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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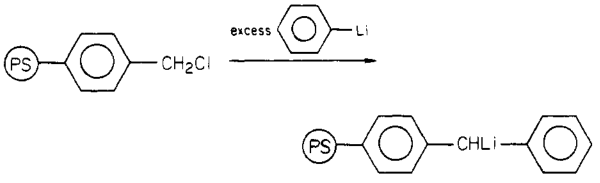
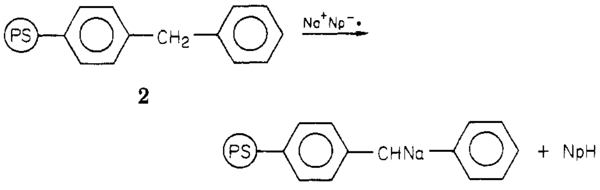
The preparation of alkali-metal derivatives of polystyrene or divinylbenzene (DVB)-cross-linked polystyrene can be accomplished by several procedures. Included among these procedures are deprotonation of the pendant aryl rings of polystyrene by *n*-butyllithium-TMEDA,[1] halogen-metal exchange between *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



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(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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(1) Grubbs, R. H.; Su, S-C. H. *J. Organomet Chem.* **1976**, *122*, 151-157.

(2) Burlitch, J. J.; Winterton, R. C. *J. Organomet. Chem* .**1978**, *159*, 299-316. The various routes to lithiated DVB-cross-linked polystyrene are critically evaluated by these authors.

(3) Weinshenker, N. M; Crosby, G. A.; Wong, J. Y. *J. Org. Chem.* **1975**, *40*, 1966-1971.

(4) Bergbreiter, D. E.; Killough, J. M. *J. Chem. Soc., Chem. Commun.* **1980**, 319-320.

(5) Cohen, B. J.; Kraus, M. A.; Patchornik, A. *J. Am. Chem. Soc.* **1981**, *103*, 7620-7629.

(6) Steitwieser, A.; Juaristi, E.; Nebenzahl, L. L. In "Comprehensive Carbanion Chemistry"; Buncel, E.; Durst, T., Eds.; Elsevier: Amsterdam, 1980; Chapter 7.

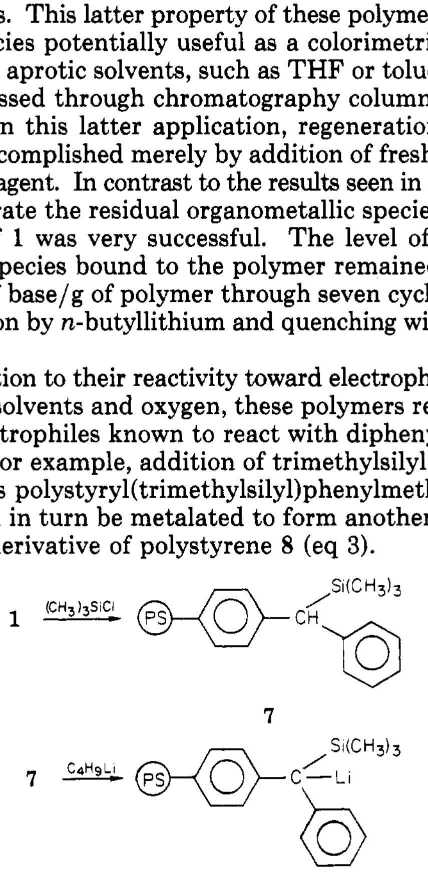
(7) Ford, W. T.; Yacoub, S. A. *J. Org. Chem.* **1981**, *46*, 819-821.

0022-3263/83/1948-5366$01.50/0

that would not re-form the same amount of organometallic species on a second *n*-butyllithium treatment. This was indeed the case. Typically the amount of residual organometallic species dropped 50% to 0.09 mequiv of base/g of polymer after one such cycle of quenching and *n*-BuLi regeneration. A further indication that the nature of the residual polymeric organometallic species had changed in this regeneration experiment was the fact that the residual organometallic polymer that was initially bluish in color was reddish after one such quenching–regeneration cycle. Regardless of the origin of these other organometallic species, they are only present at comparatively low loading (<0.10 mequiv of Li/g of polymer based on titration) and do not appear to complicate the potential applications of these organometallic polymers, which are discussed further below.

