Experimental Section

Both ^1H and ^2H NMR spectra were recorded on a Nicolet NT 360-MHz instrument. Gas chromatographic preparative collections and analyses were done on Varian Aerograph A 90-P3, Varian 1520, and Hewlett Packard 5792A instruments.

4-Formylcyclopentene was prepared in five steps by using procedures drawn from the literature. Diethyl cyclopentene-4,4-dicarboxylate, from diethyl malonate, 2 equiv of NaH, and (*Z*)-1,4-dichloro-2-butene, was hydrolyzed and decarboxylated at 180 °C to afford 4-carboxycyclopentene.[19] Reduction of the acid with $LiAlH_4$ in ether gave the alcohol;[20,21] oxidation with CrO_3 in CH_2Cl_2–pyridine provided the desired aldehyde **4** having ^1H NMR spectral characteristics in full agreement with prior observations.[21]

4-(Ethenyl-2,2-d_2)cyclopentene. Into a flame-dried, three-necked flask was placed a stir bar, 33 mL of tetrahydrofuran (freshly distilled from sodium and sodium benzophenone ketyl), and 3.00 g (8.3 mmol) of (trideuteriomethyl)triphenylphosphonium bromide. The flask was capped with a septum through which a needle was inserted to provide a nitrogen source. Then 5.7 mL of methyllithium in ether (1.5 M, 8.6 mmol, low in halide) was added to yield an orange solution which was stirred for 1 h. To this was added 33 mL of dimethyl-d_6 sulfoxide, which was freshly distilled from calcium hydride; a precipitate soon formed but then dissolved with further stirring. After the aldehyde was added (0.80 g, 8.33 mmol) and stirring was continued for another hour, the orange solution was treated with 1 mL of deuterium oxide and the product solution was poured into 400 mL of water; the dark orange phase which formed on top was removed with a Pasteur pipet and placed into 200 mL of water. Again, the upper orange phase was removed, then placed with 90 mL of water in a separatory funnel and shaken vigorously. The upper orange organic layer now amounted to about 0.5 mL; it was isolated with a small pipet, and further purification of the desired diolefin was achieved by using preparative gas chromatography on a 20% 1,2,3-tris(2-cyanoethoxy)propane (TCEP) on 50/80 mesh Chromosorb P column at 120 °C. It was identified by direct NMR comparisons with a spectrum of authentic 4-vinylcyclopentene provided by Professor P. K. Freeman.[22]

Thermolyses of 4-(ethenyl-2,2-d_2)cyclopentene were conducted by using a well-seasoned 300-mL Pyrex bulb and kinetics bath.[23] Temperature measurements employed a Hewlett-Packard Model 2802A digital thermometer; hexanes served as a bath gas. After each run at 393.1 °C, hydrocarbons were condensed from bulb to the vacuum line and examined by ^2H NMR spectroscopy and by analytical gas chromatography. Integrated ^2H absorption intensities for **5** and **6** led to estimates of mole fractions of **5**: 0.83 (at 500 min), 0.72 (810 min), and 0.62 (1261 min; Figure 1), and hence $k = 0.75 \times 10^{-5}$ s^{-1} ($\Delta G^{\ddagger}$ 55.7 kcal/mol).

An earlier estimate of the rate of this degenerate rearrangement based on a less completely deuterated sample of **5**, thermolyses in a 1-L quartz bulb at 409.6 °C, and analyses of product mixtures by ^1H NMR (Varian XL-100) gave an estimate of $k = 1.26 \times 10^{-5}$ s^{-1} ($\Delta G^{\ddagger}$ 56.4 kcal/mol) for the rate constant **5** → **6**.

Acknowledgment. We thank the National Science Foundation for support of our work on hydrocarbon rearrangements, Professor P. K. Freeman for a copy of the ^1H NMR spectrum of 4-vinylcyclopentene, and Drs. T. C. Barden, K. A. Black, and C. G. Carter for their active interest in this study.

