a variety of 2,5-disubstituted protoadamantanes,[3] 2-substituted protoadamantenes,[2] and 2-substituted isotwistanes.[3]

Experimental Section

The ^{13}C NMR spectra were taken on a JEOL FX-100 spectrometer, the ^1H NMR spectra on a Varian A-60A spectrometer, the IR spectra on a Perkin-Elmer 257 spectrophotometer, and the mass spectra on a Varian CH-7 mass spectrometer. The GLC analyses were carried out on a Varian Aerograph 1800 gas chromatograph.

2-Protoadamantenone (3). Following the reported procedure,[8] a 1:1 mixture of 2-protoadamantenone (**3**) and 10-protoadamantenone (**4**) was obtained by thermal cyclization of 7-allyloxycycloheptatriene. The ketones were not satisfactorily separated either by column chromatography or preparative GLC. We found, however, that ketone **4** formed the ethylene ketal much faster than **3**.

A solution of the sublimed crude mixture of ketones **3** and **4** (1.5 g) was stirred in ethylene glycol (10 mL) in the presence of TsOH (2.1 g) at 80–85 °C for 2 h and then poured into a mixture of KOH (0.7 g) and crushed ice. The resulting mixture was extracted with ether (3 × 25 mL), and the combined extracts were washed with water and dried. Evaporation of ether gave 1.3 g of a crude oily product which contained two GLC-detectable components (10% Carbowax 20M, 150 °C): ketone **3** and the ethylene ketal of **4** (less than 5% of unreacted **4** was present). Pure ketone **3** (0.3 g) was obtained by column chromatography on silica gel using 1:49 ether–benzene as eluent. The physical and spectral properties of **3** agree with those previously reported for this compound.[8]

8,9-Dehydro-2-adamantanone (1). A typical experiment is described. Ketone **3** (75 mg, 0.5 mmol) was stirred with 0.5 mL of 96% sulfuric acid and 2 mL of pentane at 22 °C for 3 h. Ether (10 mL) and crushed ice were added, and the layers were separated. The aqueous layer was extracted with ether (2 × 5 mL), and the combined ether extracts were washed with saturated aqueous $NaHCO_3$ and dried. Evaporation of the solvent yielded crystalline crude product which contained 15% of unreacted **3** and 85% of 8,9-dehydro-2-adamantanone (**1**) (by GLC; 10% Carbowax 20M, 150 °C). Pure ketone **1** (≥98% by GLC; 26 mg, 35% based on **3**) was easily obtained by column chromatography on Al_2O_3 (neutral, activity II) using ether as an eluent. Its melting point (205–206 °C), IR, ^1H NMR, and the mass spectral data were in complete agreement with those previously reported[1,6] for this compound; the ^{13}C NMR spectrum [δ_{Me_4Si} ($CDCl_3$) 32.2, 34.2, 37.7, 39.6, 44.0, 51.4, and 214.4 ppm] of **1** was identical to that of an authentic sample prepared by the reported[1] photoisomerization of **3**.

Ketone **1** was also obtained in 10–20% yield directly from the crude (sublimed) product mixture of the thermal cyclization of 7-allyloxycycloheptatriene by the procedure described above.

A sample of pure **1** was subjected to the same reaction conditions as **3**. Essentially no rearranged products were detected by GLC.[9]

Acknowledgment. This work was supported by a grant from the Research Council of the Republic of Croatia. We thank Professor Y. E. Rhodes for helpful discussions and Mrs. Lj. Vulić for the technical assistance.

Registry No.—**1**, 10497-56-0; **3**, 28673-75-8; **4**, 28673-76-9; **4** ethylene ketal, 64345-72-8; 7-allyoxycycloheptatriene, 28673-74-7.

