evaporated to a solid mass, and filtered through a short column of neutral alumina with 500 mL of CH_2Cl_2 as eluent. Evaporation gave the diiodide **7** (3.4 g, quantitative) which was used without further purification. Spectral data are given in Table I. Alternatively the dibromide **6** could be used in place of **8**.

(2*R*,3*R*)-*N*,*N*,*N*′,*N*′-Tetramethyl-2,3-bis[2-(tosyloxy)ethoxy]succinamide (8). The diol **5** (23 g, 78 mmol) was dissolved in a mixture of triethylamine (20 mL) and CH_2Cl_2 (20 mL) at 10 °C, and solid *p*-toluenesulfonyl chloride (30.5 g, 160 mmol) was added. The mixture was allowed to stand at ambient temperature for 24 h, diluted with a further 200 mL of CH_2Cl_2, extracted with 3 × 100 mL portions of cold 1 M HCl, dried over Na_2SO_4, and evaporated to a solid gum. The gum was triturated to a solid with a minimum of ether, and the solid was recrystallized from ether/petroleum ether to yield **8** (35.8 g, 78%), mp 105–107 °C. Spectral data are given in Table I.

(2*R*,3*R*)-*N*,*N*,*N*′,*N*′-Tetramethyl-2,3-bis(2-mercaptoethoxy)succinamide (9). The ditosylate **8** (12 g, 20 mmol) and thiourea (5 g, 70 mmol) were dissolved in 50 mL of absolute ethanol and stirred at reflux for 3 h. After removal of the solvent, the ^1H NMR spectrum of a small sample of the product showed the complete loss of the signal at δ 4.1 (CH_2OTs) and a new signal at δ 3.3 ($CH_2S^+=$). The crude isothiouronium salt was dissolved in 25 mL of 1M NaOH solution and stirred at ambient temperature for 48 h. The mixture was brought to pH 7 with HCl and extracted with $CHCl_3$ on a continuous extractor for 16 h, and the organic extract was dried with Na_2SO_4 and evaporated to a brown oil. This mixture was separated by chromatography on neutral alumina using a gradient of methanol (0.5–5% (v/v)) in $CHCl_3$. The dithiol **9** eluted at 4–5% CH_3OH (5.0 g, 78%). Spectral data are given in Table I.

(2*R*,3*R*,11*R*,12*R*)-*N*,*N*,*N*′,*N*′,*N*″,*N*″,*N*‴,*N*‴-Octamethyl-1,4,10,13-tetraoxa-7,16-dithiacyclooctadecane-2,3,11,12-tetracarboxamide (10). A solution of dithiol **9** (1.3 g, 4.0 mmol) and diiodide **8** (1.06 g, 4.0 mmol) in 100 mL of dry DMF was added dropwise over 6 h to a stirred suspension of anhydrous Cs_2CO_3 (1.43 g, 4.4 mmol) in 500 mL of dry DMF under inert atmosphere at 50 °C. The mixture was stirred a further 16 h at this temperature, the solvent was removed under vacuum, the solids were suspended in $CHCl_3$ and removed by filtration, and the solvent and residual DMF were removed by evaporation at high vacuum. The solid product was dissolved in water (100 mL) and extracted successively with 50 mL of toluene and 50 mL of ether to remove less polar impurities and then with 3 × 50 mL of CH_2Cl_2. The CH_2Cl_2 extract was purified by chromatography on silica using a gradient of methanol (0–5% (v/v)) in $CHCl_3$ as eluent to give **10**, which was recrystallized from ether/methanol (0.42 g, 18%): mp 164–169 °C; MS (CH_4, CI), *m/e* (relative intensity) 581 (40, M + 1), 536 (8, M + 1 − Me_2NH_2), 508 (19, (M + 1 − DMF) + 1) [typical fragments of tartaramide crown ethers].[5,8,15]