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Stabase-Protected 2-Chloroallylamine: A Useful Synthon for Primary Allylic Amines via Nickel-Catalyzed Cross-Coupling

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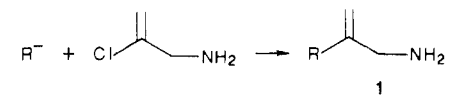
Primary allylic amines have been receiving enough attention as enzyme inhibitors[1] and natural products that methods for their synthesis have been reviewed recently.[2] New synthesis methods continue to be devised.[3]

We needed an efficient synthesis of 2-substituted allylamines in connection with our studies of mechanism-based inhibition of dopamine β-hydroxylase.[4] Many diverse and imaginative synthesis methods for primary allylic amines have been described;[2] however, nearly all require starting with a complete carbon skeleton and forming a carbon–nitrogen bond in the key step. All methodologies require multistep transformations. We wish to report a simple, one-step procedure for preparation of 2-substituted allylamines from readily available precursors by means of transition-metal-catalyzed carbon–carbon bond formation.

The most direct synthesis of a 2-substituted allylamine that we could imagine would be the coupling of a carbanion with 2-chloroallylamine[5] (eq 1). In recent years, general



(1)

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solutions to the problem of nucleophilic vinylic substitution of unactivated olefins have been reported.[6] We were attracted to the nickel-catalyzed cross-coupling reaction of vinylic and aromatic halides with Grignard reagents.[7] Kumda and co-workers have thoroughly investigated the scope of this reaction;[8] however, there are few examples

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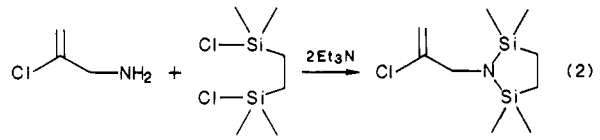
Table I. Preparation of Allylic Amines 1 by Nickel-Catalyzed Coupling of Grignard Reagents with Protected 2-Chloroallylamine 2

entry	R	[RMgBr]/[2]	product	mp (°C)[a]	yield (%)[b]
1	2-thienyl[c]	1.1	**1a**	146–156 dec	78[d]
2	Ph	1.5	**1b**	175–177	88[e]
3	4-MePh	1.4	**1c**	169–171	66[d]
4	4-MeOPh	1.5	**1d**	162–163	73[e]
5	3-MeOPh	1.4	**1e**	130–131	79[e]
6	3,4-$(MeO)_2$Ph	2.2	**1f**	188–189	42[e]
7	4-*t*-$BuMe_2SiOPh$	1.4	**1g**	*f*	92[e]
8	4-FPh	1.2	**1h**	172–173[g]	49[h]
9	3,4-Cl_2Ph	1.8	**1j**	173–174	33[d]
10	2-benzo[*b*]thienyl[c]	1.5	**1k**	231	61[d]
11	n-C_4H_9	2.0	**1l**	170.5–172.5[i]	56[d]

[a] As hydrochloride salt. [b] Isolated yield of pure primary amine. All reactions were carried out in ether using 0.005–0.01 equiv of $NiCl_2$(dppp). [c] Grignard reagent generated by exchange of $MgBr_2$ etherate with corresponding organolithium. [d] Isolated as HCl salt by method B. [e] Isolated as free base by method A. [f] Not determined. Converted to **1i** for further characterization. [g] Tosylate salt. [h] Yield of distilled free base obtained from the initially isolated HCl salt of method B. [i] Softens 103–105 °C.

in which the vinylic partner contains other useful functional groups.[9]

We protected the amino group of 2-chloroallylamine as its stabase adduct **2** using the methodology described by Magnus and co-workers (eq 2).[10] The compound was



(2)

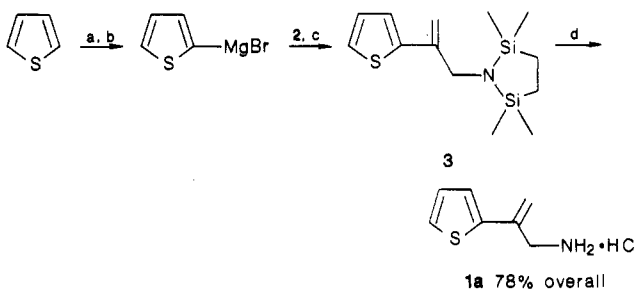
2

obtained as a colorless, distillable liquid in 92% yield. We chose the stabase protecting group because of its ease of removal and its stability in the presence of Grignard reagents.[11] Compound **2** was not extraordinarily sensitive to moisture. Samples stored in a tightly capped container at 4 °C became cloudy after several months; however, utility of the reagent appeared unaffected.

