and Beckman IR 12 spectrophotometers, respectively. NMR spectra were run on Varian T 60 A using Me_4Si as internal standard (sweep width, 100 and 500 Hz). Microanalyses were determined by Alfred Bernhardt, West Germany.

Reaction of Acetylenic Ketones Ia,b, Benzaldehydes VIIIa,b, and Acetophenones VIIIc,d with Hydrazine Carboxylic Esters II. ω-Aroylacetophenone (IIIb,c), benzaldehyde (IXa-c), and acetophenone *N*-(ethoxycarbonyl)hydrazones (IXg-i) were obtained by refluxing ethyl hydrazinecarboxylate IIa (1 mol) with acetylenic ketones Ib,c (1 mol), benzaldehydes VIIIa-c (1 mol), and acetophenones VIIId-f in ethanol for 5 h. The reaction product was worked as previously reported (*1*, *2*). ω-Aroylacetophenone (IIIe,f) and benzaldehyde *N*-(phenoxycarbonyl)hydrazones (IXd-f) were similarly prepared by using the phenyl ester IIb instead of the ethyl ester of hydrazinecarboxylic acid. Under similar conditions, the acetophenones VIIIe,f reacted with phenyl hydrazinecarboxylate IIb to give the corresponding hydrazine derivatives Xk,l in 88-92% yield, and the results are reported in Table VI. However, when phenyl hydrazinecarboxylate IIb (1 mol) was refluxed with excess of the acetophenones VIIIe,f (5 mol) in ethanol for 5 h, the product was a mixture of the acetophenone *N*-(phenoxycarbonyl)hydrazones IXk,l and the hydrazine derivatives Xk,l in which the former were predominant. Compounds IX were separated from X by extraction with cyclohexane and recrystallization from the same solvent as colorless needles (cf. Table VI), whereas compounds X, which were insoluble in cyclohexane, were crystallized from methanol-chloroform as colorless needles. The purity of all compounds was established by TLC. Compound XI was found to be identical with an authentic sample prepared by heating a mixture of acetophenone *N*-(phenoxycarbonyl)hydrazone IXl (0.01 mol) and phenyl hydrazinecarboxylate (0.01 mol) in an oil bath at 150-160 °C for 90 min.

Heating of the hydrazone derivatives IIIb,c,e,f with acetic anhydride at 120-125 °C for 3 h afforded the corresponding pyrazole derivatives Va,b,c,e,f as colorless crystals (Table VI). When the hydrazone derivatives III or the pyrazoles V were refluxed with 3% methanolic potassium hydroxide for 30 min, they gave the corresponding 5(3)-aryl-3(5)-phenylpyrazole VI identified by melting point and mixed melting point with authentic samples prepared by allowing arylbenzoylacetylene to react with hydrazine hydrate at room temperature for 2-3 min. 3-(5)-*p*-(Chlorophenyl)-5(3)-phenylpyrazole VIa had mp 214-215 °C (*2*). 3(5)-*p*-(Methoxyphenyl)-5(3)-phenylpyrazole VIb had mp 168-169 °C (*2*). Acetylation of these pyrazoles with acetic anhydride gave a product which was proved by TLC to be a mixture of VIIA and VIIB.

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Reactions of Substituted Hydrazines with Glyoxal

Robert R. Gallucci

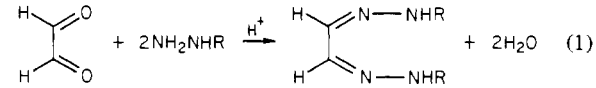
General Electric Company, Corporate Research and Development Center, Schenectady, New York 12301

Substituted hydrazines have been reacted with glyoxal to yield bis(hydrazone) derivatives. Cyclized products were not observed. Thermal decomposition of the glyoxal adducts was investigated.

The reactions of amides and urethanes with glyoxal have been shown to yield interesting and unusual products (*1-4*). However, the reactions of glyoxal with hydrazine derivatives have received less attention. This reaction has now been studied with a variety of substituted hydrazines and found to give bis(hydrazones) as the major products.

