with 0.35 g (2.07 mmol) of XeF_2 and placed into a chlorobenzene/dry ice (−44 °C) cooling bath. Next, 0.20 g (2.13 mmol) of norbornene was weighed into 4 mL of Et_2O and added dropwise to the XeF_2. Stirring was begun as soon as mechanically possible. Within 4.5 min after addition of the norbornene solution, 0.20 g of $LiBF_4$ solid was added directly to the stirred suspension with the aid of a 30-mL 14/20 jointed powder funnel. After 7.5 h solid XeF_2 was still present in the reaction suspension. The chlorobenzene/dry ice cold bath was repacked and insulated. After 23 h, the dark brown reaction solution was poured into 10 mL of distilled H_2O that contained 0.4 g of NaF. The etheral layer was washed and separated. An additional 5 mL of H_2O was added to the aqueous wash before extraction with 2 mL of Et_2O. The combined Et_2O portions were dried over anhydrous $MgSO_4$ and filtered. Seven products were isolated from the Carbowax 20 M GLPC column in the following order: **12**, **11**, unknown,[29] **3**, **2**, **1**, and **4**.

Dehydrofluorination of 2-*exo*,5-*exo*-Difluoronorbornane. A previously reported dehydrofluorination procedure that provided 7-*anti*-fluoronorbornene from **3** and 7-*syn*-fluoronorbornene from **4**, respectively,[9] was used to synthesize 5-*exo*-fluoronorbornene from 2-*exo*,5-*exo*-difluoronorbornane (**1**). Beginning with 0.103 g (0.777 mmol) of **1**, a 42% conversion to 5-*exo*-fluoronorborn-2-ene resulted. The 5-*exo*-fluoronorborn-2-ene was isolated by continuous CH_2Cl_2 extraction of the Me_2SO solvent and preparative GLPC with the Carbowax 20M column. This compound is a volatile white solid: ^1H NMR ($DCCl_3$) δ 6.32 (multiplet, 1 H), 5.88 (multiplet, 1 H), 4.72 (doublet of multiplets, J_d = 58 Hz, 1 H), 2.96 (unsymmetrical multiplet, 2 H), 1.94–1.02 (multiplets, 4 H); mass spectrum M^+ at m/e 112 (37%) with m/e 97 (53), 86 (66), 84 (100), 73 (84), and 66 (82).

Synthesis of 2-Deuterionorbornene.[30] A 100-mL three-necked round-bottomed flask was charged with 22.1 g (0.384 mol) of a 1-μm 40% Na dispersion (Gray Chemical, Inc.) in petroleum ether and mineral oil. The flask was fitted with an N_2 stopcocked inlet and identical outlet, plus an overhead mounted mechanical stirrer apparatus. Next, 20 mL of Distilled-in-Glass hexane treated with neutral alumina (pH 6.3) was added to the reaction flask. The flask was submerged into a CCl_4/dry ice cooling bath (−23 °C).

This cooled suspension was stirred at high speed while 12.0 g (0.130 mol) of *n*-chlorobutane was dried over 4A molecular seives and passed through neutral alumina (pH 6.3) prior to its combination with the hexane solvent. After all of the *n*-butyl chloride was added dropwise, the CCl_4/dry ice bath was replaced with an ice bath for 35 min. Next, the CCl_4/dry bath was again placed around the reaction flask, and 8 min later 12.0 g (0.128 mol) of norbornene in 15 mL of hexane was added dropwise to the stirred reaction suspension. The reaction solution was then stirred at ambient temperature for 22.5 h. Again, the CCl_4/dry ice bath was placed around the reaction flask for 10 min, and the system was opened to the atmosphere. Next 8.9 g of 98% D_2O *was very cautiously added dropwise* to the rapidly stirring suspension. *The reaction exothermed slightly after the first few drops of D_2O were added, but all material was contained in the reaction flask.* After D_2O addition, the cooling bath was removed, and the reaction was stirred at ambient temperature for 4.5 h. The reaction solution was transferred into a separatory funnel; then, 75 mL of H_2O and 10 mL of hexane were added to the funnel. A distinct organic layer separated; the remaining emulsion was extracted six times with three 20-mL hexane portions followed by three 40-mL diethyl ether portions. All hexane and ethereal extracts were combined, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed by fractional distillation. The undistilled liquid portion was then distilled through a microware short-path apparatus, and only the material that condensed in the water-cooled condenser was retained. Further deuteration of this 1.9-g sample met with failure; however, the 2-deuterionorbornene sample (0.7 g) was recovered and afforded the following analysis: ^1H NMR ($DCCl_3$) δ 6.04 (sharp multiplet, 1 H), 2.86 (sharp multiplet, 2 H), 1.86–0.66 (multiplets 6 H); mass spectrum M + 1 at m/e 96 (5.6), M^+ at m/e 95 (12.7), M − 1 at m/e 94 (7.5) with m/e 68 (43.0), 67 (100), and 66 (56.5).

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Registry No. 1, 61091-30-3; **2**, 61026-29-7; **3**, 36914-49-5; **4**, 36914-50-8; **5**, 71042-31-4; **6**, 71075-21-3; **11**, 695-03-4; **12**, 765-92-4; 5-*exo*-fluoronorborn-2-ene, 71042-32-5; 2-deuterionorbornene, 694-94-0; XeF_2, 13709-36-9; norbornene, 498-66-8; boron trifluoride etherate, 109-63-7.

