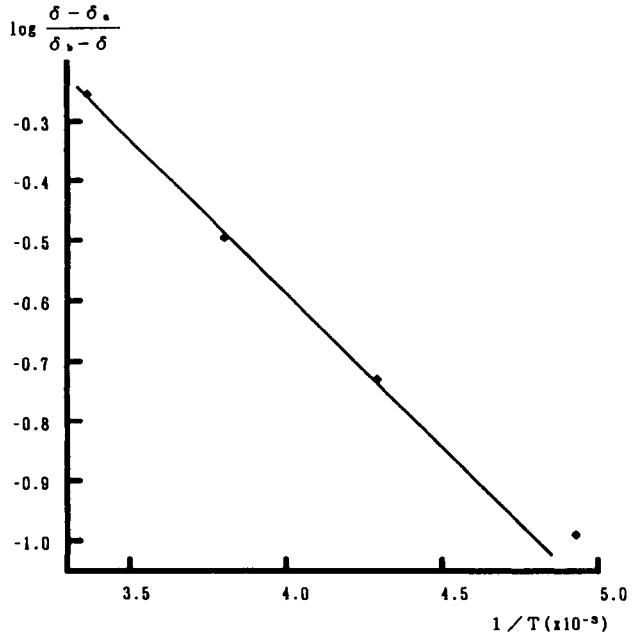

Figure 2. Plot of log $(\delta - \delta_a)/(\delta_b - \delta)$ against $1/T$.

Addition of a trace amount of NaOH to a dilute solution of 1 in $CDCl_3$, on the other hand, resolved the broad singlet into a well-defined triplet. The ^1H NMR spectrum of N-deuterated 1 showed a well-defined triplet for the signal of the C4 protons. Thus, the absence of a splitting pattern caused by C4–C5 proton coupling was due to the adjacent NH. In dilute solutions at ambient temperatures, the proton exchange between the two nitrogen atoms took place at an intermediate rate, so that the splitting pattern that arose from the coupling of the C4 and C5 protons was obscured. On raising the temperature, the exchange rate increased and the proton on nitrogen did not disturb the splitting pattern caused by the C4–C5 proton coupling. At low temperatures, or in concentrated solutions at ambient temperatures, the exchange rate slowed sufficiently to show the splitting pattern caused by the coupling of the C4 and C5 protons, but not to the point that the splitting pattern caused by the coupling of the C4 and N3 protons was revealed.

Anal. Calcd for $C_{10}H_{12}{}^{14}N^{15}NS$ (193.28): C, 62.14; H, 6.26; N, 15.01. Found: C, 62.25, 62.18; H, 6.26, 6.26; N, 14.67, 14.55.

^{15}N-Ring-Labeled 2 (2-^{15}N) and 3 (3-^{15}N). Sodium hydride suspension (220 mg) was washed with benzene, and then 3 mL of THF and 0.2 mL of HMPA were added. The mixture was cooled in ice, and a solution of 290 mg (1.5 mmol) 1-^{15}N in THF (3 mL) was added. The mixture was stirred for 30 min at 0–5 °C, and then MeI (0.3 mL) was added. The mixture was stirred for 5 h at 0–5 °C. Analysis of the mixture by TLC then showed no residual 1. Benzene and a small amount of water were added to the mixture. The mixture was then concentrated by rotary evaporator. The residue was dissolved in benzene, the solution was washed with water, dried (Na_2SO_4), and concentrated to give 330 mg of a syrup. ^1H NMR analysis showed that the syrup was a 60:40 mixture of 2 and 3 containing some HMPA. Column chromatography of the syrup ($CHCl_3$/MeOH, 98:2) gave 200 mg of crystals of 2 and an oil (3 containing some HMPA).

Crude 2-^{15}N was recrystallized from petroleum ether to give an analytical sample: mp 87–88 °C (lit.[2] mp 91 °C); ^1H NMR ($CDCl_3$) δ 2.16 (q, 5-CH_2), 2.89 (t, 6-CH_2), 3.16 (s, CH_3), 3.39 (t, 4-CH_2).