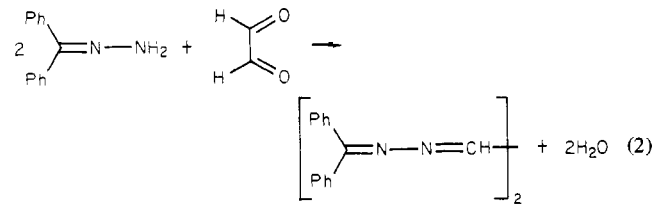
Glyoxal derivatives, **1-14** (Table I), were generally prepared by reaction of an aqueous solution of glyoxal with 2 equiv of an alcoholic solution of a hydrazine derivative, in the presence of a trace of acid. The products precipitate from solution within hours as microcrystalline solids. With few exceptions (**11** and **12**), these compounds were very insoluble. The limited solubility made isolation of these compounds easy, but purification and further reactions were hindered by the difficulty in finding suitable solvents. Fortunately, as shown by elemental analyses, the compounds were usually of reasonable purity as isolated from the reaction mixtures. In order to maintain this purity, no attempts were made to maximize yield.

Many reaction pathways are available for the addition of hydrazine derivatives to glyoxal, and we were especially concerned about the formation of cyclic products or further reaction of the initially formed hydrazones with starting material. Proton NMR spectra of saturated solutions of the glyoxal adducts in Me_2SO-d_6 were very useful in determining structure. NMR spectra, along with IR spectra and elemental analyses, showed the compounds to be of structure I. Unusual addition products similar to those seen in the reaction of glyoxal with alcohols, amides, and urethanes were not formed. The glyoxal derivatives are simple 2:1 adducts formed by nucleophilic attack on the aldehyde followed by elimination of water (eq 1).



I

Compound **13** was prepared by the reaction of 2 equiv of benzophenone hydrazone with glyoxal (eq 2).



13

In addition to information obtained from spectra, the structural assignments of the bis(hydrazones) are supported by the synthesis of some of these adducts by alternative routes.

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Table I. IR and NMR Analyses[a]