(29) This unknown trace product afforded a mass spectrum with M^+ at m/e 112 (base peak at m/e 84). This mass spectrum is similar to that obtained for 5-fluoronorborn-2-ene.

(30) J. E. Franz, C. Osuch, and M. W. Dietrich, *J. Org. Chem.*, **29**, 2922 (1964); A. A. Morton, M. L. Brown, M. E. T. Holden, R. L. Letsinger, and M. E. Maget, *J. Am. Chem. Soc.*, **67**, 2224 (1945); R. E. Finnegan and R. McNees, *J. Org. Chem.*, **29**, 3234 (1964). The sodium metalation reaction required to synthesize the 2-deuterionorbornene proved to be hazardous and quite unpredictable. In one case, the reaction was cooled too much (−78 °C) while the *n*-butyl chloride was added dropwise to the stirred sodium metal suspension. At this cold temperature an immediate conversion to *n*-butylsodium apparently did not occur causing a buildup of unreacted *n*-butyl chloride in the sodium metal suspension. Once reaction began, it quickly exothermed uncontrollably and exploded violently. Proper shielding and precautions should be instituted when attempting the described metalation reaction.

The Alkoxycarbonyl Moiety as a Blocking Group. A Generally Useful Variation of the Malonic Ester Synthesis

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A new, generally useful malonic ester synthesis has been developed on the basis of the alkoxycarbonyl moiety as a blocking group. Thus trialkyl methanetricarboxylates, symmetrical or unsymmetrical, were converted to their stable, nonhygroscopic sodio salts which were readily alkylated with multifunctional halides. Further elaboration could be carried out on the side chain, and reversion to the malonate was effected by monodecarbalkoxylation. The deblocking step occurs easily on exposure to alkoxide, diisopropylamide, or boron trichloride. When one of the esters is *tert*-butyl, anhydrous formic or trifluoroacetic acid also effects deblocking.

The alkylation of malonic esters is one of the oldest and most widely applicable of synthetic reactions.[2] It suffers from only limited side reactions, yet in some instances these side reactions, such as dialkylation, elimination, and

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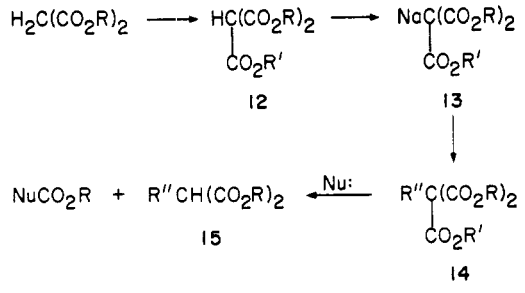
Scheme I



Michael addition, may become severe. Thus dialkylation, which is usually easily overcome by stoichiometry, becomes a major problem with reactive halides and when substitution increases the acidity of the remaining hydrogen. Also, halides themselves containing hydrogens more acidic than those of malonic ester (e.g., nitrohalides) are limited in their use.

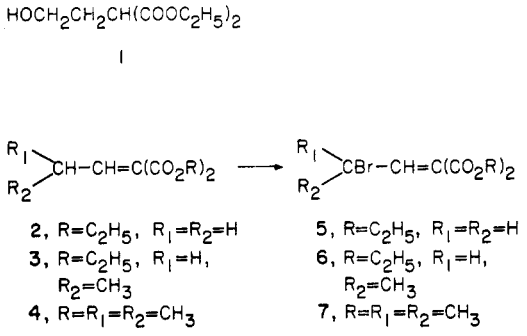
Dihalides present additional problems in that the initial (haloalkyl)malonate, when used in reaction with a nucleophile, may instead react with itself, either inter- or intramolecularly. The intramolecular cyclization is the overwhelming reaction when cyclopropane or cyclopentane rings can result.[3]

We became acutely aware of this problem in recent attempts to prepare C_2- and C_4-substituted malonic esters with displaceable groups at the end of the chain, positioned for subsequent nucleophilic displacement. The various devices attempted and the ultimate solution to this problem, which has led to a generally useful variation of the malonic ester synthesis, are the subject of this report.

For the preparation of the (2-bromoethyl)malonate, or its surrogate, we first considered the (2-hydroxyethyl)-malonate as a potential intermediate. Although the preparation of diethyl (2-hydroxyethyl)malonate (1) has been reported[4] from 2-chloroethanol and sodiomalonate, in our hands this was a poor reaction. However, alkylation with 2-(benzyloxy)ethyl chloride[5] followed by hydrogenolysis did provide an effective preparation of 1. Many attempts were then made under a variety of conditions to convert 1 to the 2-bromoethyl derivative, but all failed.

The possibility of using the corresponding cyclopropane derivative, e.g., 1,1-bis(ethoxycarbonyl)cyclopropane, was suggested by its susceptibility to ring opening by nucleophilic attack.[6] However, the harsh reaction conditions required made this procedure of no value with the nucleophiles we had in mind. The alternative of using the acylal cyclopropane (Meldrum's acid), where cleavage occurs under milder conditions,[7] also was not compatible with our nucleophiles and subsequent manipulations anticipated for the substitution products.

