(20 mL). The product was extracted with chloroform (30 mL × 3). The dried (Na_2CO_3) solution was concentrated to dryness and the residue was purified by TLC [silica gel, 4 g; $CHCl_3$–EtOH (100:3)] to give 2′-*O*-(3-methyl-2-picolyl 1-oxide)-5′-*O*-trityl-N^6-benzoyladenosine: yield, 276 mg (55.3%). On the criterion of the NMR spectra [NMR ($CDCl_3$) δ 2.26 (s, 3 H, 3″-CH_3[10]), 6.05 (d, J = 4.0 Hz, 1 H, $H_{1'}$), 8.04 (s, 1 H, H_8 or H_2)] this sample was indistinguishable with an authentic sample, prepared by an alternate route.

Synthesis of 2′-*O*-(3-Methyl-2-picolyl 1-oxide)-5′-*O*-trityl-N^6-benzoyladenosine (Alternate Route). A DMF solution (200 mL) of N^6-benzoyladenosine[11] (12 g, 32.8 mmol) was alkylated as reported[3] with 3-methyl-2-pyridyldiazomethane 1-oxide,[2] prepared from 16.8 g (55.1 mmol) of the *p*-tosylhydrazone of 2-formyl-3-methylpyridine 1-oxide in the presence of $SnCl_2 \cdot 2H_2O$ (900 mg). After workup as reported, the residue was dissolved in chloroform (200 mL) and applied to a silica gel column. The eluate corresponding to 2′-*O*-(3-methyl-2-picolyl 1-oxide)-N^6-benzoyladenosine was tritylated with 3 g (10.1 mmol) of triphenylchloromethane in pyridine (300 mL). After removal of the solvent, the residue was partitioned between saturated Na_2CO_3 solution (30 mL) and chloroform (30 mL). This process was repeated twice. The combined chloroform layer was dried (Na_2CO_3) and concentrated to dryness. A homogeneous sample of the title compound was isolated by TLC: NMR ($CDCl_3$) δ 2.26 (s, 3 H, 3″-CH_3[10]), 6.05 (d, J = 4.0 Hz, 1 H, $H_{1'}$), 8.04 (s, 1 H, H_8 or H_2). Anal. Calcd for $C_{43}H_{38}N_6O_6 \cdot H_2O$: C, 66.67; H, 5.55; N, 12.96. Found: C, 66.58; H, 5.34; N, 12.54.

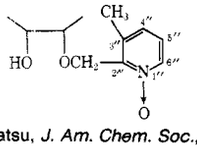
Reaction of 24 with Benzoyl Chloride. Analogous reaction of **24** (2 g, 5.15 mmol) and 3 equiv of benzoyl chloride in pyridine–DMF (1:1, v/v, 40 mL) afforded after workup presumably the *N*-benzoyloxy-rearranged product **26,** because on deblocking with methanolic ammonia the latter gave rise to adenosine rather than 2′-*O*-(3-methyl-2-picolyl 1-oxide)adenosine.

Acknowledgment. This work was financially supported by a grant from the Ministry of Education, Science and Culture to which our thanks are due. The authors also wish to thank Dr. Kyoichi A. Watanabe for helpful suggestions in the preparation of this manuscript.

Registry No.—**6,** 2683-69-4; **7,** 6890-60-4; **7**·HCl, 64314-84-7; **18,** 18868-46-7; **19,** 7719-09-7; **20,** 64314-85-8; **21,** 64314-86-9; **22,** 10242-36-1; **23**·HCl, 20979-34-4; **24,** 54657-22-6; **25,** 64314-87-0; ethyl phosphorodichloridate, 1498-51-7; trityl chloride, 76-83-5; 2′-*O*-(3-methyl-2-picolyl 1-oxide)-5′-*O*-trityl-N^6-benzoyladenosine, 64314-88-1; N^6-benzoyladenosine, 4546-55-8.

