lected by filtration, washed with water, and dissolved in methylene chloride, and the dried (sodium sulfate) methylene chloride solution was distilled to dryness. Trituration of the residue with petroleum ether (b.p. 40–60°) gave 9.7 g. of white crystals, m.p. 170–171°. Recrystallization from ethanol gave material with m.p. 170–171°; ν_{max} 1671 and 1156 cm.$^{-1}$; λ_{max} mμ (ϵ), 270 (3270), 277 (3180), 286 (2680); λ_{min} 268 (3250), 274 (3180), 283 (2500).

Anal. Calcd. for $C_{15}H_{13}NO_3S$: C, 62.70; H, 4.56; N, 4.87; S, 11.16. Found: C, 62.61; H, 4.66; N, 4.93; S, 11.21.

B. Preparation by Oxidation of 3-Methyl-2-phenyl-2*H*-1,3-benzothiazin-4(3*H*)-one.—To a solution of 3.5 g. (0.014 mole) of the thioether[7] in 25 ml. of glacial acetic acid was added 20 ml. of 30% hydrogen peroxide. The solution was allowed to stand at room temperature for 10 days and was then poured into 300 ml. of water. The resulting white precipitate was collected, washed well with water, and dissolved in methylene chloride, and the dried (sodium sulfate) methylene chloride solution was distilled to dryness. The residue was triturated with low boiling petroleum ether to give 3.3 g. of product, m.p. 170–171°, which was shown by mixture melting point and by comparison of infrared and ultraviolet spectra to be identical with material prepared by A.

2-Phenyl-2*H*-1,3-benzothiazin-4(3*H*)-one 1,1-Dioxide (VII).—To a suspension of 0.8 g. of 53.4% mineral oil dispersion of sodium hydride (0.015 mole) in 50 ml. of dimethylformamide was added a solution of 5 g. (0.015 mole) of N-(α-phenylcarbethoxymethyl)saccharin in 25 ml. of dimethylformamide, the temperature being maintained between 0 and 10°. The orange solution was stirred at room temperature for 3 hr. and then was poured into 1000 ml. of absolute ether. A gum separated, and this became a semisolid after several triturations with fresh portions of ether. The semisolid was dissolved in 150 ml. of water and on acidification of this solution with dilute hydrochloric acid there was obtained a white precipitate. This was filtered off, washed with water, and was dried *in vacuo* at 60° to give 0.7 g. of material, m.p. 177–178°. Recrystallization from ethanol yielded a product, m.p. 185–186°; ν_{max} 3200, 1680, and 1154 cm.$^{-1}$; the ultraviolet spectrum was identical with that of the corresponding N-methyl compound (VI).

Anal. Calcd. for $C_{14}H_{11}NO_3S$: C, 61.53; H, 4.06; N, 5.12; S, 11.73. Found: C, 61.37; H, 4.23; N, 5.15; S, 11.64.

On stirring a portion of this compound with 1 *N* sodium hydroxide, there was immediately noted the odor of benzaldehyde.

3-Methyl-2-phenyl-2*H*-1,3-benzothiazin-4(3*H*)-one 1-Oxide.—To a solution of 5.2 g. (0.02 mole) of 3-methyl-2-phenyl-2*H*-1,3-benzothiazin-4(3*H*)-one in 60 ml. of glacial acetic acid was added 20 ml. of 30% hydrogen peroxide. The solution was allowed to stand at room temperature for 24 hr. and was then poured into 400 ml. of ice–water. Extraction with methylene chloride followed by drying over sodium sulfate and evaporation of the solvent gave an oil. This was crystallized from 40 ml. of ethanol to yield 3.0 g. of product, m.p. 170–172°. Recrystallization did not change the melting point. Mixture melting point with a sample of the corresponding sulfone gave a 20° depression; ν_{max} 1656, 1640, 1052, no significant absorption at 1100–1200 cm.$^{-1}$; λ_{max} mμ (ϵ), 272 (2800), 280 (2750), 289 sh (2420); λ_{min} 276 (2700), 285 (2490).

Anal. Calcd. for $C_{15}H_{13}NO_2S$: C, 66.40; H, 4.83; S, 11.82. Found: C, 66.23; H, 4.80; S, 11.85.

