Synthesis and Pyrolysis of Hydrazine and Phenylhydrazine Adducts of Tetraethyl Ethylenetetracarboxylate

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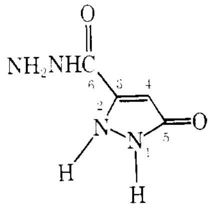
The reaction of tetraethyl ethylenetetracarboxylate with hydrazine produces 4,5,5-tricarbethoxy-3-pyrazolidinone, while reaction with phenylhydrazine produces tetraethyl phenylhydrazinoethanetetracarboxylate. Pyrolysis, or better, the lead tetraacetate oxidation of the former product, gives rise to triethyl ethylenetricarboxylate (4 and 55% yields, respectively). Pyrolysis of the phenylhydrazino adduct at 180 °C yields tetraethyl ethanetetracarboxylate (62%) and tetraethyl ethylenetetracarboxylate (20%). Evidence is presented that the previously reported reduction of tetraethyl ethylenetetracarboxylate to the saturated ester by phenylhydrazine involves the thermal decomposition of the phenylhydrazino adduct of the unsaturated ester. The product arising from the reaction of hydrazine with ethyl maleate or fumarate is shown to be 5-oxo-3-pyrazoline-3-carbohydrazide.

The products obtained from the interaction of dibasic α,β-unsaturated acids with hydrazine depend upon the solvent and reaction time. Thus maleic and fumaric acids are converted into maleic hydrazide (1,2-dihydro-3,6-pyridazinedione)[1] on short reaction times and into 5-oxo-2-pyrazoline-3-carbohydrazide[2] on longer reaction times. Esters of these acids react likewise with hydrazine to produce the substituted pyrazolinone[2] in ca. 50% yield. The product apparently arises by the dehydrogenation of the initially formed pyrazolidinone. Indeed, in most of the previously reported additions of hydrazine[3,4] and phenylhydrazine[5] to α,β-unsaturated esters, the pyrazolidinone is the major product. Methyl cinnamate, however, does not undergo cyclization with phenylhydrazine; instead the unsaturated hydrazide is formed.[5]

Because of the unusually extensive dehydrogenation observed in the reaction product of hydrazine with maleic and fumaric acids and their esters[2] (reported to form 5-oxo-2-pyrazoline-3-carbohydrazide), this reaction was reinvestigated. Spectral evidence indicates that the product obtained in this reaction is 5-oxo-3-pyrazoline-3-carbohydrazide (4) rather than the isomeric 5-oxo-2-pyrazoline previously assigned.[2] Proton NMR spectroscopy shows a vinylic hydrogen (singlet) superimposed on a broad low intensity peak, and proton-coupled ^{13}C NMR spectroscopy shows a doublet centered at 88.93 ppm (J = 178 Hz), corresponding to carbon 4, a doublet with small coupling at 138.34 ppm (J = 0.26 Hz, carbon 3), and a singlet at 160.08 ppm (coincidental carbonyls). The existence of coincidental carbonyl chemical shifts was verified by integration.[7] The ultraviolet spectrum (λ_{max} 217 nm) supports the presence of a carbon–carbon double bond rather than a carbon–nitrogen double bond[8] in the molecule.



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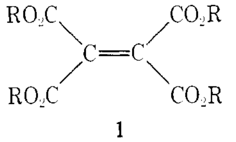
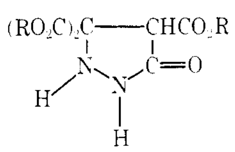
To determine whether esters of ethylenetetracarboxylic acid behave in the same way as maleic and fumaric acid esters, the interaction of 1 with hydrazine and phenylhydrazine was investigated as well as the pyrolytic behavior of the products.

The tetraethyl and tetramethyl esters (1) react readily with hydrazine in ether to give the corresponding pyrazolidinones (**2a** and **2b**) in 69 and 50% yields, respectively. The bisadduct, N,N'-bis(1,1,2,2-tetracarbomethoxyethyl)hydrazine (3; 17% yield), was isolated in addition to the pyrazolidinone in the methyl ester–hydrazine reaction.

