88 g (5.78 mmol) of Me_2SCuBr and 5 mL of Et_2O. As the resulting mixture (unchanged Me_2SCuBr still present) was warmed to −38 to −40 °C, the Me_2SCuBr dissolved and a black colloidal solid (presumably Cu^0) began to separate. While this cuprate reagent was kept at −25 to −30 °C, a solution of 782 mg (4.44 mmol) of the ester **34** in 5 mL of Et_2O was added dropwise and with stirring during 5 min. The resulting mixture was allowed to warm to 0 °C with stirring during 30 min and then was added to an aqueous solution of NH_3 and NH_4Cl and extracted with Et_2O. After the ethereal extract had been dried and concentrated, the residual liquid (1.029 g) was distilled to separate 542 mg (59%) of the ester **35** as a colorless liquid: bp 71.5–73 °C (0.07 mm); n^{25}_D 1.4878–1.4887; IR (CCl_4) 1735 cm^{-1} (ester C=O); NMR (CCl_4) δ 6.8–7.2 (5 H, m, aryl CH), 3.86 (2 H, q, J = 7 Hz, ethoxyl CH_2), 1.3–3.2 (5 H, m, CH and CH_2), 1.03 (3 H, t, J = 7 Hz, ethoxyl CH_3), and 0.75 (3 H, t, J = 7 Hz, CH_3); mass spectrum, *m/e* (relative intensity) 206 (M^+, 17), 135 (47), 132 (55), 131 (21), 119 (56), 118 (54), 117 (21), 105 (30), 91 (100), and 88 (33). The product exhibited a single GLC peak (silicone SE-52 on Chromosorb P) corresponding to the ester **35** (retention time 17.2 min) and lacked a peak corresponding to the starting ester **34** (18.6 min).

A solution of 1.218 g (5.9 mmol) of the ester **35,** 523 mg (13.1 mmol) of NaOH, and 2 mL of H_2O in 25 mL of EtOH was refluxed for 4 h and then partitioned between H_2O and Et_2O. This ethereal extract contained 35 mg (3%) of the unchanged ester. After the aqueous solution had been acidified (HCl) and extracted with Et_2O, the ethereal extract was dried, concentrated, and distilled in a short-path still (100 °C and 0.5 mm) to separate 913 mg (87%) of the acid **36** as a pale yellow liquid, n^{25}_D 1.5173, that solidified on standing, mp 50–54.2 °C. Successive recrystallization from Et_2O–pentane and pentane separated the pure acid **36** as a colorless powder: mp 59–60 °C [lit.[20] mp 62–64 °C]; IR (CCl_4) 2950 (broad, associated OH) and 1713 (carboxyl C=O) cm^{-1}; UV (95% EtOH) end absorption (ϵ 6580 at 210 nm) with a series of weak maxima (ϵ 73–244) in the region 237–268 nm; NMR (CCl_4) δ 11.88 (1 H, s, OH), 6.8–7.5 (5 H, m, aryl CH), 1.4–3.3 (5 H, m, CH and CH_2), and 0.75 (3 H, t, J = 7 Hz, CH_3); mass spectrum, *m/e* (relative intensity) 178 (M^+, 86), 150 (29), 149 (50), 132 (25), 119 (75), 118 (69), 107 (100), 105 (39), 104 (36), 103 (42), 91 (81), 79 (32), 77 (35), and 43 (24).

The solid acid **36** (824 mg or 4.62 mmol) was dissolved in 50 g of warm (50 °C) polyphosphoric acid, and the resulting solution was heated to 70–80 °C for 2 h and then poured into cold H_2O and extracted with Et_2O. The Et_2O solution was washed with aqueous $NaHCO_3$, dried, and concentrated to leave 780 mg of crude liquid product. Distillation in a short-path still (110–130 °C and 0.06 mm) separated 530 mg (72%) of the indanone **30** as a colorless liquid [lit.[21] bp 116 ° (10 mm)]: n^{25}_D 1.5482; IR (CCl_4) 1720 cm^{-1} (C=O); UV max (95% EtOH) 244.5 nm (ϵ 11 500), 288 (2450), and 293 (2480); NMR

(CCl_4) δ 7.0–8.0 (4 H, m, aryl CH), 1.1–3.5 (5 H, m, CH and CH_2), and 0.90 (3 H, t, J = 7 Hz, CH_3); mass spectrum, m/e (relative intensity) 160 (M^+, 63), 145 (37), 133 (46), 132 (100), 131 (86), 117 (29), 115 (39), 104 (29), 103 (61), 102 (29), and 77 (39).