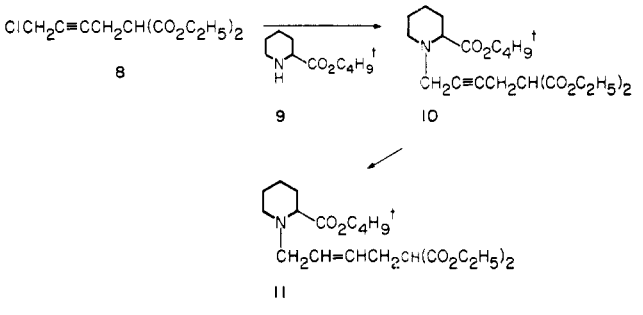
Alkylidenemalonates 2, 3, and 4 offered a more promising approach. They can be easily prepared,[8] and the double bond prevents ring formation. Moreover, bromination with *N*-bromosuccinimide (NBS) gives good yields of the corresponding allylic bromides. In the case



of the propylidene and isobutylidene derivatives 6 and 7, respectively, these allylic bromides react cleanly with secondary amines to give exclusively the unrearranged substitution products.[9] However, with the ethylidene derivative 5 the reaction takes an entirely different course. Michael addition occurs first, and the intermediate carbanion undergoes intramolecular cyclization by displacement of bromide ion, forming the aminocyclopropane.[9]

Similar frustrations were encountered in the attempted preparation of the (4-bromobutyl)malonate. Although this material has been reported[10] as a product from the reaction of 1,4-dibromobutane and the malonic ester anion, we were unable to prepare it. This failure is not surprising in view of the speed of cyclopentane formation.[3,11]

The solution appeared to be avoidance of ring closure by insertion of an unsaturation. The 1,4-dichloro-2-butenes cannot be used very effectively because of the large variety of products obtained by alkylation,[2] but 1,4-dichlorobutyne offered a favorable alternative. Thus malonic ester was alkylated to give the 4-chloro-2-butynyl derivative 8 which reacted in a straightforward manner with the nucleophile *tert*-butyl pipecolate (9) to give the N-substituted pipecolate 10. This butyne could be reduced to the butene 11 (probably cis) with a Lindlar-type catalyst. Up to this point, this approach is a good method and has avoided the previous pitfalls; however, further manipulations involving acid, which caused isomerization of the double bond, and hydrogenation, which led to significant allylic hydrogenolysis, point out its deficiencies.



As a general solution to the problems encountered in both of the above examples, we need an effective blocking

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group for a malonic ester hydrogen. Such a blocking group should tolerate subsequent nucleophilic displacements and should allow facile regeneration of the malonate active hydrogen. Another alkoxycarbonyl group seemed to offer the necessary versatility, and we have developed the methodology for implementation of this proposal.

The literature teaches that trialkyl methanetricarboxylates were first prepared in 1882,[12] and, though rarely referred to since then, convenient syntheses of both the trimethyl and triethyl esters are now available[13] from the respective malonates. Only three reports[14] have appeared on their alkylation, but these indicated the process should be straightforward. The remaining question was whether compatible conditions could be found for the deblocking step, i.e., the decarbalkoxylation.

The general approach is shown in Scheme I and consists of formation of a symmetrical or unsymmetrical triester (**12**). This is then converted to the sodio derivative **13**, alkylated to the completely substituted methane **14**, and then deblocked to regenerate the malonate **15** after the desired manipulation has been carried out with side chain R″.

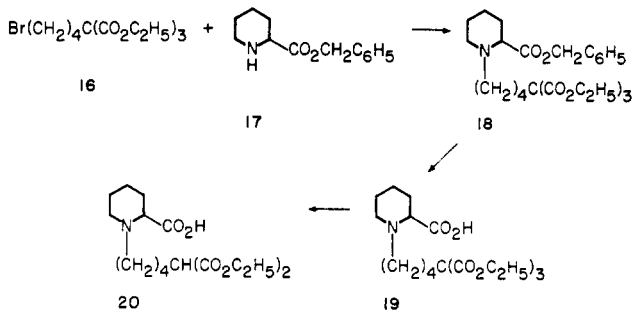
In practice, we have found that triethyl sodiomethanetricarboxylate (**13**) is easily formed and is a stable, nonhygroscopic salt that can be prepared in quantity, stored for long periods, and conveniently weighed out when needed. It is readily alkylated with alkyl halides (butyl bromide) and α,ω-dihalides (1,2-dibromoethane, 1,4-dibromobutane) to give the triesters **14** in high yields.

To develop deblocking methods, we used triethyl pentane-1,1,1-tricarboxylate as a substrate. Following an earlier observation,[15] we found that alkoxides (ethoxide, isopropoxide, *tert*-butoxide, benzyl oxide) effect this decarbalkoxylation virtually instantaneously to form the malonate and the corresponding carbonate. A small but finite amount of transesterification occurs so that if this process is to be used in the presence of other esters, as may be desirable, some side products will be introduced.

This minor disadvantage can be overcome by using lithium diisopropylamide as the nucleophile. Deblocking occurs readily below 0 °C, the only product being ethyl *N,N*-diisopropylcarbamate. Alternatively, deblocking is cleanly effected with BCl_3/CH_2Cl_2 at 5 °C. Further deblocking experiments with neutral nucleophiles such as H_2O/Me_2SO, H_2O/Me_2SO/LiCl, LiCl/pyridine, and LiI/DMF, with and without added cyanide,[16] all led to mixtures of products. However, excess LiCl in refluxing Me_2SO gave bisdecarbalkoxylation and an excellent yield of the monoester.