References and Notes

(1) R. K. Murray, Jr., T. K. Morgan, Jr., and K. A. Babiak, *J. Org. Chem.*, **40**, 1079 (1975); R. K. Murray, Jr., and K. A. Babiak, *Tetrahedron Lett.*, 319, (1974). We are grateful to Professor Murray for providing us with copies of the IR and ^1H NMR spectra of **1**.
(2) R. K. Murray, Jr., and K. A. Babiak, *Tetrahedron Lett.*, 311 (1974).
(3) R. K. Murray, Jr., and T. K. Morgan, Jr., *J. Org. Chem.*, **40**, 2642 (1975); R. K. Murray, Jr., and T. K. Morgan, Jr., *Tetrahedron Lett.*, 3299 (1973).
(4) R. K. Murray, Jr., K. A. Babiak, and T. K. Morgan, Jr., *J. Org. Chem.*, **40**, 2463 (1975).
(5) Z. Majerski, G. Karlović, S. Djigaš, and D. Stefanović, *Org. Mass Spectrom.*, **12**, 37 (1977).
(6) J. E. Baldwin and W. D. Foglesong, *J. Am. Chem. Soc.*, **90**, 4303 (1968).
(7) G. A. Olah, G. Liang, K. A. Babiak, and R. K. Murray, Jr., *J. Am. Chem. Soc.*, **96**, 6794 (1974).
(8) C. A. Cupas, W. Schumann, and W. E. Heyd, *J. Am. Chem. Soc.*, **92**, 3237 (1970).
(9) This is consistent with the formation of the stable 2-hydroxy-8,9-dehydro-2-adamantyl cation by protonation of ketone **1** in FSO_3H–SO_2ClF.[7]

Protecting Groups. 6. Interaction of 2-Picoline 1-Oxides with Acylating and Phosphorylating Agents. A Case of Product Distribution Control[1]

Yoshihisa Mizuno* and Takeshi Endo

Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo, Japan

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Previous reports from our laboratory show that the 2-picolyl 1-oxide group is potentially a useful protecting group in organic chemistry in general[2] and in oligonucleotide syntheses in particular.[1,3] The picolyl 1-oxide group can be removed from an ether, thioether, or amine (**1**, Scheme I) or from an ester **6** by treatment with an acid anhydride. The reaction may proceed by the following mechanism: O-acylation to the *N*-acyloxypyridinium salt **2** and subsequent proton abstraction from the α-methylene group of **2** by the conjugate base to afford **3**, followed by intramolecular electron transfer to complete the rearrangement from **3** to **4**.[4b]

In order to determine the scope and limitations of this protecting group, we undertook systematic studies on the interaction between picolyl 1-oxide acetate (**6**) and various acylating agents (Table I).[4] An acylating agent (3 equiv) was added portionwise to a solution of **6** in deuterated chloroform. Little spectral change of **6** occurred upon addition of acetic anhydride (**8**) or benzoyl fluoride (**13**). The spectrum of **6**, however, rapidly changed upon addition of acyl halide (except **13**), indicating the formation of the *N*-acyloxypicolinium salt **2**. A large paramagnetic shift of the H-6 signal of **6** was observed. The α-methylene signal of **2** also appeared in a lower field than that of **6** (Table I). The degree of this low-field shift of H-6 in **2** was found to be dependent upon the nature of the counterion. The largest shift was observed when the picolinium ion was associated with a hard base (Cl^-) and the smallest shift was observed when a soft base (I^-) was the counterion. The shape of the H-6 signal suggested that the strongest virtual coupling occurred with chloride and little virtual coupling was observed with iodide counterion. When bromide was the conjugate base, the long-range virtual coupling was medium.

Addition of acetyl iodide (**11**) to a preformed *N*-acetoxypicolinium chloride (**2a**, X = Cl) resulted in the formation of *N*-acetoxypicolinium iodide (**2a**, X = I) as observed by ^1H NMR spectroscopy. The bromide counterion of **2a** (X = Br) was also replaced by iodide by treatment of **2a** (X = Br) with **11**. The reverse (exchange of iodide by chloride or bromide)