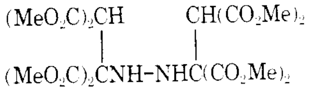


1



2

a, R = C_2H_5; b, R = CH_3

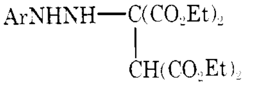


$$\begin{array}{cc} (MeO_2C)_2CH & CH(CO_2Me)_2 \\ | & | \\ (MeO_2C)_2CNH\text{-}NHC(CO_2Me)_2 & \end{array}$$

3

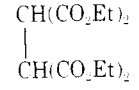
When **2a** was pyrolyzed at 260 °C (injection port of gas chromatograph), dehydrogenation and subsequent loss of nitrogen and carbon monoxide occurred, producing triethyl ethylenetricarboxylate in 4% yield. Similar dehydrogenations, followed by elimination of nitrogen and carbon monoxide, have been observed in the oxidative dehydrogenation of pyrazolidinones with mercuric oxide[3] and lead tetraacetate.[6] Accordingly, treatment of **2a** and **2b** with lead tetraacetate produced the corresponding esters of ethylenetricarboxylic acid in 55–58% isolated yields.

Treatment of an ether solution of **1a** with phenylhydrazine produced the adduct tetraethyl phenylhydrazinoethanetetracarboxylate (**5**) rather than the expected cyclized product or hydrazide. When **5** was heated to 165–175 °C in an attempt to effect cyclization, tetraethyl ethanetetracarboxylate (**6**) was produced in 45% isolated yield along with benzene, ethanol, nitrogen, and carbon dioxide. In an earlier report, Bischoff[9] found that the tetrahydrazide produced in the reaction of excess phenylhydrazine with tetraethyl ethylenetetracarboxylate was identical with the tetrahydrazide obtained from reaction of phenylhydrazine with the saturated ester **6**. In addition, **6** could be isolated from the mother liquors of the reaction mixture.



$$\begin{array}{l} ArNHNH\text{—}C(CO_2Et)_2 \\ \qquad\qquad\quad | \\ \qquad\qquad\quad CH(CO_2Et)_2 \end{array}$$

5



$$\begin{array}{l} CH(CO_2Et)_2 \\ | \\ CH(CO_2Et)_2 \end{array}$$

6

Our observations and those of Bischoff[9] suggest that adduct **5** is a probable intermediate in the reduction of tetraethyl ethylenetetracarboxylate with phenylhydrazine. Further support for the proposed intermediacy of **5** was obtained from

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Table I. Effect of Temperature and Contact Time on the Yields of Ester Products

Substance pyrolyzed	Temp,[a] °C	Relative contact time,[b] min	Yields of esters,[c] %		Relative %	
			6	1a	6	1a
5	180	6.5	62 ± 2	20 ± 3	76	24
5	270	6.5	46 ± 2	19 ± 3[d]	71	29
6	270	6.5	100			
1a	270	6.5		92 ± 2		
5	320	6.5	34 ± 2[d]	27 ± 1[d]	56	44
6	320	6.5	96 ± 1			
1a	320	6.5		78 ± 1		
5	260	5.7	*e*	*e*	71	29
5	260	9.6	*e*	*e*	57	43

[a] Temperature of GLC injection port. Column temperature was the same in each experiment. [b] Relative contact time expressed as retention time of ester **6**. [c] Yields were determined by GLC using an internal standard. Results are the average of triplicate runs, except for the second entry which was run in duplicate. [d] Experimental value uncorrected for ester decomposition. [e] Not determined.

an experiment in which **1a** was heated with excess phenylhydrazine on a steam bath for 0.5 h. Adduct **5** was isolated from an aliquot of the reaction mixture, and subsequent heating of the mixture at 170 °C (Bischoff method[9]) produced the saturated ester **6** in 27% yield. Adduct formation appears to be nearly instantaneous. The injection of an ether solution of adduct[10] or an ether solution of an equimolar mixture of phenylhydrazine and tetraethyl ethylenetetracarboxylate on GLC analysis produces the same ester mixture (77 ± 1% of **6** and 23 ± 1% of **1a**).

The pyrolysis of the phenylhydrazino adduct **5** suggests that two major competitive paths are involved, reduction and elimination, and that both temperature and contact time influence the extent of involvement of each path. Table I summarizes the effect of these parameters on the yields of the esters.

The production of ethanol and carbon dioxide during the pyrolysis of **5** as well as the fact that the elimination product yield remains nearly constant while the reduction product **6** yield decreases with increasing temperature indicate that additional competitive decomposition paths become more important at higher temperatures.

The conversion of adduct to saturated ester **6** is reminiscent of the formation of triphenylmethane from *N,N'*-bis(triphenylmethyl)hydrazine at 220 °C.[11] The facility of this latter decomposition may be attributed to the formation of the resonance-stabilized triphenylmethyl radical. Such a homolytic cleavage may also be involved in the decomposition of the adduct (**5**) since the carbethoxy substituents would tend to stabilize the radical intermediate or partially developed radical intermediate.

