difficulties were experienced. A total of 163 mg. of DPN was eventually added in increments during the course of the reaction, and after 405 minutes only 450 mg. of acetaldehyde-1-*d* was reduced. The ethanol was distilled out of the reaction mixture *in vacuo* and redistilled on a Vigreux column. The fraction collected between 70 and 98° was used entirely for the enzymatic analysis of enantiomorphic purity as described in experiment 1. The ethylidene dimethone and phenacyl lactate were analyzed for deuterium after suitable dilution.

Purification and Optical Rotation of Ethanol-1-*d*.—The ethanol was separated on a vapor phase chromatography column[32] in 0.1-ml. batches. A 5-foot column packing of Carbowax 1540 on pulverized magnesia was used with t = 100° and a helium flow rate of 50 ml. per min. Two minor impurities (probably acetaldehyde and acetic acid) appeared before the ethanol peak. The ethanol was collected in a trap chilled in alcohol–Dry Ice. The ethanol appeared about 4 to 5 minutes after injection of the alcohol mixture, and the water peak appeared after 8–9 minutes. Collection of the ethanol was interrupted the moment the water peak began to appear, or earlier. Control experiments with 95% and absolute alcohol showed that complete separation of the azeotrope was achieved. A total of 0.9 ml. of purified ethanol-1-*d* was obtained.

The rotation was determined visually in a 1-dm. polarimeter tube of 0.25-ml. capacity, with a Rudolph precision polarimeter that could be read to 0.001° under ideal conditions. The readings were taken at maximum sensitivity, but due to the small bore of the polarimeter tube, a precision of about 10% was the best that could be achieved. The zero point reference was determined with unlabeled absolute ethanol under conditions comparable to those used for taking readings with the ethanol-1-*d*. The average of a large number of readings gave $\alpha^{28}D$ −0.22 ± 0.02° (l 1). If the density at 28° is assumed to be 0.80, the ethanol-1-*d* has $[\alpha]^{28}D$ −0.28 ± 0.03°.

The rotation was also determined with a Keston polarimeter attachment[33] on a Beckman DU spectrophotometer. The rotations measured at 26° in a 0.5-dm. tube were $\alpha_{460\ m\mu}$ − 0.123°, $\alpha_{546\ m\mu}$ − 0.095°, $\alpha_{584\ m\mu}$ −0.066°. These values are regarded as only approximate.

Kinetic Measurements.—The Michaelis constants for the various alcohols were determined by measuring the initial velocity of reduction of DPN in the presence of suitable amounts of a commercial sample of alcohol dehydrogenase with a specific activity of 86,200.[27] The K_s-values were calculated from Lineweaver, Burk plots.[22] The reactions were carried out in 3 ml. of 0.05 M pyrophosphate buffer of pH 9.3. The DPN was 1.35×10^{-3} M. In each series, four to six different concentrations of alcohol were used. The measurements were made at 340 mμ in a Beckman spectrophotometer with attached thermoregulator for the cell compartment to maintain the temperature at 25°. The reaction was initiated by addition of the enzyme, the contents of the cuvette were mixed rapidly, and readings were taken every 10 or 15 seconds for at least one minute. The amount of DPNH formed was calculated from the increase in optical density.

The isopropyl alcohol and the methanol were purified according to Gilson.[34]

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The lithium aluminum deuteride was purchased on allocation from the Atomic Energy Commission. The funds for the purchase of the mass spectrometer used in this research were supplied by the Atomic Energy Commission under contract No. At(11-1)-92.

(32) K. P. Dimick and J. Corse, *Food Technology*, **8**, 360 (1956).

(33) Manufactured by Standard Polarimeter Co., 225 East 54th Street, N. Y., N. Y.

(34) L. E. Gilson, THIS JOURNAL, **54**, 1445 (1932).

CHICAGO, ILLINOIS

[CONTRIBUTION FROM THE RESEARCH LABORATORIES, AEROJET-GENERAL CORP.]