R group for compd I	compd no.	data
CH_3OOC-	1	mp 263–264 °C (decomp); 88% yield; IR 3240, 3070, 1710, 1570, 1535, 1310, 1255, 1055, 965 cm^{-1}; ^1H NMR δ 11.27 (s, 2 H), 7.67 (s, 2 H), 3.68 (s, 6 H); ^{13}C NMR δ 153.8, 142.6 (d), 52.3 (q)
EtOOC-	2	mp 287–296 °C (decomp); 88% yield (*6*); IR 3215, 3030, 3000, 1710, 1585, 1520, 1310, 1035, 880, 635 cm^{-1}; ^1H NMR δ 11.24 (s, 2 H), 7.67 (s, 2 H), 4.24–4.03 (q, 4 H), 1.29–1.15 (t, 6 H)
n-BuOOC-	3	mp 244–246 °C; 91% yield; IR 3220, 3035, 2955, 1700, 1530, 1240, 1050, 960 cm^{-1}; ^1H NMR δ 11.24 (s, 2 H), 7.66 (s, 2 H), 4.08 (t, 4 H), 1.59–1.45 (m, 8 H), 0.89 (m, 6 H)
t-BuOOC-	4	mp 228–230 °C (decomp); 85% yield; IR 3280, 2990, 1710, 1580, 1510, 1305, 1245, 1160, 1140, 960, 860 cm^{-1}; ^1H NMR δ 10.98 (s, 2 H), 7.64 (s, 2 H), 1.44 (s, 18 H)
$PhCH_2CO$-	5	mp 123–125 °C; 90% yield; IR 3210, 3060, 1660, 1545, 1260, 1175, 1070, 720 cm^{-1}; ^1H NMR (two isomers) δ 11.66 (11.55) (s, 2 H), 7.85 (7.71) (s, 2 H), 7.30 (7.27) (s, 10 H), 3.89 (3.54) (s, 4 H)
CH_3CHO-	6	mp >315 °C; 58% yield; IR 3200, 3045, 1660, 1540, 1270, 1090 cm^{-1}; ^1H NMR (two isomers) δ 11.45 (s, 2 H), 7.70–7.62 (two singlets, 2 H), 2.11–1.93 (two singlets, 6 H); ^{13}C NMR (two isomers) δ 171.89 (165.76), 143.70 (141.18), 21.58 (20.02)
PhCO-	7	mp >310 °C; 80% yield; IR 3200, 3030, 1600, 1530, 1310, 1270, 1140 cm^{-1}; ^1H NMR δ 12.05 (s, 2 H), 7.93 (s, 2 H), 7.95–7.53 (m, 12 H)
HCO-	8	mp 288–290 °C; 67% yield; IR 3170, 3040, 1660, 1575, 1405, 1200, 1040, 950, 835 cm^{-1}, ^{13}C NMR δ 165.0, 143.1; ^1H NMR δ 11.83 (s, 2 H), 8.60 (s, 2 H), 7.68 (s, 2 H)
NH_2CO-	9	mp >325 °C; 95% yield (*7*); IR 3460, 3200, 1680, 1580, 1430, 1295, 1120, 920 cm^{-1}; ^1H NMR δ 10.40 (s), 7.54 (s), 6.37 (s)
PhNHCO-	10	mp 246–247 °C; 95% yield; IR 3365, 3200, 3080, 2940, 1665, 1595, 1530, 1135 cm^{-1}; ^{13}C NMR δ 152.8, 139.5, 139.0, 128.5, 122.6, 119.7; ^1H NMR δ 11.00 (s, 2 H), 8.92 (s, 2 H), 7.73 (s, 2 H), 7.67–6.91 (m, 10 H)
Ph-	11	mp 167–168 °C; 98% yield (*7*); IR 3290, 1595, 1565, 1500, 1485, 1255, 1120, 750, 690 cm^{-1}; ^1H NMR δ 10.35 (s, 2 H), 7.65 (s, 2 H), 7.21–6.67 (m, 10 H)
p-CH_3PhSO_2	12	mp 147–149 °C; 55% yield; IR 3220, 1440, 1350, 1165, 1060, 975, 665 cm^{-1}; ^{13}C NMR δ 142.9, 142.2, 134.9, 128.2, 125.9, 20.0; ^1H NMR δ 11.85 (s, 2 H), 7.73–7.35 (m, 10 H), 2.36 (s, 6 H)
	13	mp 140–143 °C; 45% yeild; IR 1545, 1440, 1320, 1295, 1180, 1075, 985, 915, 785, 770, 690 cm^{-1}; ^{13}C NMR δ 164.8 (s), 156.4 (d), 137.5 (s), 134.7 (s), 130.5, 129.8, 129.1, 128.6, 128.2, 127.9, 127.8 (two aryl rings are not equivalent); ^1H NMR δ 8.00 (s, 2 H), 7.52–7.42 (m, 20 H), also two small unidentified peaks 8.48 and 8.40
H-	14	mp 97–100 °C; 73% yield; IR 3350, 3170, 1580, 1370, 1250, 1075 cm^{-1}; ^1H NMR 60 MHz ($CDCl_3$) δ 7.6 (s), 5.7 (s)
	16	mp ~275 °C (decomp); IR identical with Sadtler no. 13888; ^1H NMR δ 7.17–7.06 (d, 4 H), 5.27–5.21, (m, 2 H), 4.11–3.90 (q, 8 H), 1.24–1.09 (t, 6 H)
	17	^1H NMR 60 mHz δ 9.50 (s, 1 H, exch D_2O), 8.35 (s, 1 H, exch D_2O), 7.70 (s, 1 H), 4.45–4.05 (two quartets, 4 H), 1.50–1.05 (t, 9 H)
	18	mp 234–238 °C; 57% yield; IR 3360, 1600, 1570, 1505, 1490, 1255, 1145, 750, 695 cm^{-1}; ^1H NMR 60 mHz δ 9.40 (s, 2 H), 7.50, 7.30 (m, 10 H), 2.40 (s, 6 H)

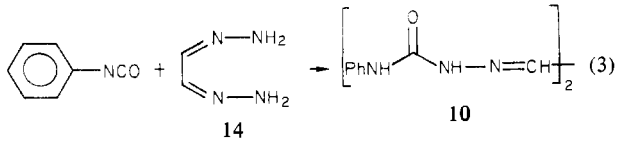
[a] IR: KBr pellets. NMR: Me_2SO-d_6, 100 mHz unless otherwise indicated. Satisfactory microanalyses, which were submitted for review, were obtained for all new compounds.

