

Table I. Formation of α -Keto Esters from α -Azido Esters

R	reaction time, ^a min	% yield ^b
CH ₃	15	50
CH ₃ CH ₂	20	86
(CH ₃) ₂ CH	30	94
Ph	2	91
PhCH ₂	45	94 ^c

^a Time for complete evolution of nitrogen at 25 °C.

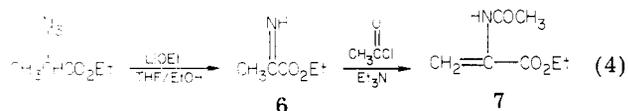
^b GLC yields, determined with internal standard, unless otherwise noted. In all cases, removal of solvent left a residue of essentially pure (¹H NMR analysis) α -keto ester.

^c Yield of distilled product.

aqueous sodium hydroxide/THF resulted in disappearance of starting ester by GLC analysis but no nitrogen was evolved.

Addition of 4 (R = Me) to 1 equiv of sodium ethoxide in ethanol at 25 °C gave slow (8 h) and quantitative evolution of nitrogen. Hydrolysis of the yellow reaction mixture gave minor amounts (<10%) of ethyl pyruvate (5, R = Me). Similar reactions conducted in THF solution were much faster, and reasonable rates (<15 min) could be achieved even with catalytic amounts (0.5–0.05 equiv) of ethanolic sodium ethoxide. These reaction mixtures turned light yellow and quenching gave 50–70% yields of 5 (R = Me). However, even with scrupulous protection from atmospheric oxygen and moisture, our stock solutions of ethanolic sodium ethoxide deteriorated rapidly. To obtain maximum yields of 5 it was necessary to use freshly prepared solutions of the alkoxide. Fortunately, lithium ethoxide served equally well and solutions of this base can be conveniently generated as needed by injection of *n*-butyllithium into small amounts of ethanol. Yields of α -keto esters obtained by adding azido esters to THF/ethanol suspensions of lithium ethoxide are shown in Table I.

Attempts to isolate ethyl 2-iminopropanoate (6) by distillation of unhydrolyzed reaction mixtures were unsuccessful. The pot contents turned dark on heating and eventually formed a nonvolatile tar. However, careful evaporation of solvent at 25 °C from freshly prepared reaction mixtures gave a residue of essentially pure 6 as judged by ¹H NMR analysis. Alternatively, addition of triethylamine and acetyl chloride to the unhydrolyzed reaction mixture gave a 60% isolated yield of the corresponding *N*-acetyl derivative 7 (eq 4).



More simply, verification of dehydroamino ester formation was obtained by reaction of 4 with lithium ethoxide in CCl₄/ethanol solution. Direct ¹H NMR analysis of the reaction mixtures indicated essentially quantitative formation of dehydroamino esters [3, R = Me, Et (a mixture of imino and enamine esters was formed), and Ph].

Both α -keto esters and dehydroamino esters are compounds of biological importance.^{4,5} The present procedure

offers advantages in both simplicity and availability of starting materials over previously reported procedures.^{6,7}

Experimental Section

All solvents were distilled before use. Acetyl chloride, *n*-butyllithium, ethyl 2-bromopropanoate, ethyl 2-bromobutanoate, and 2-bromo-2-phenylacetic acid were obtained from Aldrich Chemical. Ethyl 2-bromo-3-methylbutanoate was prepared by the method of Rathke.⁸ 2-Bromo-3-phenylpropanoic acid was prepared by the method of Marvel⁹ and esterified by standard procedures. All reactions were conducted under argon atmosphere. Gas chromatographic data were obtained on a Varian 920 chromatograph equipped with a 4 ft \times 0.25 in. column packed with 10% Carbowax 20M terephthalate on Chromosorb G. ¹H NMR spectra were recorded on a Varian T-60 spectrometer and are reported in parts per million relative to Me₄Si. Infrared spectra were taken on a Perkin-Elmer 237 B spectrometer, using polystyrene as a reference. Mass spectra were obtained with a Finnegon 4000 GC/MS. Melting points are uncorrected. Yields of azides are not maximized and ranged from 50–85%.

General Procedure for Preparation of Azides (4). Ethyl 2-azidopropanoate¹⁰ (4, R = Me). Ethyl 2-bromopropanoate (65 mL, 0.50 mol) was added to a suspension of sodium azide (49 g, 0.76 mol) in 50 mL of dimethylformamide at 25 °C and stirred for 2.5 h. After addition of 200 mL of water, the solution was extracted with two 50-mL portions of CH₂Cl₂. The combined organic layers were washed with 200 mL of water, dried (MgSO₄), and concentrated in vacuo. Distillation afforded 51.01 g (72%) of 4 (R = Me) as a clear, colorless oil: bp 36–40 °C (0.5 torr); ¹H NMR (CDCl₃) 4.18 (q, 2 H), 3.90 (q, 1 H), 1.42 (d), and 1.28 (t) (total 6 H); IR (neat) 2100 (s, CN₃), 1745 (s, C=O) cm⁻¹; mass spectrum, *m/e* 143 (M⁺), 73, 70, 56, 42.