Anal. Calcd for $C_{11}H_{14}{}^{14}N^{15}NS$ (207.32): C, 63.72; H, 6.82; N, 13.99. Found: C, 63.83, 63.69; H, 6.82, 6.83; N, 13.73, 13.60.

No attempt to isolate 3-^{15}N from the syrup was made. 3-^{15}N: MS *m/e* 207 (M^+, 28), 206 ($(M-1)^+$, 100), 192 ($(M-CH_3)^+$, 6), 178 ($(M-(CH_2)_2-1)^+$, 18), 150 ($(M-(CH_2)_3{}^{15}N)^+$, 11), 149 ($(M-(CH_2)_3{}^{15}N-1)^+$, 27), 106 ($(PhNMe)^+$, 60); ^1H NMR ($CDCl_3$) δ 1.80 (q, 5-CH_2), 2.92 (t, 6-CH_2), 3.24 (s, CH_3), 3.70 (t, 4-CH_2).

Acknowledgment. The authors thank Dr. Jacques Reuben (Hercules Incorporated, USA) for helpful suggestions.

An Improved Synthesis of Ethyl *N*-(Methoxycarbonyl)-2,5-dihydro-1*H*-pyrrole-3-carboxylate[1]

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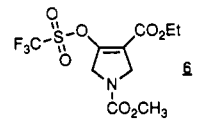
The title compound (4, Scheme I) has been used as a key intermediate in the synthesis of racemic supinidine (5)[3] and due to the functionality embodied within is envisioned as a useful precursor for many target compounds that incorporate a pyrroline or pyrrolidine ring.[4] The published route to 4 involves reduction of the pyrrolidone 1[5] to give a mixture of alcohols, which were converted to the benzoate esters 3. Base-induced elimination resulted in dihydropyrrole 4 in 34% overall yield from 1.

Because of the potential for 4 to serve as a pivotal intermediate in the construction of cyclic alkaloids and other important compounds,[6] attempts were made to improve on the synthesis of this important heterocycle. Thus, although 1 could readily be converted to the tosylhydrazone,[7a] attempts to decompose the crystalline derivative with methyllithium in ether or sodium methoxide in ethylene glycol[7b] to produce 4 were unsuccessful. Likewise, attempts to reduce the crude bis(dimethylamino) phosphonamide derivative of 1 with lithium[8] failed also. In addition, treatment of 1 with chlorotrimethylsilane and zinc metal in tetrahydrofuran[9] resulted in destruction of the starting material and none of the desired product could be isolated.

In an earlier report on palladium-catalyzed coupling of vinyl triflates with organotin compounds,[10] Stille and coworkers observed that vinyl triflates B could be reduced to olefins C with tributyltin hydride (Scheme II). We felt that this methodology might be suitable for the conversion of 1 to 4. Thus, the keto ester 1 was treated with trifluoromethanesulfonic anhydride in the presence of 1,8-bis(*N*,*N*-dimethylamino)naphthalene or 2,6-lutidine[11] to give the vinyl triflate 6. The crude triflate was reduced