N-Nitrosoamides. VI. Nitrosocarbamates and Nitrosoamides of Amino Acids. The Preparation of Diazoacetic and Diazopropionic Esters[1]

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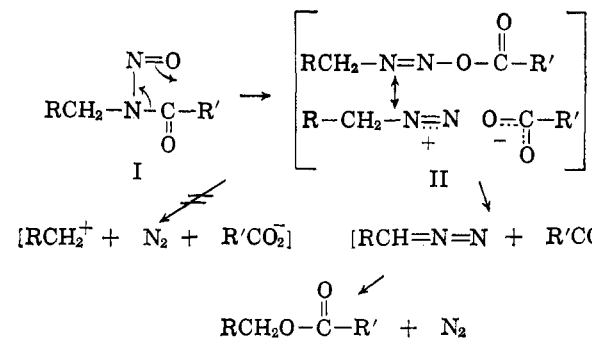
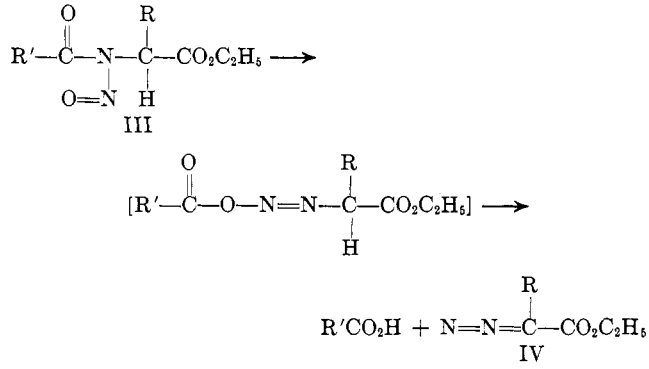
N-Nitrosoamides of primary carbinamines (I) decompose to give the corresponding esters *via* a reaction

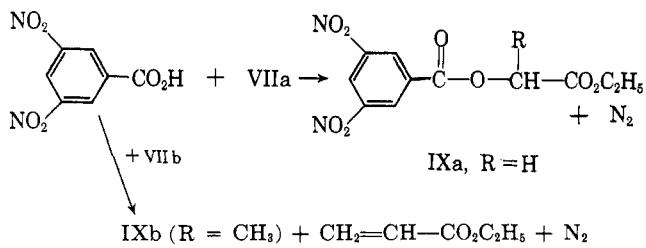


series involving diazo alkanes as intermediates.[3] The carbonium ion pathway, found for the decomposition of nitrosoamides of secondary carbinamines,[1] is not followed, presumably because of the relatively high energy of a primary carbonium ion (formed by the loss of nitrogen from II). The decomposition of nitrosoamides or nitrosocarbamates of amino acid esters (III) also yields the corresponding diazo compound (IV), which, in this case, can be isolated because of the low general reactivity of α-diazocarbonyl compounds. We report here the decomposition of several of these nitroso compounds.[4]



N-Nitrosocarbamates.—These derivatives of glycine and alanine were readily prepared by the acylation of the corresponding esters, and subsequent nitrosation of the carbamates with either nitrogen tetroxide or nitrous acid. The pyrolysis of compounds VIa and VIb at 125–135° and 50–100 mm. (under conditions whereby the product was distilled from the reaction vessel) led to *ca.* 70% yields of the corresponding diazo esters (Scheme I).

The diazo esters were identified through their infrared spectra, and assayed by the reaction with 3,5-dinitrobenzoic acid. These dinitrobenzoate derivatives, which apparently have not been reported previously, were prepared from ethyl chloroacetate and ethyl lactate for comparison purposes. The diazo