Scheme I

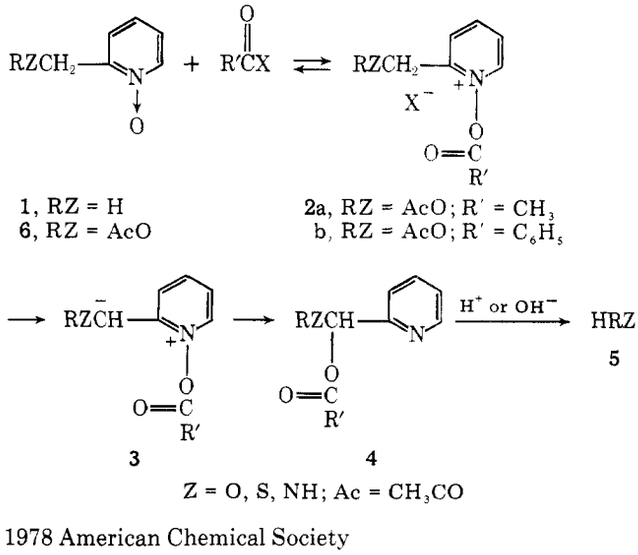

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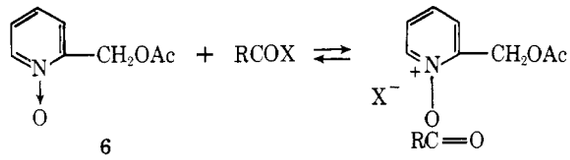
Table I. Reaction of 2-Picolyl 1-Oxide Acetate (6) with Acylating Agents



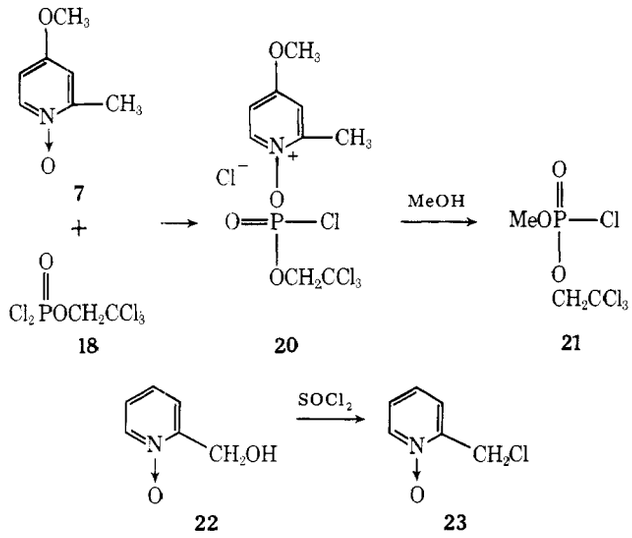
6

2a, R = CH_3
b, R = C_6H_5

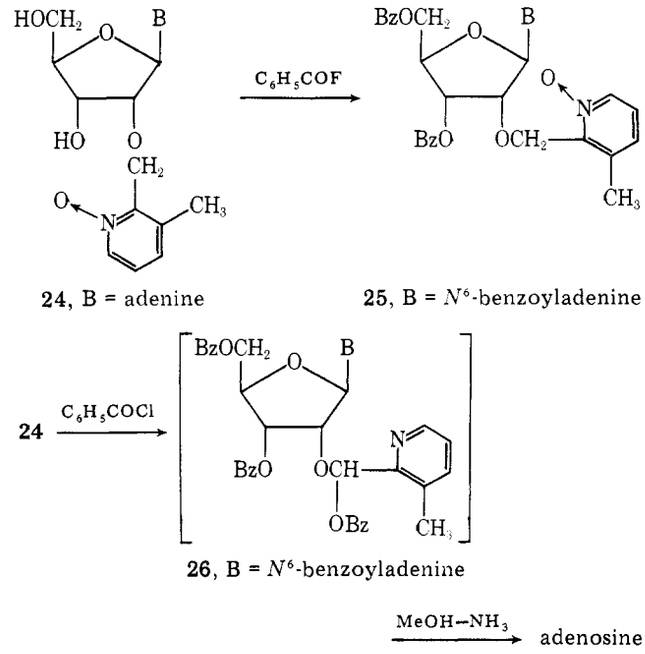
Acylating agent	Registry no.	Chemical shift (δ) of product 2[a] H-6	α-Methylene	Registry no.
Acetic anhydride (8)	108-24-7	8.25 t	5.35 s	64332-63-4
Acetyl chloride (9)	75-36-5	10.54 br s	5.62 s	64314-78-9
Acetyl bromide (10)	506-96-7	10.27 br d	5.61 s	64314-79-0
Acetyl iodide (11)	507-02-8	9.96 d	5.60 s	64314-80-3
Chloroacetyl chloride (12)	79-04-9	9.98 d	5.56 s	64314-81-4
Benzoyl fluoride (13)	455-32-3	8.19 t	5.34 s	64314-82-5
Benzoyl chloride (14)	98-88-4	Undetd	5.22 br s	64314-83-6
Benzoyl bromide (15)	618-32-6	10.24 d	5.75 s	64332-61-2

[a] Relative to the internal Me_4Si signal, and $CDCl_3$ was used as the solvent. Signals are quoted as s (singlet), d (doublet), br d (broad doublet), and t (triplet).

