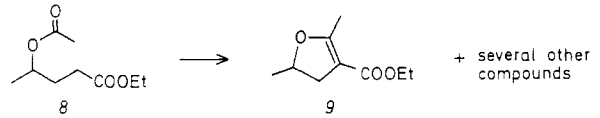
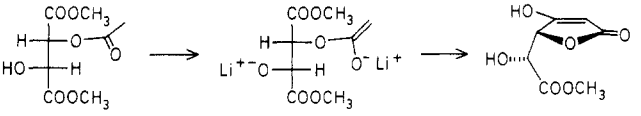


8 9

However, initially attempted syntheses from the diacetate or the acetate benzoate of dimethyl (*R,R*)-tartrate led to deep red crude reaction products from which no cyclized products could be isolated; benzoic acid was obtained from the latter starting material (ca. 50% yield). It seems reasonable to assume that these two starting esters, like dimethyl 2-acetoxybutanedioate (see above), undergo elimination faster than they undergo ring closure.

On the other hand, when the monoacetate **10**[7] was treated with 3.5 equiv of lithium bis(trimethylsilyl)amide in THF (-78 °C, 1 h), ring closure occurred, and after hydrolysis, **11** crystallized during workup (78% yield).



10 11

This difference in reactivity between **10** and the diacetate of dimethyl tartrate can be rationalized by assuming that the base rapidly converts the α-hydroxy group of **10** into a lithium oxido group which then prevents 1,2-elimination of the β-acetoxy group by lowering the acidity of the α hydrogen. The use of a lithium oxido group to prevent 1,2-elimination of an adjacent group has, to the best of our knowledge, not been reported before.

Experimental Section

Tetrahydrofuran (THF) was freshly distilled over $LiAlH_4$. An atmosphere of N_2 was used in all reactions involving amide bases. NMR spectra were recorded by using a JEOL JNM-FX 100 instrument. Unless otherwise stated, chemical shifts are related to internal tetramethylsilane.

General Procedure. Synthesis of 4-Hydroxy-5(*S*)-methyl-2(5*H*)-furanone ((*S*)-γ-Methyltetronic Acid) (5). A solution of lithium bis(trimethylsilyl)amide (15 mmol) in THF (40 mL) was prepared from the commercially available (Aldrich) 1 M solution in THF or from butyllithium (15 mmol) in ether (13 mL) and hexamethyldisilazane (20 mmol) in THF (30 mL, 15 min, ca. 10 °C). The solution of the base was cooled to -78 °C, and a solution of ethyl 2(*S*)-acetoxypropanoate[8] (1.00 g, 6.29 mmol) in THF (40 mL) was added with stirring over a period of 30 min. The reaction mixture was kept at -78 °C for 1 h and then poured into 2 M HCl (20 mL). The two layers were separated, the aqueous layer was washed once with EtOAc, the combined organic layers were dried with NaCl(s) and concentrated, and CH_2Cl_2 was added. Drying with Na_2SO_4 and evaporation of the solvent left a solid residue (0.76 g, 107%), mp 103-108 °C, which on ^1H NMR analysis proved to be almost pure γ-methyltetronic acid; estimated yield, >95%. Recrystallization from EtOAc-light petroleum ether gave 0.50 g (70%; 83% on the 4-g scale); mp 112-115 °C; $[\alpha]^{22}_D$ +19.3°; $[\alpha]^{22}_{546}$ +23.9° (*c* 0.5, H_2O).[5] ^1H and ^{13}C NMR spectra show that **5** in $CDCl_3$ is a mixture (≈3:7) of keto and enol forms: ^1H NMR ($CDCl_3$) δ 11.5 (very broad), 5.06 (s, olefinic H), 4.92 (q, 1 H), 3.23 (α-H of keto form), 1.53 (d, 3 H). In $(CD_3)_2SO$ only the enol form was observed: ^{13}C NMR, 183.3, 173.1, 87.2, 74.9, and 17.8 ppm (calibrated against solvent signal, 39.6 ppm); these shifts are similar to those obtained with CD_3OD as solvent.[9] This solvent dependence was somewhat unexpected since the usual experience is that the enol form decreases as the solvent polarity increases.