Metalations of 2 can be successfully carried out in flasks in toluene or ether suspensions or in chromatography columns packed with a tetrahydrofuran (THF) slurry of 2. Alkali-metal derivatives of 2 are all highly colored insoluble solids and react rapidly with oxygen or protic species such as water or alcohols. The rapidity of the reaction is readily apparent since the characteristic color (the intense color of these polymers makes them effectively appear black) of these anionic polymers immediately disappears. This latter property of these polymers makes these species potentially useful as a colorimetric drying agents for aprotic solvents, such as THF or toluene, that can be passed through chromatography columns loaded with 1. In this latter application, regeneration of 1 is readily accomplished merely by addition of fresh organolithium reagent. In contrast to the results seen in attempts to regenerate the residual organometallic species, regeneration of 1 was very successful. The level of organometallic species bound to the polymer remained at 0.80 mequiv of base/g of polymer through seven cycles of deprotonation by *n*-butyllithium and quenching with methanol.

In addition to their reactivity toward electrophiles such as protic solvents and oxygen, these polymers react with other electrophiles known to react with diphenylmethyl anions. For example, addition of trimethylsilyl chloride to 1 forms polystyryl(trimethylsilyl)phenylmethane (7), which can in turn be metalated to form another organometallic derivative of polystyrene 8 (eq 3).



(3)

8

The loading of metal species on these polymers was determined titrimetrically by quenching suspensions of these organometallic polymers with methanol and titrating the water-soluble base so formed. Typical loadings (expressed as milliequivalents of base/gram of polymer) are as follows: **1**, 0.8; **3**–**5**, 0.6; **6**, 0.5; **8**, 0.75.

The polymeric anions derived from 2 can be used as reagents to prepare "clean" solutions of various stabilized carbanions. For example, 0.3 mmol of fluorene is quantitatively deprotonated by 1 g of 1 to form a THF solution of the lithium salt of fluorene on the basis of UV–visible spectroscopy and deuteration of the fluorenyl anion. Polymers 3–6 behave similarly. The only differences among the various derivatives of 2 in deprotonation of fluorene was that the time required for complete deprotonation of fluorene based on spectral analysis of aliquots and titration of aliquots for soluble base was 90 min for 1 and 3, 45 min for 4, 30 min for 5, and 10 min for 6. Ketones can also be deprotonated (THF, −78 °C, 4 h) by these polymeric bases as evidenced by their alkylation with methyl iodide. The solutions of alkali-metal enolates prepared in this way are fairly dilute (<0.3 N) and the amount of ketone deprotonated varied. This experimental problem reflects in part the heterogeneity of these reactions. The yield of soluble alkali-metal enolates in these reactions also varies because of the differing electrophilicity and basicity of different ketones or ketone derivatives. The major side reaction appeared to generally be loss of ketone from solution, possibly by 1,2-addition of the polymeric organometallic reagent to the carbonyl. Aldol condensation products were also present in some cases. Ketones successfully deprotonated with 1 included (GC yields of methylated ketones given in parentheses) the following: 2-butanone (37%), 3,3-dimethyl-2-butanone (56%), acetophenone (27%), and camphor (39%). Less acidic carbonyl derivatives such as 2-butanone dimethylhydrazone were not deprotonated at all under similar conditions. Although these deprotonation reactions of ketones would not be synthetically useful, they may nonetheless still be useful in physical studies of carbanions especially when no soluble byproducts are present.[5]

Experimental Section[8]

General Procedure for the Preparation of Polystyrylphenylmethane (2). In a typical procedure , 100 g of chloromethylated polystyrene (2% DVB cross-linked, 200–400 mesh) was weighed into a 1-L flame-dried round-bottomed flask. THF (700 mL) was added to this polymer to give a slurry of the solvent swollen polymer, which was then cooled to −78 °C. Addition of 150 mL of 1.6 N phenyllithium in a benzene–ether solution followed by overnight shaking led to formation of 1. Initially, the polymer in this reaction turns a deep red color, which becomes darker as the reaction proceeds until the final polymer superficially appears nearly black. Protonaton of this lithiated polymer by pouring the polymer slurry into 400 mL of methanol produced the light yellow polymer 2, which was then extracted for 12 h in a Soxhlet extraction apparatus with hot THF.