Table II. Thermal Gravimetric Analysis of Decomposition

compd	onset of wt loss,[a] °C	end rapid wt loss, °C (%)	total wt loss at 400 °C, %
1	265	305 (68)	76
2	285	320 (72)	76
3	255	295 (68)	78
4	235	275 (91)	93
5	310	355 (83)	87
6	275	370 (95)	96
7	355	405 (95)	
9	265	315 (53)	67
10	255	300 (68)	78
11	210	290 (66)	78
12	260	340 (77)	84
14	160	170 (74)	96
16	220	310 (73)	81
17	170	290 (57)	82
18	250	305 (86)	93

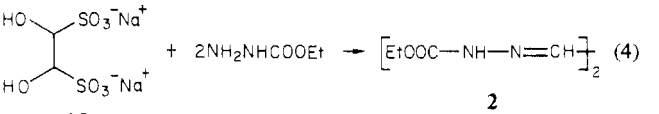
[a] Some samples showed a small weight loss <5% below this temperature.

Compound **10** was prepared by the addition of phenyl isocyanate to **14**, as shown in eq 3.



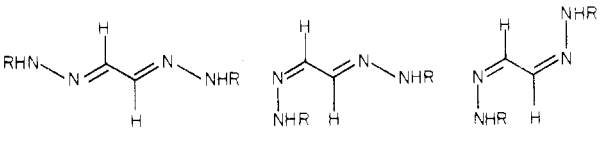
14 10

A compound whose spectra were identical with those of **9** was formed when 2 equiv of the semicarbazone of acetone was reacted with glyoxal in aqueous acid. The reaction is formally an exchange between the ketone semicarbazone and the aldehyde. Alternative synthesis of adducts (**1–13**) can be achieved by reaction of the bisulfite addition product of glyoxal (**15**) with substituted hydrazines. This synthesis was demonstrated with ethyl carbazate (eq 4).



15 2

The proton NMR spectra of adducts **1–14** show H—C=N protons at δ 12.05–11.0 and NH absorbances at δ 7.93–7.62. Other absorbances are as expected (Table I). Although the derivatives can exist as three possible isomers (II–IV), most



II III IV

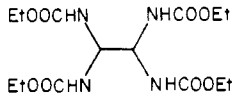
adducts appeared to be present as single stereoisomers (**5**, **6**, and **9** are exceptions showing two sets of NMR signals). Judging by the simplicity of the NMR spectra, the products are one of the symmetric isomers (II or IV), probably the trans–trans isomer (II).

The reaction showed no sign of cyclic products although such compounds have been formed in similar cases and are not unreasonable products in this instance (*5*). Analyses of the

products, which were generally formed in high yield (Table I), indicate that the condensation involves 2 equiv of substituted hydrazine. Spectral analyses firmly establish the glyoxal adducts as bis(hydrazones). No significant amounts (>5%) of byproducts are observed.

In order to further explore the possibility of cyclization, **10** was heated in Me_2SO-d_6. No change was apparent by heating to 125 °C. Similarly, no change in the NMR spectrum was observed upon addition of HCl (other than broadening of the NH absorbance). NMR spectra taken in CF_3COOH were similar to those taken in Me_2SO-d_6. Compounds **1–13** were stable under the reaction conditions showing no further addition even when excess hydrazine derivative was present. In addition, dimethylformamide (DMF) solutions of compound **1** showed no reaction in an attempted reduction using sodium borohydride or sodium cyanoborohydride. An attempted Diels–Alder addition of **1** with dimethyl acetylenedicarboxylate to form a dihydropyrazine failed to yield product.

