the barrier to C–H migration. In fact, a significant substituent effect might be anticipated in light of the observation by Moss and co-workers[7] that methylchlorocarbene, $CH_3\ddot{C}Cl$, undergoes addition to olefins in competition with unimolecular isomerization to vinyl chloride. By contrast, the methyl group in $CH_3\ddot{C}OH$ is expected to have little effect on the barrier to O–H migration. This is consistent with our data. Our observation of ≥90% O–H migration indicates that the barrier to C–H migration must exceed that for O–H migration by at least 3.3 kcal/mol.

We are presently attempting to spectroscopically characterize the carbene formed via mechanism 1a and to determine the isomerization kinetics for mechanism 1b. Chemical trapping of the carbene is also being investigated.

Experimental Section

NMR spectra were recorded on a Varian EM-390 spectrometer using $CDCl_3$ as a solvent with tetramethylsilane as an internal standard. IR spectra were recorded on a Beckman IR-8 or a Perkin-Elmer 180 spectrometer using 7–10-cm gas cells equipped with NaCl windows. Pyruvic acid was obtained from Aldrich Chemical Co. and was vacuum distilled prior to use. Pyruvic acid-*O-d* was prepared via deuterium exchange with D_2O and was determined to be 90% deuterated at oxygen by NMR.

Pyrolysis of Pyruvic Acid. Pyrolyses were accomplished by flash distilling pyruvic acid through a heated quartz tube (6-mm i.d., 15-cm heated length, 500 °C) under vacuum (pressure ~10 torr) and trapping the effluent at 77 K. We estimate residence times in the heated quartz tube to be ca. 10 ms. IR analysis of the effluent indicated the presence of CO_2 and CH_3CHO. NMR analysis after removal of the CO_2 indicated the presence of CH_3CHO. The extent of reaction was essentially quantitative.

Pyrolysis of Pyruvic Acid-*O-d*. Pyrolyses of pyruvic acid-*O-d* were accomplished as indicated above with the exception that prior to a sequence of 3–5 runs, D_2O was flash distilled through the pyrolysis system. The D_2O effluent was removed from the trap prior to the pyruvic acid-*O-d* pyrolyses. Products from these pyrolyses were analyzed by IR and NMR spectroscopy as indicated above. In a control experiment, pyruvic acid-*O-d* was flash distilled through the pyrolysis tube at a tube temperature of ca. 100 °C. Under these conditions, negligible pyrolysis was found to occur. The recovered pyruvic acid was determined by NMR to be ≳80% deuterated at oxygen.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this work.

Registry No. Pyruvic acid, 127-17-3; methylhydroxycarbene, 30967-49-8.

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A Regiospecific, Convergent Route to 2,3-Disubstituted Cyclopentanones†

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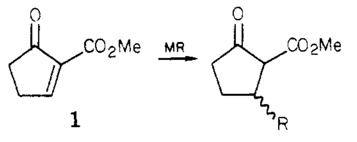
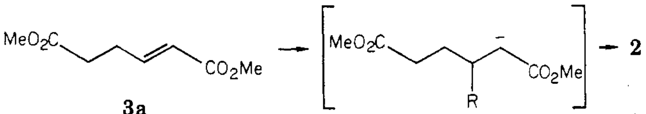
The 2,3-disubstituted cyclopentanones include many biologically active compounds, including the 11-deoxyprostaglandins[1] and the cyclopentanoid antibiotic antitumor agents such as sarkomycin.[2] A conceptually attractive route to these compounds begins with conjugate addition of organometallic reagents to enone **1**.[3] The resulting



1 **2**

(1)

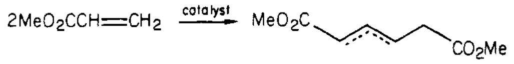
2-carbomethoxycyclopentanones can then be transformed by standard methods into a variety of useful cyclopentanoids. However, compound **1** is unstable, difficult to prepare, and polymerizes in the presence of many nucleophiles.[3b] It occurred to us that eq 2, a conjugate addition/cyclization utilizing dimethyl hex-2-enedioate, **3a**, would represent an attractive alternative to eq 1. Tandem conjugate addition/cyclization reactions related to eq 2 have been reported.[4] The practicality of this approach depends on the ready availability of **3a**, and therefore a high yield synthesis of **3a** by dimerization of methyl acrylate was first developed.