Scheme II



Scheme III



could not be effected. These experiments established that the *N*-acetoxypicolinium ion is a soft acid and forms a most stable salt with a soft base, such as iodide, and it cannot form a stable salt with a very hard base such as fluoride.

The effect of halide ion (counterion) upon the rate of overall rearrangement (1 → 4) was examined by taking advantage of the unique chemical shift of a sharp singlet due to the lateral α-methylene group of **2**. As the rearrangement proceeded the methylene signal decreased. It was found that only acyl chlorides were effective. Benzoyl fluoride (**13**) and acyl bromides were even less effective than acetic anhydride (**8**). The ineffectiveness of **13** in overall rearrangement (1 → 4) is apparently due to the inability of **13** to react with **6** to form **2**. Acetyl bromide (**10**) or benzoyl bromide (**15**) forms a stable *N*-acyloxypicolinium salt **2**. The conjugate base (Br^-), however, is less basic so that it does not abstract a proton as effectively from the α-methylene group as the chloride ion does. It was also found that benzoyl chloride (**14**) is several orders more efficient than acetyl chloride (**9**) in promoting the rearrangement. This may be explained by the difference of ease with which intramolecular electron transfer (from **3** to **4**) takes place. The carbonyl group of the *N*-benzoyloxy derivative **2b** is a better electron acceptor than that of the *N*-acetoxy analogue **2a** due to high conjugation of the benzoyl system. Anisoyl chloride or *p*-nitrobenzoyl chloride (**16**) was found as effective as **14**. Thus, the electronic nature of the para substituent is much less significant than conjugation of the system in the rearrangement.

Ethyl phosphorodichloridate[5] (**17**) or 2,2,2-trichloroethyl phosphorodichloridate[6] (**18**) did not react with **6**. Treatment of 4-methoxy-2-picoline 1-oxide[7] (**7**) with **18**, however, gave rise to *N*-(2,2,2-trichloroethylchlorophosphoryl)picolinium chloride (**20**) as judged by the ^1H NMR spectrum. Addition of methanol to **20** led to an immediate displacement of the spectrum of **20** by that of the hydrochloride salt of **7** with the concomitant appearance of a methyl signal [at δ 3.99 (J = 14.4 Hz)] due to the methyl group of methyl 2,2,2-trichloroethyl phosphorochloridate (**21**) (see Scheme II).

These results clearly showed that the electron-releasing methoxy group at position 4 favors the formation of quaternary salt **20**, and the phosphorus in **20** is sufficiently electrophilic to phosphorylate methanol. Thus, compound **20** has

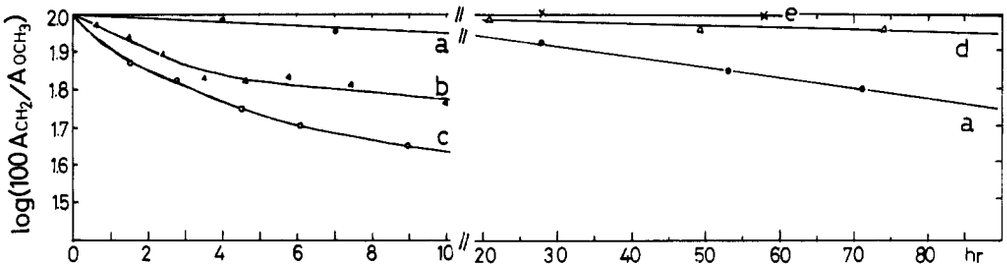


Figure 1. Rearrangement rate of the *N*-acyloxy group to the side chain. Time course of the integration of lateral methylene protons of **6** with reference to methyl protons of an internal standard (*p*-nitrotoluene or *p*-bromoanisole) on treatment of **6** with a variety of acylating agents. A_{CH_2} and A_{OCH_3}, the integration of lateral methylene protons of **6** and that of methyl protons of an internal standard, respectively. (a) 2-Pyridinemethanol 1-oxide (**6**) and Ac_2O (**8**); (b) **6** and $ClCH_2COCl$ (**12**); (c) **6** and BzCl (**14**); (d) **6** and AcBr (**10**); (e) **6** and BzF (**13**). For details of the reaction conditions, see the Experimental Section.

characteristics of an "active" ester and is a good acyl transfer agent with a reasonably electrophilic phosphorus.