The Mannich Reaction of 2,2-Dinitro-1-alkanols with Ammonia, Glycine and Hydrazine[1]

BY MILTON B. FRANKEL AND KARL KLAGER

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The Mannich condensation of 2,2-dinitro-1-alkanols with ammonia, glycine and hydrazine has been studied and the importance of the pH in these reactions has been shown. 2,2-Dinitro-1-alkanols condense readily with ammonia in a buffered medium to give the corresponding bis-substituted amines. The condensation of these nitroalcohols with glycine gives a mono substituted product at a pH of 7 and a disubstituted product at a pH of 9. The reaction of methyl 5-hydroxy-4,4-dinitropentanoate with glycine results in the formation of 5,5-dinitro-2-piperidone-N-acetic acid. The condensation of 2,2-dinitropropanol with hydrazine gives bis-N,N'-(2,2-dinitropropyl)-hydrazine.

The Mannich reaction with *gem*-dinitroparaffins was first reported by Feuer and co-workers[2] who described the condensation of 2,2-dinitro-1,3-propanediol and sodium 2,2-dinitroethanol with glycine and ethanolamine. Feuer reported that the pH, the reaction temperature and the mole ratio of the reactants have a pronounced effect on the course of this reaction. Independent of this work, we studied the Mannich reaction of various 2,2-dinitro-1-alkanols with ammonia, glycine and hydrazine.

Inasmuch as the 2,2-dinitro-1-alkanols are converted in basic medium to the corresponding aci salts of 1,1-dinitroalkanes and formaldehyde,[3] this work was directed to a study of the influence of pH on the Mannich reaction in these systems. We observed that the reaction of 2,2-dinitro-1-alkanols with ammonium hydroxide gave little or no yield of the Mannich condensation product. However, it was found that if the solution was buf-

(1) Presented before the Division of Organic Chemistry at the 131st meeting of the American Chemical Society, Miami, Florida.

(2) H. Feuer, G. B. Bachman and W. May, THIS JOURNAL, **76**, 5124 (1954).

(3) P. Duden and G. Ponndorf, *Ber.*, **38**, 2031 (1905).

fered by using ammonium acetate instead of ammonium hydroxide, the condensation occurred readily. Thus, if an aqueous solution of ammonium acetate and the 2,2-dinitro-1-alkanols was warmed to 60°, quantitative yields of the bis-(2,2-dinitroalkyl)-amines separated on cooling. In this manner were prepared 2,2,6,6-tetranitro-4-azaheptane (Ia), 3,3,7,7-tetranitro-5-azanonane (Ib) and 4,4,8,8-tetranitro-6-azaundecane (Ic).

$$2RC(NO_2)_2CH_2OH + NH_3 \xrightarrow[\text{Buffer}]{\text{HOAc}} [RC(NO_2)_2CH_2]_2—NH$$

Ia, R = CH_3
Ib, R = CH_3CH_2
Ic, R = $CH_3CH_2CH_2$

Condensation of methyl 5-hydroxy-4,4-dinitropentanoate and ammonium acetate gave dimethyl 4,4,8,8-tetranitro-6-aza-1,11-undecanedioate (II). Compound II was prepared more conveniently by the direct condensation of the aci-sodium salt of methyl 4,4-dinitrobutyrate, formaldehyde and ammonium acetate.

$$2CNO_2CH_2CH_2CO_2CH_3 \\ \| \\ NO_2Na$$

$$+ 2CH_2O \longrightarrow 2HOCH_2C(NO_2)_2CH_2CH_2CO_2CH_3$$

$$\xrightarrow[\text{HOAc}]{NH_3} \quad \downarrow \begin{matrix} NH_3 \\ HOAc \end{matrix}$$

$$[CH_3O_2CCH_2CH_2C(NO_2)_2CH_2]_2—NH$$
II

When amino acids or their esters were used in the condensation with 2,2-dinitro-1-alkanols, the importance of the *p*H in determining the course of the reaction was strikingly illustrated. The condensation of 2,2-dinitropropanol and methylglycine at a *p*H of 7 gave methyl 5,5-dinitro-2-azahexanoate (III), while the condensation of 2,2-dinitropropanol and glycine at a *p*H of 9 or higher, gave bis-(2,2-dinitropropyl)-glycine (IV). The structure of IV was confirmed by analysis and by the preparation of the corresponding methyl ester and acid chloride.

When methyl 5-hydroxy-4,4-dinitropentanoate was condensed with the sodium salt of glycine the expected methyl 4,4-dinitro-6-azaoctanedioic acid (V), cyclized to form 5,5-dinitro-2-piperidone-N-acetic acid (VI). The structure of VI was confirmed by analysis and by conversion into a monomethyl ester derivative VII.

