NMR data, and S.C.T. wishes to thank the Council of Scientific and Industrial Research, New Delhi, for the Postdoctoral fellowship award.

Registry No.—**I**, 106-22-9; *cis*-**III**, 876-17-5; *trans*-**III**, 876-18-6; *N*-iodosuccinimide, 516-12-1.

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(5) The presence of dehydrocitronellol in the reaction mixture was confirmed by TLC and GLC only. The authentic sample was prepared by the reaction of citronellyl acetate with NBS and subsequent dehydrobromination and hydrolysis of the bromo derivative (cf. ref 4).
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(7) The citronellol used was of 95% purity; $[\alpha]^{20}_{D}$ +1.5°.
(8) The ratio of the *cis*- and *trans*-(rose oxide) was calculated from GLC only.

Reinvestigation of the Synthesis of 2′-Deoxyadenosylhomocysteine[1]

Yueh Wang and Harry P. C. Hogenkamp*

Department of Biochemistry, University of Minnesota, Minneapolis, Minnesota 55455

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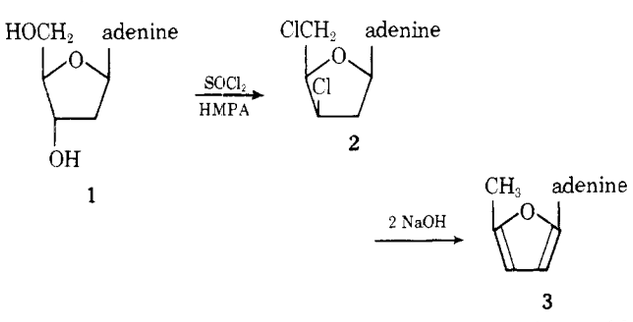
Recently two laboratories described convenient methods for the preparation of *S*-adenosylhomocysteine and some of its analogues.[2,3] Both methods employ the hexamethylphosphoramide–thionyl chloride reagent of Kikugawa and Ichino[4] to prepare the 5′-chloro-5′-deoxynucleosides, which upon condensation with either DL-homocysteine thiolactone in 2 N alkali[2] or DL-homocystine in sodium and liquid ammonia[3] yield the desired products. Borchardt and co-workers[3] reported the syntheses of *S*-adenosylhomocysteine and its analogues containing N^6-methyladenine, N^6-methyl-3-deazaadenine, and 7-deazzaadenine, as well as 2′- and 3′-deoxyadenosine. The purported synthesis of the last two analogues is surprising in light of our earlier observations that chlorination of 2′-deoxyadenosine by the method of Kikugawa and Ichino[4] does not yield 5′-chloro-2′,5′-dideoxyadenosine but rather the dichlorinated nucleoside, 9-(3,5-dichloro-2,3,5,-trideoxy-β-D-*threo*-pentofuranosyl)adenine (**2**).[5] Condensation of this dichloronucleoside with L-homocysteine could lead to the disubstituted analogue, 9-(3,5-dihomocysteinyl-2,3,5-trideoxy-β-D-*erythro*-pentofuranosyl)adenine, or the two monosubstituted analogues, 9-(3-chloro-5-*S*-homocysteinyl-2,3,5-trideoxy-β-D-*threo*-pentofuranosyl)adenine and 9-(5-chloro-3-*S*-homocysteinyl-2,3,5-trideoxy-β-D-*erythro*-pentofuranosyl)adenine.



These compounds would be expected to undergo elimination reactions under the basic conditions of the condensation reactions. Indeed, McCarthy and co-workers[6] have demonstrated that a similar compound, 2′,5′-dideoxy-5′-*S*-ethyl-3′-*O*-*p*-toluenesulfonyl-5′-thioadenosine, is converted to 9-(5-methyl-2-furyl)adenine (**3**) via two base-catalyzed elimination reactions when treated with potassium *tert*-butoxide in dimethyl sulfoxide.