When an ethereal solution of **2** was combined with 0.007 molar equiv of (1,3-bis(diphenylphosphino)propane)nickel(II) chloride ($NiCl_2$(dppp))[12] and treated with an ethereal solution of 2-thienylmagnesium bromide,[13] the desired substitution product was obtained in good yield (Scheme I). Deprotection of the product allylic amine **3** was accomplished simply by treatment of an ethereal solution with excess of ethanolic HCl. The product hydrochloride **1a** precipitated in pure form in 78% yield based on **2**. When the catalyst was omitted, only unreacted **2** was detected on GC analysis of the reaction mixture after 21 h at room temperature. Compound **1a** is a potent mechanism-based inhibitor of dopamine β-hydroxylase, formerly prepared in a five-step sequence.[4]

The utility of the method is indicated in Table I. In general, aromatic Grignard reagents coupled effectively. Progress of the coupling reaction was conveniently monitored by capillary GC and **2** was usually consumed within 0.5–4 h, depending on the Grignard reagent. We noted, however, that methoxy-substituted-Grignard reagents

Scheme I[a]



1a 78% overall

[a] (a) *n*-BuLi/Et_2O; (b) $MgBr_2$·OEt_2; (c) 0.7 mol % $NiCl_2$(dppp); (d) HCl/EtOH/Et_2O.

(entries 4–6) reacted more slowly than phenylmagnesium bromide (entry 2), requiring, in the case of entry 6, 3 days to proceed to completion. In all cases, the major side product was the biaryl derived from homo coupling. The halogen-substituted Grignards (entries 8,9) gave rise to unidentified aromatic side products observable in the ^1H NMR spectrum of the crude products, possibly a result of nickel-catalyzed substitution of ring halogen.[14] The reaction of (2-benzo[*b*]thienyl)magnesium bromide (entry 10) led to a similar observation, possibly a result of nickel-catalyzed cleavage of the carbon–sulfur bond.[15] The silyl ether **1g** (entry 7) was subsequently deprotected to provide 2-(4-hydroxyphenyl)allylamine (**1i**) in 62% yield, also a potent inhibitor of dopamine β-hydroxylase. The literature synthesis of **1i** required five steps and proceeded in less than 5% overall yield.[1e] *n*-Butylmagnesium bromide coupled readily, suggesting that the methodology is also applicable to aliphatic Grignard reagents.

An additional observation is pertinent. We found that the Grignard reagent derived from (4-*tert*-butyldimethylsiloxy)iodobenzene coupled only very slowly, giving only 5% conversion by GC after 3 days (compare entry 2, Table I). We could find no indication in the literature that iodide-derived Grignard reagents are resistant to coupling and this result is difficult to explain on the basis of published mechanism studies.[16]

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(16) Tamao, K.; Sumitani, K.; Yoshihisa, K.; Zembayashi, M.; Fujioka, A.; Kodama, S.; Nakajima, I.; Isao, N.; Minato, A.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1958 and references cited therein.

The nickel-catalyzed coupling of Grignard reagents with stabase-protected 2-chloroallylamine (**2**) is a simple, economical, virtual one-step method for preparing 2-substituted allylamines and represents a significant improvement over former syntheses of these biologically interesting compounds.[17]

Experimental Section

Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. Proton NMR spectra were determined on either a Varian EM-360 or a Varian XL-300 instrument and are reported in ppm downfield from $(CH_3)_4Si$ internal standard (δ). Mass spectra were obtained on a Finnegan 4000 spectrometer interfaced to an Incos 2000 data system. GC analyses were performed on a HP 5890 gas chromatograph equipped with a DB5-durabond (0.25 μm × 15 m) capillary column. Elemental analyses were provided by the Analytical Chemistry Dept., Merrell Dow Research Institute, Cincinnati, OH.