(2*R*,3*R*,11*R*,12*R*)-1,4,10,13-Tetraoxa-7,16-dithiacyclooctadecane-2,3,11,12-tetracarboxylic Acid (11). The tetraamide **10** (130 mg, 0.22 mmol) was dissolved in 2 mL of D_2O, 200 μL of concentrated HCl was added, and the mixture was heated at 80 °C for 18 h. ^1H NMR showed complete loss of methyl amide resonances. The mixture was diluted with 5 mL of H_2O and passed down a short column of Dowex 50 H (H^+ form, 200 mesh, 10 g of resin) and eluted with H_2O until the eluent was neutral. The combined acidic eluent was concentrated to 2 mL at a temperature below 35 °C by using high vacuum. Silver oxide was freshly precipitated from $AgNO_3$ (600 mg) and tetramethylammonium hydroxide pentahydrate (800 mg) in 5 mL of H_2O. The Ag_2O was washed until neutral and suspended in 5 mL of H_2O, and the concentrated eluent (above) was added. The solid slurry was agitated periodically for 30 min, the solids were settled by centrifugation, and the supernatant was filtered through a 0.45-μm filter to remove traces of suspended solid. This solution (ca 6 mL) was again passed through a Dowex column as above, and the combined acidic fractions were concentrated to approximately 1 mL as previously. This sample was free of Cl^- (no precipitate with Ag^+) and free of Ag^+ (no precipitate with Cl^-). Evaporation at high vacuum gave the tetraacid **11** as a pale yellow brittle foam (75 mg, 71%). The elemental analysis indicated this product to be the monohydrate. This was confirmed by titration: equivalent weight calculated for **11**, 113 g/equiv; for **11**·H_2O, 122.5 g/equiv; found, 121.7 g/equiv. The parent hexaoxa tetraacid forms a similar hydrate,[8] but it is not known if this is a specific complex of H_2O.

Acknowledgment. This ongoing research was supported by the National Sciences and Engineering Research Council of Canada.

Registry No. **1**, 26549-65-5; **2**, 17739-45-6; **3**, 96388-83-9; **4**, 100190-94-1; **5**, 100190-95-2; **6**, 100190-96-3; **7**, 100190-97-4; **8**, 100190-98-5; **9**, 100190-99-6; **10**, 100191-00-2; **11**, 100191-01-3; 2-bromoethanol, 540-51-2; thiourea, 62-56-6.

Transient Protection. 2. One-Flask Synthesis of 6-*O*-[(4-Nitrophenyl)ethyl]-2′-deoxyguanosine Nucleosides

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Received December 14, 1984

Transient protection of both the 3′- and 5′-hydroxyl groups of **1a** or of the 3′-hydroxyl group of **1b**, followed by Mitsunobu alkylation with 2-(4-nitrophenyl)ethanol gave the O^6-protected nucleosides **4a** or **4b** in good yield in a one-flask procedure. Similar reactions with 3-hydroxypropionitrile or 2-(phenylsulfonyl)ethanol, however, were unsuccessful. Reaction of **1b** without 3′-hydroxyl protection led to formation of a stable $N^3 \rightarrow 3'$ cyclonucleoside, **7a**.

Results and Discussion

The degradation of guanine nucleosides during oligonucleotide synthesis is a well known phenomenon.[1] The findings by Reese[2,3] and by Hata[4,5] that guanine residues are subject to both O^6 sulfonylation with condensing reagents and to O^6 phosphorylation with activated nucleotides implicated the O^6 position as the source of this degradation. We then devised a sulfonylation/displacement route for specific O^6 alkylation of deoxyguanosine and showed that O^6 protection with any of several β-substituted ethyl derivatives completely eliminated reaction of the base with condensing agents.[6] Moreover, we reported use of three of these protecting groups, the (nitrophenyl)ethyl, cyanoethyl, and (phenylthio)ethyl groups, in the syntheses of several short oligonucleotides.[7-9]

We simplified our sulfonylation/displacement route by replacing the 5′- and 3′-*tert*-butyldimethylsilyl protecting groups originally used with a 5′-dimethoxytrityl and a 3′-levulinyl group.[9] We also attempted to use transient protection instead of the levulinyl group, but this route never gave satisfactory results. Recently, Pfleiderer has reported an alternative route for introduction of the (nitrophenyl)ethyl group via a Mitsunobu reaction.[10,11] For