2-Methyl[tetrahydropyran-3-spirocyclopentane]-4,6-dione (7). Ethyl acetoacetate was alkylated with 1,4-dibromobutane[10] and the product reduced with sodium borohydride.[11] The resulting secondary alcohol was acetylated with acetic anhydride-/4-(dimethylamino)pyridine[12] to obtain ethyl 1-(1-acetoxyethyl)cyclopentane-1-carboxylate (**6**) in a yield of 51%; bp 80-82 °C (2 mmHg); ^1H NMR ($CDCl_3$) δ 5.22 (q, 1 H), 4.12 (q, 2 H), 2.3-1.4 (m, 11 H, including a 3-H singlet at 2.02), 1.24 (t, 3 H), 1.17 (d, 3 H).

The intramolecular Claisen condensation of **6** was carried out according to the general procedure, but the reaction mixture was kept at -50 to -55 °C for 3 h before hydrolysis. Workup as above and crystallization from ether-light petroleum ether gave a 76% yield of **7**: mp 76-79 °C; ^1H NMR ($CDCl_3$) δ 4.58 (q, 1 H), 3.58 and 3.42 (AB spectrum, 2 H, J_{AB} = 20.0 Hz), 2.2-1.4 (m, 8 H), 1.38 (d, 3 H); ^{13}C NMR ($CDCl_3$, 77.17 ppm) 204.8, 167.6, 78.9, 58.3, 44.4, 32.8, 29.6, 26.3 (double intensity, probably two carbons), 16.3 ppm. Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.92; H, 7.74. Found: C, 65.92; H, 7.62.

Methyl 2-Deoxy-L-*threo*-hex-2-enarate 1,4-Lactone (11). Monoacetate **10**[7] (1 g) was allowed to react with lithium bis(trimethylsilyl)amide (3.5 equiv) according to the general procedure. After hydrolysis, the organic layer was separated and the aqueous layer extracted twice with ethyl acetate. The combined organic layers were dried (Na_2SO_4) and the solvents evaporated. More ethyl acetate was added and then evaporated. After a further addition of ethyl acetate, the solution was concentrated to about 2 mL. On addition of methylene chloride (ca. 10 mL) **11** crystallized (78% yield). After recrystallization from THF-methylene chloride it showed the following: mp 126-130 °C; $[\alpha]^{22}_D$ +95° (*c* 0.5, H_2O); ^1H NMR [$(CD_3)_2SO$ + 2 drops of 40% DCl in D_2O] δ 5.10 (d, 1 H, *J* = 2.0 Hz), 4.49 (d, 1 H, *J* = 2.0 Hz), 3.71 (s, 3 H); ^1H NMR [$(CD_3)_2SO$] δ 6.0 (broad, 1 H), 4.94 (s, 1 H), 4.79 (s, 1 H), 4.41 (s, 1 H), 3.69 (s, 3 H); ^{13}CNMR [$(CD_3)_2SO$] 178.6, 173.2, 171.6, 89.6, 79.6, 68.1, 52.2 ppm (calibrated against solvent signal, 39.6 ppm). Anal. Calcd for $C_7H_8O_6$: C, 44.69; H, 4.29. Found: C, 44.54; H, 4.28.

Acknowledgment. This work has been supported by the National Swedish Board For Technical Development.

Registry No. **5**, 22886-01-7; **6**, 88377-35-9; **7**, 88377-36-0; **10**, 36065-06-2; **11**, 88377-37-1; ethyl 2(*S*)-acetoxypropanoate, 20918-91-6; ethyl acetoacetate, 141-97-9; 1,4-dibromobutane, 110-52-1.

(7) Hungerbühler, E.; Seebach, D.; Wasmuth, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 958-960.
(8) Commercially available ethyl (*S*)-lactate was acetylated according to Fryzuk, M. D.; Bosnich, B. *J. Am. Chem. Soc.* **1978**, *100*, 5491-5494.
(9) Jacobsen, J. P.; Reffstrup, T.; Boll, P. M. *Acta Chem. Scand., Ser. B* **1977**, *B31*, 756-760.
(10) Goldsworthy, L. J. *J. Chem. Soc.* **1934**, 377-378.
(11) Barnett, J. E. G.; Kent, P. W. *J. Chem. Soc.* **1963**, 2743-2747.
(12) Steglich, W.; Höfle, G. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 981.
(13) Clutterbuck, P. W.; Raistrick, H.; Reuter, F. *Biochem. J.* **1935**, *29*, 1300-1309.
(14) Boll, P. M.; Sörensen, E.; Balieu, E. *Acta Chem. Scand.* **1968**, *22*, 3251-3255.