To further increase the scope of this method, we explored the use of an unsymmetrical triester. The *tert*-butyl diethyl methanetricarboxylate (**13**) was best prepared from *tert*-butyl ethyl malonate and ethyl chloroformate. Alkylation of its sodium salt proceeded as did previous alkylations. Now deblocking required the removal of a *tert*-butyl ester, and this was easily done in formic or trifluoroacetic acid at room temperature. Thus, depending on the triester, deblocking conditions are available that include alkoxide, diisopropylamide, boron trichloride, and formic or trifluoroacetic acid.

Scheme II



A comprehensive illustration of the utility of this new method is shown in Scheme II. Bromopentane triester **16** with benzyl pipecolate (**17**) gave a good yield of the N-alkylated pipecolate ester **18**. Hydrogenolysis then converted benzyl ester **18** to the N-substituted pipecolic acid **19**. Treatment of this amino acid with ethoxide/ethanol resulted in clean decarbethoxylation, and the pure *N*-[5,5-bis(ethoxycarbonyl)-*n*-pentyl]pipecolic acid (**20**) was obtained as its hydrochloride. Further applications of this method, particularly for the preparation of intermediates in the syntheses of 1-azabicyclo compounds via iminium salts,[17] are under investigation.

Experimental Section[18]

2-(Benzyloxy)ethyl chloride, bp 97–98 °C (5 mm) [lit.[5] bp 124 °C (20 mm)], was prepared in 79% yield from 2-(benzyloxy)ethanol and thionyl chloride following the literature procedure.[5]

Diethyl [2-(benzyloxy)ethyl]malonate, bp 138–140 °C (1 mm) [lit.[5] bp 213 °C (20 mm)], was prepared by the same method as used for the corresponding propyl compound.[19]

Diethyl (2-Hydroxyethyl)malonate (1). A mixture of 2.00 g (9.0 mmol) of diethyl [2-(benzyloxy)ethyl]malonate and 0.22 g of 10% palladium on charcoal in 40 mL of 95% ethanol was hydrogenated at room temperature and 50 psi for 16 h by using a Parr hydrogenation apparatus. The catalyst was removed by filtration and the solvent evaporated to give 1.10 g (80%) of an oil which was not further purified: IR 3330, 2875, 1710 cm^{-1}; NMR δ 1.25 (t, 6 H, J = 6 Hz), 2.00 (m, 2 H), 2.67 (s, 1 H, OH), 3.40 (t, 1 H, J = 7 Hz), 3.58 (t, 2 H, J = 5.5 Hz), 4.28 (q, 4 H, J = 6 Hz).

Diethyl (4-Chloro-2-butynyl)malonate (8). To a solution of sodium (2.2 g, 94 mmol) dissolved in absolute ethanol was added diethyl malonate (30.0 g, 28.6 mL, 188 mmol), and the mixture was heated to 60 °C with stirring for 1 h. After the solution was cooled to room temperature and ether added (25 mL), a solution of 1,4-dichloro-2-butyne (11.6 g, 94 mmol) in 50 mL of ether cooled to 5 °C was added quickly, and the resulting mixture was stirred briefly and then left at room temperature for 20 h. The mixture was then poured into water (200 mL), the layers were separated, the aqueous layer was extracted with ether (3 × 100 mL), and the combined organic phase was washed with water and saturated brine. The solution was dried and evaporated, and the residue was short-path Claisen distilled to 80 °C (0.01 mm) and Kugelrohr distilled to 150 °C (0.01 mm). The Kugelrohr-distilled fraction was redistilled, bp 135–137 °C (1.5 mm), to give 9 g (36.5 mmol, 39%) of 8 as a colorless liquid: NMR δ 1.3 (t, 6 H), 2.8 (m, 2 H),

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(18) All solvents were dried over $MgSO_4$ prior to evaporation in vacuo with a Berkeley rotary evaporator. NMR spectra were determined in $CDCl_3$ solution with internal Me_4Si, and IR spectra were recorded for liquid films unless otherwise indicated. Elemental analyses were performed by the Analytical Laboratory, Department of Chemistry, University of California, Berkeley.

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3.6 (m, 1 H), 4.1 (m, 2 H), 4.3 (q, 4 H); IR 2930, 2210 (weak), 1720, 1360, 1255, 1230 cm^{-1}. Anal. Calcd for $C_{11}H_{15}ClO_4$: C, 53.6; H, 6.1. Found: C, 53.6; H, 6.2.