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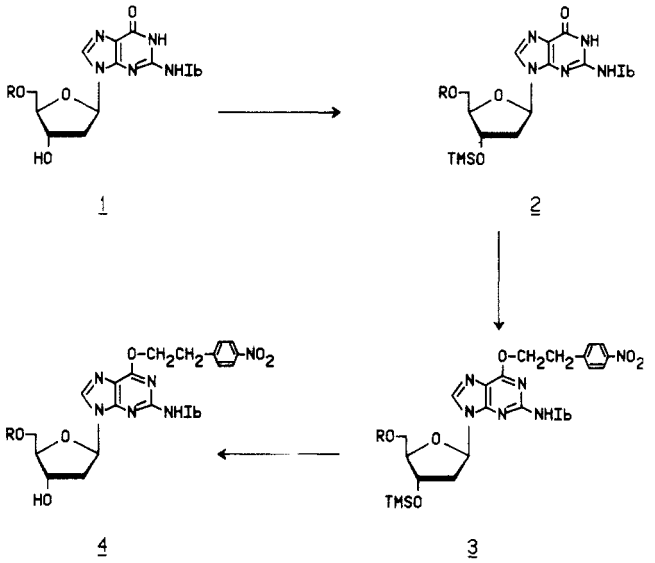
0022-3263/86/1951-0755$01.50/0

hydroxyl protection the Pfleiderer procedure uses isobutyryl groups which are removed by ammonolysis after the Mitsunobu alkylation. The (nitrophenyl)ethyl group is not cleaved by these conditions, although a more labile group such as the cyanoethyl group would be.[6] It appeared to us that if the Mitsunobu alkylation could be combined with transient hydroxyl protection it might lead to an exceptionally facile and general route for O^6 protection. Transient protection would eliminate the ammonolysis step and could therefore allow synthesis of more labile derivatives such as the O^6 cyanoethyl. The results of this investigation are presented below.

The protected derivative ultimately required for oligonucleotide synthesis must have a 5′-protecting group, of which the 4,4′-dimethoxytrityl (DMT) group is the most common. Since, in principle, this group could be introduced equally well either before or after O^6 protection we have explored both the route starting from N^2-isobutyryl deoxyguanosine (**1a**) and from its 5′ DMT derivative (**1b**).



1 2 3 4

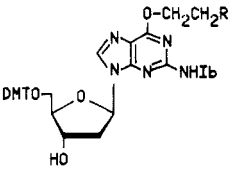
a, R = H
b, R = 4,4′-dimethoxytrityl
c, R = Me_3Si

Treatment of a dioxane solution of either **1a** or **1b** with *N*-(trimethylsilyl)imidazole (2.3 equiv for **1a**; 1.3 equiv for **1b**) gives the Me_3Si derivatives **2c** or **2b**, respectively. The addition of 3.5 equiv each of triphenylphosphine, (nitrophenyl)ethanol, and diethyl azodicarboxylate effects rapid O^6 alkylation to give **3c** or **3b**. Overall reaction of **1a**/**1b** to **3c**/**3b** generally requires less than 1 h.

Excess 1 M HF in pyridine is then added to cleave the Me_3Si groups (15 min), and the reaction mixture is partitioned between methylene chloride and aqueous $NaHCO_3$. Concentration of the organic layer and crystallization of the residual gum from ether or ethyl acetate gives **4a**/**4b** in somewhat variable yield. The crystallization is complicated by the presence of triphenylphosphine oxide, diethyl hydrazinedicarboxylate, and imidazole. While it is possible to remove these byproducts chromatographically for both **4a** and **4b**, the separation from **4b** is by far the more difficult. The best route is therefore to start from **1a**, since the product, **4a**, is easily separated from the triphenylphosphine oxide and diethyl hydrazinedicarboxylate. This partially purified **4a**, still containing some imidazole, is then reacted in the normal fashion with 4,4′-dimethoxytrityl chloride to give **4b**, which is now readily purified. The overall yield of crystalline **4b** by either route is 60–70%.