Improved Selectivity in the Preparation of Some 1,1-Difunctionalized 3-Cyclopentenes. High-Yield Synthesis of 3-Cyclopentenecarboxylic Acid

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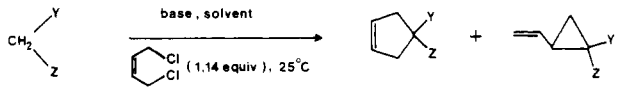
Although 3-cyclopentenecarboxylic acid (**3**, eq 1) has frequently been used as a starting material in synthesis,[1]

(1) (a) Grubs, E. J.; Lee, D. J.; Bellettini, A. G. *J. Org. Chem.* **1966**, *31*, 4069. (b) Wilt, J. W.; Massie, S. N.; Dabek, R. B. *Ibid.* **1970**, *35*, 2803. (c) Portoghese, P. S.; Lattin, D. L. *J. Heterocycl. Chem.* **1972**, *9*, 395. (d) David, S.; Lepine, M. C.; Lubineau, A. *Bull. Soc. Chim. Fr.* **1972**, 3580. (e) Givens, R. S.; Rademacher, D. R.; Kongs, J.; Dikerson, J. *Tetrahedron Lett.* **1974**, 3211. (f) Williams, T. R.; Sirvio, L. M. *J. Org. Chem.* **1980**, *45*, 5082. (g) Rastetter, W. H.; Phillion, D. P. *Ibid.* **1981**, *46*, 3204. (h) David, F. *Ibid.* **1981**, *46*, 3512. (i) Paulsen, H.; Maass, U. *Chem. Ber.* **1981**, *114*, 346. (j) Cremer, S. E.; Blankenship, C. *J. Org. Chem.* **1982**, *47*, 1626.

0022-3263/84/1949-0928$01.50/0

Table I. Solvent and Base Effects on the Cycloalkylation of Malonic Esters and Nitriles

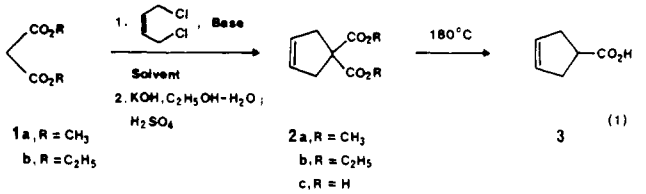


I II III

entry	I	base (equiv)	solvent	time, h	II:III[a]	isolated yield, %
1	Y = Z = $CO_2C_2H_5$ (1b)	CaH_2 (2.1)	DMF	120	95:5	73 (2b + 4b)
2	1b	LiH (2.5)	DMF	96	93:7	86 (2b + 4b)
3	1b	NaH (2.0)	DMF	24	87:13	80 (2b + 4b)
4	1b	DBU[b] (2.1)	DMF	24	71:29	
5	1b	K_2CO_3 (2.5)	DMF	120	70:30	
6	1b	Cs_2CO_3 (2.2)	DMF	120	65:35	
7	1b	$(n\text{-}C_4H_9)_4N^+F^-$ (2.3)	DMF	72	62:38	
8	1b	LiH (2.5)	DME	120	98.5:1.5	
9	1b	LiH (2.5)	$(CH_3)_2CO$	96	96:4	
10	1b	LiH (2.5)	HMPA	72	95:5	
11	1b	LiH (2.5)	CH_3CN	96	89:11	
12	1b	LiH (2.5)	$(CH_3)_2SO$	96	87:13	
13	1b	LiH (2.5)	$t\text{-}C_4H_9OH$	96	83:17	
14	1b	KO-t-C_4H_9 (2.4)	CH_3OH	24	34:66	
15	Y = Z = CO_2CH_3 (1a)	LiH (2.5)	DME	120	>99:<1	78 (2a)
16	1a	LiH (2.5)	$(CH_3)_2CO$	96	98:2	69 (2a)
17	1a	LiH (2.5)	DMF	72	95:5	83 (2a)
18	1a	NaOH-TEBA[c]	H_2O	14	67:33[d]	
19	Y = Z = CO_2-t-C_4H_9	LiH (2.5)	DMF	96	96:4	
20	Y = CN, Z = CO_2CH_3	LiH (2.4)	DMF	72	93:7	
21	Y = CN, Z = CO_2CH_3	LiH (2.4)	DME	72	97:3	66 (5a)[e]
22	Y = Z = CN	LiH (2.4)	DMF	60	100:0	82 (5b)