Most adducts were stable to their melting point where they decomposed with evolution of gas (Table I). Gas-chromatographic–mass-spectroscopic analysis showed the "gases" to be a very complex mixture, including a fraction which could be condensed at room temperature. Separation and identification of all volatile products of decomposition of the various glyoxal adducts was not achieved. Decomposition of some of these compounds was studied by thermal gravimetric analysis (TGA) (Table II). For the purposes of comparison, 1,1,2,2-tetrakis-(ethoxycarbonylamino)ethane (TCE), **16**, the bis(ethyl carbazate)



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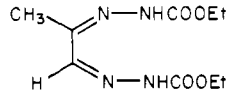
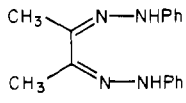


17



18

of 1,2-propanedione, **17**, and the bis(phenylhydrazone) of 2,3-butanedione, **18**, are included. Almost all compounds investigated showed a rapid weight loss over a relatively narrow temperature range. This behavior is in agreement with the rapid evolution of gas observed when these compounds are melted. (Exceptions which melt before decomposition are noted in Table I.)

Experimental Section

General. All melting points were taken on a Thomas-Hoover apparatus and are uncorrected. IR spectra were taken on a Perkin-Elmer 457 grating infrared spectrophotometer as KBr pellets. NMR spectra were taken on a Varian XL100 or T60 spectrometer in Me_2SO-d_6. TGA analyses were done on a Du Pont 990/951 thermal gravimetric analyzer. Samples were heated under nitrogen at 10 °C/min. Unless otherwise indicated, starting materials were commercially available and were used as received.

***Preparation of Glyoxal Adducts* (1–13).** A 40% aqueous glyoxal solution was dissolved in methanol and added to the appropriate amount of hydrazine derivative in methanol. A few drops of glacial acetic acid were added, and the reaction was stirred until a precipitate formed. A few hours after this, the product was separated by filtration and washed with methanol. No attempt was made to improve yields or isolate a second crop. The preparation of the methyl carbazate derivative of glyoxal, **1**, is given in illustration of the technique. A 40% aqueous glyoxal solution (14.5 g, 0.1 M), dissolved in 50 mL of methanol, was added to a solution of 18.9 g of methyl carbazate (0.21 M) dissolved in 150 mL of methanol. Five drops of glacial acetic acid were added. After 5 min, a white precipitate appeared; the reaction was stopped after 1 h and the product filtered off; yield 17.75 g (88%), mp 263–264 °C. IR, NMR and elemental analyses of compounds **1–13** are presented in Table I. Compounds **2**, **9**, and **11** have been previously prepared by similar methods (**6**, **7**). Analyses were made on materials as isolated from the reaction mixture. Compound **18** was made by the reaction of 2,3-butanedione with phenylhydrazine as described for the glyoxal adducts. Attempts to recrystallize these materials from a variety of solvents were fruitless. The compounds were purified by washing with methanol–water and methanol.

***Preparation of* 2 *from Glyoxal Bisulfite*.** Glyoxal sodium bisulfite (5.0 g, 0.02 M) was suspended in 200 mL of distilled water with 3.91 g of ethyl carbazate (0.38 M). Not all of the solids dissolved. A drop of acetic acid was added and the reaction was stirred at room temperature for 18 h. A white solid which was different in texture from the starting materials was filtered from solution. A second crop was not isolated. The compound was washed several times with water–methanol and then with methanol. IR spectra were identical with that of the corresponding product of ethyl carbazate and aqueous glyoxal (3.3 g, 76%).

***Preparation of* 10 *from Phenyl Isocyanate and* 14.** The glyoxal-hydrazine adduct **14** was prepared by adding an aqueous solution of glyoxal to a large excess of hydrazine in MeOH. Product was isolated by removing solvent on a rotary evaporator until crystals formed. The crystals were filtered from solution. The hydrazine-glyoxal adduct, (0.30 g) was dissolved in THF and reacted with 0.83 g of phenyl isocyanate. The product precipitated from solution as a yellow solid, 0.9 g (80%). The IR spectrum (KBr) was identical with that of the compound formed by addition of phenylsemicarbazide to glyoxal (**10**).

***Preparation of Osazone* 17.** A solution of acetol (2.0 g, 0.03 M) in ethanol was added dropwise to a stirred solution of ethyl carbazate in ethanol (11.2 g, 0.11 M). After 2 h at room temperature, the solution was concentrated to give a colorless oil. Washing the oil with ethanol–water gave white crystals (3.2 g, 49%).

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