Anal. Calcd for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.35; H, 7.56.

Electrochemical Measurements. Polarographic and cyclic voltammetry measurements employed a custom-made polarographic module, utilizing solid-state amplifiers, that followed the typical three-electrode design. Descriptions of the cell, working electrodes, reference electrode, reagent purification, and measurement procedures have been published previously.[22] For cyclic voltammetry measurements that involved anion radicals with short half-lives (0.01 s or less), we found it advantageous to use a previously described[22e] cell design in which the tube leading to the reference electrode was placed directly above an inverted spherical Hg-coated Pt working electrode and both electrodes were surrounded by a cylindrical Pt gauze counter electrode. All measurements were performed at 25 °C in anhydrous DMF containing 0.5 M n-Bu_4NBF_4 as the supporting electrolyte. The results of these measurements are summarized in Table IV.

Preparation of p-Methoxystyrene (23). Following a previously described procedure,[23] a mixture of 50.0 g (0.28 mol) of p-methoxycinnamic acid, 5.0 g of Cu powder, and 100 mL of quinoline was heated to boiling during 40 min and then held at the boiling point for 15 min while the volatile materials were allowed to distill from the reaction flask. The yellow liquid distillate was decanted from a small amount of the solid starting acid that had codistilled, and then it was partitioned between Et_2O and aqueous 6 M HCl. The ethereal layer was dried, concentrated, and distilled to separate 20.25 g (54%) of the styrene **23** as a colorless liquid: bp 60–64 °C (1.7 mm); n^{25}_D 1.5600–1.5670 [lit.[23] bp 77–80 °C (3 mm), n^{20}_D 1.5609–1.5620]; IR (CCl_4) 1628 (C=C) and 908 (CH=CH_2) cm^{-1}; UV max (95% EtOH) 259 nm (ε 18 100), 292 (2450), and 303 (1420); NMR (CCl_4) δ 6.2–7.3 (5 H, m, aryl CH and vinyl CH), 5.45 (1 H, d of d, J = 1 and 17 Hz, vinyl CH), 4.98 (1 H, d of d, J = 1 and 11 Hz, vinyl CH), and 3.57 (3 H, s, OCH_3); mass spectrum, m/e (relative intensity) 134 (M^+, 100), 119 (20), and 91 (20).

Preparation of the Acid Derivatives 25 and 27. A solution of 11.41 g (100 mmol) of N_2CHCO_2Et in 13.42 g (100 mmol) of the styrene **23** was added dropwise and with stirring during 40 min to 4.80 g (35.8 mmol) of the styrene **23** while the temperature of the mixture was maintained at 130–145 °C.[7b] The resulting solution was heated to 130 °C for an additional 12 h, during which time the color of the solution turned from orange to red to amber. The resulting mixture was fractionally distilled to separate 7.74 g of low boiling fractions (bp 38–52 °C (0.11–0.13 mm); n^{25}_D 1.5595–1.5653) containing (NMR analysis) the unchanged olefin **23.** Subsequent distillation fractions contained 12.06 g (55%) of the crude ester **25** as a liquid, bp 52–145 °C (0.13 mm), that solidified on standing, mp 58–74 °C. Recrystallization from pentane separated 6.21 g of ester **25** (a mixture of cis and trans isomers) as fractions of colorless crystals melting within the range 76–83 °C. Repeated recrystallization from pentane afforded a sample of the trans ester **25** as colorless plates: mp 81.1–82.8 °C (lit.[24] mp 83–84 °C); IR (CCl_4) 1727 cm^{-1} (ester C=O); UV max (95% EtOH) 232 nm (ε 14 900), 279.5 (1690), 282 (1650), and 289 shoulder (1190); nmr ($CDCl_3$) δ 6.8–7.1 (4 H, m, aryl CH), 4.18 (2 H, q, J = 7 Hz, ethoxyl CH_2), 3.75 (3 H, s, OCH_3), and 0.9–2.8 (7 H, m, CH_3 and cyclopropyl CH and CH_2); mass spectrum, m/e (relative intensity) 220 (M^+, 78), 191 (46), 175 (55), 174 (32), 165 (31), 163 (30), 148 (45), 147 (100), 146 (49), 145 (49), 131 (31), 115 (37), 103 (30), and 91 (27).

