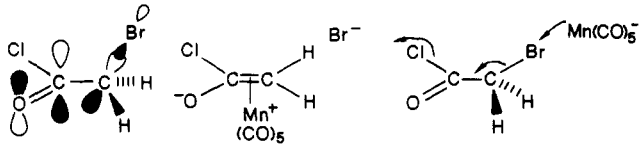
From these results, one can probably exclude, for the mechanism of the ketene forming reaction, the transient formation of a (α-bromoacyl)manganese (like **3**) followed by elimination of $Mn(CO)_5Br$. Additionally, in eq 2, such an intermediate would leave the bromine and manganese on opposite sides of a double bond and spatially distant, an unlikely scenario for rapid vinyl ketene formation.

The normal reactivity of **2** and an acyl halide is the very rapid formation of the acyl manganese compound. The complete circumvention of this "normal" reaction by the ketene forming mechanism implies that the latter reaction rate would have to be very rapid indeed, *exactly as one finds*.

In treating the eq 1 or 2 reactions in terms of a HOMO–LUMO interaction, the C–Br bond has been oriented perpendicular to the carbonyl group plane in the computed [12] LUMO of the α-bromoacyl chloride **5**. This LUMO has π-character, and a direct attack from underneath could lead smoothly with Br^- loss to the π-complex ion pair **6**, which might then collapse to $Mn(CO)_5Br$, Cl^- and ketene. Complex **6** has close analogies in cyclopentadienyliron dicarbonyl complexes.[13] However, a direct attack on **5** via the α-bromine looks like an even more straightforward mechanism (electron transfer?), i.e. structure **7**.



5 **6** **7**

In summary, we believe that this new synthetic procedure offers a convenient small-scale preparation of ketene and monoalkyl ketenes and a synthesis of vinyl ketenes free of pyrolysis coproducts.

We are extending this investigation to the generation of other reactive ketenes, as well as investigating the utility of other metal-centered nucleophiles in carrying out these reactions.

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada for generous financial support.

Registry No. 1 ($R_1 = R_2 = H$), 463-51-4; 1 ($R_1 = CH_3$, $R_2 = H$), 6004-44-0; 1 ($R_1 = CH_3CH_2$, $R_2 = H$), 20334-52-5; 1 ($R_1 = R_2 = CH_3$), 598-26-5; 1 (R_1 = vinyl, $R_2 = H$), 50888-73-8; 1 (R_1 = vinyl, R_2 = methyl), 83897-55-6; **2a**, 52542-59-3; $BrCH_2COCl$, 22118-09-8; $BrCH(CH_3)COCl$, 7148-74-5; $BrCH(CH_2CH_3)COBr$, 26074-52-2; $BrC(CH_3)_2COCl$, 20469-89-0; $BrC(CH_3)_2COBr$, 20769-85-1; $BrCH_2CH{=}CHCOCl$, 51544-74-2; $BrCH_2CH{=}C(CH_3)COCl$, 103500-00-1.

Supplementary Material Available: Experimental procedure, apparatus, and NMR specta of the ketenes (3 pages). For ordering information see any current masthead page.

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Received June 18, 1986

Modification of Guanine Bases: Reaction of N^2-Acylated Guanine Nucleosides with Dichloro-(*N*,*N*-diisopropylamino)phosphine

Summary: N^2-acylated guanine nucleosides (acyl = benzoyl, isobutyryl, acetyl) reacted rapidly with dichloro-(*N*,*N*-diisopropylamino)phosphine in the presence of diisopropylethylamine to give novel phosphitylated tricyclic guanine nucleoside derivatives in 60–96% yield.

Sir: We wish to describe the synthesis and structure determination of novel phosphitylated tricyclic guanine nucleoside derivatives. These derivatives are readily formed by the reaction of N^2-acylated guanine nucleosides (widely used in nucleotide synthesis) with dichloro-(*N*,*N*-diisopropylamino)phosphine (**1**) in the presence of diisopropylethylamine (**2**). These novel derivatives were unexpectedly detected during a ^{31}P NMR study of the reaction of N^2-acylated guanine nucleosides with chloro-(*N*,*N*-diisopropylamino)methoxyphosphine (**3**), a reagent commonly used for the preparation of nucleoside-3′-*O*-[1,2] and 5′-*O*-(*N*,*N*-diisopropylamino)phosphoramidites,[3] key intermediates in the chemical synthesis of DNA and RNA molecules. Dichloro-(*N*,*N*-diisopropylamino)phosphine (**1**) was obtained as an impurity during the preparation of reagent **3**.