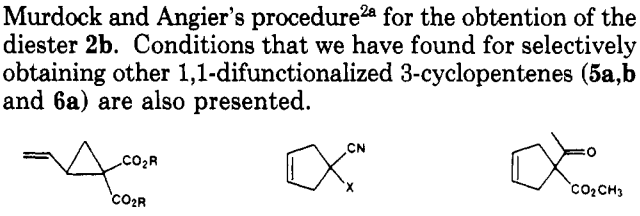
[a] Ratio determined by VPC (10% Carbowax 20 M). [b] DBU:1,8-diazabicyclo[5.4.0]undec-7-ene. [c] TEBA:benzyltriethylammonium chloride, see ref 8. [d] Ratio determined after esterification with diazomethane. [e] Contains 3% of the corresponding vinylcyclopropane isomer III.

there is, surprisingly, no very satisfactory method for its preparation to be found among those that have been reported.[2] Most often, this acid has been prepared by the method of Murdock and Angier,[2a] which involves cycloalkylation of diethyl malonate with *cis*-1,4-dichloro-2-butene ($NaOC_2H_5$ in C_2H_5OH) to give **2b** (along with the isomeric diester **4b**), followed by hydrolysis and fractional crystallization to yield pure **2c** and then decarboxylation to afford **3** (eq 1). The overall yield through this procedure



is 19–33%.[1d,2a] *cis*-1,4-Dibromo-2-butene has been used in lieu of *cis*-1,4-dichloro-2-butene; however, the overall yield is only 16%.[2b] Schmid and Wolkoff[2c] have reported the selective obtention of **2b** by the rearrangement at 400–425 °C of the vinylcyclopropane derivative **4b**, secured from diethyl malonate and *trans*-1,4-dichloro-2-butene, and the conversion of **2b** as before to acid **3** (32% overall yield). Alternatively, **3** has been prepared from cyclopentadiene in five steps in 19% overall yield.[1j]

Recently, we required large amounts of acid **3** for work on a total synthesis of (±)-hirsutic acid C[3] and found the previous methods, as described, to be unsuitable. In this paper we detail a much improved synthesis of **3**—70% overall yield from dimethyl malonate (**1a**)—that we have developed, which is based primarily on a modification of Murdock and Angier's procedure[2a] for the obtention of the diester **2b**. Conditions that we have found for selectively obtaining other 1,1-difunctionalized 3-cyclopentenes (**5a,b** and **6a**) are also presented.



4a, R = CH_3
b, R = C_2H_5

5a, X = CO_2CH_3
b, X = CN

6a

The cycloalkylation of diethyl malonate with *cis*-1,4-dichloro-2-butene in ethanol in the presence of sodium ethoxide gives, essentially as reported, a ca. 6:4 mixture (VPC) of **2b** and the vinylcyclopropane isomer **4b**, respectively, in 63% yield [lit.[2a] 67%; lit.[2c] 59%, 58:42, **2b**:**4b**]. However, we have found the ratio of these products to be highly sensitive to changes in the base and the solvent and to a lesser extent the R groups of the starting malonic ester (Table I). From the results presented in Table I, it can be seen that the ratio of II to III, in general, increases (a) with increasing hardness of the cation,[4] (b) in going from protic to nonprotic solvents, and (c) slightly, in changing from diethyl to dimethyl malonate.

Although the combination dimethyl malonate–lithium hydride with dichlorobutene produces a higher ratio of **2a** to **4a** in DME than in DMF (>99:<1 vs. 95:5, entries 15 and 17),[5] the isolated yield of **2a** (mp 61 °C) is higher with DMF as the solvent (83% vs. 78%), and therefore this solvent is preferred. When these conditions (i.e., those of entry 17) are used for the formation of **2a**, pure acid **3** can

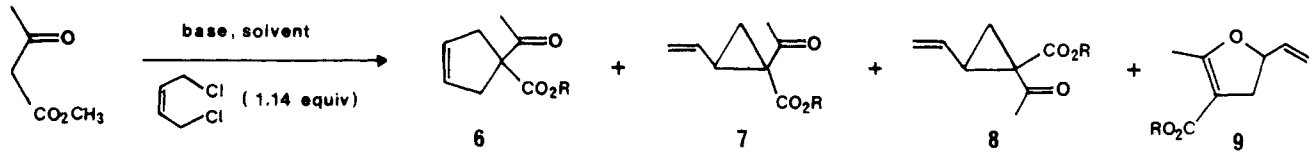
(2) (a) Murdock, K. C.; Angier, R. B. *J. Org. Chem.* **1962**, *27*, 2395. (b) Meinwald, J.; Gassman, P. G.; Crandall, J. K. *Ibid.* **1962**, *27*, 3366. (c) Schmid, G. H.; Wolkoff, A. W. *Ibid.* **1967**, *32*, 254. See also ref 1d and 1j.