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.96; H, 7.32.

A solution of 3.34 g (15 mmol) of the ester **25,** 1.05 g (26 mmol) of NaOH, and 2.6 mL of H_2O in 15 mL of EtOH was refluxed for 15 h and then diluted with H_2O and distilled to remove most of the EtOH. After the resulting basic aqueous solution had been extracted with Et_2O, it was cooled, acidified (HCl), and again extracted with Et_2O. This latter ethereal extract was dried and concentrated to leave 2.72 g (93%) of the acid **27** as a white powder, mp 112.1–113.9 °C. Recrystallization from a $CHCl_3$–hexane mixture gave the trans acid **27:** mp 113–114 °C (lit. trans acid mp 113.2–114.2[25] and 114–114.5 °C,[24] cis acid mp 100.8–101 °C[25]); IR ($CHCl_3$) 2950 (broad, associated OH) and 1690 (carboxyl C=O) cm^{-1}; UV max (95% EtOH) 231 nm (ε 14 200), 278.5 (1650), and 281.5 (1630); NMR (CD_3COCD_3) δ 7.83 (1 H, broad, OH), 6.7–7.2 (4 H, m, aryl CH), 3.76 (3 H, s, OCH_3), and 1.0–2.7 (4 H, m, cyclopropyl CH and CH_2); mass spectrum, m/e (relative intensity) 192 (M^+, 57), 147 (100), 131 (32), 115 (31), 105 (36), 103 (36), 91 (36), and 77 (56).

Table IV. Electrochemical Reduction of Ketones

ketone (concn, M × 10^3)	polarography $E_{1/2}$ (V) vs. SCE	n	i_d, μA	cyclic voltammetry $E_{1/2}$ (V) vs. SCE	half-life, s
48 (1.1–2.8)	−2.03	1.0	32–37	−2.05	0.08
49 (0.8–1.1)	−2.01	1.4	28–46	−2.03	0.3
19 (0.6–1.8)	−2.03	0.9	12–17	−2.03	0.001
8 (0.98)	−1.82[a]	0.8[a]		−1.82	0.005

[a] These values were described previously in ref 3.

Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.73; H, 6.29. Found: C, 68.68; H, 6.33.

Reduction of the Ketone 19. A. With $LiAlH_4$. A solution of 1.44 g (10 mmol) of the ketone **19** in 20 mL of Et_2O was added dropwise and with stirring during 5 min to a solution of 0.57 g (15 mmol) of $LiAlH_4$ in 80 mL of Et_2O. After the resulting solution had been stirred at 25 °C for 24 h, EtOAc was added to consume the excess $LiAlH_4$ and the mixture was partitioned between Et_2O and H_2O. The organic layer was washed with aqueous NaCl, dried, and concentrated to leave 1.36 g (93%) of a waxy solid, mp 40–69 °C, containing (IR, NMR, and TLC analysis; silica gel coating with an EtOAc–hexane eluent, 15:85 v/v) a mixture of the alcohol **44** (ca. 29%, R_f 0.36) and the alcohol **45** (ca. 71%, R_f 0.29) but lacking IR absorption attributable to the starting ketone **19.** This mixture was subjected to low-pressure liquid chromatography on silica gel with EtOAc–hexane eluent (1:4 v/v) to separate 595 mg of early fractions containing (NMR analysis) various mixtures of alcohols **44** and **45** and 449 mg of later fractions containing alcohol **45** as colorless needles, mp 82–82.9 °C. Repeated chromatography of these latter fractions afforded the pure (NMR analysis) alcohol **45:** mp 85.2–86 °C (lit.[11b] mp 85.5–87.5 °C); IR (CCl_4) 3574 and 3370 cm^{-1} (OH); NMR ($CDCl_3$) δ 6.8–7.5 (4 H, m, aryl CH), 5.55 (1 H, broad d, J = 6 Hz, O–CH), 1.7–2.7 (3 H, m, OH and cyclopropyl CH), 0.6–1.2 (1 H, m, cyclopropyl CH), and 0.2–0.6 (1 H, m, cyclopropyl CH); mass spectrum, m/e (relative intensity) 146 (M^+, 30), 145 (26), 131 (32), 129 (25), 128 (100), 127 (27), 117 (94), 116 (82), 115 (72), 63 (27), 51 (30), and 39 (21).