2,2-Dinitropropanol and hydrazine react under buffered *p*H conditions to form bis-N,N′-(2,2-dinitropropyl)-hydrazine (VIII).

Oxidation of VIII with bromine in methanol solution yielded azo-(2,2-dinitropropane) (IX), a remarkably stable compound melting without decomposition at 101–101.5°. The results of the study of the decomposition of IX were rather surprising, since it is known that aliphatic azo compounds are thermally unstable and decompose into free radicals with the liberation of nitrogen.[4] However, azo-(2,2-dinitropropane) was almost quantitatively recovered after two hours refluxing in either toluene or chlorobenzene. Even after refluxing for 90 minutes in *o*-dichlorobenzene, 50% of the starting material was recovered. In the latter solvent the evolution of nitrogen dioxide was observed.

The physical properties and yields of the Mannich condensation products are listed in Table I.

Experimental[5,6]

3,3,7,7-Tetranitro-5-azanonane (Ib).—This preparation is typical of the condensation of 2,2-dinitro-1-alkanols and ammonium acetate. A mixture of 30.0 g. (0.18 mole) of 2,2-dinitrobutanol,[7] 50 ml. of water and 30.0 g. (0.39 mole) of ammonium acetate was warmed to 60° for 20 minutes. The reaction mixture was cooled and the product was collected and dried, giving 28.0 g. (99%) of a cream-colored solid, m.p. 57–61°. Recrystallization from isopropyl alcohol gave white plates, m.p. 66–67°.

Dimethyl 4,4,8,8-Tetranitro-6-aza-1,11-undecanedioate (II). (a) From Methyl 5-Hydroxy-4,4-dinitropentanoate.—A mixture of 30.0 g. (0.13 mole) of methyl 4,4-dinitro-5-hydroxypentanoate,[8] 75 ml. of water and 30.0 g. (0.39 mole) of ammonium acetate was heated on the steam-bath for 10 minutes, on cooling a cream-colored solid separated. The product was collected, washed with water and dried to give 25.4 g. (88.6%) of a cream-colored solid, m.p. 65–69°. Recrystallization from methanol gave white needles, m.p. 79–80°.

(b) From Aci-sodium Salt of Methyl 4,4-Dinitrobutyrate.—Five hundred ml. of concentrated ammonium hydroxide, 800 ml. of water and 500 ml. of glacial acetic acid were mixed together. The temperature was allowed to rise to 60–70°, at which point a solution of 1000 g. (equivalent to 850 g. or 3.97 moles of dry salt containing 15% moisture) of the aci-sodium salt of methyl 4,4-dinitrobutyrate,[8] 2000 ml. of water and 324 g. (4.0 moles) of 37% formalin was added over a period of 15 minutes. The reaction mixture was stirred at 60° for one hour and then cooled to 10°. The solid product was collected, washed with water and dried *in vacuo* over potassium hydroxide to give 480 g. (56.8%) of cream-colored solid, m.p. 66–69°. Recrystallization from methanol gave white needles, m.p. 79–80°.

Methyl 5,5-Dinitro-3-azahexanoate (III).—A mixture of 12.6 g. (0.1 mole) of methylglycine hydrochloride,[9] 65 ml. of water, 15 g. (0.1 mole) of 2,2-dinitropropanol[7] and 8.2 g. (0.1 mole) of sodium acetate was heated at 70–85° for one hour. The reaction mixture was cooled and extracted with methylene chloride. The extracts were dried and concentrated *in vacuo* leaving 17.1 g. (77.3%) of a yellow oil.

The amine was identified by conversion to the corresponding nitraza derivative. Methyl 5,5-dinitro-3-azahexanoate, 2.2 g. (0.01 mole), was dissolved in 20 ml. of acetic anhydride and added to 20 ml. of 99% nitric acid at 0–5°. After stirring for 10 minutes the mixture was poured onto ice. The product was collected, washed with water and dried *in vacuo* over potassium hydroxide to give 1.64 g. (61.4%) of white solid, m.p. 76–79°. Recrystallization from isopropyl ether raised the melting point to 80–81°.