We next explored the use of this transient protection/Mitsunobu alkylation sequence for synthesis of the O^6-cyanoethyl derivative **5a**. In this case the reaction of 3-hydroxypropionitrile with **1b** under conditions identical to those used for synthesis of **4b** gave none of the expected product. Reactions using 2-(phenylsulfonyl)ethanol were also unsuccessful. Apparently for these alcohols the Mitsunobu intermediate (**6**) undergoes elimination much faster than it does the desired O^6 alkylation. The cyanoethyl and (phenylsulfonyl)ethyl groups are much more reactive to β-elimination than is the (nitrophenyl)ethyl group, and the dehydration of alcohols having acidic adjacent hydrogens under Mitsunobu conditions is known.[12] Even using a 10-fold excess of the alkylation reagents we could not detect any product formation. We did determine that the product, if formed, would be stable in the reaction mixture by similarly treating a sample of **5a** prepared by the sulfonylation/displacement route. Thus even using transient protection it has not been possible to extend the Mitsunobu reaction to preparation of the more labile derivatives **5a** or **5b**.

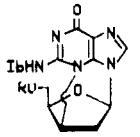
$$RCH_2CH_2OP^+(C_6H_5)_3$$
6



5a, R = CN
b, R = $SO_2C_6H_5$

DMT = 4,4′-dimethoxytrityl

Since in **1b** the primary (5′) hydroxyl group is protected we wondered if it might be possible to directly alkylate this compound under the Mitsunobu conditions without transient protection of the secondary (3′) hydroxyl group. When this reaction was carried out a nonpolar, higher R_f (TLC) product was detected, along with **4b** as the major product. This same nonpolar product was produced exclusively when **1b** was reacted with only triphenylphosphine and diethyl azodicarboxylate, i.e., with no (nitrophenyl)ethanol present. The product was purified by chromatography and crystallized in 85% yield. The shift in the UV absorption maximum from 265 nm, for **1b**, to 279 nm suggested that a cyclonucleoside had been produced. This product was carefully detritylated and further characterized by ^1H and ^{13}C NMR and elemental analysis. The NMR spectral data obtained for **7a** and **7b** are listed in Table I along with similar data on **1b**, for comparison. The largest chemical shift differences occur



7a, R = 4,4′-dimethoxytrityl
b, R = H

for C_3' and H_3'. The C_3' resonance in **7b** is 16.7 ppm upfield while the H_3' resonance is 1.18 ppm downfield of the respective signals in **1b**. In addition, C_4 and C_5 are shifted downfield by 8.9 and 4.4 ppm, respectively. These

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Table I. NMR Data of 1b and 7a,b[a]

^{1}H NMR chem shifts, ppm				^{1}H NMR coupling constants,[b] Hz			^{13}C NMR chem shifts, ppm		
H	1b	7a	7b	J	1b	7b	C	1b	7b
H8	8.24	7.80	7.97	$J_{1',2'}$	6.5	0.0	C2	148.4	150.8
H1′	6.21	6.35	6.38	$J_{1',2''}$	6.5	4.0	C4	147.9	139.0
H2′	2.55	2.59	2.73	$J_{2',2''}$	−13.2	−12.8	C5	120.1	115.7
H2″	2.27	2.29	2.51	$J_{2',3'}$	5.9	0.0	C6	154.8	154.4
H3′	4.36	5.80	5.54	$J_{2'',3'}$	3.6	3.6	C8	137.3	135.0
H4′	3.84	4.61	4.38	$J_{3',4'}$	3.0	4.0	C1′	82.9	82.5
H5′	3.61	3.10	3.52	$J_{4',5'}$	5.2	4.2	C2″[c]	38.4	38.8
H5″	3.50	3.10	3.31	$J_{4',5''}$	5.2	5.2	C3′	70.3	53.6
(*i*-Pr)*H*	2.76		2.56	$J_{5',5''}$	−11.7	−12.4	C4′	87.6	86.0
(*i*-Pr)C*H*$_3$	1.13	1.05, 0.91	1.11, 0.10	$J_{5',5'\text{-OH}}$	5.5	6.0	C5′	61.3	59.9
				$J_{3',3'\text{-OH}}$	4.0		(*i*-Pr)C=O	180.0	190.0
							(*i*-Pr)CH	34.7	34.4
							(*i*-Pr)CH$_3$	18.8	19.6, 19.3