3a

(2)

The catalytic tail-to-tail dimerization of methyl acrylate (eq 3) has been reported.[5] Unfortunately, we found that



(3)

Δ^2 isomer **3a**
Δ^3 isomer **3b**

each of the known catalysts had severe limitations for the practical synthesis of **3a**. In particular, predominant formation of isomeric **3b**, limited catalyst life, or further oligomerization of product dimers were problems. We have now discovered that the loosely coordinated cationic palladium complex $Pd(NCMe)_4(BF_4)_2$[6,7] affords very high yields of **3a** under mild conditions, particularly in the presence of anhydrous $LiBF_4$. Thus, treatment of neat methyl acrylate with 0.005 equiv of palladium catalyst[8] and 0.16 equiv of $LiBF_4$ at 40 °C for 30 h afforded after distillation a 93% yield of dimers consisting of 93–96% of the

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† Contribution No. 3243.

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(8) The amount of palladium catalyst can be further diminished by addition of a nonligating reoxidant such as benzoquinone (cf. ref 5c) or VOF_3.

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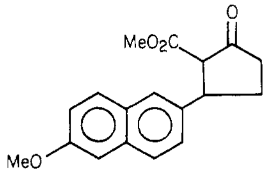
Table I. 3-Substituted 2-Carbomethoxycyclopentenones from Conjugate Addition/Cyclization of 3a

product	R	conditions	R_f[a]	yield,[b] %
2a	methyl	normal[c]	0.41	76
2b	*n*-butyl	normal	0.51	71
2c	*sec*-butyl	normal	0.44	42
2d	neopentyl	normal	0.55	68
2e	vinyl	normal	0.43	42
2f	phenyl	0 °C	0.38	66
2g	2-methoxy-6-naphthyl	catalytic[d]	0.27	53

[a] TLC (30% EtOAc/hexane); see Experimental Section. [b] Percent yield based on **3a**. [c] Normal conditions indicate stoichiometric reaction of $LiCuR_2$ at −25 °C. [d] CuCl-catalyzed reaction of Grignard reagent; see Experimental Section.

trans Δ^2 isomer.[9] We have found this mixture of products to be suitable for use in the subsequent addition/cyclization reaction. However, if the pure trans Δ^2 isomer is desired, it can readily be isolated. In this regard we take advantage of the fact that, at high conversions, **3a** precipitates from the reaction mixture as large analytically pure crystals of its 1:1 adduct with $LiBF_4$.[10]

Tandem conjugate addition/cyclization of **3a** with lithium dialkylcuprates proceeds readily at −25 °C. A 2-fold excess of cuprate is required because an enolizable β-dicarbonyl system is produced. Isolated yields for several alkyl, vinyl, and aryl cuprates ranged from 40% to 80% as summarized in Table I. In each case the product consists overwhelmingly of a single isomer, which by NMR is the trans diastereomer. In one case we have extended this reaction to a copper-*catalyzed* Grignard reaction. Thus, the Grignard reagent from 2-bromo-6-methoxynaphthalene was added to **3** in the presence of 5% CuCl to afford cyclopentanone **2g** in 53% yield. The limited electrophilicity of enoate esters[11] imposes some limitations on the nature of the nucleophile R^- used in eq 2. Lithium di-*tert*-butylcuprate afforded only a low yield of the expected adduct, while KCN, Et_2AlCN, 2-potassiocyclohexanone, and 2-lithio-1,3-dithiane failed to produce cyclopentanoid products.