The early chromatographic fractions (containing mixtures of alcohols **44** and **45**) from several reactions were combined and rechromatographed to separate the alcohol **44** as a colorless oil that thus far has not crystallized (lit.[11b] mp 67–68.5 °C). However, the spectral properties of the sample correspond to those previously reported[11b] for alcohol **44:** IR (CCl_4) 3565 and 3310 cm^{-1} (OH); NMR ($CDCl_3$) δ 6.8–7.6 (4 H, m, aryl CH), 4.88 (1 H, partially resolved multiplet, O–CH), 1.8–2.9 (3 H, m, OH and cyclopropyl CH), 0.9–1.5 (1 H, m, cyclopropyl CH), and −0.1–0.2 (1 H, m, cyclopropyl CH); mass spectrum, m/e (relative intensity) 146 (M^+, 13), 145 (25), 131 (42), 129 (27), 128 (85), 127 (29), 117 (100), 116 (42), 115 (57), 91 (28), 77 (28), 63 (33), 51 (49), 50 (24), and 39 (38).

B. With Li in NH_3. To a cold (−33 °C) solution of 139 mg (20 mg-atom) of Li in 100 mL of NH_3 was added dropwise and with stirring during 2 min a solution of 1.44 g (10 mmol) of the ketone **19** and 740 mg (10 mmol) of t-BuOH in 20 mL of Et_2O. The resulting solution, from which the blue color was discharged as the last of the ketone solution was added, was stirred for 5 min and neutralized by the addition of excess solid NH_4Cl, and then the NH_3 was allowed to evaporate. The residue was partitioned between Et_2O and H_2O, and the organic layer was washed with aqueous NaCl, dried, and concentrated. The residual colorless semisolid (1.506 g) was triturated with Et_2O to separate several fractions of the crude dihydro dimer **43** (total 335 mg, 23%), melting within the range 181–187.5 °C. Concentration of the mother liquors from this separation left 1.124 g of crude liquid product. NMR and GLC analyses allowed us to conclude that neither tetralin nor either of the isomeric alcohols **44** or **45** was present in any significant quantity. An aliquot of this product mixture was mixed with a known weight of $PhCH_2CH_2Ph$ (an internal standard) for GLC analysis (silicone SE-30 on Chromosorb P; apparatus was calibrated with known mixtures). The crude product contained the tetralol **41** (24% yield; eluted as the corresponding olefin with retention time 12.1 min), a mixture of the tetralone **42** and the starting ketone **19** (25.4 min, not resolved, total yield ca. 30%), and $PhCH_2CH_2Ph$ (43.5 min). Under the same GLC conditions the retention times for tetralin and the alcohols **44** and **45** (not resolved, eluted from the GLC column as naphthalene) were 11.4 and 13.1 min and the dihydro dimer **43** was not eluted. A 977-mg aliquot of the crude liquid product was chromatographed on silica gel with

EtOAc–hexane eluent (15:85 v/v) to separate 153 mg (12%) of early fractions containing tetralone **42** (identified with an authentic sample by comparison of IR and NMR spectra) followed by 110 mg (9%) of the starting ketone **19** (identified by comparison of IR and NMR spectra). Subsequent chromatographic fractions contained 505 mg of various mixtures of the tetralol **41** and a second solid product. Further purification by preparative TLC separated 279 mg (19%) of the tetralol **41** (identified with an authentic sample by comparison of IR and NMR spectra) and 89 mg of a colorless solid, mp 148.5–149.7 °C, believed to be a second stereoisomer of the dihydro dimer **43**: IR ($CHCl_3$) 3560, 3460 (OH), and 1670 (conjugated C=O) cm^{-1}; mass spectrum, *m/e* (relative intensity) 273 (20), 272 (82), 244 (74), 243 (32), 239 (22), 230 (42), 229 (45), 228 (28), 216 (40), 215 (100), 141 (29), 129 (22), 128 (73), 116 (29), 115 (76), 91 (23), 77 (23), 63 (28), 51 (28), 40 (97), and 39 (35).