Experimental Section

Pyrolytic gas chromatographic experiments were carried out at various injection port temperatures using a 4 ft (180 °C) or a 6 ft (200 °C) × 0.125 in, 3% Silar 5CP column. Quantities of ester products were measured by electronic integration using *N*-methylcarbazole as an internal standard. A flame ionization detector and a carrier gas flow rate of 35 mL/min were used. Preparative GLC separations of products were carried out on a 10 ft × 0.375 in, 20% Dexsil 300 column heated isothermally at 125 °C (8 min) and then programmed at 4 °C/min to 250 °C. Proton NMR spectra were taken on a Varian Model T-60 spectrometer, ^{13}C NMR spectra were taken on a Varian CFT-20 spectrometer, UV spectra were taken on a Beckman Model 26 spectrometer, and mass spectra were taken on a Hitachi Perkin-Elmer RMU-6E mass spectrometer. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

4,5,5-Tricarbethoxy-3-pyrazolidinone (2a). To a stirred, refluxing solution of 3.8 g (12 mmol) of tetraethyl ethylenetetracarboxylate in 150 mL of ether was added 0.40 g (12 mmol) of 95% hydrazine dropwise. After refluxing for an additional 1.5 h, the reaction mixture was cooled and filtered to remove suspended yellow particles. Removal of the solvent produced a colorless oil which solidified on standing. Recrystallization from benzene–pentane yielded 2.5 g (69%) of white crystals, mp 75–79 °C. An analytical sample prepared by additional recrystallizations melted at 78.5–80 °C; ^{1}H NMR ($CDCl_3$) δ 1.17 (t, 9 H, CH_3), 4.00–4.47 (m, 7 H, CH_2 and CH), 5.53 (s, 1 H, NH), 8.83 (s, 1 H, N–H); ^{13}C NMR ($CDCl_3$) δ 13.87 (CH_3), 53.62 (C-4), 62.50, 62.99, 63.29 (CH_2's), 72.76 (C-5), 165.82, 166.50, 166.91, 169.14 (C=O groups). A coupled ^{13}C NMR spectrum confirmed the preceding assignments.

Anal. Calcd for $C_{12}H_{18}N_2O_7$: C, 47.68; H, 6.00; N, 9.27. Found: C, 47.82; H, 6.10; N, 9.19.

When ethanol was used as solvent, the yields of adduct varied widely (24–80%).

Triethyl Ethylenetricarboxylate. A solution of 2.01 g (6.65 mmol) of 4,5,5-tricarbethoxy-3-pyrazolidinone in 10 mL of benzene was added to a stirred suspension of 5.67 g of lead tetraacetate in 10 mL of benzene over a period of 20 min. A gas was evolved during the addition. After standing overnight, the mixture was filtered and the filtrate was shaken vigorously with ca. 5 mL of ethylene glycol, separated, extracted with 5% $NaHCO_3$, and washed several times with water. After drying over Na_2SO_4 and removal of the solvent, distillation produced 0.89 g (55%) of colorless oil: bp 118–122 °C (1.8 mm) [lit.[12] bp 155–156 °C (11 mm)]; ^{1}H NMR ($CDCl_3$) grouping of 3 triplets centered at δ 1.30 (CH_3 groups), grouping of 3 quartets centered at δ 4.32 (CH_2 groups), and a singlet at δ 6.80 (vinylic H), area ratio 9:6:1; ^{13}C NMR ($CDCl_3$) δ 13.98 (CH_3 groups), 61.81, 62.03, 62.51 (CH_2 groups), 130.10 (vinylic CH), 139.12 (vinylic C), 162.33, 163.60, 164.22 (C=O groups); MS (70 eV) *m/e* (relative intensity) 199 (9, M^+ – OEt), 171 (87, M^+ – COOEt), 154 (10), 143 (100), 126 (15), 125 (21); IR (neat) 2980, 2940, 2900, 1725, 1635, 1470, 1450, 1395, 1375, 1350, 1250, 1190, 1100, 1070, 1030, 920, 870, 800, 785, 695 cm^{-1}.