(Polystyrylphenylmethyl)lithium (1). The lithium salt of 2, which was formed in situ in the preparation of 2 from chloromethylated polystyrene, was normally prepared by addition of an organolithium reagent such as phenyllithium or *n*-butyllithium to an ether, THF, or toluene slurry of 2. In the case of *n*-butyllithium addition to THF or ether slurries of 2, the reaction mixture was cooled to −78 °C during the addition of the alkyllithium reagent. Overnight shaking of the reaction mixture on a wrist-action shaker at room temperature formed a deeply colored suspension of 1.

Deprotonation of 2 by Alkali-Metal Naphthalene Derivatives. Formation of the sodium, potassium, rubidium, and cesium salts of 2 was accomplished by addition of a standardized solution of the appropriate alkali-metal naphthalene anion to a THF slurry of 2. In these cases, reaction was evidenced by the rapid (0.5 h) decolorization of the solution and concomitant formation of the highly colored organometallic polymer.

Formation of 7 and 8. Addition of excess chlorotrimethylsilane to a suspension of 1 in benzene–ether at −78 °C followed by shaking for 24 h at room temperature led to formation of 7, which was isolated by filtration. The product polymer was washed with THF in a Soxhlet extraction apparatus for 1 day to remove

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(8) Unexceptional inert-atmosphere techniques were used in all reactions involving organometallic reagents; cf.: Brown, H. C. "Organic Syntheses via Boranes"; Wiley-Interscience: New York, 1975.

any soluble impurities. Suspension of 7 in an ether or hydrocarbon solvent followed by *n*-butyllithium addition and shaking at room temperature overnight led to formation of the purplish polymer 8.

Analysis of Polymers 1, 3–6, and 8. The loading of organometallic species on these polymers was estimated on the basis of the amount of soluble base detected in an acid–base titration of a methanol quench of known amounts of these polymers. In these analyses, the organometallic polymers were typically washed with dry THF until the THF washes contained no basic species in order to remove any soluble bases that might be present. In such cases, addition of THF to the solid organometallic polymer formed suspensions of polymer that contained no soluble base as determined by acid–base titration of aliquots of the solutions over these polymers. Addition of these suspensions to excess methanol produced methoxide base, which was subsequently titrated with standardized HCl to a phenolphthalein endpoint.

General Procedure for Deprotonation Reactions. A weighed amount of polymer (ca. 2 g) was placed in a flame-dried flask under a nitrogen atmosphere and swollen with ca. 12 mL of THF, and the resulting suspension of swollen polymer was then cooled to −78 °C. Deprotonation with *n*-BuLi as described above followed by washing with THF until no excess soluble base was detected in the washes produced 1, which was then used for a deprotonation reaction. Addition of 10 mL of THF and cooling of the polymer suspension to −78 °C followed by addition of 0.25 mmol of a weak carbon acid substrates and 2 h of stirring (at −78 °C for ketones to produce the desired enolate and at room temperature for fluorene) yielded a solution of the desired stabilized carbanion. In the case of deprotonation of a ketone substrate, transfer of the enolate solution formed in this fashion from the flask containing the polymer to a separate flask at −78 °C followed by addition of excess methyl iodide led to formation of methylated product whole yield was determined by GC relative to an internal hydrocarbon standard. Fluorene anion was detected by UV-visible spectroscopy, by titration of the organometallic species in solution and by ^{13}C NMR spectroscopic analysis of the product of a deuterium oxide quench.

Acknowledgment. Support of this research by the Office of Naval Research and the Texas A&M Center for Energy and Mineral Resources is gratefully acknowledged.

Registry No. Fluorene, 86-73-7; 2-butanone, 78-93-3; 3,3-dimethylbutanone, 75-97-8; acetophenone, 98-86-2; camphor, 76-22-2.