[a] In Me_2SO-d_6, except 7a ^{1}H NMR was run in $CDCl_3$. [b] Estimated precision: ±0.2 Hz. [c] Under one CH_3 resonance of Me_2SO-d_6.

chemical shift changes are consistent with an $N^3 \rightarrow 3'$ cyclonucleoside. Furthermore, H_1' appears as a doublet, with a 1′,2′ coupling of 0 Hz and a 1′,2″ coupling of 4.0 Hz, while the 2′,3′ coupling is close to 0 Hz and the 2″,3′ coupling is 3.6 Hz. These small trans couplings are typical for the N-type sugar conformation expected for an $N^3 \rightarrow 3'$ cyclonucleoside, in which these dihedral angles should approach 90°.[13] The cis couplings observed, however, are somewhat smaller than would be expected. We were able to observe an NOE of 8% between H_8 and H_1', which is consistent with the syn structure of the cyclonucleoside. Finally, the two methyl groups in the N^2-isobutyryl group are nonequivalent in both the ^{1}H and ^{13}C NMR, in accord with the restricted rotation expected for **7b**.

The formation of purine $N^3 \rightarrow 5'$ cyclonucleosides and pyrimidine $O^2 \rightarrow 3'$ cyclonucleosides during Mitsunobu acylation or phosphorylation has been reported,[14] but to our knowledge this guanine $N^3 \rightarrow 3'$ cyclonucleoside has not been reported or characterized previously. The combination of transient protection with Mitsunobu alkylation offers a simple, effective route for O^6 protection of guanine with the (nitrophenyl)ethyl group. However, this route is not applicable to more labile protecting groups, such as the cyanoethyl group, which at present can only be introduced by a sulfonylation/displacement sequence.[6,9]

Experimental Section

General Methods. Thin-layer chromatography was performed on Eastman Chromatogram sheets (silica gel No. 18181, indicator No. 6060) in methylene chloride containing 3% methanol. Flash chromatography was carried out on EM silica gel 60, 230–400 mesh. Pyridine and dioxane were refluxed over and then distilled from calcium hydride. *N*-(Trimethylsilyl)imidazole was obtained from Petrarch Systems or Aldrich Chemical Co. Melting points were determined on a Thomas-Hoover apparatus and are uncorrected.

Preparation of 1 M HF in Pyridine. To ca. 25 mL of pyridine was added 2.0 mL of 49% aqueous HF. The solution was concentrated to ca. 5 mL, 25 mL of pyridine was added, and the solution was again concentrated. The coevaporation was repeated a third time, and the residue was then diluted with dry pyridine to a final volume of 50 mL (1 M HF/pyridine).

2-*N*-Isobutyryl-6-*O*-[2-(4-nitrophenyl)ethyl]-2′-deoxyguanosine (4a). To 1.7 g (5 mmol) of **1a** dried by evaporation of dioxane and suspended in 20 mL of dioxane was added 1.7 mL (11.5 mmol) of *N*-(trimethylsilyl)imidazole. The mixture was stirred for 15 min and 4.3 g (16.5 mmol) of triphenylphosphine, 2.8 g (16.5 mmol) of 2-(4-nitrophenyl)ethanol, and 2.6 mL (16.5 mmol) of diethyl azodicarboxylate were added successively. The reaction was allowed to proceed at room temperature for 20 min whereupon 25 mL of the above 1 M HF/pyridine solution was added. After a further 15 min the reaction mixture was poured into 150 mL of 5% aqueous sodium bicarbonate. This solution was extracted with three 50-mL portions of methylene chloride. The combined organic layers were concentrated under vacuum, and the residue was dissolved in a mixture of 10% methanol in methylene chloride. Ethyl acetate was then added to induce crystallization. Filtration gave 1.2 g (48%) of **4a**: mp, NMR, and UV were consistent with those reported in the literature.[11] The filtrate was concentrated and the residue purified by chromatography on silica gel, using a step gradient of methanol in methylene chloride as eluant. The combined product-containing fractions were concentrated to a dry foam to give an additional 0.5 g (22%) of **4a** for a total yield of 1.7 g (70%).