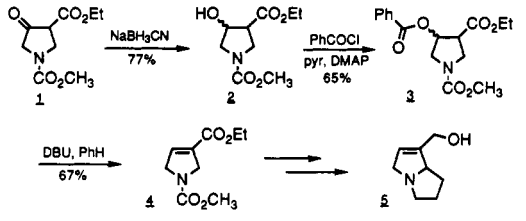
6

with tributyltin hydride in the presence of catalytic tet-

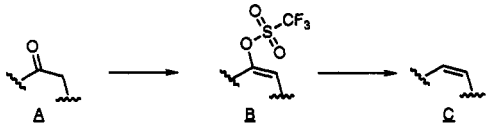
(1) In memory of Professor John K. Stille, May 8, 1930–July 19, 1989.
(2) Present address: Alcon Laboratories, Inc., 6201 South Freeway, Fort Worth, TX 76134.
(3) Macdonald, T. L.; Narayanan, B. A. *J. Org. Chem.* **1983**, *48*, 1129.
(4) For a review of pyrrolizidine alkaloids, see: Robins, D. J. *Adv. Heterocycl. Chem.* **1979**, *24*, 247.
(5) Kuhn, R. *Chem. Ber.* **1956**, *89*, 1423.
(6) Pinder, A. R. *Nat. Prod. Rep.* **1985**, *2*, 181.
(7) (a) Recrystallized from methanol, mp 199–200 °C dec; ^1H NMR (DMSO-d_6, 270 MHz) δ 9.60 (br s, 1 H), 7.72 (d, J = 7.5 Hz, 2 H), 7.40 (d, J = 7.5 Hz, 2 H), 4.42 (s, 2 H), 4.20 (s, 2 H), 4.08 (q, J = 7.5 Hz, 2 H), 3.70 (s, 3 H), 2.58 (br s, 1 H), 2.49 (s, 3 H), 1.20 (t, J = 7.5 Hz, 3 H); IR (KBr) 3350, 1685, 1640, 1595, 1335, 1100 cm^{-1}. (b) Shapiro, R. H. *Org. React.* **1976**, *23*, 405.
(8) Ireland, R. E.; Muchmore, D. C.; Hengartner, U. *J. Am. Chem. Soc.* **1972**, *94*, 5098.
(9) (a) Motherwell, W. B. *J. Chem. Soc., Chem. Commun.* **1973**, 935. (b) Hodge, P.; Khan, M. N. *J. Chem. Soc., Perkin Trans. I* **1975**, 809.
(10) Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 3033.
(11) For leading references on triflate chemistry see: (a) Stang, P. J.; White, M. R. *Aldrichemica Acta*, **1983**, *16*, 14 and (b) Stang, P. J.; Hanack, M.; Subramanian, L. R. *Synthesis* **1982**, *2*, 85.

0022-3263/91/1956-3197$02.50/0

Scheme I



Scheme II



rakis(triphenylphosphine)palladium(0), which produced 4 in 63–70% overall yield from 1 after purification.

In summary, significant improvement on the published route to the title compound was made, and the method described herein should provide ready access to other related derivatives.

Experimental Section[12]

3-(Ethoxycarbonyl)-*N*-(methoxycarbonyl)-2,5-dihydro-1*H*-pyrrol-4-yl Trifluoromethanesulfonate (6). Pyrrolidone 1[5] (1.7 g, 7.9 mM) and 1,8-bis(*N*,*N*-dimethylamino)naphthalene (Proton sponge, 1.8 g, 8.7 mM) were dissolved in dry dichloromethane (20 mL). The solution was cooled to 0 °C in an ice bath and trifluoromethanesulfonic anhydride (1.42 mL, 8.5 mM) was added dropwise over 10 min. The mixture was stirred for 3–4 h at room temperature, filtered through coarse silica gel (Merck 60–200 mesh), and then concentrated under reduced pressure. The reside was used crude in the next experiment. An analytical sample of 6 was obtained by flash chromatography (SiO_2, hexane/ethyl acetate, 3:1): mp 52 °C (hexane); ^1H NMR ($CDCl_3$, 270 MHz) δ 4.45 (s, 4 H), 4.31 (q, J = 7.2 Hz, 2 H), 3.76 (s, 3 H), 1.34 (t, J = 7.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 159.9, 154.7, 125.6, 119.8, 61.9, 53.0, 51.4 (t, J = 13.4 Hz), 50.9, 30.5, 14.0; IR ($CHCl_3$) 1710, 1670, 1390, 1122 cm^{-1}. Anal. Calcd for $C_{10}H_{12}NO_7SF_3$: C, 34.58; H, 3.48; N, 4.03. Found: C, 34.53; H, 3.49; N, 3.99.