References and Notes

(1) For part 5, see Y. Mizuno, T. Endo, and T. Nakamura, *J. Org. Chem.*, **40,** 1391 (1975).
(2) (a) Y. Mizuno, K. Linn, K. Tsuchida, and K. Ikeda, *J. Org. Chem.*, **37,** 39 (1972); (b) T. Endo, K. Ikeda, Y. Kawamura, and Y. Mizuno, *J. Chem. Soc., Chem. Commun.*, 673 (1973); (c) K. Ikeda, K. Tsuchida, Y. Monma, and Y. Mizuno, *J. Heterocycl. Chem.*, **11,** 321 (1974); (d) Y. Mizuno and K. Ikeda, *Chem. Pharm. Bull.*, **22,** 2889 (1974).
(3) Y. Mizuno, T. Endo, and K. Ikeda, *J. Org. Chem.*, **40,** 1385 (1975).
(4) The reactions of aromatic amine *N*-oxides with acylating agents have been extensively studied: (a) E. Ochiai, "Aromatic Amine *N*-oxides", Elsevier, Amsterdam, 1967, pp 173–203, 290–301; (b) V. J. Traynelis in "Mechanism of Molecular Migrations", Vol. 2, B. S. Thyagarajan, Ed., Interscience, New York, N.Y., 1969, pp 1–42; (c) A. R. Katritzky and J. M. Lagowski, "Chemistry of Heterocyclic *N*-oxides", Academic Press, New York, N.Y., 1971, pp 1–50.
(5) B. C. Saunders, G. J. Stacy, F. Wied, and I. G. E. Wieding, *J. Chem. Soc.*, 695 (1948).
(6) (a) G. R. Owen, C. B. Reese, C. J. Ranson, J. H. Boom, and J. D. H. Hersheid, *Synthesis*, 704 (1974); (b) W. Geward, W. J. Green, and R. J. Phillips, *J. Chem. Soc.*, 1148 (1954); (c) F. Eckstein and I. Rizk, *Chem. Ber.*, **102,** 2362 (1969).
(7) (a) I. Suzuki, *Yakugaku Zasshi*, **68,** 126 (1948); (b) E. Profft and G. Schulz, *Arch. Pharm. (Weinheim, Ger.)*, **294,** 292 (1961); (c) M. Endo and T. Nakanishi, *Yakugaku Zasshi*, **80,** 875 (1960).
(8) A new type of neighboring group participation in acylation involving an *N*-oxide group will be the subject of part 7 in this series (Y. Mizuno and T. Endo, *J. Org. Chem.*, accompanying paper in this issue).
(9) M. Hamana, B. Umezawa, Y. Goto, and K. Noda, *Chem. Pharm. Bull.*, **8,** 692 (1960).
(10) Double prime for the numbering, e.g., 3″-CH_3, refers to the protecting group, and the numbering of the pyridine ring is as follows.



(11) T. Ukita and H. Hayatsu, *J. Am. Chem. Soc.*, **84,** 1879 (1962).

Organofunctional Alkylstannanes via Michael-Type Additions[1]

Henry G. Kuivila* and George H. Lein, Jr.

Department of Chemistry, State University of New York at Albany, Albany, New York 12222

Received April 21, 1977

Organostannanes have been shown to be useful as intermediates in a variety of organic syntheses such as the preparation of vinyl-[2,3] and allylalkalis[4] and other species.[5,6] Their utility could be increased with the availability of organofunctional organotins which can be easily synthesized. To this end, in part, we have been studying the scope and mechanisms of reactions of organostannylalkalis with functional organic compounds and have reported some results recently.[7,8] We wish to report preliminary observations on Michael-type additions of trimethylstannylsodium to α,β-unsaturated esters, ketones, and nitriles. Gilman and Rosenberg[9] reported that triphenylstannyllithium fails to react with either benzophenone or benzalacetophenone in ether.[9] Recently, Hudec reported the addition of trimethylstannyllithium in the presence of copper(I) iodide in THF to α,β-unsaturated ketones.[10] Tri-*n*-butylstannylmagnesium chloride has been shown to undergo Michael-type addition to unhindered α-β-unsaturated ketones, but 1,2 addition occurred if the β-carbon was dialkylated.[11] Still has observed that either 1,2 addition or Michael addition can be brought about using only trialkylstannyllithium without copper(I) iodide.[12]