1-(2-Chloro-3-propenyl)-2,2,5,5-tetramethyl-2,5-disilazole (2). To a magnetically stirred solution of 1.84 g (20 mmol) of 2-chloroallylamine in 10 mL of CH_2Cl_2 under N_2 was added 6.13 mL (44 mmol) of triethylamine. Then a solution of 4.73 g (22 mmol) of 1,1,4,4-tetramethyl-1,4-dichlorosilethylene (Petrarch Systems, Inc.) in 10 mL of CH_2Cl_2 was added dropwise while maintaining the temperature below 25 °C with an ice bath. A precipate formed. After 2 h the mixture was partitioned between CH_2Cl_2 and saturated $NaHCO_3$ solution. The aqueous phase was extracted with two portions of CH_2Cl_2 and the combined CH_2Cl_2 extracts were dried over K_2CO_3 and concentrated. Bulb-to-bulb distillation (70 °C, 1.5 torr) provided 4.35 g (92%) of colorless liquid: ^{1}H NMR ($CDCl_3$) δ 5.38 (t, 1 H, J = 2.1 Hz, vinylic), 5.23 (t, 1 H, J = 1.5 Hz, vinylic), 3.54 (dd, 2 H, J_1 = 2.1 Hz, J_2 = 1.5 Hz, CH_2N), 0.77 (s, 4 H, CH_2Si), 0.08 (s, 12 H, $SiCH_3$); MS (CI/CH_4), m/z 234 (30, MH^+), 218 (40, M − CH_3), 198 (M − Cl), 161 (M − $CH_2Si(CH_3)_2$), 92 (100, 2-chloroallylammonium), 75 (20, 2-chloroallyl cation).

Anal. Calcd for $C_9H_{20}ClNSi_2$: C, 46.22; H, 8.62; N, 5.99. Found: C, 46.16; H, 8.72; N, 5.80.

General Coupling Procedure. Grignard reagents were generated by stirring an excess of 99.98% Mg turnings (Reade Manufacturing Co., Inc.) with the appropriate halo compound in anhydrous ether under N_2. When necessary a small crystal of I_2 or a few drops of 1,2-dibromoethane were added to initiate the reaction. Aliquots were analyzed for unreacted halo compound by GC to assure completeness of the Grignard formation. The stabase group was removed from the initially formed coupling product by either of two methods. **Method A.** The crude product was subjected to flash chromatography on silica gel eluting with a mixture of 1% concentrated NH_4OH, 9% CH_3OH, and 90% $CHCl_3$ to provide the free base. **Method B.** The crude product was diluted with ether, chilled in an ice bath, and treated with excess ethanolic HCl. After 5 min the HCl salt of the desired product was removed by filtration, washed with ether, and recrystallized. The following two procedures are typical.

β-Methylene-β-thienylethanamine Hydrochloride (1a). To a solution of 200 μL (2.5 mmol) of thiophene in 5 mL of ether under Ar was added 1.25 mL of 2.2 M *n*-BuLi/hexane (2.75 mmol). The resulting pale yellow cloudy solution was stirred for 45 min and then was cooled in an ice/CH_3OH bath and 775 mg (3.0 mmol) of $MgBr_2$ etherate was added all at once. The mixture was allowed to warm to 23 °C. After 30 min, 16 mg (0.03 mmol) of $NiCl_2$(dppp) was added, followed immediately by a solution of 528 mg (2.25 mmol) of **2** in 5 mL of ether. The resulting dark brown reaction mixture was stirred at 23 °C for 1 h, then was quenched with 25 mL of saturated $NaHCO_3$, and diluted with more ether. The ether layer was separated and the aqueous phase was washed with two portions of ether. The combined ether solutions were dried over K_2CO_3 and filtered. The product was isolated by method B, providing 312 mg (78%) of **1a** (after recrystallization from 2-propanol) [mp 146–156 °C dec (lit.[4] mp 140–145 °C dec] chromatographically and spectroscopically identical with a sample prepared by the literature method: ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 8.60 (br s, 3 H, NH_3^+), 7.54 (d, 1 H, $J_{3,4}$ = 5.1 Hz, H-3 of thiophene), 7.29 (d, 1 H, $J_{5,4}$ = 3.3 Hz, H-5), 7.09 (dd, 1 H, $J_{4,3}$ = 5.1 Hz, $J_{4,5}$ = 3.3 Hz, H-4), 5.62 (s, 1 H, olefinic), 5.32 (s, 1 H, olefinic), 3.88 (s, 2 H, CH_2N); MS (CI/CH_4); m/z 140 (100, MH^+), 123 (30, $MH^+ - NH_3$).