(3) Greene, A. E.; Luche, M. J.; Deprés, J. P. *J. Am. Chem. Soc.* **1983**, *105*, 2435.

(4) For reviews on the hard and soft acid–base concept, see: Pearson, R. G. In "Advances in Linear Free-Energy Relationships"; Chapman, N. B., Shorter, J., Eds.; Plenum Press: New York, 1972; pp 281–319. Ho. T. L. "Hard and Soft Acids and Bases Principle in Organic Chemistry"; Academic Press: London, 1977.

(5) There is no conversion of **4a** to **2a** under these reaction conditions; diester **4a**, prepared from dimethyl malonate and *trans*-1,4-dibromo-2-butene, can be recovered unchanged after 1 week.

Table II. Solvent and Base Effects on the Cycloalkylation of Methyl Acetoacetate



a, R = CH_3; b, R = C_2H_5

entry	base	solvent	temp, °C	time, h	6:7 + 8[a]	isolated, yield, %
1	LiH (2.4)	DME-HMPA (93:7)	65	72	96.5:3.5	65 (6a-8a)
2	LiH (2.5)	DMF	25	48	66:34	75 (6a-8a)
3	NaH (2.2)	DMF	25	18	32:68	
4	KO-t-C_4H_9 (2.2)	DMF	25	14	30:70	
5	K_2CO_3 (2.4)	$(CH_3)_2SO$	25	48	20:80	
6	K_2CO_3 (2.6)	CH_3OH	25	96	3:97	
7	K_2CO_3 (2.6)	C_2H_5OH	25	96	3:97	72 (6b-8b)[b]

[a] Determined by VPC (10% Carbowax 20 M); ca. 2% of 9 is formed in each of these reactions. [b] Transesterification.

be quite easily obtained in up to 70% overall yield from **1a** with no purification necessary other than a final distillation (eq 1).[6] This improved synthesis of **3** should prove quite useful. Interestingly, under similar reaction conditions methyl cyanoacetate and malononitrile are also converted highly selectively and in good yield to the corresponding cyclopentene derivatives **5a** and **5b** (entries 21 and 22, respectively).[7]

A similar high selectivity has been obtained in the cycloalkylation of methyl acetoacetate with *cis*-1,4-dichloro-2-butene. It has been reported[7a,b] that the use of ethyl acetoacetate and sodium ethoxide in ethanol at reflux gives in 72% yield a mixture of the four isomers **6b–9b** (Table II), with **7b** being the major product (ca. 70% of the mixture). By using conditions only slightly different from those employed above, we have been able to selectively generate the cyclopentene isomer **6a** (Table II, entry 1); the use of potassium carbonate in ethanol, on the other hand, produces selectively the cyclopropyl derivatives **7b** and **8b** (82:18) (entry 7). Isomers **6b** and **7b**, upon treatment with aqueous potassium hydroxide, afford 4-acetylcyclopentene and 4-cycloheptenone, respectively.[7a,b]

In conclusion, several usefully functionalized cyclopentenes can now be easily obtained selectively and in good yield from inexpensive reagents. This greater availability should enhance the attractiveness of these compounds as starting materials for synthesis.

Experimental Section

General Methods. Dimethylformamide, dimethyl sulfoxide, 1,2-dimethoxyethane, and hexamethylphosphoric triamide were dried over calcium hydride. Acetone was dried over 3-Å molecular sieves. Methanol and ethanol were distilled from magnesium turnings. Melting and boiling points are uncorrected. IR spectra were recorded on a Perkin-Elmer Model 397 instrument as neat liquid films. ^1H NMR spectra were recorded on a Bruker WP 80 SY instrument with Me_4Si as the internal reference in CCl_4 solution. Microanalyses were carried out by the Central Service of the CNRS.