***tert*-Butyl Pipecolate (9).** Pipecolic acid (10 g, 77.5 mmol) was dissolved in 2 N NaOH (38.8 mL) and cooled in an ice–water bath. Benzyl chloroformate (15.4 g, 12.8 mL, 90 mmol) and 2 N NaOH (58 mL) were added simultaneously dropwise over a period of 20 min with stirring, which was continued for 1.5 h. Water (50 mL) was added, the mixture was extracted with ether (3 × 50 mL), the aqueous layer was then layered with ether, and 6 N H_2SO_4 was added to pH 1.9 in the cold mixture. The phases were separated, and the aqueous phase was extracted with two more portions of ether. The combined ether extracts were washed with water, dried, and evaporated to give 15.2 g (57 mmol, 75% yield) of *N*-(benzyloxycarbonyl)pipecolic acid which was dissolved in dichloromethane (115 mL) in a pressure bottle and cooled in ice. Concentrated sulfuric acid (1 mL) was added slowly, and then isobutylene (60 mL, 36 g, 0.64 mol) was poured in, and the bottle was shaken at 20 °C for 18 h. After being cooled in ice/CH_3OH, the bottle was opened and the contents poured into 5% $NaHCO_3$ (200 mL). The CH_2Cl_2 phase was washed with water and dried and the solvent evaporated to give *tert*-butyl *N*-(benzyloxycarbonyl)pipecolate (17 g, 53 mmol, 93% yield): IR 1685, 1720 cm^{-1}. This ester was dissolved in absolute ethanol (200 mL) and hydrogenated over PtO_2 (1.5 g) at 50 psi of H_2 for 24 h. The catalyst was removed and the solvent evaporated to give, after Kugelrohr distillation at 70–75 °C (0.1 mm), 7.9 g (42.5 mmol, 81% yield) of *tert*-butyl pipecolate: NMR δ 1.1–2.0 (m, 6 H), 1.5 (s, 9 H), 2.3–3.4 (m, 3 H), 3.3 (s, 1 H); IR 3460, 2930, 1735, 1360 cm^{-1}.

***tert*-Butyl *N*-[5,5-Bis(ethoxycarbonyl)-2-pentynyl]pipecolate (10).** Diethyl (4-chloro-2-butynyl)malonate (8; 10.4 g, 41.5 mmol), anhydrous potassium carbonate (15 g), and benzene/DMF (1/1, 50 mL) were stirred, and *tert*-butyl pipecolate (9; 7.0 g, 37.8 mmol) in benzene/DMF (1/1, 30 mL) was added over a period of 8 h to the halide solution at 80 °C. The heating was continued for another 9 h, and the mixture was cooled and poured into cold 1 N HCl (300 mL). After being separated, the aqueous layer was extracted with ether (2 × 75 mL), adjusted to pH 10 by the addition of K_2CO_3, and extracted again with ether. The combined ether extracts were washed with water and evaporated, and the residue was dissolved in benzene and washed with water (2 × 50 mL). Evaporation of the benzene gave analytically pure product: 11.4 g, 29 mmol, 76% yield; GC (5-ft glass column, 5% SE-30, 225 °C, He at 125 mL/min) R_t 3 min 16 s; NMR δ 1.3 (t, 6 H), 1.3–2.0 (m, 15 H), 2.2–3.2 (m, 5 H), 3.3–3.7 (m, 3 H), 4.2 (q, 4 H); IR 2920, 1750, 1735, 1360, 1150 cm^{-1}. Anal. Calcd for $C_{21}H_{33}NO_6$: C, 63.8; H, 8.4; N, 3.5. Found: C, 63.9; H, 8.3; N, 3.6.

***tert*-Butyl *N*-[5,5-Bis(ethoxycarbonyl)-2-pentenyl]pipecolate (11).** To a solution of *tert*-butyl *N*-[5,5-bis(ethoxycarbonyl)-2-pentynyl]pipecolate (10; 2.0 g, 5 mmol) in ethanol (25 mL) was added 5% Pd on $BaSO_4$ (40 mg) and freshly distilled quinoline (2 drops). This mixture was hydrogenated at 50 psi of H_2 for 24 h, the catalyst was filtered off, and the solvent was removed. Kugelrohr distillation of the residue gave 1.63 g (4.1 mmol, 81% yield) of pure olefinic ester 11: bp 150–160 °C (0.01 mm); GC (4-ft glass column, 3% OV-17, 240 °C, He at 100 mL/min) R_t 4 min; NMR δ 1.3 (t, 6 H), 1.0–2.0 (m, 15 H), 2.1–3.5 (m, 8 H), 4.2 (q, 4 H), 5.4–5.7 (m, 2 H); IR 2920, 1735, 1360, 1150 cm^{-1}. Anal. Calcd for $C_{21}H_{35}NO_6$: C, 63.4; H, 8.9; N, 3.5. Found: C, 63.2; H, 8.7; N, 3.5.

Triethyl methanetricarboxylate (12, R = R′ = C_2H_5) was prepared by a literature method:[13] NMR δ 1.25 (t, 9 H), 4.15 (s, 1 H), 4.20 (q, 6 H).

Triethyl sodiomethanetricarboxylate (13, R = R′ = C_2H_5) was prepared by adding with stirring a solution of 1.26 g of sodium in 15 mL of absolute ethanol to a solution of 12.70 g of triethyl methanetricarboxylate in 40 mL of anhydrous ether, cooled in an ice bath. The white sodium salt that precipitated was collected, washed with anhydrous ether, and dried in vacuo to give 11.30 g (83%) of 13[15] as a nonhygroscopic white powder.