Bis-(2,2-dinitropropyl)-glycine (IV).—A solution of 7.5 g. (0.1 mole) of glycine, 4.0 g. (0.1 mole) of sodium hydroxide and 50 ml. of water was mixed with 15.0 g. (0.1 mole) of 2,2-dinitropropanol. The temperature rose to 42° and the yellow solution formed was allowed to stand overnight. Upon addition of dilute sulfuric acid a viscous, colorless oil separated and solidified on standing. The product 15.6 g. (92.0%) was collected and recrystallized from methanol-water to give white crystals, m.p. 123–124°.

Methyl Bis-(2,2-dinitropropyl)-glycine.—A mixture of 20 g. (0.059 mole) of bis-(2,2-dinitropropyl)-glycine, 100 ml. of methanol and 10.0 ml. of concentrated sulfuric acid was refluxed for 90 minutes. The solution was diluted with 250 ml. of methylene chloride and washed with water, 5% sodium carbonate solution and water. The solvent was evaporated to yield 14.0 g. (67.3%) of white solid. Recrystallization from methanol–ether gave crystals, m.p. 94–95°.

(4) C. G. Overberger, *et al.*, THIS JOURNAL, **77**, 4651 (1955), and preceding papers in this series.

(5) All melting points are uncorrected.

(6) Microanalyses by Dr. A. Elek, Elek Microanalytical Laboratory, 4763 W. Adams Blvd., Los Angeles, Calif.

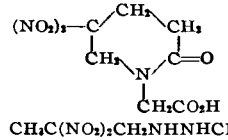
(7) O.S.R.D. Report No. 2016, Nov. 15, 1943.

(8) K. Klager, *J. Org. Chem.*, **16**, 161 (1951).

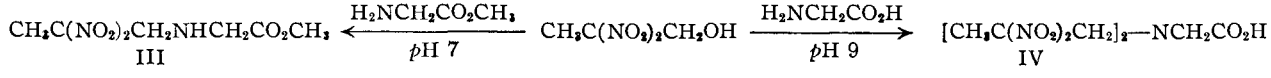
(9) C. Harries and M. Weiss, *Ann.*, **327**, 365 (1903).

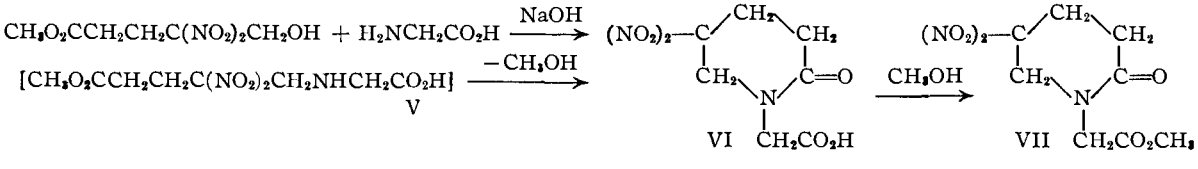
TABLE I

MANNICH CONDENSATION PRODUCTS

2,2-Dinitro-1-alkanol	Amine	Product	Yield, %	M.p., °C.	Recryst. solvent	Formula	Analyses, % Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
$CH_3C(NO_2)_2CH_2OH$	NH_3	$[CH_3C(NO_2)_2CH_2]_2$–NH	90.4	67–68	Isopropyl alcohol	$C_5H_{11}N_3O_5$	25.63	3.94	24.91	25.90	4.09	24.80
$CH_3CH_2C(NO_2)_2CH_2OH$	NH_3	$[CH_3CH_2C(NO_2)_2CH_2]_2$–NH	99.0	66–67	Isopropyl alcohol	$C_8H_{16}N_3O_5$	31.07	4.89	22.65	31.06	4.98	21.73
$CH_3CH_2CH_2C(NO_2)_2CH_2OH$	NH_3	$[CH_3CH_2CH_2C(NO_2)_2CH_2]_2$–NH	85.2	100–100.5	Ethanol	$C_{10}H_{19}N_3O_5$	35.61	5.68	20.77	35.78	5.58	19.75
$CH_3O_2CCH_2CH_2C(NO_2)_2CH_2OH$	NH_3	$[CH_3O_2CCH_2CH_2C(NO_2)_2CH_2]$–NH	88.6	79–80	Methanol	$C_{12}H_{17}N_3O_{13}$	33.89	4.50	16.47	33.91	4.52	16.86
$CH_3C(NO_2)CH_2OH$	$NH_2CH_2CO_2CH_3$	$CH_3C(NO_2)_2CH_2NHCH_2CO_2CH_3$[a]	77.3	80–81	Isopropyl alcohol	$C_6H_{10}N_4O_8$	27.07	3.79	21.05	27.20	4.09	21.43
$CH_3C(NO_2)_2CH_2OH$	$NH_2CH_2CO_2H$	$[CH_3C(NO_2)_2CH_2]_2$–NCH_2CO_2H	92.0	123–124	Methanol–water	$C_8H_{12}N_3O_{12}$	28.32	3.83	20.65	28.52	3.73	20.74
$CH_3O_2CCH_2CH_2C(NO_2)_2CH_2OH$	$NH_2CH_2CO_2H$		61.5	128–130	Ether	$C_7H_9N_3O_7$	34.01	3.67	17.00	34.37	3.92	17.62
$CH_3C(NO_2)_2CH_2OH$	NH_2NH_2	$CH_3C(NO_2)_2CH_2NHNHCH_2C(NO_2)_2CH_3$	73	85–86	Chloroform	$C_6H_{12}N_6O_8$	24.33	4.09	28.37	24.98	4.12	27.65