5′-*O*-(Dimethoxytrityl)-2-*N*-isobutyryl-6-*O*-[2-(4-nitrophenyl)ethyl]-2′-deoxyguanosine (4b). Method A. To 2.8 g (4.3 mmol) of **1b** in 20 mL of dioxane was added 0.83 mL (5.6 mmol) of *N*-(trimethylsilyl)imidazole. The mixture was stirred for 15 min, and 4.2 g (16.0 mmol) of triphenylphosphine, 2.7 g (16.0 mmol) of 2-(4-nitrophenyl)ethanol, and 2.5 mL (16.0 mmol) of diethyl azodicarboxylate were added successively. The reaction was allowed to proceed at room temperature for 20 min whereupon 25 mL of the above 1 M HF/pyridine solution was added. After a further 15 min the reaction mixture was poured into 150 mL of 5% aqueous sodium bicarbonate. This solution was extracted with three 50-mL portions of methylene chloride. The combined organic layers were concentrated under vacuum, and the residue was purified by chromatography on silica gel using a gradient of methanol in a mixture of petroleum ether–methylene chloride (1:9) as eluant. The combined product-containing fractions were concentrated to a dry foam to give 2.4 g (71%) of **4b**. A sample of **4b** crystallized from diethyl ether had the same mp, NMR, and UV reported previously.[9]

Method B. To 2.4 g (5 mmol) of **4a** in 25 mL of dry pyridine were added 2.5 g (7.5 mmol) of 4,4′-dimethoxytrityl chloride, 1.0 mL (7.5 mmol) of triethylamine, and 15 mg (0.12 mmol) of 4-(dimethylamino)pyridine. After 4 h the reaction was poured into 100 mL of 5% aqueous sodium bicarbonate. The solution was then extracted with three 50-mL portions of methylene chloride. The combined organic layers were then purified by chromatography on a silical gel as reported above for method A to give 3.5 g (90%) of **4b**. A sample crystallized from diethyl ether had the same mp, NMR, and UV reported previously.[9]

2-*N*-(Isobutyryl-9-(2,3-dideoxy-β-D-*threo*-pentofuranosyl)-($N^3 \rightarrow 3'$)-cycloguanine (7b). To 2.56 g (4 mmol) of **1b** and 5.24 g (20 mmol) of triphenylphosphine dissolved in 20 mL of dry dioxane was added 3.2 mL (20 mmol) of diethyl azodicarboxylate. After 30 min. the reaction was poured into 100 mL of 2% $NaHCO_3$ and then extracted with three 50-mL portions of methylene chloride. The combined organic layers were con-

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centrated under vacuum. The residue was purified by flash chromatography on silica gel using a step gradient of methanol in methylene chloride as eluant. The appropriate product fractions were combined and concentrated to a gum. Crystallization by diffusion of diethyl ether into a methylene chloride solution of this gum gave 2.12 g (3.4 mmol 85%) of **7a**: UV_{max} (CH_3OH) 279 nm; UV_{min} 238 nm.

To a 250 mg portion of **7a** dissolved in 1 mL of methylene chloride was added 20 mL of 2% trichloroacetic acid in methylene chloride. After 40 min. the reaction was poured into 20 mL of 2% $NaHCO_3$ and then extracted with two 20-mL portions of methylene chloride. The combined organic layers were concentrated under vacuum. The residue was purified by flash chromatography on silica gel, using a step gradient of methanol in methylene chloride as eluant. The appropriate product fractions were combined and concentration to a gum. Crystallization by diffusion of diethyl ether into a methylene chloride solution of this gum gave 85 mg (69%) of **7b**: UV_{max} (CH_3OH) 279 nm (ϵ 23.1×10^3); UV_{min} 238 nm (ϵ 3.7×10^3); mp 209-211 °C. Anal. Calcd for $C_{14}H_{17}N_5O_4$: C, 52.63; H, 5.38; N, 21.94. Found: C, 52.41; H, 5.19; N, 21.63.