Triethyl 3-Bromopropane-1,1,1-tricarboxylate (14, R = R′ = C_2H_5, R″ = $BrCH_2CH_2$). To 8.40 g (33.0 mmol) of triethyl sodiomethanetricarboxylate (13) dissolved in 40 mL of benzene/DMF (1/1) was added 12.40 g (66.0 mmol) of 1,2-dibromoethane, and the solution was heated at 90 °C for 10 h. The mixture was cooled to room temperature and filtered, more benzene was added to the filtrate, and the DMF was washed out by extraction with water. After the solvent was dried and evaporated, 10.15 g of residue resulted which was Kugelrohr distilled to yield 9.44 g (91%) of product: NMR δ 1.25 (t, 9 H), 2.52 (m, 2 H), 3.45 (m, 2 H), 4.18 (q, 6 H). MS Calcd for $C_{12}H_{20}O_6Br$: *m/e* 399.0449, 341.0427. Found: *m/e* 339.0444, 341.0424.

Triethyl 5-Bromopentane-1,1,1-tricarboxylate (14, R = R′ = C_2H_5, R″ = $Br(CH_2)_4$). Triethyl sodiomethanetricarboxylate (13; 10.0 g, 39.4 mmol) was dissolved in 100 mL of benzene/DMF (1/1). 1,4-Dibromobutane (17.0 g, 78.8 mmol) was then added, the solution was heated at 85 °C for 20 h, and 100 mL of benzene was added after cooling. This solution was then washed three times with H_2O, dried, and fractionally distilled. The product was collected at 120–125 °C (0.05 mm): yield 9.95 g (27 mmol, 70%); NMR δ 1.3 (t, 9 H), 1.5–2.4 (m, 6 H), 3.25–3.6 (m, 2 H), 4.25 (q, 6 H); IR 3025, 1740, 1355, 1250 cm^{-1}. Anal. Calcd for $C_{14}H_{23}O_6Br$: C, 45.8; H, 6.3. Found: C, 46.0; H, 6.3.

Triethyl pentane-1,1,1-tricarboxylate (14, R = R′ = C_2H_5, R″ = $CH_3(CH_2)_3$) was prepared by following the same procedure as above from triethyl sodiomethanetricarboxylate (25.4 g, 0.1 mol) and 1-bromobutane (27.4 g, 0.2 mol) in 260 mL of benzene/DMF (1/1), giving product boiling at 125–130 °C (1 mm) [lit.[14] bp 152–154 °C (10 mm)] in 85% yield (24.5 g, 0.85 mol): NMR δ 1.3 (t, 9 H), 0.6–2.3 (m, 9 H), 4.2 (q, 6 H); IR 3100, 1750, 1360, 1260 cm^{-1}.

Decarbethoxylation of Triethyl Pentane-1,1,1-tricarboxylate to Diethyl Pentane-1,1-dicarboxylate. All of the following reactions were monitored by GC on a 5-ft glass column packed with 5% SE-30 at 150–160 °C and a He flow of 60 mL/min. The retention time of the triester was 5.0 min and that of the diester was 1.5 min. The other product of the reaction, the carbonate or carbamate, was identified by comparison with an authentic sample.

A. With Alkoxide. To alcohol-free sodium alkoxide (methoxide, ethoxide, isopropoxide, benzyl oxide, 6.25 mmol) suspended in 15 mL of solvent (Me_2SO, THF, DMF) was added the triester (5 mmol) in 5 mL of the same solvent. GC analysis showed the reaction was complete and quantitative before 10 min had elapsed at room temperature. For preparative experiments, equal volumes of benzene and 1 N HCl were added, and the organic layer was separated, washed three times with H_2O, dried, and distilled.

B. With Lithium Diisopropylamide. The triester (0.4 g, 1.39 mmol) in THF (2.5 mL) was added at once to a solution of LDA [from the addition of an *n*-butyllithium/hexane solution (2.5 M, 0.85 mL, 2.1 mmol) to a mixture of diisopropylamine (0.25 g, 2.5 mmol) in 2.5 mL of THF] at 0 °C with stirring. After 1.5 h GC showed only peaks corresponding to the diester and ethyl *N*,*N*-diisopropylcarbamate.

C. With Boron Trichloride. The triester (0.9 g, 3 mmol) was mixed with methylene chloride (9 mL) and cooled to 5 °C in an ice bath. Boron trichloride gas was bubbled in slowly for 3 h, then cold 10% aqueous Na_2CO_3 was added, and the organic phase was separated, dried, and evaporated. GC analysis showed the presence of only the malonate.

Decarbethoxylation of Triethyl Pentane-1,1,1-tricarboxylate to Ethyl Hexanoate. This reaction was monitored by GC as above. The retention time of the monoester was 1.0 min at 120–125 °C. A mixture of the triester (0.5 g, 1.7 mmol), lithium chloride (0.22 g, 5.2 mmol), water (0.03 mL, 1.7 mmol), and Me_2SO (3 mL) was heated at reflux for 2 h. The cooled reaction mixture was then diluted with water (6 mL) and hexane (3 mL), and NaCl was added to saturate the aqueous phase. GC analysis of the organic phase showed ethyl hexanoate as the only product.