2g

Compounds **2** represent a general class of versatile synthetic intermediates. A wide variety of techniques exist for the subsequent alkylation[12] and decarboxylation[13] to afford the corresponding 2,3-disubstituted cyclopentanones. Moreover, 5-substituents could presumably be incorporated by means of the corresponding dianions.[14]

Cyclopentanone **2e** has been converted by Tsuji into methyl dihydrojasmonate[15] and 18-hydroxy estrone.[16] The potential utility of naphthyl derivatives such as **2g** for synthesis of steroids has likewise been demonstrated.[17]

Experimental Section

General Methods. ^1H NMR spectra were determined on a Nicolet NT 360WB spectrometer as solutions in $CDCl_3$. Chemical shifts are reported in parts per million downfield from the internal reference tetramethylsilane. Couplings (J) are in hertz. Reactions were carried out under an atmosphere of dry nitrogen. Neopentyllithium was prepared as a 0.48 M solution by treating excess lithium powder with neopentyl chloride in hexane. Vinyllithium (Orgmet) and all other lithium reagents (Alfa) were commercial materials. Methyl acrylate and acetonitrile were dried over 4-Å molecular sieves. All other chemicals were reagent grade materials used as received. Flash chromatography was carried out on 230–400 mesh silica (EM Reagents) following the procedure of Still.[18] The R_f values indicated in Table I refer to thin-layer chromatography on 2.5 × 10 cm, 250-μm analytical plates coated with silica gel HLF with 30% (v/v) ethyl acetate in hexane as eluent. Tetrakis(acetonitrile)palladium(II) tetrafluoroborate was prepared according to the literature procedure.[6]

Preparation of *trans*-Dimethyl Hex-2-enedioate (3a). A mixture of methyl acrylate (100 mL, 95.6 g, 1.11 mol), lithium tetrafluoroborate (18 g, 0.19 mol), and $Pd(NCMe)_4(BF_4)_2$ (2.66 g, 0.006 mol) was heated at 40 °C for 30 h. The product was added to 200 mL of 10% $NaHCO_3$ and was extracted with 3 × 100 mL of ether. The combined organics were dried ($MgSO_4$), and the solvent and unreacted monomer were removed in vacuo. Distillation at 62–67 °C at 0.5 torr afforded 89.0 g (93%) of dimers. Capillary column GC (Carbowax) indicated three minor components at retention times of 6.74 (2.3%), 7.06 (1.2%), and 7.19 min (3.8%). The principal component (7.33 min, 92.7%) was isoretentive with authentic *trans*-**3a**. All components were shown to be isomers of **3** by GC–mass spectroscopy. Anal. Calcd for $C_8H_{12}O_4$: C, 55.80; H, 7.03. Found: C, 55.78; H, 6.87.

Preparation of 2-Carbomethoxy-3-methylcyclopentanone (2a). To a suspension of copper(I) iodide (19.0 g, 0.10 mol) in dry ether (200 mL) at −25 °C was added rapidly dropwise methyllithium as a 1.6 M solution in ether (125 mL, 0.20 mol). A solution of **3a** (6.8 g, 0.04 mol) in ether (50 mL) was then added dropwise. Stirring was continued for 0.5 h at −25 °C whereupon methanol (10 mL) was added and the solution was allowed to warm to room temperature. The mixture was then stirred with saturated aqueous ammonium chloride (250 mL). Extraction with ether (3 × 100 mL), drying ($MgSO_4$), and removal of solvent at reduced pressure followed by flash chromatography over 500 g of silica afforded **2a** (4.70 g, 76%): ^1H NMR δ 1.19 (d, J = 7, 3 H), 1.51 (m, 1 H), 2.1–2.5 (m, 3 H), 2.59 (m, 1 H), 2.80 (d, J = 11, 1 H), 3.78 (s, 3 H). Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.75. Found: C, 61.60; H, 7.78.

Similarly prepared were the following. **2b**: ^1H NMR δ 0.90 (dist t, J = 7, 3 H), 1.15–1.65 (m, 7 H), 2.1–2.5 (m, 3 H), 2.57 (m, 1 H), 2.85 (d, J = 11, 1 H), 3.75 (s, 3 H). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.99; H, 9.36.