In order to resolve this inconsistency, we have reinvestigated the synthesis of the analogue of *S*-adenosylhomocysteine involving 2′-deoxyadenosine under reaction conditions used in both laboratories.[2,3] Our results demonstrate that chlorination of 2′-deoxyadenosine with thionyl chloride in hexamethylphosphoramide yields exclusively 9-(3,5-dichloro-2,3,5-trideoxy-β-D-*threo*-pentofuranosyl)adenine (**2**). Paper chromatography of the crude reaction mixture in three solvent systems showed only **2** and adenine. Under the conditions of the condensation reactions, **2** undergoes two eliminations and an isomerization to 9-(5-methyl-2-furyl)adenine (**3**). The NMR spectra of **3** readily confirm its structure; the 270-MHz ^{1}H NMR spectrum shows the C-5′ protons as a three-proton singlet while the ^{13}C NMR spectrum shows a prominent resonance in the methyl region. Further evidence for the isomerization was obtained by conducting the reaction in a mixture of sodium deuterioxide and deuterioethanol. The ^{13}C NMR spectrum of the crystalline product demonstrates that one atom of deuterium is incorporated at carbon-5′, which now appears as a triplet, while the ^{1}H NMR spectrum indicates the presence of only two C-5′ protons. The ^{1}H NMR and ^{13}C NMR spectra also show that substitution of deuterium has occurred at C-8. The 80-MHz ^{1}H NMR spectra of **3** and its 5′-monodeuterio derivative are also in accordance with the assigned structures. The C-3′ proton of **3** appears as a set of quartets due to the long-range coupling of the three C-5′ protons, while for the deuterio derivative the C-3′ proton appears as a set of triplets.

This two-step reaction sequence provides a most convenient synthetic route to these unsaturated purine derivatives.

Experimental Section

Melting points were measured on a hot stage equipped with a microscope and are not corrected. Pulse proton and carbon-13 nuclear magnetic resonance spectra were recorded with a Bruker 270-MHz, a Varian CFT-20, and a Varian XL-100-15 spectrometer; chemical shifts are recorded in parts per million downfield from tetramethylsilane. Ultraviolet spectra were recorded with a Cary Model 15 spectrophotometer. Descending chromatography on Whatman No. 1 paper was conducted with the following solvent systems: 1-butanol–ethanol–water (50:15:35), *sec*-butyl alcohol–ammonium hydroxide–water (50:14:36), 1-butanol–acetic acid–water (40:10:50). Nucleosides on paper chromatograms were detected by their absorption of ultraviolet light; homocysteine derivatives were located with ninhydrin.

5′-Chloro-5′-deoxyadenosine and 9-(3,5-dichloro-2,3,5-trideoxy-β-D-*threo*-pentofuranosyl)adenine were prepared as described before.[5]

***S*-Adenosylhomocysteine. Method 1.** To a solution of L-homocysteine thiolactone hydrochloride (1.15 g, 7.49 mmol) in 12 mL of 2 N sodium hydroxide was added 1.0 g (3.5 mmol) of 5′-chloro-5′-deoxyadenosine. The reaction mixture was stirred vigorously at 80 °C for 1.5 h and then acidified to pH 6 with dilute acetic acid. The solution was applied to an ion-exchange column (2 × 60 cm of Dowex 50-X2, 200–400 mesh, NH_4^+ form) and eluted with water. The fractions containing the desired product were pooled and evaporated to dryness, and the residue was crystallized from water–methanol to yield 520 mg (39%) of *S*-adenosyl-L-homocysteine: mp 195–199 °C (lit.[3] 212 °C).

Method 2. To a solution of L-homocystine (400 mg, 1.5 mmol) in 50 mL of liquid ammonia was added sufficient sodium to give a blue solution. Solid ammonium chloride was then added to just discharge the color. 5′-Chloro-5′-deoxyadenosine (600 mg, 2.1 mmol) was added and the reaction mixture was stirred at −33 °C for 12 h. The reaction mixture was evaporated to dryness, the residue was dissolved in water, and the desired product was purified as described above: yield 393 mg (49%); mp 198–202 °C; UV λ_{max} (pH 1) 257 nm (ϵ 12.8 × 10^3); UV λ_{max} (pH 7) 259 nm (ϵ 14.3 × 10^3); UV λ_{max} (pH 11) 259 nm (ϵ 14.1 × 10^3); ^{1}H NMR (Me_2SO-d_6) 1.84, 1.99 (2 m, 2, C_βH), 2.64 (t, 1, $J_{\alpha,\beta}$ = 7.5 Hz, C_αH), 2.79, 2.95 (2 m, 2, C_γH), 3.31 (q, 2, $J_{5'a,5'b}$ = −15.0 Hz,