Diethyl *tert*-Butyl Sodiomethanetricarboxylate (13, R = C_2H_5, R′ = *t*-C_4H_9). Ethyl *tert*-butyl malonate (3.7 g, 0.02 mol) was added to sodium sand (0.46 g, 0.02 mol) in THF (40 mL), and the mixture was heated at 50 °C with stirring for 4 h after which it was cooled to 5 °C. Ethyl chloroformate (3.3 g, 2.9 mL, 0.03 mol) in THF (5 mL) was added dropwise with vigorous stirring over a period of 5 min. The temperature was then raised to 50 °C for 0.5 h at which time GC analysis showed complete

consumption of starting material. The mixture was poured into cold 1 M phosphate buffer (100 mL, pH 2.5), ether (40 mL) was added, the layers were separated, and the aqueous portion was extracted with ether (2 × 25 mL). The combined ether phase was washed with water and saturated brine and dried, the solvent was evaporated, and the light yellow residue was Kugelrohr distilled at 80–85 °C (0.01 mm) to yield 3.1 g (0.012 mol, 60%) of product. To this diethyl *tert*-butyl triester (1.9 g, 7.3 mmol) dissolved in ether (8 mL) and cooled to 5 °C was added with stirring a solution of sodium in ethanol (2.9 mL of 2.5 M solution, 7.5 mmol, from dissolving 0.4 g of sodium in 7 mL of ethanol). After the addition was completed, the stirring was continued for 10 min. The white paste was transferred to a fritted glass funnel, washed with ether, and dried in vacuo; yield 1.7 g (6 mmol, 85%). Anal. Calcd for $C_{12}H_{19}O_6Na$: C, 51.1; H, 6.8. Found: C, 50.7; H, 6.7.

Diethyl *tert*-Butyl Pentane-1,1,1-tricarboxylate (14, R = C_2H_5, R′ = C_4H_9, R″ = $CH_3(CH_2)_3$). Diethyl *tert*-butyl sodiomethanetricarboxylate (3.0 g, 10.6 mmol) was dissolved in benzene/DMF (1/1, 30 mL). 1-Bromobutane (2.9 g, 20 mmol) was added, the solution was heated at 75 °C with stirring for 16 h and then cooled to room temperature, 50 mL of water and 40 mL benzene were added, and, after thorough mixing, the organic layer was separated and washed twice with water. After the solvent was dried and evaporated, the crude product was Kugelrohr distilled: bp 100–110 °C (0.1 mm); yield 2.7 g (8.6 mmol, 86%). Anal. Calcd for $C_{16}H_{28}O_6$: C, 60.7; H, 8.9. Found: C, 60.4; H, 8.7.

Diethyl *n*-Butylmalonate (15) by Decarbo-*tert*-butoxylation of Diethyl *tert*-Butyl Pentane-1,1,1-tricarboxylate (14). The unsymmetrical triester in either 100% formic or trifluoroacetic acid (1.0 mL/0.1 g of triester) was stirred at room temperature for 3 h. An aliquot, quenched by addition of aqueous K_2CO_3 and extracted into CH_2Cl_2, was analyzed by GC and showed the presence of only diethyl *n*-butylmalonate as the product.

Benzyl Pipecolate (17). Pipecolic acid (52.7 g, 0.41 mol), *p*-toluenesulfonic acid monohydrate (85.5 g, 0.45 mol), and benzyl alcohol (130 g, 125 mL) were dissolved in 250 mL of toluene and heated at reflux for 48 h, with a Dean–Stark trap to remove water. The mixture was cooled, poured into 1.5 L of water, and extracted with ether (3 × 300 mL). The aqueous layer was made alkaline with excess solid K_2CO_3 and then extracted with ether (3 × 300 mL). After the ether extracts were washed with water (2 × 100 mL) and dried, the ether was evaporated to give a crude product containing the desired ester and benzyl alcohol. This product was Claisen distilled [bp 100–103 °C (0.05 mm)], followed by Kugelrohr distillation, to obtain 58 g (88%) of pure (GC) benzyl pipecolate: IR 2900, 1725, 1440, 1180 cm^{-1}; NMR δ 1.2–2.1 (m, 7 H), 2.3–3.4 (m, 3 H), 5.1 (s, 2 H), 7.35 (s, 5 H).

Benzyl *N*-[5,5,5-Tris(ethoxycarbonyl)-*n*-pentyl]pipecolate (18). Benzyl pipecolate (17; 4.15 g, 19 mmol), triethyl 5-bromopentane-1,1,1-tricarboxylate (8.7 g, 23.7 mmol), benzene/DMF (1/1, 65 mL), and anhydrous K_2CO_3 (9.75 g, 71 mmol) were heated at 85 °C with vigorous stirring for 17 h. The mixture was cooled, poured into 1 M H_3PO_4 (250 mL), and extracted with ether (3 × 100 mL). The aqueous acidic solution, cooled in an ice bath, was adjusted to pH 10 with K_2CO_3 and extracted with ether (3 × 100 mL). The ether was evaporated, benzene was added, and the benzene was washed with H_2O (2 × 75 mL), dried, and evaporated to yield 4.9 g (10.3 mmol, 53%) of **18**: NMR δ 1.25 (t, 9 H), 1.0–3.3 (m, 17 H), 4.2 (q, 6 H), 5.1 (s, 2 H), 7.3 (s, 5 H); IR 3000, 1745, 1360, 1255 cm^{-1}. Anal. Calcd for $C_{27}H_{39}NO_8$: C, 64.1; H, 7.8; N, 2.8. Found: C, 64.3; H, 7.7; N, 2.8.