Compound **1** was prepared by the reaction of phosphorous trichloride (1 equiv) and diisopropylamine (2 equiv) in ether (0 °C) in 67% isolated yield.[4] This material showed spectroscopic properties (^{31}P NMR, $\delta_{CDCl_3} = 169.8$ ppm) identical with those of the impurity in our original phosphite reagent **3** (^{31}P NMR, $\delta_{CDCl_3} = 184.2$ ppm). When nucleoside **4a** (1.0 mmol), the dichloroaminophosphine reagent **1** (1.1 mmol), and diisopropylethylamine (7.8 mmol) were combined (3 mL of $CHCl_3$, 20 °C, 20 min), **5a** was isolated as a yellow solid, mp 93–97 °C, $C_{41}H_{71}N_6O_6PSi_3$,[5] in 96% yield after silica gel chromatography (dichloromethane as eluant; R_f 0.64, 1:6 chloroform–ether).

The structure of **5a** was established by spectroscopic means. The ^{31}P NMR spectrum showed two resonance signals at 93.7 and 93.5 ppm. The UV spectrum (EtOH) was indicative of the extended ring system: λ_{max} (ϵ) 377 sh (8700), 356 (14 100), 344 (14 500), 262 (19 500). The ^1H NMR and the coupled INEPT ^{15}N NMR showed no indication of the two NH signals present in guanosine **4a**.[6] Further evidence for the structure of this product was provided by the ^{13}C and ^{15}N NMR and IR spectra. The ^{13}C NMR resonance of the carbonyl group of the benzoyl moiety of **4a** appears as a singlet at 167.14 ppm, while in the tricyclic derivative **5a**, this carbon signal is coupled to phosphorus and appears as a doublet centered at 160.58 (isomer 1) and 160.53 ppm (isomer 2) with $^2J_{^{13}C-^{31}P} = 6.0$ and 6.9 Hz, respectively. The upfield shift experienced by this carbon strongly suggests that the amido carbonyl

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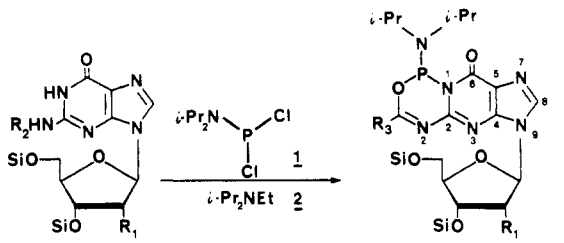
(4) During the preparation of this manuscript Tanaka et al. reported the synthesis of this reagent: Tanaka, T.; Tamatsukuri, S.; Ikehara, M. *Tetrahedron Lett.* **1986**, *27*, 199–202.

(5) Satisfactory microanalyses, UV, FAB mass spectra, and ^1H, ^{13}C, and ^{31}P NMR data were obtained for each compound here reported.

(6) ^1H NMR ($CDCl_3$) in ppm from Me_4Si. **4a**: 12.12 (NH), 8.62 (NH, D_2O exchangeable). INEPT ^{15}N NMR ($CDCl_3$) in ppm from $^{15}NH_4NO_3$: [0.3 M **4a**] 224.8 (N7, $J_{N7-H8} = 11.6$ Hz), 149.7 (N9, $J_{N9-H8} = 8.3$ Hz), 129.0 (*N1*, $J_{N1-H1} = 91.6$ Hz), 106.7 (N2, $J_{N2-H2} = 94.8$ Hz). 0.6 M **5a**: 225.1, 224.1 (N7, isomers 1, 2, $J_{N7-H8} = 11.6$, 11.6 Hz, respectively), 149.9, 149.8 (N9, isomers 1, 2, $J_{N9-H8} = 6.6$, 8.3 Hz, respectively).

0022-3263/86/1951-3559$01.50/0

Scheme I



Si= TBDMSi

a, R_1= OSi; R_2= Bz — a, R_1= OSi; R_3= Ph; 96%.

b, R_1= H ; R_2= Bz — b, R_1= H ; R_3= Ph; 93%.

c, R_1= H ; R_2= iBu — c, R_1= H ; R_3= iPr; 67%.

d, R_1= H ; R_2= Ac — d, R_1= H ; R_3= CH_3; 60%.