A Method for the Determination of the pK_a of the α-Hydrogen in Amino Acids Using Racemization and Exchange Studies

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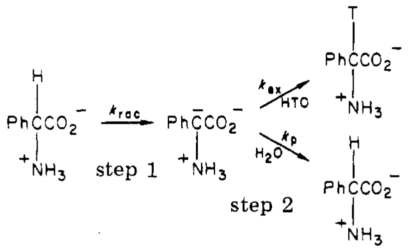
A mechanism for the racemization of amino acids, which was recently reported in this journal by Smith and Sivakua,[1] is shown below: The absence of a kinetic isotope



effect in step 2, as evidenced by the rate of reprotonation (k_p) equaling that of tritium exchange (k_{ex}), indicated that step 1, abstraction of the methine hydrogen, is the rate-controlling step. We are now reporting another racemization study, focusing on step 1, which shows that this step does display a kinetic isotope effect with a k_H/k_D value of 2.0 (Figure 1). This indicates that deprotonation is indeed the slower, rate-controlling step. A new exchange study, using deuterium oxide instead of tritiated water, confirms that step 2, of the above mechanism, is not influenced by the strength of bond reformation (Figure 2). Similar findings have previously been reported.[2,3] In view of these data, it seems reasonable to assume that step 2 is predominantly a diffusion-controlled process and that the rate of reprotonation (k_p) can be assumed to be equal to the diffusion-controlled rate (k_d) in the solvent.

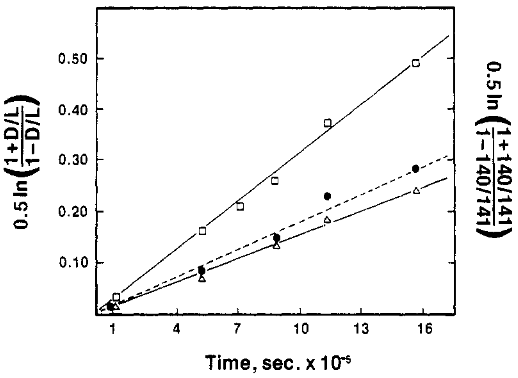


Figure 1. Rate of racemization L (left ordinate) and rate of exchange (right ordinate) of L-alanine-*2-H* and L-alanine-*2-d*: (□) H, (△ D, and (●) exchange.

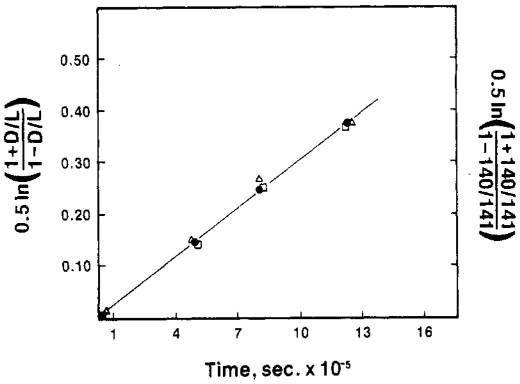


Figure 2. Rate of racemization (left ordinate) and rate of exchange (right ordinate) of L-alanine-*2-H* in D_2O and H_2O: (□) H_2O, (△) D_2O, and (●) exchange.

Table I. α-Hydrogen pK_a Values

amino acid	$10^7 k_{rac}$,[a,b] s^{-1}	pK_a
alanine	17.7	16.5
valine	5.9	17.0
isoleucine	7.8	16.9
leucine	11.7	16.7
phenylalnine	34.8	16.2
D-phenylglycine	788.8	14.9

[a] Determined at 139.0 °C, pH 7.6 in 0.05 M NaH_2PO_4. $k_d = 6 \times 10^{10}\ M^{-1}\ s^{-1}$. [b] Reference 1.

If this mechanism is valid, it should allow the calculation of the pK_a of the α-hydrogen of any amino acid, for which k_{rac} has been determined, via eq 1. Calculations of the

$$\mathrm{p}K_a = -\log k_{rac}/k_d \tag{1}$$

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[1] Smith, G. G.; Sivakua, T. *J. Org. Chem.* **1983**, *48*, 627.

[2] Matsuo, H.; Kawazoe, Y.; Sato, M.; Ohnishi, M.; Tatsuno, T. *Chem. Pharm. Bull.* **1967**, *15*, 391.

[3] Matsuo, H.; Kawazoe, Y.; Sato, M.; Ohnishi, M.; Tatsuno, T. *Chem. Pharm. Bull.* **1970**, *18*, 1788.