Treatment of 2-pyridylmethanol 1-oxide (**22**) with thionyl chloride (**19**) afforded 2-picolyl chloride 1-oxide[2a] (**23**) which was isolated in crystalline form as its hydrochloride salt in good yield. It was not possible, however, to establish whether or not this chlorination reaction proceeded via the cyclic intermediate involving the *N*-oxide group.

In summary, we wish to emphasize that the present work[8] suggests that it may be possible for us to control the competing pathways (rearrangement, nonrearrangement, or acylating pathways) that a combination of 3-methyl-2-picolyl 1-oxide protected substrate, e.g., **24**, with an acylating agent undergoes. For example, to remove the 3-methyl-2-picolyl 1-oxide group, benzoyl chloride (**14**) may be an appropriate reagent. On the other hand, to introduce any acyl group without affecting the protecting group already present, acyl fluoride may be a reagent of choice. Thus, treatment of 2′-*O*-(3-methyl-2-picolyl 1-oxide)adenosine (**24**) in DMF–pyridine with excess benzoyl fluoride afforded $O^{3'},O^{5'},N^6$-tribenzoyl-2′-*O*-(3-methyl-2-picolyl 1-oxide)adenosine (**25**) in 89% yield. Analogous reaction of **24** and **14** failed to give **25** but instead presumably an *N*-benzoyloxy-rearranged product (**26**), because on deblocking with methanolic ammonia the latter gave rise to adenosine in excellent yield rather than 2′-*O*-(3-methyl-2-picolyl 1-oxide)adenosine (see Scheme III).

Experimental Section

General. Melting points and boiling points are uncorrected. UV spectra were determined on a Hitachi spectrometer, type T4. NMR spectra were determined on a Hitachi R24 instrument. Unless otherwise specified, the chemical shifts are reported in parts per million downfield from tetramethylsilane. Thin-layer chromatography (TLC) was run on glass plates coated with silicic acid. Elemental analysis was performed by Misses Chizuko Ohara and Hiroko Matsumoto of our Faculty of Pharmaceutical Sciences to whom our thanks are due. Solvents were evaporated on a rotary evaporator under water-aspirator pressure using a water bath at ca. 40 °C. The progress of reactions was routinely followed by either TLC or NMR spectrometry.

Reaction products were characterized or determined by TLC. Samples were spotted on precoated silica gel plates and developed to a distance of ca. 15 cm with a solvent system, $CHCl_3$–EtOH, whose composition depends on the cases.

Benzoyl fluoride was obtained from Aldrich Chemical Co., Milwaukee, Wis. Benzoyl bromide, benzoyl iodide, and other acylating agents are of analytical grade and were obtained from Wako Pure Chemical Co.

2-Picolyl 1-oxide acetate [**6**, mp 142–143 °C (crystallized from MeOH–AcOEt)],[9] 4-methoxy-2-picoline 1-oxide [mp 77–78 °C (crystallized from acetone)],[7] and ethyl phosphorodichloridate [bp 63–64 °C (19 mm)][5] were prepared according to reported methods. 2,2,2-Trichloroethyl phosphorodichloridate (**18**) [bp 116–118 °C (14 mm)] was also prepared by a reported method.[6]

Interaction between 2-Picolyl 1-Oxide Acetate (6) and Acylating Agents. NMR spectra of a mixture of **6** (100 mg, 0.598 mmol) and 3 equiv of acetylating agent (AcX: X = OAc, **8**; Cl, **9**; Br, **10**; or I, **11**) in 0.3 mL of chloroform-d_6 were taken at 29 °C. In the case of aroyl halide (BzX: X = F, **13**; Cl, **14**; or Br, **15**), the spectra were similarly determined, except that *p*-bromoanisole (0.179 mmol, 0.3 equiv) was used as the internal standard. δ values of signals arising from H-6 are listed in Table I.

Reactions of Aromatic Amine *N*-Oxides (6 or 7) with Phosphorylating Agents. Interaction of **6** or **7** with **18**, as well as the reaction of *N*-(2,2,2-trichloroethylchlorophosphoryl)picolinium chloride (**20**) with methanol were similarly followed as above.