4,5,5-Tricarbomethoxy-3-pyrazolidinone (2b) and *N,N'*-Bis(1,1,2,2-tetracarbomethoxyethyl)hydrazine (3). The procedure is the same as that used in the formation of **2a**. From 5.20 g (20 mmol) of tetramethyl ethylenetetracarboxylate in 400 mL of anhydrous ether and 0.68 g of 95% hydrazine, there was obtained after recrystallization from $CHCl_3$–CCl_4 2.58 g (50%) of the pyrazolidinone as white crystals: mp 118–119 °C; ^{1}H NMR (Me_2CO-d_6) δ 2.97 (s, 2 H), 3.70 (s, 3 H), 3.74 (s, 3 H), 3.75 (s, 3 H), 3.97 (s, 1 H); ^{13}C NMR (Me_2CO-d_6) δ 53.29, 53.80, 54.14, 54.38, 73.47, 167.29, 167.86, 168.51, 169.07; MS (70 eV) *m/e* (relative intensity) 229 (1, M^+ – OMe), 201 (37, M^+ – CO_2Me), 169 (100), 137 (32), 59 (55), 53 (29).

Anal. Calcd for $C_9H_{12}N_2O_7$: C, 41.54; H, 4.65; N, 10.77. Found: C, 41.60; H, 4.35; N, 10.78.

Removal of the solvent from the filtrate left an oil which on recrystallization from methanol yielded 0.95 g (17%) of **3** as white crystals, mp 120–123 °C. Further recrystallization produced a melting point of 124–125 °C; ^{1}H NMR (Me_2CO-d_6) δ 3.60 (s, CH_3), 3.64 (s, CH_3), 4.05 (s, CH), 5.02 (s, NH); ^{13}C NMR (Me_2CO-d_6) δ 52.81 (J = 150 Hz, OCH_3), 55.29 (J = 145 Hz, C-2), 72.81 (J = 0.7 Hz, C-1), 166 (C=O), 168 (C=O); MS (70 eV) *m/e* (relative intensity) 552 (2, M^+), 521 (<1, M^+ – OMe), 493 (7, M^+ – COOMe), 229 (100), 201 (54), 171 (94), 169 (69), 141 (83).

Anal. Calcd for $C_{20}H_{28}N_2O_{16}$: C, 43.48; H, 5.11; N, 5.07. Found: C, 43.68; H, 5.21; N, 5.06.

Trimethyl Ethylenetricarboxylate. A solution of 2.00 g (7.69 mmol) of **2b** in 15 mL methylene chloride was added over a period of 40 min to 9.09 g of lead tetraacetate in 20 mL of methylene chloride. After standing for 3 h, the reaction mixture was worked up as described for the ethyl ester. The oil thus obtained solidified (1.27 g, 82%) and melted at 28–33 °C. Distillation yielded 0.90 g (58%): bp 83–85 °C (0.07–0.15 mm) [lit.[12] bp 141 °C (12 mm)]; mp 36–38 °C (lit.[12] mp 40–41 °C); ^{1}H NMR (CCl_4) δ 3.84 (s, 3 H), 3.88 (s, 3 H), 3.89

(s, 3 H), 6.99 (s, 1 H, vinylic H); IR (neat) 3000, 2950, 1730, 1650, 1440, 1360, 1270, 1210, 1175, 1075, 1020, 985, 900, 850, 785, 695 cm^{-1}.

5-Oxo-3-pyrazoline-3-carbohydrazide (4). After refluxing a mixture of 3.60 g (20.9 mmol) of diethyl fumarate and 30.3 g (60.6 mmol) of hydrazine hydrate for 3 h and cooling, there was obtained a yellow oil. The oil was dissolved in water and treated with 5 mL of acetic acid, and the precipitate was collected by filtration (1.04 g). Recrystallization from water yielded 0.83 g of white solid. The product melted at 247–255 °C only if placed on the hot stage at 240 °C (lit.[2] mp 253–254 °C). After several recrystallizations from water, melting and resolidification occurred at 258 °C. If the sample was placed on the hot stage at temperatures lower than ca. 258 °C, melting was not observed. This sample was found to contain 0.6 mol water of hydration, while earlier reports[2] indicate 0.75 mol water of hydration. An analytical sample was prepared by recrystallization several times from water: UV (H_2O) λ_{max} 217 nm (log ϵ 3.96); ^{1}H NMR (Me_2CO-d_6) δ 6.03 (s, superimposed on a low broad peak ranging from 4–8 ppm); ^{13}C NMR[7] (Me_2CO-d_6) δ 88.9 (J = 178 Hz), 138.34 (J = 0.26 Hz), 160.08; MS (70 eV) m/e 111 ($M^+ - NHNH_2$). The product from reaction of hydrazine with diethyl maleate exhibited an identical ^{13}C NMR spectrum.