Ethyl 2-azidobutanoate (4, R = Et) was prepared as above: bp 38–40 °C (0.15 torr); NMR (CDCl₃) 4.20 (q, 2 H), 3.73 (t, 1 H), 1.82 (m, 2 H), 1.30 (t) and 1.00 (t) (total 6 H); IR (neat) 2100 (s, CN₃), 1745 (s, C=O) cm⁻¹; mass spectrum, *m/e* 157 (M⁺), 84, 73, 69, 56.

Ethyl α -azidoisovalerate¹¹ (4, R = (CH₃)₂CH) was prepared as above: bp 45–45.5 °C (0.35 torr); NMR (CDCl₃) 4.13 (q, 2 H), 3.57 (d, 1 H), 2.08 (m, 1 H), 1.27 (t) and 1.00 (dd) (total 9 H); IR (neat) 2090 (s, CN₃), 1730 (s, C=O) cm⁻¹; mass spectrum *m/e* 171 (M⁺), 102, 70, 43.

Ethyl 2-azidophenylacetate¹² (4, R = Ph) was prepared as above: bp 85–88 °C (0.05 torr); NMR (CDCl₃) 7.28 (s, 5 H), 4.87 (s, 1 H), 4.08 (q, 2 H), 1.10 (t, 3 H); IR (neat) 2100 (s, CN₃), 1735 (s, C=O) cm⁻¹; mass spectrum, *m/e* 205 (M⁺), 163, 132, 104, 77, 51.

Ethyl 2-azido-3-phenylpropanoate¹³ (4, R = PhCH₂) was prepared as above: bp 107–107.5 °C (0.05 torr); NMR (CDCl₃) 7.10 (s, 5 H), 3.8–4.3 (m, 3 H), 2.85–3.10 (dd, 2 H), 1.15 (t, 3 H); IR (neat) 2100 (s, CN₃), 1700 (s, C=O) cm⁻¹; mass spectrum, *m/e* 219 (M⁺), 191, 176, 91.

General Procedure for Preparation of Dehydroamino Esters (3). Ethyl 2-iminopropanoate (3, R = Me). Ethanol (0.05 mL, 0.8 mmol) was added to *n*-butyllithium (1.6 M, 0.32 mL, 0.5 mmol) in hexane. The mixture was dissolved in 5 mL of CCl₄ at 25 °C. Ethyl 2-azidopropanoate (4, R = Me) was added dropwise and stirred at 25 °C until 125 mL (5 mmol) of N₂ was evolved (20 min). Benzene (0.22 mL, 2.5 mmol) was added, and the yield was determined by ¹H NMR¹⁴ analysis: yield 100%; ¹H NMR (CCl₄) 10.91 (br s, 1 H), 4.24 (q, 2 H), 2.29 (s, 3 H), 1.41 (t, 3 H).

Ethyl 2-iminobutanoate (3, R = Et) was prepared as above: yield 100%¹⁴ (mixture of imine and enamine); partial ¹H NMR

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(CCl₄) for imine, 2.64 (q, 2 H); partial NMR (CCl₄) for enamine, 5.54 (q, 1 H, *J* = 7 Hz), 1.70 (d, 3 H, *J* = 7 Hz).

Ethyl 2-iminophenylacetate (3, R = Ph) was prepared as above: yield 100%; ¹H NMR (CCl₄) 10.5 (s, 1 H), 7.3-8.0 (m, 5 H), 4.20 (q, 2 H), 0.85 (t, 3 H).

N-Acetyl-2,3-dehydroalanine (7). Imine 3 (R = Me) was prepared as above. Triethylamine (0.77 mL, 5.5 mmol) was added and the solution cooled to 0 °C. Acetyl chloride (0.54 mL, 5.5 mmol) was added dropwise. The mixture was filtered, concentrated in vacuo, and the residue purified by bulb-to-bulb distillation, giving 0.42 g (58%) of pale yellow oil; ¹H NMR (CDCl₃) 8.20 (br s, 1 H), 6.58 (s, 1 H), 5.90 (br s, 1 H), 4.40 (q, 2 H), 2.27 (s, 1 H), 1.46 (t, 3 H).

General Procedure for Preparation of α -Keto Esters (5). **Ethyl 2-Oxobutanoate (5, R = Et).** Ethanol (0.05 mL, 0.8 mmol) was added to *n*-butyllithium (1.6 M, 0.32 mL, 0.5 mmol) in hexane. The mixture was dissolved in 5 mL of THF and stirred at 25 °C. Ethyl 2-azidobutanoate (0.76 mL, 5.0 mmol) was added dropwise. After 20 min at 25 °C, 125 mL (5 mmol) of N₂ had evolved, and the reaction was quenched with 2 mL of 3 N HCl. The solution was extracted with two 10-mL portions of ether. The combined organic layers were dried (K₂CO₃) and concentrated in vacuo. The yield was 86% as determined by GLC: ¹H NMR (CDCl₃) 4.13 (q, 2 H), 2.70 (q, 2 H), 1.23 (t, 3 H), 1.00 (t, 3 H); 2,4-DNP, mp 139-140.5 °C (lit.¹⁵ mp 141-142 °C); mass spectrum, *m/e* 310 (M⁺).