When 50 mmol of trimethylstannylsodium in THF was added to 50 mmol of ethyl cinnamate and 100 mmol of ethanol in THF, a rapid reaction ensued to yield 60–75% ethyl 3-phenyl-3-(trimethylstannyl)propionate: IR 1730 cm^{-1}; ^{13}C NMR (C β to CO 29.96 ppm; $^3J(^{119}Sn-^{13}C{=}O)$ = 30.8 Hz indicated that the trimethylstannyl group was β rather than α to the carbonyl.[13,14] If the trimethylstannylsodium and the ester were first combined and the alcohol added after 1 min, none of the adduct was obtained; polymeric material and hexamethylditin were the major products. These observations show that, under the conditions used, the addition of trimethylstannylsodium to the ester (eq 1) and the reaction of the resulting enolate with ethyl alcohol (eq 2) are extremely fast compared with the reaction between ethyl alcohol and stannylsodium. A further transformation of the stannane formed in eq 3 results in the formation of hexamethylditin (eq 4). Prolonged standing of the initial reaction mixture before workup resulted in the ethanolysis of adduct **2** to ethyl 3-phenylpropionate, due to the lability of the benzylic trimethylstannyl group.

$$PhCH{=}CHCOOEt + Me_3SnNa \rightarrow \underset{\mathbf{1}}{[(Me_3Sn)C(Ph)HCHCOOEt]^-Na^+} \quad (1)$$

$$\mathbf{1} + EtOH \rightarrow EtONa + \underset{\mathbf{2}}{(Me_3Sn)C(Ph)HCH_2COOEt} \quad (2)$$

$$Me_3SnNa + EtOH \rightarrow Me_3SnH + EtONa \quad (3)$$

$$2Me_3SnH \rightarrow (Me_3Sn)_2 + H_2 \quad (4)$$

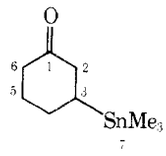
The reaction of ethyl acrylate with trimethylstannylsodium under similar conditions provided 48–53% yields of ethyl 3-trimethylstannylpropionate. If the reaction was carried out at −78 °C with workup after warming to room temperature, the yield of adduct was 45%.

The reaction of trimethylstannylsodium with mesityl oxide

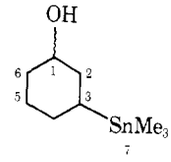
0022-3263/78/1943-0750$01.00/0

in THF with 2-propanol as the proton source at ambient temperature provided 49% 4-methyl-4-(trimethylstannyl)-2-pentanone.[11] The results obtained with mesityl oxide contrast strikingly with the formation of the 1,2 adduct when tri-*n*-butylstannylmagnesium chloride is used and suggest a means of controlling the direction of addition.

The reaction of 2-cyclohexenone with trimethylstannylsodium at −78 °C using ethanol as a proton source provided 3-(trimethylstannyl)cyclohexanone (**3**) contaminated with a small amount of 3-(trimethylstannyl)cyclohexanol (**4**). The yield of ketone was 50%. When a twofold excess of trimethylstannylsodium was used, the ratio of **4** to **3** increased to 3:1. Separation by high pressure liquid chromatography (HPLC) provided pure **4**, apparently a single geometrical isomer.[14] Treatment of 1 equiv of cyclohexanone and 2 equiv of ethanol with 1 equiv of trimethylstannylsodium in THF at ambient temperature led to 90% reduction of the ketone to cyclohexanol in 44 h. Hexamethylditin was the major tin-containing product.



3



4

Under conditions similar to those described above, methyl vinyl ketone, isophorone, and divinyl sulfone gave little or no adduct.

The observations recorded and cited above demonstrate that Michael-type acceptors can undergo 1,4 addition, 1,2 addition, and reduction of the 1,4 adduct upon treatment with trialkylstannylanionoids. They also reflect the importance of the various reaction parameters in directing the course of the reactions and yields of products.

Experimental Section

The IR spectra were recorded on Beckman IR-8 and IR-10 instruments. The C NMR spectra were recorded at 25.15 MHz on a Varian HA-100D spectrometer interfaced to a Digilab FTS-3 pulse and data system. The spectra were 8K or 14K Fourier-transformed, recorded at bandwidths of 2000 Hz. ^{1}H NMR spectra were recorded on a Varian A-60A instrument. All chemical shifts are recorded in ppm downfield from internal $(Me_4)Si$. Multiplicities are indicated by the first letters of the descriptives singlet, doublet, triplet, quartet, or multiplet, and relative areas are indicated in parentheses. Coupling constants are for ^{119}Sn if not specified.