[a] Identified by conversion to the corresponding nitraza derivative whose melting point and analyses are given in the table.





Anal. Calcd. for $C_9H_{15}N_5O_{10}$: C, 30.60; H, 4.24; N, 19.83; OCH_3, 8.78. Found: C, 31.17; H, 4.49; N, 20.11; OCH_3, 8.19.

Bis-(2,2-dinitropropyl)-glycyl Chloride.—A mixture of 78 g. (0.23 mole) of bis-(2,2-dinitropropyl)-glycine and 190 ml. of thionyl chloride was refluxed overnight. The solution was evaporated to dryness *in vacuo*, leaving a brown solid. Recrystallization from chloroform gave white crystals, 41.0 g. (50%), m.p. 64–65°.

Anal. Calcd. for $C_8H_{12}N_5O_9Cl$: C, 26.86; H, 3.38; N, 19.14; Cl, 9.91. Found: C, 27.48; H, 3.68; N, 19.27; Cl, 9.70.

5,5-Dinitro-2-piperidone-N-acetic Acid (VI).—A solution of 7.5 g. (0.1 mole) of glycine, 4.0 g. (0.1 mole) of sodium hydroxide and 50 ml. of water was mixed with 22.2 g. (0.1 mole) of methyl 5-hydroxy-4,4-dinitropentanoate. A yellow solution was formed and the temperature rose to 38°. The mixture was allowed to stand overnight. Acidification with dilute sulfuric acid caused an oil to separate, which soon crystallized. The product was collected, washed with water and dried to give 15.2 g. (61.5%) of white solid. Recrystallization from methanol–water and ether gave colorless crystals, m.p. 128–130°. This compound gave a negative test for the methoxyl group.

Methyl 5,5-Dinitro-2-piperidone-N-acetate (VII).—A mixture of 20.0 g. (0.081 mole) of 5,5-dinitro-2-piperidone-N-acetic acid, 150 ml. of methanol and 10 ml. of concentrated sulfuric acid was refluxed for 90 minutes. The solution was diluted with 250 ml. of methylene chloride and washed with water, 5% sodium carbonate solution and water. After drying over sodium sulfate, the solvent was evaporated leaving crystals. Recrystallization from methanol gave 16.0 g. (75.8%) of product, m.p. 126–130°. The mixed melting point with the free acid (m.p. 128–130°) was depressed to 105–111°.

Anal. Calcd. for $C_8H_{11}N_3O_7$: C, 36.79; H, 4.26; N, 16.09. Found: C, 37.51; H, 4.33; N, 16.32.

Bis-(2,2-dinitropropyl)-hydrazine (VIII).—A solution of 52.0 g. of 85% hydrazine hydrate, 300 ml. of water and 75 ml. of glacial acetic acid was heated to 60°. At this temperature a solution of 50.0 g. (0.33 mole) of 2,2-dinitropropanol in 150 ml. of methanol was added within 15 minutes. A viscous oil immediately separated. The mixture was stirred at 60° for one hour. After cooling the oily layer crystallized to give 36 g. (73.0%) of white solid, m.p. 83–85°. Recrystallization from ether or chloroform gave colorless prisms, m.p. 85–86°.