Ethyl pyruvate (5, R = Me) was prepared as above: yield 50%; ¹H NMR (CDCl₃) 4.31 (q, 2 H), 2.45 (s, 3 H), 1.50 (t, 3 H); 2,4-DNP, mp 154.5-155 °C (lit.¹⁶ mp 154.5-155 °C); mass spectrum, *m/e* 296 (M⁺).

Ethyl α -oxoisovalerate (5, R = (CH₃)₂CH) was prepared as above: yield 94%; NMR (CDCl₃) 4.25 (q, 2 H), 3.20 (m, 1 H),

1.35 (t, 3 H), 1.17 (d, 6 H); 2,4-DNP, mp 172.5-173.5 °C (lit.¹⁷ mp 171.5-172 °C); mass spectrum, *m/e* 324 (M⁺).

Ethyl phenylglyoxylate (5, R = Ph) was prepared as above: yield 91%; ¹H NMR (CDCl₃) 7.20-8.00 (m, 5 H), 4.37 (q, 2 H), 1.23 (t, 3 H); 2,4-DNP, mp 161-162.5 °C (lit.¹⁸ mp 162-163.5 °C); mass spectrum, *m/e* 358 (M⁺).

Ethyl phenylpyruvate (5, R = PhCH₂) was prepared as above. The residue was purified by bulb-to-bulb distillation, affording a 94% yield of clear, light yellow oil identified as the keto ester containing a small amount of enol:¹⁹ ¹H NMR (CDCl₃) of keto form, 7.25 (s, 5 H), 4.30 (q, 2 H), 4.15 (s, 2 H), 1.40 (t, 3 H); 2,4-DNP, mp 132.5-133 °C (lit.²⁰ mp 132.5-133 °C); mass spectrum, *m/e* 372 (M⁺).

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Registry No. 3 (R = Me), 75213-99-9; 3 (R = Et), 75214-00-5; 3 (R = Ph), 75214-01-6; 4 (R = Me), 71754-74-0; 4 (R = Et), 2571-38-2; 4 (R = (CH₃)₂CH), 75214-02-7; 4 (R = Ph), 75214-03-8; 4 (R = PhCH₂), 75214-04-9; 5 (R = Et), 15933-07-0; 5 (R = Me), 617-35-6; 5 (R = Me) 2,4-DNP derivative, 17767-38-3; 5 (R = (CH₃)₂CH), 20201-24-5; 5 (R = Ph), 1603-79-8; 5 (R = Ph) 2,4-DNP derivative, 3602-40-2; 5 (R = PhCH₂), 6613-41-8; 5 (R = PhCH₂) 2,4-DNP derivative, 50838-93-2; 7, 23115-42-6; ethyl 2-bromopropanoate, 535-11-5; ethyl 2-bromobutanoate, 533-68-6; ethyl 2-bromo-3-methylbutanoate, 609-12-1; ethyl α -bromobenzenoacetate, 2882-19-1; ethyl α -bromobenzenepropanoate, 39149-82-1; lithium ethoxide, 2388-07-0; 5 (R = Et) 2,4-DNP derivative, 75214-05-0; 5 (R = (CH₃)₂CH) 2,4-DNP derivative, 50838-92-1.

(14) Yields based on integration of product peaks relative to benzene standard.

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Synthesis of Triamantane

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Triamantane, the third member of the diamondoid hydrocarbon series, has been synthesized efficiently in five easy stages from norbornadiene. Acid-catalyzed rearrangement of the norbornadiene [4 + 4] dimer, binor S (5), either in solution using silver perchlorate or in the gas phase on silica gel, gives two hexacyclic olefins (13 and 14) suitable (without separation) for further elaboration: [4 + 2] cycloaddition with butadiene gives C₁₈ adducts whose hydrogenated forms (26 and 27) are converted by aluminum chloride catalyzed rearrangement into triamantane in 60% yield. By use of isoprene instead of butadiene in the cycloaddition stage the synthesis can be modified to produce 9-methyltriamantane. The mechanism of the binor S rearrangement is discussed.

The diamondoid hydrocarbons adamantane (1)¹ and diamantane (2)^{2,3} are best prepared by Lewis acid catalyzed rearrangement of tetrahydrodicyclopentadiene (3) and tetrahydrobinor S (4), respectively.^{4,5} These precursors

are readily available, the former from hydrogenation of cyclopentadiene dimer and the latter from hydrogenolytic opening of the cyclopropane rings of the [4 + 4] norbornadiene dimer, binor S (5).⁶ Although triamantane (6), the third member of the diamondoid series, has also been synthesized by rearrangement routes, the polycycles (7)⁷

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