$C_{5'}H$), 4.03 (q, 1, $J_{2',3'}$ = 10.0 Hz, $J_{3',4'}$ = 6.0 Hz, $C_{3'}H$), 4.17 (q, 1, $C_{2'}H$), 4.73 (t, 1, $J_{4',5'}$ = 6.0 Hz, $C_{4'}H$), 5.90 (d, 1, $J_{1',2'}$ = 5.2 Hz, $C_{1'}H$), 7.30 (s, 2, NH_2), 8.16 (s, 1, C_2), and 8.37 ppm (s, 1, C_8); ^{13}C NMR (D_2O) 28.78 (C-5'), 31.44 (C-γ), 34.56 (C-β), 54.76 (C-α), 73.24 (C-3'), 74.52 (C-2'), 84.0 (C-4'), 88.37 (C-1'), 119.18 (C-5), 140.55 (C-8), 149.25 (C-4), 153.38 (C-2), 155.88 (C-6), and 174.83 ppm (COO^-).

Reaction of **2** with L-homocysteine thiolactone hydrochloride in 2 N sodium hydroxide or with L-homocystine in sodium and liquid ammonia was described above for 5'-chloro-5'-deoxyadenosine and examination of the reaction mixtures by paper chromatography showed only **3** and no condensation products. From these reaction mixtures **3** could be isolated in approximately 50% yield.

9-(5-Methyl-2-furyl)adenine (3). 9-(3,5-Dichloro-2,3,5-trideoxy-β-D-*threo*-pentofuranosyl)adenine (**2**, 500 mg, 1.64 mmol) was suspended in a mixture of 6 N sodium hydroxide (2.7 mL) and ethanol (5.3 mL) and stirred at 70 °C for 10 min. During this time the reactant dissolved and a new precipitate formed. The reaction mixture was stored at 4 °C overnight to yield 204 mg (58%) of **3**. Recrystallization from ethanol provided **3** as colorless needles: mp 235–236 °C (mp 205–215 °C dec when heated slowly) (lit.[6] 236–237 °C); $[\alpha]^{22}_D$ 0°; UV λ_{max} (pH 1) 252 nm (ϵ 21.3 × 10^3); UV λ_{max} (pH 7) 252 nm (ϵ 19.3 × 10^3); UV λ_{max} (pH 11) 251 nm (ϵ 18.8 × 10^3); ^1H NMR (270 MHz) (Me_2SO-d_6) 2.34 (s, 3, $C_{5'}H$), 6.32 (s, 1, $C_{3'}H$), 6.60 (d, 1, $J_{2',3'}$ = 3.0 Hz, $C_{2'}H$), 7.47 (s, 2, NH_2), 8.21 (s, 1, C_2H), and 8.40 ppm (s, 1, C_8H); ^1H NMR (80 MHz) (Me_2SO-d_6) 2.34 (q, 3, $J_{2',5'}$ = 0.30 Hz, $J_{3',5'}$ = 1.1 Hz, $C_{5'}H$), 6.30 (oct, 1, $J_{2',3'}$ = 3.1 Hz, $C_{3'}H$), 6.59 (q, 1, $C_{2'}H$, 7.40 (s, 2, NH_2), 8.21 (s, 1, C_2H), and 8.38 ppm (s, 1, C_8H); ^{13}C NMR (Me_2SO-d_6) 17.00 (C-5'), 105.90 and 111.33 (C-2' and C-3'), 121.90 (C-5), 142.66 (C-8 and C-4'), 152.81 (C-1'), 152.98 (C-4), 157.19 (C-2), and 159.81 ppm (C-6).

[5'-^{2}H,8-^{2}H]-9-(5-Methyl-2-furyl)adenine (4). **2** (500 mg, 1.64 mmol) was suspended in a mixture of 7.5 N sodium deuterioxide (2.1 mL) and deuterioethanol (5.9 mL) and heated at 70 °C for 10 min. The reaction mixture was worked up as described above to yield 185 mg (52%) of crystalline **4**: mp 235–236 °C; ^1H NMR (80 MHz) (Me_2SO-d_6) 2.34 (m, 2, $C_{5'}H$), 6.30 (sx, 1, $J_{2',3'}$ = 3.1 Hz, $J_{3',5'}$ = 1.1 Hz, $C_{3'}H$), 6.59 (d, 1, $C_{2'}H$), 7.40 (s, 2, NH_2), 8.21 (s, 1, C_2H); ^{13}C NMR (Me_2SO-d_6) 16.61 (t, $J_{C\text{-}^2H}$ = 20.0 Hz, C-5'), 105.94 and 111.43 (C-2' and C-3'), 122.06 (C-5), 142.90 (C-4'), 153.08 (C-1'), 153.18 (C-4), 157.40 (C-2), and 160.08 ppm (C-6).