Anal. Calcd for C_7H_9NS·HCl: C, 47.86; H, 5.74; N, 7.97. Found: C, 47.83; H, 5.92; N, 7.95.

β-Methylene-β-phenylethanamine (1b). A solution of phenylmagnesium bromide (from 0.39 g (16 mmol) of Mg and 2.0 g (12.8 mmol) of bromobenzene in 20 mL of ether) was added via syringe to a magnetically stirred mixture of 0.040 g (0.074 mmol) of $NiCl_2$(dppp) and 2.0 g (8.6 mmol) of **2** in 20 mL of ether under N_2. The catalyst dissolved and the exothermic reaction mixture warmed to reflux. The mixture was stirred at ambient temperature for 16 h after which time GC analysis revealed no unreacted **2**. Saturated $NaHCO_3$ was added, the layers were separated, and the aqueous layer was extracted with ether. The combined ether extracts were dried over Na_2SO_4 and filtered, and the product was isolated as a colorless oil (1.01 g, 88%) by method A: ^{1}H NMR (60 MHz, $CDCl_3$) δ 7.37 (s, 5 H, Ph), 5.34 (s, 1 H, olefinic H), 5.18 (s, 1 H, olefinic H), 3.74 (br s, 2 H, CH_2N), 1.51 (br s, 2 H, NH_2). Treatment with etheral HCl gave a white solid, mp 175–177 °C (lit.[1d] mp 178–179 °C).

β-Methylene-β-(4-methylphenyl)ethanamine hydrochloride (1c) was prepared according to the procedure used for **1b** and the product hydrochloride was obtained by method B and recrystallized from EtOH/ether: mp 169–171 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 8.25 (br s, 3 H, NH_3^+), 7.41 (d, 2 H, J = 8.4 Hz, ring H), 7.22 (d, 2 H, J = 8.4 Hz, ring H), 5.64 (s, 1 H, olefinic H), 5.32 (s, 1 H, olefinic H), 3.90 (s, 2 H, CH_2N), 2.32 (s, 3 H, CH_3); MS (EI/70 eV), m/z 147 (100, M^+), 132 (60, M − CH_3), 130 (40, M − NH_3).

Anal. Calcd for $C_{10}H_{13}N$·HCl: C, 65.39; H, 7.68; N, 7.63. Found: C, 65.37; H, 7.72; N, 7.77.

β-Methylene-β-(4-methoxyphenyl)ethanamine (1d) was prepared by the procedure used for **1b** and isolated as the free base by method A: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, 2 H, J = 9 Hz, ring H), 6.82 (d, 2 H, J = 9 Hz, ring H), 5.23 (s, 1 H, olefinic H), 5.08 (s, 1 H, olefinic H), 3.78 (s, 3 H, OCH_3), 3.58 (s, 2 H, CH_2N), 1.34 (br s, 2 H, NH_2); MS (EI/70 eV), m/z 163 (90, M^+), 134 (90, M − CH_2=NH), 133 (100, M − CH_2NH_2). The HCl salt (recrystallized from EtOH/ether) had mp 162–163 °C.

Anal. Calcd for $C_{10}H_{13}NO$·HCl: C, 60.15; H, 7.06; N, 7.02. Found: C, 60.10; H, 6.93; N, 6.99.