In a second comparable experiment involving reduction of 1.44 g (10 mmol) of the ketone **19** with 143 mg (21 mg-atom) of Li and 740 mg (10 mmol) of *t*-BuOH in 20 mL of Et_2O and 100 mL of NH_3, the isolated dihydro dimer **43** (mp 182.6–187.7 °C) amounted to 187 mg (13%). The semisolid (1.23 g) recovered from the mother liquor exhibited TLC spots (silica gel coating; EtOAc–hexane eluent, 15:85 v/v) corresponding to tetralone **42** (R_f 0.50), the starting ketone **19** (R_f 0.40), and two (or more) more slowly eluted components (R_f 0.32 and 0.21) but lacked a spot corresponding to tetralin (R_f 0.86). This mixture was subjected to low-pressure liquid chromatography (silica gel with EtOAc–hexane eluent) to separate early fractions containing 203 mg (14%) of tetralone (**42**) followed by 74 mg (5%) of the starting ketone **19**. Both materials **42** and **19** were identified with authentic samples by comparison of IR and NMR spectra. Subsequent chromatographic fractions (506 mg) contained (IR and NMR analyses) mixtures of mainly tetralol (**41**) and the dihydro dimer **43** (or its stereoisomer), and the final fractions contained 30 mg (total yield 217 mg or 15%) of the dihydro dimer **43**, mp 186–187.5 °C. The intermediate fractions were subjected to preparative TLC to separate 186 mg (13%) of tetralol (**41**) and 22 mg of a solid, mp 147.2–150 °C, believed to be a stereoisomer of the dihydro dimer **43**. The fractions containing the tetralol (**41**) were distilled in a short-path still (ca. 80 °C at 0.15 mm) to separate the tetralol as a colorless liquid, $n^{25}D$ 1.5628. This material was identified with an authentic sample [bp 85–87 °C (0.35 mm); $n^{25}D$ 1.5620–1.5629; prepared in 75% yield by the reduction of tetralone with $LiAlH_4$] by comparison of IR and NMR spectra.

The dihydro dimer crystallized from a $CHCl_3$–hexane mixture as colorless needles: mp 188–189.9 °C; IR ($CHCl_3$) 3562, 3390 (OH), and 1675 (conjugated C=O) cm^{-1}; UV max (95% EtOH) 251.5 nm (ε 10 600), 279.5 (1760), and 297 (1680); NMR ($CDCl_3$) δ 6.7–8.2 (7 H, m, aryl CH), 6.1–6.4 (1 H, m, aryl CH), 3.3–3.6 (1 H, m, benzylic CH), 1.4–2.9 (7 H, m, aliphatic CH and OH), 0.8–1.4 (1 H, m, cyclopropyl CH), and 0.2–0.7 (1 H, m, cyclopropyl CH); mass spectrum, *m/e* (relative intensity) 290 (M^+, 0.4), 147 (11), 146 (100), 145 (57), 117 (12), and 115 (19).

Anal. Calcd for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25. Found: C, 82.73; H, 6.27.

In an experiment where 10 mmol of the ketone **19** was reduced with 20 mg-atom of Li in a mixture of 100 mL of NH_3 and 20 mL of Et_2O with no added *t*-BuOH, 386 mg (27%) of the dihydro dimer **43**, mp 182.3–185 °C, was isolated from the crude product by trituration with Et_2O. Although the residual product contained (GLC analysis) some tetralol (**41**) and tetralone (**42**), the bulk of the material separated by subsequent chromatography was 734 mg of the crude dihydro dimer **43** (and/or its stereoisomer), mp 128–182 °C.

Structure Determination of Dihydro Dimer 43. A plate-like crystal fragment with approximate dimensions 0.5 × 0.7 × 0.3 mm was mounted on a glass fiber with epoxy cement. Unit cell parameters and the orientation matrix were determined on a Syntex $P2_1$, four-circle diffractometer equipped with a graphite monochromator (Bragg 2θ angle = 12.2°) using Mo Kα radiation at a takeoff angle of 6.75°. A total of 15 reflections whose 2θ values ranged from 7.24 to 19.33° were machine-centered and used in least-squares refinement of the lattice parameters and orientation matrix. Unit cell parameters obtained were the following:[26] a = 8.619 (4) Å, b = 14.803 (6) Å, c = 11.463 (3) Å, β = 92.26 (3)°, and V = 1462 Å^3. The calculated density of 1.32 g cm^{-3} for 4 molecules per unit cell agrees with the experimental density of 1.31 (1) g cm^{-3} measured by the flotation method using aqueous zinc chloride solution at room temperature. ω scans of several low 2θ angle reflections gave peak widths at half-height of less than 0.20°, indicating a satisfactory mosaic spread for the crystal.