2c: ^1H NMR δ 0.85–0.95 (m, 6 H), 1.17 (m, 1 H) 1.4–1.6 (m, 3 H), 2.1–2.5 (m, 3 H), 2.56 (m, 1 H), 2.95 and 2.97 (2 d s, J = 11, 1 H total), 3.75 (s, 3 H). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.80; H, 9.31.

2d: ^1H NMR δ 0.95 (s, 9 H), 1.38 (dd, J = 8, 14, 1 H), 1.45–1.6 (m, 2 H), 2.2–2.55 (m, 3 H), 2.64 (m, 1 H), 2.86 (d, J = 11, 1 H), 3.75 (s, 3 H). Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.54; H, 9.34.

2e: ^1H NMR δ 1.72 (m 1 H), 2.1–2.6 (m, 3 H), 3.05 (d, J = 11, 1 H), 3.1–3.3 (m, 1 H), 3.75 (s, 3 H), 5.09 (d, J = 11, 1 H), 5.16 (d, J = 17, 1 H), 5.75–5.85 (m, 1 H). Anal. Calcd for $C_9H_{12}O_3$:

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[9] A unique feature of this catalyst system is that under similar conditions methyl methacrylate is likewise converted to a 94:6 mixture of Δ^2- and Δ^3-dimethyl 2,4-dimethylhexenedioates (25 °C, 63% isolated yield).

[10] The adduct could be obtained in 89% yield based on $LiBF_4$ charged. Anal. Calcd for $C_8H_{12}BLiF_4O_4$: C, 36.13; H, 4.55. Found: C, 36.00; H, 4.58. Extractive workup of this adduct produced **3a** of >99% isomeric purity by GC.

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C, 64.27; H, 7.19. Found: C, 64.10; H, 7.41.

2f: mp 71–73 °C; ^{1}H NMR δ 2.01 (m, 1 H), 2.4–2.7 (m, 3 H), 3.37 (d, J = 12, 1 H), 3.72 (s, 3 H), 3.82 (dt, J = 6, 12, 1 H), 7.2–7.4 (m, 5 H). Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.73; H, 6.33.

Preparation of 2-Carbomethoxy-3-(6-methoxy-2-naphthyl)cyclopentanone (2g). The Grignard reagent was prepared from 2-bromo-6-methoxynaphthalene (9.48 g, 40 mmol) and magnesium turnings (1.0 g, 41 mmol) in tetrahydrofuran (50 mL). To the filtered Grignard solution was added copper(I) chloride (0.10 g, 1.0 mmol), and the mixture was cooled to 0 °C. A solution of **3a** (3.44 g, 20 mmol) was added dropwise and the solution was stirred an additional 0.5 h at 0 °C and then 0.5 h at room temperature. The product was poured into saturated aqueous ammonium chloride (150 mL) with rapid stirring. The mixture was extracted with chloroform (3 × 50 mL) and the combined organics were back-extracted with H_2O (50 mL). The solvent was removed in vacuo from the dried ($MgSO_4$) product. The resultant light brown residue was taken up in chloroform (25 mL) and added dropwise to 200 mL of hexane to free it from most of the side product 2-methoxynaphthalene. Precipitated crude **2g** was collected by filtration. Flash chromatography over 500 g of silica afforded pure **2g** (3.18 g, 53%): mp (toluene/heptane) 142–145 °C; ^{1}H NMR δ 2.0–2.2 (m, 1 H), 2.45–2.7 (m, 3 H), 3.45 (d, J = 12, 1 H), 3.71 (s, 3 H), 3.92 (s, 3 H), 3.94 (partially obscured dt, J = 6, 12, 1 H), 7.1–7.8 (m, 6 H). Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.47; H, 6.08. Found: C, 72.32; H, 6.06.

Registry No. **2a**, 18067-33-9; **2b**, 87682-82-4; **2c**, 87682-83-5; **2d**, 87682-84-6; **2e**, 75351-19-8; **2f**, 87682-85-7; **2g**, 2741-86-8; (E)-**3a**, 70353-99-0; $Pd(NCMe)_4(BF_4)_2$, 21797-13-7; $LiBF_4$, 14283-07-9; 2-bromo-6-methoxynaphthalene, 5111-65-9; methyl acrylate, 96-33-3.