β-Methylene-β-(3-methoxyphenyl)ethanamine (1e) was obtained as a colorless oil by the procedure used for **1b** and isolated by method A: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (dd, 1 H, $J_{4,5}$ = 7.6 Hz, $J_{4,3}$ = 8.3 Hz, H-4 of ring), 7.00 (ddd, 1 H, $J_{5,4}$ = 7.6 Hz, $J_{5,2}$ = 2 Hz, $J_{5,3}$ = 1 Hz, H-5), 6.95 (br t or unresolved dd, 1 H, J = 2–3 Hz, H-2), 6.84 (ddd, 1 H, $J_{3,4}$ = 8.3 Hz, $J_{3,2}$ = 2.8 Hz, $J_{3,5}$ = 1 Hz, H-3), 5.35 (s, 1 H, olefinic H), 5.22 (s, 1 H, olefinic H), 3.82 (s, 3 H, OCH_3), 3.69 (s, 2 H, CH_2N), 1.80 (br s, 2 H, NH_2); MS (CI/CH_4), m/z 164 (100, MH^+), 147 (30, $MH^+ - NH_3$). The HCl salt (recrystallized from 2-propanol) had mp 130–131 °C (lit.[18] mp 136 °C).

Anal. Calcd for $C_{10}H_{13}NO$·HCl: C, 60.15; H, 7.06; N, 7.02. Found: C, 60.35; H, 7.19; N, 7.02.

β-(3,4-Dimethoxyphenyl)-β-methyleneethanamine (1f) was obtained as a colorless oil by the procedure used for **1b**, isolated by method A, and subsequently converted to the HCl salt and recrystallized from EtOH: mp 188–189 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 8.20 (br s, 3 H, NH_3^+), 7.08 (d, 1 H, $J_{2,6}$ = 1.8 Hz, H-2 of ring), 7.05 (dd, 1 H, $J_{6,5}$ = 8.1 Hz, $J_{6,2}$ = 1.8 Hz, H-6), 6.98 (d, 1 H, $J_{5,6}$ = 8.1 Hz, H-5), 5.62 (s, 1 H, olefinic H), 5.28 (s, 1 H, olefinic H), 3.92 (s, 2 H, CH_2N), 3.81 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3); MS (CI/CH_4), m/z 194 (100, MH^+), 177 (20, $MH^+ - NH_3$).

Anal. Calcd for $C_{11}H_{15}NO_2$·HCl: C, 57.52; H, 7.02; N, 6.10. Found: C, 57.37; H, 7.09; N, 5.78.

β-[4-(*tert*-Butyldimethylsiloxy)phenyl]-β-methyleneethanamine (1g) was obtained as a colorless oil by the procedure used for **1b** and isolated by method A. Treatment with ethereal HCl gave the hydrochloride as a sticky solid: ^{1}H NMR (300 MHz,

(17) 2-Chloroallylamine was prepared by the procedure of footnote 5 on 200-g scale with no change in yield.

(18) Bey, P. U.S. Pat. 4 454 158.

$CDCl_3$) δ 8.45 (br s, 3 H, NH_3^+), 7.22 (AA'BB' doublet, 2 H, J = 8.8 Hz, H-2 and H-6 of ring), 6.90 (AA'BB' doublet, 2 H, J = 8.8 Hz, H-3 and H-5) 5.54 (s, 1 H, olefinic H), 5.43 (s, 1 H, olefinic H), 3.99 (s, 2 H, CH_2N), 0.97 (s, 9 H, *t*-Bu), 0.19 (s, 6 H, CH_3); MS (CI/CH_4), m/z 264 (100, MH^+), 248 (20, M - CH_3), 206 (10, M - C_4H_9). The product was further characterized by deprotection to give **1i**.