Dimethyl 3-Cyclopentene-1,1-dicarboxylate (2a). Typical Procedure. To a stirred solution of 13.2 g (0.100 mol) of dimethyl malonate in 150 mL of dry dimethylformamide at 0 °C under nitrogen was added, in one portion, 2.00 g (0.250 mol) of lithium hydride. After the evolution of hydrogen ceased (2 h), 12.0 mL (14.3 g, 0.114 mol) of *cis*-1,4-dichloro-2-butene was added and the mixture was then allowed to warm to room temperature. After 72 h, the resulting mixture was diluted with 20% ether in hexane and poured into cold water. The organic layer was washed with water and brine and dried over sodium sulfate, and the solvent was removed to give 17.3 g of a mixture of the diesters **2a** and **4a**, as a white crystalline solid (mp 55–57 °C), in a ca. 95:5 ratio (VPC). Recrystallization from hexane of 1.82 g of this mixture afforded 1.60 g (83%) of **2a** as white needles, mp 58–59 °C. An additional recrystallization produced the analytical sample of **2a**: mp 61 °C; IR (Nujol) 3065, 1730 cm^{-1}; ^1H NMR δ 2.94 (s, 4 H), 3.69 (s, 6 H), 5.55 (s, 2 H).

Anal. Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.44; H, 6.57.

3-Cyclopentenecarboxylic Acid (3).[2] Impure **2a** (mixture of **2a** and **4a**, 95:5) was converted to acid **3** by the method of Murdock and Angier.[2a] To a solution of 24.2 g (ca. 0.131 mol) of impure **2a** (prepared from 0.140 mol of dimethyl malonate) in 260 mL of 80% aqueous ethanol was added 23.5 g (0.356 mol) of 85% potassium hydroxide. The mixture was stirred at 40–50 °C for 14 h and then concentrated to eliminate the ethanol. The aqueous phase was washed with 150 mL of 20% ether in hexane, 100 g of ice was added, and the resulting mixture was cautiously treated with 21.3 mL of concentrated sulfuric acid. The acidified aqueous phase was extracted three times with 200-mL portions of ethyl acetate, which were dried over sodium sulfate, and then evaporated under reduced pressure to give 19.50 g of crude diacid **2c** as a white crystalline solid, mp 162–165 °C (lit.[2a] mp 170–172 °C). The crude diacid **2c** was heated with an oil bath at 180 °C. After 1 h, gas evolution ceased and the residual oil was distilled under reduced pressure to give 11.04 g (70% overall yield from dimethyl malonate) of **3**:[2] bp 70 °C (1 mm) [lit.[2a] bp 83–84 °C (2 mm)]; IR 3075, 2650, 1715, 1625 cm^{-1}; ^1H NMR δ 2.67 (distorted d, 4 H), 2.90–3.35 (m, 1 H), 5.63 (s, 2 H), 11.97 (s, 1 H).

Methyl 1-Cyano-3-cyclopentenecarboxylate (5a). To a stirred solution of 2.97 g (30.0 mmol) of methyl cyanoacetate in 45 mL of dry 1,2-dimethoxyethane under nitrogen was added 0.576 g (72.0 mmol) of lithium hydride. After the evolution of hydrogen ceased (5 h), 3.6 mL (4.3 g, 34 mmol) of *cis*-1,4-dichloro-2-butene was added to the mixture. After 72 h at room temperature, the mixture was diluted with 30% ether in hexane and then poured into cold water. The usual workup followed by distillation under reduced pressure afforded 3.00 g (66%) of **5a**, containing 3% of the corresponding vinylcyclopropane isomers. Compound **5a**: bp 73–75 °C (1 mm); IR 3060, 2240, 1750, 1620 cm^{-1}; ^1H NMR δ 3.05

(6) In that the preparation of *tert*-butyl 1-methyl-3-cyclopentenecarboxylate,[3] an intermediate in our synthesis of hirsutic acid, requires two steps from acid **3**, we attempted to secure it directly from *tert*-butyl propionate and *cis*-1,4-dichloro-2-butene in THF in the presence of LDA. Disappointingly, vinylcyclopropane formation is preferred by ca. 2 to 1.