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Registry No. **1a**, 68892-42-2; **1b**, 68892-41-1; **4a**, 82921-57-1; **4b**, 90678-72-1; **7a**, 100205-38-7; **7b**, 100190-48-5; 2-(4-nitrophenyl)ethanol, 100-27-6.

Cyclopropane Derivatives through Charge-Directed Conjugate Addition Reactions of Unsaturated Acylphosphoranes

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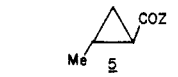
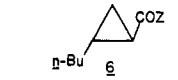
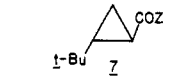
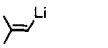
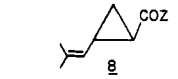
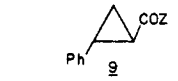
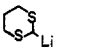
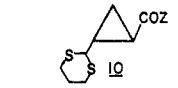
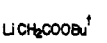
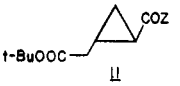
There has been considerable interest over the years in the construction of cyclopropane derivatives through Michael-initiated intramolecular alkylation reactions of γ-halo Michael acceptors. Allylic substitution and 1,2-addition processes are often competing, if not dominant, side reactions. Certain doubly activated alkylidenemalonate derivatives bearing a γ-leaving group give cyclopropyl derivatives in good yields when treated with nucleophiles such as cyanide,[1] methoxide,[1] thiolate,[1c] and borohydride.[1c]

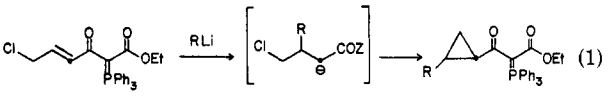
The singly activated 4-halocrotonate system also undergoes such reactions but only with certain stabilized nucleophiles such as lithium thiolates,[2] certain sulfur-based carbanions,[3] and the enolates of some esters.[4] More powerful nucleophiles generally are not successfully employed. Methyl 4-bromocrotonate and phenylmagnesium bromide give, after saponification of the reaction mixture, *trans*-2-phenylcyclopropanecarboxylic acid in only 13% yield.[5] Michael acceptors with the structural features necessary for cyclopropane formation (good γ-leaving groups) generally undergo reduction reactions with organocopper reagents.[6]

Table I. Reaction of 1 with Nucleophiles

RLi	Product[a]	Yield(%)[b]
MeLi		91
n-BuLi		91
t-BuLi		77
		67
PhLi		84
		76
		91

[a] COZ = C(O)C(Ph_3P)COOEt. [b] Isolated.

We have previously shown that unsaturated acylphosphoranes undergo charge-directed conjugate addition reactions with a wide range of nucleophiles[7] and that such reactions may be used to initiate intramolecular cyclization reactions leading to five- and six-membered rings.[8] We now report that chlorinated acceptor 1 reacts with a variety of nucleophiles heretofore not successfully employed in addition-initiated cyclopropanation reactions giving cyclopropane derivatives[3] as shown in eq 1. When coupled

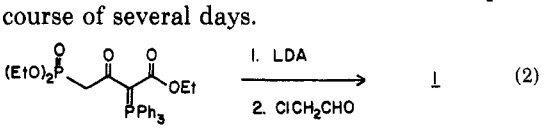


(1)

1 2 3

with the functional group transformations previously developed for such acylphosphoranes, a variety of cyclopropyl carboxyl[9] and ketone[10] derivatives become available by this process.

Acceptor 1 is readily prepared by Emmons-Wadsworth-Horner condensation of anhydrous chloroacetaldehyde[11] with the lithium salt of phosphonate 4 (eq 2).[12] Crystalline 1 is stable for months but solutions decompose over the course of several days.



(2)

4

Treatment of 1 with a variety of organolithium reagents in THF results in the formation of cyclopropyl derivatives

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