Azo-(2,2-dinitropropane) (IX).—A solution of 5.0 g. (0.017 mole) of bis-(2,2-dinitropropyl)-hydrazine in 50 ml. of methanol was cooled to 0° and bromine was added with vigorous stirring until the bromine was no longer bleached. The temperature was kept below 5° by means of external cooling. After a short time crystals precipitated, which were collected and washed with absolute ether. Recrystallization from methanol gave 2.3 g. (46.3%) of colorless crystals, m.p. 101–101.5°.

Anal. Calcd. for $C_6H_{10}N_6O_8$: C, 24.49; H, 3.43; N, 28.57. Found: C, 24.85; H, 3.49; N, 28.80.

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AZUSA, CALIFORNIA

[CONTRIBUTION FROM THE IPATIEFF HIGH PRESSURE AND CATALYTIC LABORATORY, DEPARTMENT OF CHEMISTRY, NORTHWESTERN UNIVERSITY]

Sodium and Potassium Alkoxides as Catalysts for Carbanion Reactions of Hydrocarbons[1]

BY HERMAN PINES AND LUKE SCHAAP[2]

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Sodium and potassium alkoxides, when heated to decomposition temperatures, catalyze carbanion reactions such as the dehydrogenation of *d*-limonene, double bond isomerization of olefins, and the side chain alkylation of alkylarenes. Alkoxides of tertiary alcohols are far more effective than those of primary or secondary alcohols. A mechanism for the alkoxide decomposition is proposed, and some similar reactions are discussed.

Organosodium compounds and sodium hydride have been reported to be catalysts for certain reactions that apparently proceed by carbanion mechanism: (a) isomerization of olefins, (b) dehydrogenation of monocyclic terpenes, (c) side chain alkylation of alkylarenes by olefins.[3]

It has been found that potassium *t*-butoxide can promote reactions a, b as well as c at temperatures of 250–300°, which cause alkoxide decomposition, but that it is most effective for b. Reaction c is promoted by a trace of hydroxide ion with the *t*-alkoxide. An autoclave was used, the experiments being of 4–12 hours duration. Limonene changed into *p*-cymene in yields of 95–97% using either potassium *t*-butoxide or *t*-pentoxide, whereas it dropped to 3–4% with the isopropoxide, 1.5% with the methoxide, and 0% with the phenoxide or with no alkoxide. The experimental data obtained are summarized in Table I. The solid residue from the *t*-butoxide experiments, on acidification, yielded some 3,5-dimethylphenol and isovaleric acid.

Potassium *t*-butoxide caused 8% isomerization of 1-*p*-menthene on heating for 5.5 hours at 260–265°. The same catalyst, containing a trace of potassium hydroxide, was effective for the formation of *n*-propylbenzene from ethylene and toluene at 279–291°, or *t*-pentylbenzene (containing a trace of 1,1-dimethylindan) from cumene and ethylene. The experimental conditions and yields are summarized in Table II.

Methane was found in the reactions catalyzed by potassium *t*-butoxide while small amounts of ethane as well as methane were obtained from the experiments carried out with potassium *t*-pentoxide. The presence of methane is due to the decomposition of the alkoxide at 280° as shown in Experiment 8. No methane was produced however when powdered potassium hydroxide in *t*-butyl alcohol was heated to the same temperature (ex-

(1) Paper IX of the series of Base Catalyzed Reactions. For paper VIII see H. Pines and M. Kolobielski, THIS JOURNAL, **79**, 1698 (1957).

(2) Predoctoral Fellow: Universal Oil Products Company, 1954–1955, Standard Oil Company (Indiana) 1955–1956.

(3) (a) H. Pines, J. A. Vesely and V. N. Ipatieff, THIS JOURNAL, **77**, 347 (1955); (b) **77**, 554 (1955); (c) H. Pines and H. E. Eschinazi, *ibid.*, **77**, 6314 (1955); (d) **78**, 1178 (1956); (c) H. Pines and V. Mark, *ibid.*, **78**, 4316 (1956); (f) H. Hart, *ibid.*, **78**, 2619 (1956); (g) A. A. Morton and E. J. Lanpher, *J. Org. Chem.*, **20**, 839 (1955); (h) **21**, 93 (1956).