(7) Ethyl 1-cyano-3-cyclopentenecarboxylate and 3-cyclopentene-1,1-dicarbonitrile (**5b**) have been prepared through the thermal rearrangement of the corresponding vinylcyclopropane isomers; see: Cho, I.; Ahn, K. D. *Taehan Hwahakhoe Chi* **1978**, *22*, 158; *Chem. Abstr.* **1979**, *90*, 38368*x*. Ethyl 1-acetyl-3-cyclopentenecarboxylate (**6b**) and **5b** have been obtained in 30% and 44% yields, respectively, by using *cis*-1,4-dichloro-2-butene and DBU in DMF; see: Oediger, H.; Möller, F. *Liebigs Ann. Chem.* **1976**, 348. Compound **6b** has also been synthesized by using *cis*-1,4-dichloro-2-butene and sodium ethoxide; see: (a) Bahurel, Y.; Collonges, F.; Menet, A.; Pautet, F.; Poncet, A.; Descotes, G. *Bull. Soc. Chim. Fr.* **1971**, 2203. (b) Wilson, R. S.; Wiesler, D. P. *Synth. Commun.* **1980**, 339.

(8) Singh, R. K.; Danishefsky, S. *J. Org. Chem.* **1975**, *40*, 2969.

(br s, 4 H), 3.83 (s, 3 H), 5.69 (br s, 2 H).

Anal. Calcd for $C_8H_9O_2N$: C, 63.56; H, 6.00. Found: C, 63.34; H, 6.04.

3-Cyclopentene-1,1-dicarbonitrile (5b).[7] To a stirred solution of 2.64 g (40.0 mmol) of malononitrile in 60 mL of dry DMF at 0 °C under nitrogen was added 0.77 g (96 mmol) of lithium hydride. After the evolution of hydrogen ceased (2 h), 4.8 mL (5.7 g, 46 mmol) of *cis*-1,4-dichloro-2-butene was added and the reaction mixture was allowed to warm to room temperature. After 60 h, the mixture was diluted with 50% ether in hexane and poured into cold water. The usual workup followed by distillation under reduced pressure gave 3.87 g (82%) of pure **5b**:[7] bp 66–68 °C (1 mm); IR 3070, 2250, 1620 cm^{-1}; ^1H NMR δ 3.19 (s, 4 H), 5.81 (s, 2 H).

Anal. Calcd for $C_7H_6N_2$: C, 71.16; H, 5.12. Found: C, 70.89; H, 5.21.

Methyl 1-Acetyl-3-cyclopentenecarboxylate (6a). Typical Procedure. To a stirred solution of 5.80 g (50.0 mmol) of methyl acetoacetate in 93 mL of dry 1,2-dimethoxyethane and 7 mL of dry hexamethylphosphoric triamide at 0 °C under nitrogen was added 0.960 g (120 mmol) of lithium hydride. After the evolution of hydrogen ceased (1 h), 6.0 mL (7.1 g, 57 mmol) of *cis*-1,4-dichloro-2-butene was added and the mixture was heated in an oil bath at 65 °C for 72 h. The resulting mixture was then cooled, diluted with 25% ether in hexane, and poured into water. The usual workup followed by distillation under reduced pressure afforded 5.50 g (65%) of **6a**, containing 3% of the corresponding vinylcyclopropane isomers **7a** and **8a**. Compound **6a**: bp 74–76 °C (1 mm); IR 3060, 1740, 1715, 1625 cm^{-1}; ^1H NMR δ 2.09 (s, 3 H), 2.97 (s, 4 H), 3.71 (s, 3 H), 5.53 (br s, 2 H).

Anal. Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 64.16; H, 7.43.

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Registry No. **1a**, 108-59-8; **1b**, 105-53-3; **2a**, 84646-68-4; **2b**, 21622-00-4; **2c**, 88326-51-6; **3**, 7686-77-3; **4a**, 17447-60-8; **4b**, 7686-78-4; **5a**, 88326-52-7; **5b**, 58920-81-3; **6a**, 88326-53-8; **6b**, 33626-80-1; **7a**, 88326-54-9; **7b**, 74379-81-0; **8a**, 88326-55-0; **8b**, 74379-82-1; **9a**, 88326-56-1; **9b**, 33626-83-4; I (Y = Z = CO_2-*t*-C_4H_9), 541-16-2; I (Y = CN, Z = CO_2CH_3), 105-34-0; I (Y = Z = CN), 109-77-3; II (Y = Z = CO_2-*t*-C_4H_9), 88326-57-2; III (Y = Z = CO_2-*t*-C_4H_9), 88326-58-3; III (Y = CN, Z = CO_2CH_3), 88326-59-4; methyl acetoacetate, 105-45-3; *cis*-1,4-dichloro-2-butene, 1476-11-5.