Axial photographs indicated that the crystal belonged to the monoclinic system. Intensity data for 0 and upper levels were collected at a rapid scan rate and the intensities examined carefully for systematic absences. The absence of $h = 2n + 1$ for $0k0$ reflections and $h + l = 2n + 1$ for $h0l$ reflections is consistent with only space group $P2_1/n$ (a nonstandard setting of $P2_1/c$, No. 14[27]).

Intensity data were collected using θ–2θ scans with X-ray source and monochromator settings identical with those used for determination of the unit cell parameters. A variable scan rate of from 2.93 to 29.3° per min was used, and a scan width of 2.0° was sufficient to collect all of the peak intensity. Stationary background counts were measured at the beginning (*bgd*1) and end (*bgd*2) of each scan with a total background to scan time ratio of 1.0. No significant fluctuations were observed in the intensities of three standard reflections (4,0,0; 0,4,0; 0,0,6) monitored every 97 reflections. Intensities (I) were calculated by subtracting the sum of the two background counts (*bgd*1 + *bgd*2) from the total scan count (CT). Standard deviations were assigned to the intensities according to the formula $\sigma(I) = (CT + bgd1 + bgd2)^{1/2}$. From a total of 2857 reflections collected in a complete quadrant $k \geq 0$, $l \geq 0$ of data out to $2\theta = 50°$, 1602 were accepted as statistically above background ($I \geq 3\sigma(I)$). Lorentz and polarization corrections were made in the usual way; no corrections were made for absorption.

The structure was solved[28] by direct methods utilizing the program MULTAN to generate phases. E values were calculated for all nonzero reflections. The 260 largest E values were used as input for MULTAN, and it automatically produced a set of phases with an absolute figure-of-merit of 1.25 and ψ_0 of 0.18 × 10^3; the resulting E map revealed the positions of all nonhydrogen atoms. Hydrogen positions were located from a combination of difference Fourier peaks and calculations based on ideal geometry after three cycles of full-matrix least-squares refinement. Further cycles of least-squares refinement, varying a scale factor, coordinates of all nonhydrogen atoms, anisotropic temperature parameters for all nonhydrogen atoms, not varying the positions of the hydrogens, and fixing the isotropic temperature parameters of all hydrogen atoms at 5.0 caused the refinement to converge[30] to R = 0.048 and R_w = 0.040 (199 variables, 1602 reflections). Final positional and thermal parameters are available as supplementary material, and a list of calculated and observed structure factors may be obtained from the authors.

Registry No.—**8,** 1145-92-2; **9,** 5771-62-0; **22,** 100-42-5; **23,** 637-69-4; *cis*-**24,** 946-38-3; *trans*-**24,** 946-39-4; *cis*-**25,** 67478-53-9; *trans*-**25,** 6142-64-9; *cis*-**26,** 939-89-9; *trans*-**26,** 939-90-2; *trans*-**27,** 34919-28-3; *cis*-**28,** 62624-90-2; *trans*-**28,** 939-87-7; **29,** 65731-99-9; **30,** 19832-99-6; **31,** 22351-56-0; **32,** 19832-98-5; **33,** 1590-08-5; **34,** 103-36-6; **35,** 67478-54-0; **36,** 5669-17-0; **37,** 495-40-9; **38,** 67478-55-1; **39,** 22731-65-3; **40,** 67478-56-2; **41,** 529-33-9; **42,** 529-34-0; **43,** 67478-57-3; **44,** 57378-74-2; **45,** 57378-75-3; **48,** 83-33-0; **49,** 13623-25-1; $PhCH_2CH_2Ph$, 103-29-7; N_2CHCO_2Et, 623-73-4; *p*-methoxycinnamic acid, 830-09-1.

Supplementary Material Available: Tables of atomic coordinates and isotropic temperature factors (Table V) and anisotropic thermal parameters (Table VI) (2 pages). Ordering information is given on any current masthead page.

References and Notes

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spectra were determined with a Perkin-Elmer Model 257 infrared recording spectrophotometer fitted with a grating. The UV spectra were determined with a Cary Model 14 or a Perkin-Elmer Model 202 recording spectrophotometer. The proton NMR spectra were determined at 60 mHz with a Varian Model A-60 or T-60-A NMR spectrometer, and the ^{13}C NMR spectra were determined at 25 mHz with a JEOL Model PFT-100 Fourier transform spectrometer. The chemical shift values are expressed in δ values (ppm) relative to a Me_4Si internal standard. The mass spectra were obtained with an Hitachi (Perkin-Elmer) Model RMU-7 mass spectrometer. All reactions involving strong bases or reactive organometallic intermediates were performed under a nitrogen atmosphere.