Determination of the Relative Areas under the Signal Arising from the α-Methylene of 6 Interacting with Acylating Agents. An aromatic amine *N*-oxide **6** (103 mg, 0.616 mmol, 1 equiv), *p*-bromoanisole (83.8 mg, 0.448 mmol, 0.72 equiv), and 3 equiv of acylating agent (**13**, **8**, **12**, or **14**) were dissolved in 0.3 mL of chloroform-d_6. NMR spectra of the mixture were determined at 36 °C. A two-proton signal arising from the α-methylene of **6** appeared at δ 5.5, whereas a three-proton singlet due to the methyl group of *p*-bromoanisole appeared at δ 4.0. The areas under the signal of the former relative to that of the latter were determined at intervals (from 10 min to 80 h after the mixing, see Figure 1).

With aroyl chloride such as *p*-nitrobenzoyl or *p*-anisoyl chloride, the same results were obtained as with **14**. Acetyl chloride (**9**) gave the same time profile as chloroacetyl chloride (**12**). With acetyl bromide (**10**) the relative area remained virtually constant throughout the determination for up to 48 h, showing that rearrangement of the acyloxy group to the side chain did not take place under the above conditions.

Reaction of 2-Pyridinemethanol 1-Oxide (22) with Thionyl Chloride (19). To a suspension of **22** (5.0 g) in chloroform (70 mL) was added, with stirring at −15 °C, a solution of **19** (6.3 g) in chloroform (30 mL). A complete solution soon resulted and then a white precipitate deposited. The mixture was added to dry *n*-hexane (200 mL). The solid was collected by filtration and dried in vacuo. TLC and NMR examination showed that 2-picolyl chloride 1-oxide (**23**) HCl salt was formed (rather than free 2-picolyl chloride). The yield was 4.6 g (63%).[2a]

Reaction of 2′-*O*-(3-Methyl-2-picolyl 1-oxide)-N^6-benzoyladenosine (24) with Benzoyl Fluoride (13). Synthesis of $O^{3'},O^{5'},N^6$-Tribenzoyl-2′-*O*-(3-methyl-2-picolyl 1-oxide)adenosine (25). A suspension of 2′-*O*-(3-methyl-2-picolyl 1-oxide)adenosine[3] (2 g, 5.15 mmol) in a mixture of DMF (20 mL) and pyridine (20 mL) was treated with **13** (10 g, 80.6 mmol) at 40 °C for 2 days. The resulting solution was concentrated to dryness. The residue was partitioned between 30 mL of a saturated Na_2CO_3 solution and 30 mL of chloroform. This process was repeated twice. The combined chloroform solution was dried over Na_2SO_4. The salt was filtered off. The filtrate was concentrated to dryness. The residue was chromatographed over silica gel (100 g). The band corresponding to **25** was collected: yield, 3.2 g (89%); NMR ($CDCl_3$) δ 2.08 (s, 3 H, 3″-CH_3),[10] 6.36 (d, J = 5.6 Hz, $H_{1'}$), 8.30 (s, H_8 or H_2), 8.60 (s, 1 H, H_8 or H_2). Anal. Calcd for $C_{38}H_{33}N_6O_8 \cdot \frac{1}{3}H_2O$: C, 64.58; H, 4.72; N, 11.89. Found: C, 64.75; H, 4.48; N, 11.71.

To a solution of **25** (479 mg, 0.68 mmol) in pyridine (20 mL) was added 10 mL of 2 N sodium hydroxide solution. The solution then became turbid and ethanol was added until a homogeneous solution was obtained. It required 35 mL of ethanol. The solution was kept at room temperature for 5 min and then neutralized with cooling with 15 mL of acetic acid and concentrated to dryness in vacuo. The residue was purified with TLC to afford 2′-*O*-(3-methyl-2-picolyl 1-oxide)-N^6-benzoyladenosine (ca. 330 mg). Without further purification, this sample was dissolved in 20 mL of pyridine and treated with trityl chloride (300 mg, 1.07 mmol) at 30 °C for 2 days. The solvent was removed. The residue was neutralized with saturated Na_2CO_3 solution

(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.

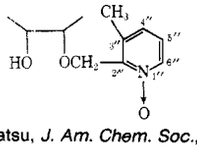
Reaction of 24 with Benzoyl Chloride. Analogous reaction of **24** (2 g, 5.15 mmol) and 3 equiv of benzoyl chloride in pyridine–DMF (1:1, v/v, 40 mL) afforded after workup presumably the *N*-benzoyloxy-rearranged product **26,** because on deblocking with methanolic ammonia the latter gave rise to adenosine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

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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

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