(benzoyl) in **5a** has been converted into an sp^2 carbon of the type OC=N.[7] The infrared spectrum (carbonyl region) of guanosine **4a** shows two absorptions at 1710 and 1670 cm^{-1}, which have been assigned to C6=O (lactam) and C=O (benzoyl) groups, respectively,[8] while the tricyclic guanosine derivative **5a** showed these absorptions at 1710 and 1620 cm^{-1}. The lowering of the vibrational frequency of the C=O (benzoyl) group is consistent with the ^{13}C NMR results, both indicating an increase single bond character of the C–O bond. Assignments of ^{15}N NMR resonances to specific nitrogens of **4a** and **5a**[9] have been made on the basis of nitrogen–hydrogen coupling constants[6] and ^{15}N NMR studies of nucleosides previously reported.[10,11] The signal at 129.7 ppm corresponding to N1 in compound **4a** is shifted downfield to 141.2 ppm in **5a** and as expected, exhibited coupling to phosphorous with $^1J_{^{15}N-^{31}P}$ coupling of 57 Hz.[12] The N2 resonance of **4a** experienced a downfield shift of 82 ppm upon conversion to **5a**, consistent with a change of hybridization of this nitrogen.[12] The addition of a third ring in **5a** shifted the N3 resonance 35 ppm downfield compared to N3 in **4a**, and this shift is indicative of the greater degree of aromatic character of the pyrimidine ring which is now the central ring of the tricyclic base. Finally, the FAB mass spectrum of **5a** showed the ions MH^+ and $(B + 2H)^+$ at m/e 859 and 385, respectively.

The formation of **5a** from **4a** could arise via reaction of 1 with N1 followed by a rapid intramolecular cyclization with the N^2-benzoyl group. As expected, the cyclization did not occur with O^6-protected, N^2-tritylated, or N^2-unprotected guanosines. The N^2-benzoyl-, N^2-isobutyryl-, and N^2-acetyl-2′-deoxyguanosines **4b–d** also afforded the corresponding modified 2′-deoxyguanosines **5b–d** in good yields (Scheme I). Compound **5a** is a "protected" guanosine since quantitative reconversion of **5a** to **4a** occurs within 5 min upon treatment with 3% trichloroacetic acid ($CHCl_3$) at 20 °C.

The modification of guanine bases described herein provides a new series of novel guanine nucleoside analogues. It also introduces a new base-protecting group for guanine nucleosides which can be removed under midly acidic conditions.

Acknowledgment. We thank NSERC for financial assistance. We also thank J. A. Montgomery for recording FAB mass spectra and Dr. T. Phan for recording ^{15}N NMR spectra. M.D. acknowledges scholarship funds from the Faculty of Graduate Studies, McGill University.

Registry No. 1, 921-26-6; **4a**, 72429-33-5; **4b**, 103477-30-1; **4c**, 90362-51-9; **4d**, 51549-44-1; **5a**, 103457-17-6; **5b**, 103457-18-7; **5c**, 103457-19-8; **5d**, 103457-20-1.

(7) Wehrli, F. W.; Wirthlin, T. *Interpretation of Carbon-13 NMR Spectra*; Heyden and Son: London, 1978; pp 31–33, 104–106.

(8) The IR (carbonyl region) spectrum of 5,3,2-*O*-trisilyl (TBDMS) guanosine (N^2-unprotected) shows an absorption band at 1700 cm^{-1}.

(9) ^{15}N NMR (C_6H_6, 20% C_6D_6) in ppm from $^{15}NH_4NO_3$. 1.4 M **4a**: 227.4 (N7), 162.3 (N3), 149.1 (N9), 129.7 (N1), 107.5 (N2). 1.4 M **5a**, isomers 1, 2: 230.0, 228.1 (N7), 197.4, 197.0 (N3), 189.4, 189.0 (N2), 149.6, 149.5 (N9), 141.2, 141.0 (N1, $^1J_{^{15}N-^{31}P}$ = 56.5, 56.8 Hz, respectively), 85.2, 85.0 (diisopropylamine N, $^1J_{^{15}N-^{31}P}$ = 89.2, 88.9 Hz, respectively). Note: Because N2 and N3 signals in **5a** are very close together, it is conceivable that the assignments may be reversed.

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Received June 19, 1986