Solutions of trimethylstannylsodium were prepared by stirring hexamethyldistannane for 12 h with 4 equiv of the metal cut into small pieces in THF, which had been dried by distillation from potassium benzophenone ketyl, an atmosphere of nitrogen or argon being maintained throughout the preparation and subsequent reaction of the alkali-metal derivative. Solutions for further use were removed by syringe through a serum cap, or the entire solution was filtered into the reaction flask through a small wad of cotton which retained unreacted metal.

General Reaction Procedure. The procedure described here for ethyl acrylate was generally used for synthetic scale preparations. To a solution of 6.1 g (61 mmol) of ethyl acrylate and 5.5 g (120 mmol) of ethanol in 200 mL of tetrahydrofuran (THF) cooled to −78 °C was added 66 mmol of trimethylstannylsodium in 33 mL of THF over about 30 min with stirring. The reaction mixture was allowed to warm to room temperature. The mixture was quenched with 60 mL of water and extracted with two 60-mL portions of pentane, which were combined and concentrated and the product distilled: bp 36 °C (0.26 Torr); yield 7.1 g (45%). The ^{1}H NMR spectrum was in accord with that reported for ethyl 3-(trimethylstannyl)propionate.[16]

Ethyl cinnamate was used in a similar procedure, but the product decomposed on distillation. However, GLPC using 15% Apiezon L on 60–80 mesh Chromosorb W provided pure product. Yields were estimated at 65–75%: IR 1730 and 520 cm^{-1} (C=O and Sn–C); ^{13}C NMR phenyl C 145.6 ($^2J(^{119}Sn-^{13}C)$ = 31.25 Hz), 125.7 ($^3J(^{119}Sn-^{13}C)$ = 22.25 Hz), 123.9, 128.3; $CH(SnMe_3)$ 30.0; CH_2 36.8 ($J(^{119}Sn-^{13}C)$ = 727 Hz); C=O 172.7 ($^3J(^{119}Sn-^{13}C)$ = 30.8 Hz); CH_2O 59.9; CH_3 14.2; CH_3Sn 9.68 ($^1J(^{119}Sn-^{13}C)$ = 322 Hz); ^{1}H NMR −0.04 (J = 52.0 Hz, 9); $(CH_3)_3Sn$ 1.15 (t, 3, 2.85 (s, 3), 4.07 (q, 2, 7.0 (m, 5),

Anal. Calcd for $C_{14}H_{22}O_2Sn$: C, 49.30; H, 6.51. Found: C, 49.41; H, 6.41.

Acrylonitrile yielded 3-(trimethylstannyl)acrylonitrile (81%) identical with a sample prepared by the addition of trimethylstannane to acrylonitrile.[16]

Mesityl oxide yielded 4-methyl-4-(trimethylstannyl)-2-pentanone (49%): bp 40 °C (0.05 Torr), ^{1}H NMR −0.06 (s, J = 52.0 Hz, 9, $(CH_3)_3Sn$), 1.00 (s, J = 62 Hz, $(CH_3)_2CSn$), 2.02 (s), 2.42 (J = 68 Hz, CH_2Sn).

Anal. Calcd for $C_9H_{20}SnO$: C, 41.11; H, 7.67. Found: C, 41.11; H, 7.83.

Cyclohexenone provided 40% of the expected adduct and 7% of its reduction product if workup was conducted after 2 h of reaction time. If the reaction was allowed to proceed for 44 h, equal amounts of alcohol and ketone were obtained. Use of 2 equiv of trimethylstannylsodium also gave this latter distribution after 2 h and a 3:1 ratio of alcohol to ketone after 44 h.

The products were separated by HPLC using 4 ft × 1/8 in Porasil columns with chloroform as an eluant.

3-(Trimethylstannyl)cyclohexanone: ^{13}C NMR (210.6 ($^3J(^{119}Sn-^{13}C)$ = 58 Hz, C_1), 45.7 ($^2J(^{119}Sn-^{13}C)$ = 15 Hz, C_2), 25.3 ($^1J(^{119}Sn-^{13}C)$ = 376 Hz, C_3), 29.5 (^2J (not defined), C_4), 30.8 ($^3J(^{119}Sn-^{13}C)$ = 69 Hz, C_5), 42.1 ($^1J(^{119}Sn-^{13}C)$ = 316 Hz, C_6), −11.6, (J = 320 Hz, $SnCH_3$).[15]

Anal. Calcd for $C_9H_{18}SnO$: C, 41.43; H, 6.95. Found: C, 40.98, H, 6.98.