β-(4-Fluorophenyl)-β-methyleneethanamine 4-methylbenzenesulfonate salt (1h) was prepared by the procedure used for **1b** and isolated initially as the HCl salt in 56% yield according to method B. The salt, although spectroscopically pure, proved difficult to recrystallize and was converted to the free base and bulb-to-bulb distilled (90-100 °C, 2.5 torr) to provide a colorless oil in 49% yield based on **2**. Addition of 1.0 equiv of 1.0 M *p*-TsOH in EtOH to an ether solution of the free base gave a tosylate salt which was recrystallized from CH_3CN to give colorless needles: mp 172-173 °C; ^1H NMR (300 MHz, $(CD_3)_2SO$) δ 8.10 (br s, 3 H, NH_3^+), 7.57 (dd, 2 H, J_{HH} = 9.0 Hz, J_{HF} = 5.4 Hz, H-2 and H-6 of ring), 7.48 (d, 2 H, J = 7.8 Hz, H-2' and H-6' of tosylate), 7.25 (dd, 2 H, J_{HH} = 9.0 Hz, J_{HF} = 8.8 Hz, H-3 and H-4), 7.12 (d, 2 H, J = 7.8 Hz, H-3' and H-4'), 5.65 (s, 1 H, olefinic H), 5.35 (s, 1 H, olefinic H), 3.94 (s, 2 H, CH_2N), 2.29 (s, 3 H, CH_3); MS (CI/CH_4), m/z 173 (70, *p*-$TsOH_2^+$), 3.94 (s, 2 H, CH_2N), 2.29 (s, 3 H, CH_3); MS (CI/CH_4), m/z 173 (70, *p*-$TsOH_2^+$) 152 (100, MH^+), 135 (50, MH^+ - NH_3), 132 (40, MH^+ - HF), 123 (20, MH^+ - CH_2=NH).

Anal. Calcd for $C_9H_{10}FN \cdot C_7H_8O_3S$: C, 59.43; H, 5.61; N, 4.33. Found: C, 59.28; H, 5.77; N, 4.28.

β-(4-Hydroxyphenyl)-β-methyleneethanamine Hydrochloride (1i). To a mixture of 0.80 g (2.7 mmol) of **1g**, 10 mL of water, and 4 mL of THF was added 1.50 g (25.8 mmol) of anhydrous KF. The mixture was stirred at ambient temperature for 16 h, then was saturated with NaCl, and diluted with 25 mL of THF. The layers were separated and the aqueous layer was extracted with more THF (2 × 50 mL). The combined extracts were dried over $MgSO_4$ and concentrated to dryness. The residue was taken up in CH_3OH and treated with methanolic HCl and then concentrated to dryness. The residue was recrystallized from 2-propanol to afford 0.31 g (62%) of dark crystals: mp 172 °C (lit.[1e] mp 175 °C); ^1H NMR (300 MHz, $(CD_3)_2SO$) δ 9.70 (br s, 1 H, OH), 8.30 (br s, 3 H, NH_3^+), 7.34 (d, 2 H, J = 9 Hz, H-2 and H-6 of benzene ring), 6.97 (d, 2 H, J = 9 Hz, H-3 and H-5), 5.51 (s, 1 H, olefinic H), 5.21 (s, 1 H, olefinic H), 3.85 (br s, 2 H, CH_2N); MS (EI/70 eV), m/z 149 (100, M^+), 132 (50, M - NH_3), 120 (80), 119 (60, M - CH_2NH_2), 91 (50).

Anal. Calcd for $C_9H_{11}NO \cdot HCl$: C, 58.22; H, 6.52; N, 7.54. Found: C, 58.40; H, 6.44; N, 7.54.

β-(3,4-Dichlorophenyl)-β-methyleneethanamine (1j) was prepared by the procedure used for **1b**, isolated by method A, and subsequently converted to the HCl salt, mp 173-174 °C, after recrystallization from CH_3CN: ^1H NMR (300 MHz, $(CD_3)_2SO$) δ 8.48 (br s, 3 H, NH_3^+), 7.83 (d, 1 H, $J_{2,6}$ = 1.8 Hz, H-2 of ring), 7.68 (d, 1 H, $J_{5,6}$ = 9.0 Hz, H-5), 7.54 (dd, 1 H, $J_{6,5}$ = 9.0 Hz, $J_{6,2}$ = 1.8 Hz, H-6), 5.79 (s, 1 H, olefinic H), 5.53 (s, 1 H, olefinic H), 3.93 (s, 2 H, CH_2N); MS (CI/CH_4), m/z 202 (100, MH^+), 185 (40, MH^+ - NH_3).