Efficient Syntheses of (±)-β-Cuparenone. Conjugate Addition of Organozinc Reagents

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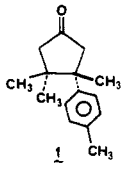
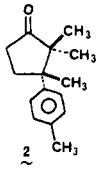
β-Cuparenone (**1**), isolated with α-cuparenone (**2**) from "mayur pankhi",[1] has been synthesized numerous times.[2]

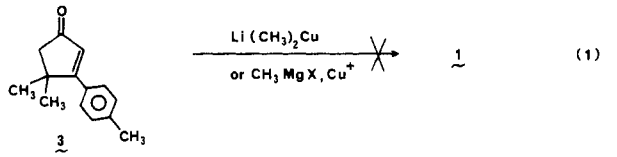


1



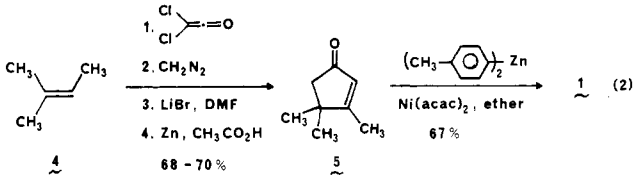
2

Successful conjugate addition-based approaches to β-cuparenone, however, have yet to be reported, which is not too surprising in light of the vicinal quaternary centers present in this molecule. In fact, Casares and Maldonado[2d] have reported 4,4-dimethyl-3-*p*-tolylcyclopentenone (**3**) to be "inert both to lithium dimethylcuprate and copper catalyzed methyl Grignard 1,4 additions", while others[3] have noted exclusive 1,2-addition in similar attempts to convert this enone to **1** (eq 1). This apparent impasse has



led to several alternative approaches; each of these, however, suffers from poor yields, a lack of selectivity, a large number of steps, or the need for difficultly accessible reagents.[2a-g] In this note we describe two straightforward and efficient conjugate addition-based syntheses of β-cuparenone that illustrate the largely unrecognized potency of organozinc reagents in this type of reaction.[4]

The known trimethylcyclopentenone **5**[5] could be easily obtained in improved overall yield through three-carbon annelation[6] of inexpensive β-isoamylene (**4**), as outlined in eq 2. The overall yield of pure **5** was reproducibly



68–70% and only a final chromatographic purification was necessary. While this enone as expected[2d,3] proved quite resistant to several copper-assisted conjugate addition techniques[4] for the introduction of a *p*-tolyl group, nickel acetylacetonate catalyzed conjugate addition of readily prepared di-*p*-tolylzinc (Li, C_7H_7Br, $ZnBr_2$, ether, ultrasonic irradiation)[4,7] was found to proceed smoothly *and produce in 67% yield (46% overall from* **4***) pure* (±)-β-*cuparenone* (**1**). Only a trace amount, if any, of the corresponding 1,2-addition product was formed in this reaction.

A second high-yield synthesis of β-cuparenone illustrates a similar application of another organozinc reagent (eq 3). Enone **3**, available in 50–60% yield from *p*-tolualdehyde,[2d,8]

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(2) (a) Lansbury, P. T.; Hilfiker, F. R. *Chem. Commun.* **1969**, 619. (b) Mane, R. B.; Rao, G. S. K. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1806. (c) Leriverend, P. *Bull. Soc. Chim. Fr.* **1973**, 3498. Leriverend, M. L.; Leriverend, P. *C. R. Acad. Sci., Ser. C* **1975**, *280*, 791. See also: Leriverend, M. L.; Vazeux, M. *J. Chem. Soc., Chem. Commun.* **1982**, 866. (d) Casares, A.; Maldonado, L. A. *Synth. Commun.* **1976**, *6*, 11. (e) Paquette, L. A.; Fristad, W. E.; Dime, D. S.; Bailey, T. R. *J. Org. Chem.* **1980**, *45*, 3017. (f) Jung, M. E.; Radcliffe, C. D. *Tetrahedron Lett.* **1980**, 4397. (g) Halazy, S.; Zutterman, F.; Krief, A. *Ibid.* **1982**, 4385. For syntheses of α-cuparenone, see: Greene, A. E.; Lansard, J. P.; Luche, J. L.; Petrier, C. *J. Org. Chem.* **1983**, *48*, 4763 and references cited therein.

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(7) The reagent obtained by using magnesium in place of lithium also gave **1** but in slightly lower yield.

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