***N*-[5,5,5-Tris(ethoxycarbonyl)-*n*-pentyl]pipecolic Acid (19).** Benzyl *N*-[5,5,5-tris(ethoxycarbonyl)-*n*-pentyl]pipecolate (18; 2.5 g, 5.0 mmol), dissolved in absolute ethanol (50 mL), was hydrogenated over Pd/C (10%, 0.25 g) for 20 h. After filtration and evaporation of the filtrate, the residue was triturated with ether/hexane (85/15, 5 mL). Cooling resulted in **19**: mp 91–94 °C; 1.9 g (4.6 mmol, 92%); NMR δ 1.3 (t, 9 H), 1.3–3.8 (m, 17 H), 4.2 (q, 6 H), 9.3 (br s, 1 H); IR ($CHCl_3$) 3075, 1740, 1630, 1380 cm^{-1}. Anal. Calcd for $C_{20}H_{33}NO_8$: C, 57.8; H, 8.0; N, 3.4. Found: C, 57.7; H, 7.9; N, 3.5.

***N*-[5,5-Bis(ethoxycarbonyl)-*n*-pentyl]pipecolic Acid (20) Hydrochloride.** *N*-[5,5,5-Tris(ethoxycarbonyl)-*n*-pentyl]pipecolic acid (19; 1.0 g, 2.4 mmol) was added to a solution of sodium (0.115 g, 5.0 mmol) in ethanol (10 mL) and stirred at room temperature for 10 min. The solution was then cooled in an ice bath, cold 2 N HCl (5 mL, 200 mol % based on sodium used) was added slowly, and the acidic ethanol/water solution was evaporated to give an oily solid. This material was triturated with hot *tert*-butyl alcohol, the NaCl was removed, and the *tert*-butyl alcohol was evaporated, leaving 0.85 g (2.24 mmol, 93%) of **20**·HCl as a glass: NMR δ 1.3 (t, 6 H), 1.0–3.6 (m, 18 H), 4.2 (q, 4 H), 9.2 (s, 1 H); IR ($CHCl_3$) 3100, 2480, 1735, 1600, 1520, 1200 cm^{-1}. Anal. Calcd for $C_{17}H_{30}NO_6Cl$: C, 53.8; H, 8.0; N, 3.7. Found: C, 54.0; H, 8.2; N, 3.6.

Registry No. 1, 63972-17-8; 8, 71170-77-9; 9, 71170-78-0; 10, 71170-79-1; (*Z*)-11, 71170-80-4; 12 (R = R′ = C_2H_5), 6279-86-3; 12 (R = C_2H_5; R′ = *t*-C_4H_9), 71170-90-6; 13 (R = R′ = C_2H_5), 68922-87-2; 13 (R = C_2H_5; R′ = *t*-C_4H_9), 71170-81-5; 14 (R = R′ = C_2H_5; R″ = $BrCH_2CH_2$), 71170-82-6; 14 (R = R′ = C_2H_5; R″ = $Br(CH_2)_4$), 71170-83-7; 14 (R = R′ = C_2H_5; R″ = $CH_3(CH_2)_3$), 3272-32-0; 14 (R = C_2H_5; R′ = *t*-C_4H_9; R″ = $CH_3(CH_2)_3$), 71170-84-8; 15 (R = C_2H_5; R″ = $CH_3(CH_2)_3$), 133-08-4; 17, 38068-75-6; 18, 71170-85-9; 19, 71170-86-0; 20·HCl, 71170-87-1; 2-(benzyloxy)ethyl chloride, 17229-17-3; 2-(benzyloxy)ethanol, 622-08-2; diethyl [2-(benzyloxy)ethyl]malonate, 41478-45-9; diethyl malonate, 105-53-3; 1,4-dichloro-2-butyne, 821-10-3; pipecolic acid, 535-75-1; *N*-(benzyloxycarbonyl)pipecolic acid, 71170-88-2; *tert*-butyl *N*-(benzyloxycarbonyl)pipecolate, 71170-89-3; 1,2-dibromoethane, 106-93-4; 1-bromobutane, 109-65-9; 1,4-dibromobutane, 110-52-1; ethyl *tert*-butyl malonate, 32864-38-3.

3,8-Thionanedione 1,1-Dioxide. Synthesis and Solid-State Conformation[1]

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The title compound is conveniently prepared in 80% overall yield by ozonolysis at −78 °C of the cycloadduct of SO_2 with 1,2-dimethylenecyclohexane. Single-crystal X-ray analysis establishes that the nine-membered ring adopts a twist-chair–chair conformation in which the sulfur atom and the midpoint of the C(5)–C(6) bond lie on a noncrystallographic C_2 axis, but the ring shape differs significantly from that of cyclononane in order to accommodate transannular dipole···dipole interactions. Crystals are orthorhombic, space group $P2_12_12_1$, with a = 8.963 (4) Å, b = 15.403 (7) Å, c = 6.724 (3) Å, and Z = 4. Atomic positional and thermal parameters were refined by full-matrix least-squares calculations to R = 0.032 over 913 statistically significant reflections.

We recently reported[2] a simple method to obtain diketo derivatives of the rare phosphorus heterocycles with seven to nine members in the ring. The method employs the cycloaddition of a diene with a trivalent phosphorus halide

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