Acknowledgments. The authors thank Drs. J. M. Wood and R. L. Thrift of the Freshwater Biological Institute for the 270-MHz ^1H NMR spectra and Dr. N. A. Matwiyoff of the Los Alamos Scientific Laboratory for the use of the Varian XL-100 spectrometer.

Registry No.—**2**, 63162-55-0; **3**, 6979-90-4; **4**, 64784-77-6; L-homocysteine thiolactone hydrochloride, 31828-68-9; 5'-chloro-5'-deoxyadenosine, 892-48-8; *S*-adenosyl-L-homocysteine, 979-92-0; L-homocystine, 626-72-2.

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Synthesis of Methyl Arylmethyl 2,2-Dimethyl-3-(2-methyl-1-propenyl)cyclopropylphosphonates as Potential Insecticides

Jack R. Reid* and Robert S. Marmor

Lorillard, A Division of Loews Theatres, Inc., Greensboro, North Carolina 27420

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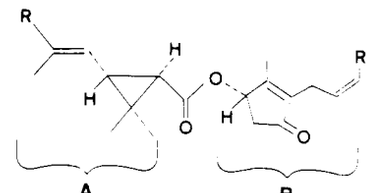
The interest generated by the insecticidal properties and low mammalian toxicity of the extracts of pyrethrum flowers has prompted many detailed investigations into the chemical nature of the chrysanthemate esters.[1-3] The esters **1** have been isolated and synthesized along with numerous synthetic analogues. Many of the previous investigations have dealt with a modification of the 2-methyl-1-propenyl group attached to the acid functionality A[5,6] or the replacement of the cyclopentenone alcohol moiety B by other suitable alcohols.[4] Many of these synthetic analogues exhibit enhanced insecticidal activity and a lowered rate of degradation when compared to the natural materials.[7] A heteroatom modification of the carboxylic function has not been reported. We now report the successful synthesis of compounds related to the chrysanthemate esters **1** in which the carboxylic function has been replaced by a phosphonic function.



1

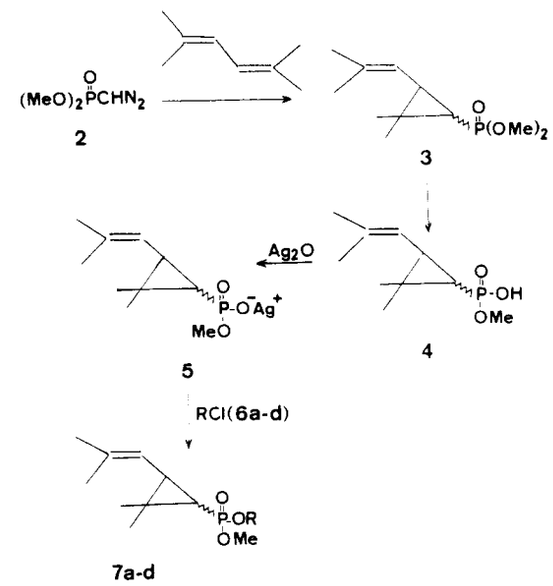
R=Me, $COOCH_3$
R'=Me, Et, $CH{=}CH_2$

The synthesis of ethyl chrysanthemate by Staudinger[9] was accomplished by the reaction of ethyl diazoacetate and 2,5-dimethyl-2,4-hexadiene. The availability of dimethyl diazomethylphosphonate[8] prompted us to attempt the synthesis of the phosphonochrysanthemates using a similar procedure.

Dimethyl diazomethylphosphonate (**2**) was treated with an excess of 2,5-dimethyl-2,4-hexadiene in methylene chloride in the presence of copper powder to give dimethyl 2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropylphosphonate (**3**). Although the cis/trans structural isomers could be separated by gas chromatography, no attempt was made to use the individual structural or optical isomers for our initial investigations. The esters which we chose to prepare were the phosphorus analogues of the chrysanthemate esters reported to have high insecticidal properties.

The diester **3** was selectively saponified to yield monomethyl 2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropylphosphonic acid (**4**). This acid was converted into its silver salt, silver methyl 2,2-dimethyl-3-(2-methyl-1-propenyl)-

Scheme I



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