Ethyl *N*-(Methoxycarbonyl)-2,5-dihydro-1*H*-pyrrole-3-carboxylate (4). In a dry 100-mL round-bottom flask flushed with dry argon, tetrakis(triphenylphosphine)palladium(0) (147 mg, 0.127 mM) and lithium chloride (808 mg, 19.1 mM, dried overnight at 0.1 mmHg) were mixed with dry THF (20 mL). The crude triflate 6 (2.0 g, 6.35 mM) in dry THF (20 mL) was added rapidly. Freshly distilled tributyltin hydride (2.07 mL, 7.68 mM) was added slowly over 2 min, and the mixture was heated at reflux for 3 h and cooled then diluted with hexane (40 mL). The reaction mixture was washed with 5% aqueous ammonium hydroxide (3 × 50 mL) and saturated sodium chloride (2 × 100 mL), filtered through silica gel, and then concentrated under reduced pressure. The residue was purified by flash chromatography (SiO_2, hexane/ethyl acetate, 3:1) to yield 0.89 g (70%) of a white solid with spectral characteristics identical with the literature values:[3] mp 75 °C (hexane/ethyl acetate); ^1H NMR ($CDCl_3$, 270 MHz) δ 6.74 (br d, J = 9.0 Hz, 1 H), 4.40–4.32 (complex m, 4 H), 4.24 (q, J = 7.0 Hz, 2 H), 3.74 (s, 3 H), 1.31 (t, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 67.5 MHz), δ 162.4, 155.1, 136.2, 132.3, 60.6, 54.1, 52.4, 51.8, 14.1; IR ($CHCl_3$) 1692, 1630 cm^{-1}.

(12) All reagents were obtained from Aldrich Chemical Co., Inc., Milwaukee, WI, and were used without further purification except where noted. Melting points are uncorrected.

Acknowledgment. Financial support was received from the National Science Foundation and is gratefully acknowledged.

Additions and Corrections

Vol. 55, 1990

Charles A. Panetta,* Stephanie M. Garlick, H. Dupont Durst, Frederick R. Longo, and J. Richard Ward. Synthesis of 4-Alkyl-2-iodosobenzoic Acids: Potent Catalysts for the Hydrolysis of Phosphorus Esters.

Page 5202, replace Phosphorous in title with Phosphorus.

Page 5203, column 1, line 1, replace phosphorous with phosphorus.

Yoshinori Yamamoto* and Naoki Asao. Copper Azide as a New Reagent for Syn-S_N2 Displacement of γ-Sulfonyloxy α,β-Unsaturated Esters.

Page 5303. **CAUTION**: Copper azide should be handled carefully behind a safety screen in a hood. Avoid heating this compound or shocking the reagent (see: Fedoroff, B. T.; et al. *Encyclopedia of Explosives and Related Items*, Vol. 1; Picatinny Arsenal: Dover, NJ, 1960; pp A534–A535). We appreciate Dr. Horst G. Adolph at Naval Surface Warfare Center for bringing this to our attention.

Vol. 56, 1991

John S. Lomas,* Sylvette Briand, and Dominique Fain. Reactions of Thermally Generated *tert*-Butyl and Di(*tert*-alkyl)ketyl Radicals in Toluene: Cage Effects and Hydrogen Transfer.

Page 166. Professor H. Fischer (Zurich) has informed us of unpublished data from his Laboratory (Dütsch, H. Doctoral Thesis, 1982; Münger, K. Doctoral Thesis, 1985) on hydrogen transfer from toluene to the *tert*-butyl radical. The Arrhenius plot of these data (log A = 5.9; E_a = 6.9 kcal mol^{-1}) intersects ours (log A = 9.8; E_a = 14.4 kcal mol^{-1}) at about 145 °C, all our data lying above Fischer's plot and the greatest difference between the two plots corresponding to a factor of 4.

Michael Lehd and Frank Jensen*. Improved Radical Stabilization Energies.

Page 884. The AUHF method was originally developed by T. Kovar and T. Clark and consequently ref 4 should include the following: (b) Kovar, T.; Clark, T. Manuscript in preparation.