Polystyrene-Bound Analogues of Alkali-Metal Diphenylmethyl Anions

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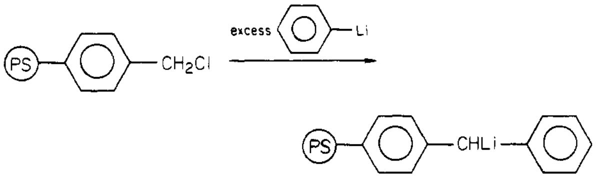
Received June 14, 1983

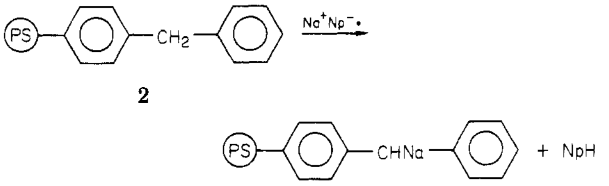
The preparation of alkali-metal derivatives of polystyrene or divinylbenzene (DVB)-cross-linked polystyrene can be accomplished by several procedures. Included among these procedures are deprotonation of the pendant aryl rings of polystyrene by n-butyllithium–TMEDA,[1] halogen–metal exchange between n-butyllithium and brominated or iodinated polystyrene,[2] transmetalation reactions of alkyllithium reagents and mercurated polystyrene,[3] electron transfer to form polystyrene-bound alkali-metal aromatic radical anions,[4] and deprotonation of polymer-bound weak carbon acids.[5] In this report, we describe a very simple and convenient method we have developed for formation of alkali-metal derivatives of commercially available DVB-cross-linked polystyrenes. This method involves the in situ generation and deprotonation of a polymeric analogue of diphenylmethane derived from commercially available Merrifield resin (chloromethylated polystyrene). The resulting organometallic polymers have reactivity comparable to their soluble diphenylmethyl anion ananogues as is shown by the experiments detailed below in which alkali-metal salts of **2** are used to form various stabilized carbanions.

Commercially available chloromethylated DVB-cross-linked polystyrene, Merrifield resin, reacts readily with excess phenyllithium in ether–benzene suspensions to form (polystyrylphenylmethyl)lithium **1** (eq 1). This polymer can than be treated with an ether solution of an alcohol to form the neutral polystyrene-bound diphenylmethane analogue **2**. Polymer **2** reacts with an organolithium reagent such as n-butyllithium or phenyllithium to regenerate **1** or can be treated with sodium, potassium, rubidium, or cesium naphthalene to form the sodium, potassium, rubidium, or cesium species **3**–**6**, respectively (eq 2).



(1)

1



2

(2)

3

The organometallic polymers formed in reactions like 1 and 2 strictly speaking are more like tolylphenylmethyl anions (the ion-pair pK_a of tolylphenylmethane can be estimated at ca. 34 vs. 33 for diphenylmethane[6]) than diphenylmethyl anions. These polymers evidently also contain small amounts of other basic organometallic impurities. Control experiments in which Merrifield resin is treated with excess n-butyllithium and then washed to remove any soluble base also produced a colored organometallic polymer. The organometallic species formed in this case have not been completely identified. In part, they must contain some diarylmethyl units since chloromethylation of polystyrene does introduce additional diarylmethyl cross-links.[7] However, cross-linking during chloromethylation is unlikely to introduce the amount of acidic diaryl-substituted methylene groups suggested by titration. On the basis of the qualitatively different color (more bluish) of this organometallic polymer, we think that other species are present as well. For example, instead of nucleophilic addition of an organolithium reagent to the polymeric benzyl chloride, some deprotonation could have occurred as a side reaction. Coupling of the anions so formed with other reactive sites on the polymer could then have formed stilbene cross-links that could have reacted with an alkyllithium reagent like n-butyllithium to give a polymeric lithium radical anion. If this were the case, reaction of the organometallic polymer formed when Merrifield resin has been treated with excess n-butyllithium with a protic solvent should form a neutral polymer

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