Anal. Calcd for $C_4H_6N_4O_2 \cdot 0.6H_2O$: C, 31.42; H, 4.74; N, 36.63. Found: C, 31.53; H, 4.77; N, 36.81.

Tetraethyl Phenylhydrazinoethanetetracarboxylate (5). A solution of 3.24 g (30 mmol) of phenylhydrazine in 50 mL of ether was added over a period of 0.5 h to a stirred, refluxing solution of **1a** (9.48 g, 30 mmol) in 270 mL of ether. After 2.5 h of additional heating, cooling, and solvent evaporation, there was obtained, after recrystallization from 95% ethanol, 11.3 g (89%) of white crystals: mp 77–78 °C; ^{1}H NMR (CCl_4) δ 1.04–1.42 (two overlapping triplets, 12 H, CH_3), 3.92–4.28 (two overlapping quartets with a superimposed singlet, 9 H, CH_2 and CH), 4.70 (s, 1 H, NH), 6.04 (s, 1 H, NH), 6.60–7.72 (m, 5 H, aromatic); IR ($CHCl_3$) 3540, 3430, 3330, 2980, 2940, 2900, 1740 (broad), 1605, 1510, 1470, 1450, 1400, 1375, 1330, 1305, 1230 (broad), 1120, 1100, 1040, 890, 870, 700 cm^{-1}.

Anal. Calcd for $C_{20}H_{28}N_2O_8$: C, 56.59; H, 6.65; N, 6.60. Found: C, 56.75; H, 6.70; N, 6.65.

Reaction of 1a with Excess Phenylhydrazine. When **1a** (6.0 g, 19.0 mmol) was added to 3.0 g (27.8 mmol) of phenylhydrazine, the mixture became warm. After heating on a steam bath for 0.5 h and cooling, the mixture crystallized. A portion of the solid was recrystallized from 95% ethanol, mp 76–78 °C. The IR spectrum was identical with that obtained from **5**, and a mixture melting point was not depressed.

Upon heating the remaining reaction mixture at 150–170 °C for 0.5 h and cooling, there was obtained, after recrystallization from 95% ethanol, 1.61 g (27%) of **6**, mp 72–73 °C. The IR spectrum was identical with that obtained from an authentic sample of **6**, and a mixture melting point was not depressed.

Pyrolysis of 5. A 50-mL three-neck round-bottom flask containing 4.00 g (9.42 mmol) of **5** and equipped with a reflux condenser and a helium inlet was purged with helium (60 mL/min) and then heated to 165–175 °C for 0.5 h. The gases which evolved were collected and analyzed by infrared spectroscopy. The spectrum of the mixture contained all of the bands found in the vapor phase spectra of authentic samples of benzene and ethanol, and the presence of carbon dioxide was inferred from absorptions at 2360 and 2330 cm^{-1}. A high-resolution mass spectrum of the gas sample showed an m/e at 28.006, which corresponds to nitrogen. The reaction mixture, after cooling (3.28 g), was recrystallized from 95% ethanol, giving 1.15 g of **6**, mp 70–71.5 °C. The IR spectrum was identical with that obtained from an authentic sample, and a mixture melting point was not depressed. The mother liquors deposited 126 mg of unknown material (mp 228–230 °C). After concentration and refrigeration of the filtrate, there was obtained an additional 0.21 g of **6**, total yield 1.36 g (45%). TLC of the remaining oil (1.50 g) showed the presence of at least 5 components.

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Registry No.—**1a**, 6174-95-4; **1b**, 1733-15-9; **2a**, 66483-30-5; **2b**, 66483-29-2; **3**, 66483-28-1; **4**, 66483-27-0; **5**, 66483-31-6; **6**, 632-56-4; hydrazine, 302-01-2; triethyl ethylenetricarboxylate, 13049-86-0; trimethyl ethylenetricarboxylate, 51175-48-5; phenylhydrazine, 100-63-0.

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(10) The phenylhydrazino adduct **5** undergoes pyrolysis on injection into a gas chromatograph to form tetraethyl ethanetetracarboxylate (**6**) and tetraethyl ethylenetetracarboxylate (**1a**) as major volatile products. Phenylhydrazine and benzene were also produced. Products were separated by preparative GLC and identified by comparisons of retention times and infrared spectra in the cases of the esters **1a** and **6** and of retention time and ultraviolet spectrum in the case of benzene.

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