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(30) $R = \sum(|F_o| - |F_c|)/\sum|F_o|$ and $R_w = [\sum w(|F_o| - |F_c|)^2/\sum w(|F_o|)^2]^{1/2}$.

Base-Catalyzed Isomerization of *cis*- and *trans*-2,2-Dimethyl-3-formylcyclopropanecarboxylates. Nature of the Base-Stable Cis Intermediate

Paul R. Ortiz de Montellano* and Stephen E. Dinizo

Department of Pharmaceutical Chemistry, School of Pharmacy and Liver Center, University of California, San Francisco, California 94143

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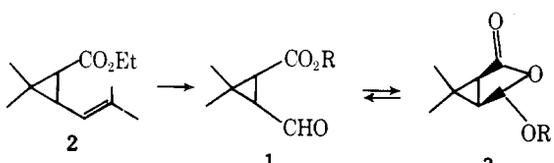
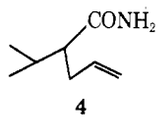
A mixture of isomers of ethyl 2,2-dimethyl-3-formylcyclopropanecarboxylate (**1b**), obtained by ozonolysis of commercial ethyl chrysanthemate, undergoes rapid transesterification and isomerization to the *trans* methyl ester in 15 min at 25 °C in sodium methoxide–methanol. Reaction at this temperature for 24 h rather than 15 min, or refluxing for 3 h, results in the accumulation of a relatively base-stable cis intermediate which is hydrolyzed under acid conditions to hydroxy lactone **3c**. The intermediate has been isolated and identified as the dimethyl acetal of *cis*-2,2-dimethyl-3-formylcyclopropanecarboxylic acid (**9**) instead of the previously postulated methoxy lactone **3a**, although methoxy lactone **3a** is implicated as a precursor of the accumulated dimethyl acetal. Anhydrous sodium ethoxide–ethanol can also be used for conversion of a mixture of isomers of **1b** to the pure trans isomer, but it cannot be used for the preparation of the cis isomer, since reaction of **1b** in this medium for 24 h at 25 °C results exclusively in the formation of the *hydrolysis* product *trans*-2,2-dimethyl-3-formylcyclopropanecarboxylic acid. A reaction scheme which rationalizes these observations is suggested. The isomerically pure *cis*- and *trans*-2,2-dimethyl-3-vinylcyclopropanecarboxylic acids and amides have been prepared from the corresponding formyl precursors **3c** and **1a**.

Methodology for stereospecific preparation of 2,2-dimethyl-3-formylcyclopropanecarboxylates (1), particularly



2 1 3

a, R = Me
b, R = Et
c, R = H



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the thermodynamically less stable cis isomers, is of considerable current interest because of the pivotal role these structures play in elaboration of vinyl-modified chrysanthemic acid analogues, essential components of the highly promising pyrethroid insecticides.[1,2] Among methods reported in recent years for the synthesis of isomerically pure *cis*- and *trans*-2,2-dimethyl-3-formylcyclopropanecarboxylates,[3] that disclosed by J. Martel of Roussel UCLAF is particularly ingenious.[4] It involves ozonolysis of *trans*-methyl chrysanthemate (**2a**) to give trans ester aldehyde **1a**, which is converted in refluxing sodium methoxide–methanol to a latent form of the cis isomer, essentially uncharacterized but assigned structure **3a** in the patent.[4] This unisolated precursor is directly hydrolyzed under acidic conditions to hydroxy lactone **3c**, the preferred tautomeric form of the desired *cis*-**1c**.

Our interest in this process stems from our desire, in connection with a study of the destruction of cytochrome P450 by 2-isopropyl-4-pentenamide (**4**),[5,6] to synthesize the conformationally restricted analogues, *cis*- (**5**) and *trans*-2,2-dimethyl-3-vinylcyclopropanecarboxamide (**6**). The procedure outlined by Martel was particularly attractive because of the ready commercial availability of a mixture of *cis*- and *trans*-ethyl chrysanthemates. To our surpirse, only poor and erratic yields of **3c** were obtained when a mixture of isomers of ethyl chrysanthemate was subjected to the literature procedure reported for the pure *trans*-methyl ester.[4] Subsequent detailed studies, the results of which are presented here, demonstrate that the isomerization process is a complex one

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