Anal. Calcd for $C_9H_9Cl_2N \cdot HCl$: C, 45.32; H, 4.22; N, 5.87. Found: C, 45.50; H, 4.27; N, 6.04.

β-Methylene-β-(2-benzo[*b*]thienyl)ethanamine hydrochloride (1k) was prepared by the procedure used for **1a** and isolated by method B: mp 231 °C; ^1H NMR (300 MHz, $(CD_3)_2SO$) δ 8.35 (br s, 3 H, NH_3^+), 7.95 (m, 1 H, benzene H), 7.82 (m, 1 H, benzene H), 7.63 (s, 1 H, H-3 of thiophene), 7.41 (m, 1 H, benzene H), 7.38 (m, 1 H, benzene H), 5.75 (s, 1 H, olefinic H), 5.50 (s, 1 H, olefinic H), 4.02 (s, 2 H, CH_2N); MS (CI/CH_4), m/z 190 (100, MH^+), 173 (20, MH^+ - NH_3), 149 (10, M - CH_2NH_2).

Anal. Calcd for $C_{11}H_{11}NS \cdot HCl$: C, 58.52; H, 5.36; N, 6.20. Found: C, 58.75; H, 5.38; N, 6.19.

β-Methylenehexanamine hydrochloride (1l) was prepared by the procedure used for **1b** and isolated by method B: mp 170.5-172.5 °C (softens at 103-105 °C); ^1H NMR (300 MHz, $(CD_3)_2SO$) δ 8.28 (br s, 3 H, NH_3^+), 5.09 (s, 1 H, olefinic H), 4.99 (s, 1 H, olefinic H), 3.35 (s, 2 H, CH_2N), 2.06 (t, 2 H, J = 7.3 Hz, allylic H), 1.2-1.5 (m, 4 H, remaining methylene H), 0.89 (t, 3 H, J = 7.1 Hz, CH_3); MS (EI/70 eV), m/z 114 (7, M + H), 113 (2, M^+), 96 (15, M - NH_3), 84 (10, M - CH_2=CHC(=CH_2)CH_2NH_3), 81 (30), 70 (80, M - CH_2C(=CH_2)CH_2NH_2), 56 (100, M - C_4H_9).

Anal. Calcd for $C_7H_{15}N \cdot HCl$: C, 56.18; H, 10.78; N, 9.36. Found: C, 56.01; H, 10.59; N, 9.35.

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Inorganic-Solid-Supported Potassium Thiocyanate: Study of Reagent Preparation and a Convenient Synthesis of *tert*-Alkyl Thiocyanates

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The development of inorganic reagents adsorbed on high surface area supports has received much attention during the last decade and several common metal salts have thus been simply activated to produce valuable reagents for the organic synthetic chemist.[1,2] Our previous studies have shown that considerable improvement in reagent reactivity and selectivity may be gained by careful selection of support material and control of salt dispersion by optimization of loading and drying conditions.[3-5] The activation of KCN in the presence of alumina has been reported[6] and we recently developed highly reactive KCN-Al_2O_3 reagents,[7] enabling facile cyanation, with the use of infrared spectroscopy to study the metal cyanide-support interaction.[8]

Our attention was turned toward thiocyanation since although the reaction of metal thiocyanates with alkyl halides represents a valuable synthesis of organic thiocyanates, important intermediates for heterocyclic syntheses,[9] the literature contained only two short communications reporting silica gel supported potassium thiocyanate reagents for syntheses of some primary alkyl thiocyanates[10] and thiiranes.[11] We now report the use of infrared spectroscopy to enable straightforward monitoring of reagent preparation and show that some highly reactive supported reagents can be prepared. These allow some hitherto troublesome syntheses of *tert*-alkyl thiocyanates to be performed in moderate yield but with a high degree of selectivity and convenience.

Results and Discussion

Among the inorganic supports which were previously investigated for KSCN, the effectiveness was reported to

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