3-(Trimethylstannyl)cyclohexanol: ^{13}C NMR (insufficiently pure sample for determination of J values) 71.6 (C_1), 40.2 (C_2), 22.6 (C_3), 29.9 (C_4), 27.5 (C_5), 36.2 (C_6), −11.8 (CH_3Sn).

Anal. Calcd for $C_9H_{20}SnO$: C, 41.11; H, 7.67. Found: C, 40.83; H, 7.53.

Registry No.—Ethyl acrylate, 140-88-5; trimethylstannylsodium, 16643-09-7; ethyl 3-(trimethylstannyl)propionate, 17490-11-8; ethyl cinnamate, 1103-36-6; ethyl β-(trimethylstannyl)cinnamate, 64010-80-6; mesityl oxide, 141-79-7; 4-methyl-4-(trimethylstannyl)-2-pentanone, 63831-56-1; cyclohexanone, 930-68-7; 3-(trimethylstannyl)cyclohexanone, 63831-50-5; 3-(trimethylstannyl)cyclohexanol, 64010-81-7; acrylonitrile, 107131; 3-(trimethylstannyl)acrylonitrile, 64010-82-8.

References and Notes

(1) This research was supported by the National Science Foundation. We thank Dr. K. R. Wursthorn for providing the ^{13}C NMR spectra.
(2) D. Seyferth and M. A. Weiner, *Chem. Ind. (London)*, 402 (1959); *J. Am. Chem. Soc.*, **83**, 3583 (1961).
(3) D. Seyferth and L. G. Vaughan, *J. Am. Chem. Soc.*, **86**, 883 (1964).
(4) D. Seyferth and M. A. Weiner, *J. Org. Chem.*, **26**, 4797 (1961); C. S. Johnson, M. A. Weiner, J. S. Waugh, and D. Seyferth, *J. Am. Chem. Soc.*, **83**, 1306 (1961).
(5) E. J. Corey and R. H. Wolenberg, *J. Am. Chem. Soc.*, **96**, 5581 (1974); **40**, 3788 (1975).
(6) E. J. Corey and R. H. Wollenberg, *J. Org. Chem.*, **40**, 2265 (1975); E. J. Corey, P. Ulrich, and J. M. Fitzpatrick, *J. Am. Chem. Soc.*, **98**, 222 (1976).
(7) H. G. Kuivila and K. R. Wursthorn, *Tetrahedron Lett.*, 4357 (1975).
(8) H. G. Kuivila and K. R. Wursthorn, *J. Organomet. Chem.*, **105**, C6 (1976).
(9) H. Gilman and S. D. Rosenberg, *J. Org. Chem.*, **18**, 1554 (1953).
(10) J. Hudec, *J. Chem. Soc., Perkin Trans. 1*, 1020 (1975).
(11) J-C. LaHournere and J. Valade, *J. Organomet. Chem.*, **33**, C7 (1971).
(12) W. C. Still, private communication. We appreciate receiving this information prior to its publication.
(13) D. Doddrell, I. Burfitt, W. Kitching, M. Bullpitt, R. J. Mynott, J. L. Considine, H. G. Kuivila, and R. H. Sarma, *J. Am. Chem. Soc.*, **96**, 1940 (1974); H. G. Kuivila, J. L. Considine, R. H. Sarma, and R. J. Mynott, *J. Organomet. Chem.*, **111**, 179 (1976).
(14) A. J. Leusink, H. A. Budding, and J. W. Marsam, *J. Organomet. Chem.*, **9**, 286 (1967).
(15) The chemical shift values are in good agreement with those calculated on the basis of the additivity effect of substituents on the cyclohexane ring: ref 13 and G. C. Levy and G. Nelson, "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists," Wiley, New York, N.Y., 1972, p 45.
(16) H. G. Kuivila, J. E. Dixon, P. L. Maxfield, N. M. Scarpa, T. M. Topka, K-H. Tsai, and K. R. Wursthorn, *J. Organomet. Chem.*, **86**, 89 (1975).