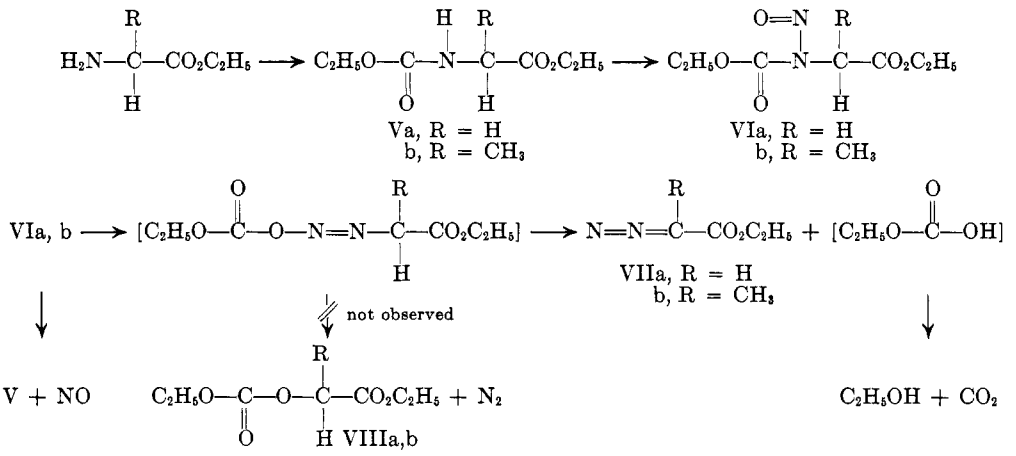
(1) Paper V in this series: E. H. White and C. A. Aufdermarsh, Jr., *J. Am. Chem. Soc.*, **83**, 1179 (1961).

(2) Taken in part from a thesis submitted by R. J. Baumgarten to the Faculty of the Graduate School at The Johns Hopkins University in partial fulfillment of the requirements for the Ph.D. degree.

(3) E. H. White and C. A. Aufdermarsh, Jr., *J. Am. Chem. Soc.*, **83**, 1174 (1961).

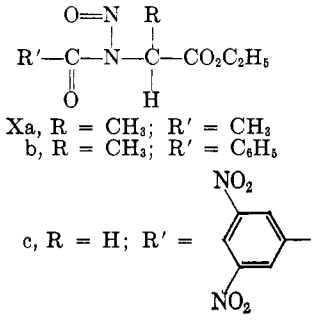
(4) Preliminary results were given by E. H. White, *ibid.*, **77**, 6013 (1955).

SCHEME I



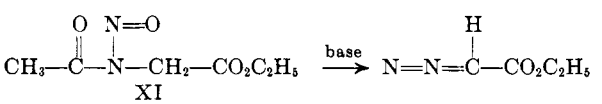
esters were pure as obtained from the reaction. The reaction sequence represents, therefore, a convenient method for the preparation of diazoacetic esters and related compounds. One by-product was found; this is the relatively nonvolatile carbamate V. We have observed the thermal denitrosation of N-nitrosocarbamates in a number of other cases, and, in addition, Newman and Weinberg[5] have shown that some related N-nitrosooxazolidones also undergo pyrolytic denitrosation. The corresponding carbonates (VIII) were not detected among the reaction products.

N-Nitrosamides.—Extension of the reaction to several N-nitrosoamides was less successful. Com-



pounds Xa and Xb yielded mixtures of ethyl diazopropionate and the corresponding acid ($R'CO_2H$) on pyrolysis, whereas compound Xc yielded principally the starting amide, presumably a result of denitrosation catalyzed by the rather strong acid, 3,5-dinitrobenzoic acid.

Ethyl Diazoacetate.—This compound has usually been made by the reaction of nitrous acid with ethyl glycinate.[6] Recently, Reimlinger[7] reported a synthesis based on the reaction of ethyl N-acetyl-N-nitrosoglycinate (XI) with barium oxide. We have found



that sodium ethoxide may also be used as the base; however, the simplest method proved to be the reaction of tetraethylenepentamine with the nitrosoamide under conditions whereby the ethyl diazoacetate could be distilled out of the reaction vessel as it was formed.[8]

(5) M. S. Newman and A. E. Weinberg, *J. Am. Chem. Soc.*, **79**, 2814 (1957).
(6) N. E. Searle, *Org. Syn.*, **36**, 25 (1956).
(7) H. Reimlinger, *Angew. Chem.*, **72**, 33 (1960).
(8) We thank Dr. G. Maier for this experiment.

Experimental

Ethyl N-carbethoxyglycinate (Va) ($n^{19.5}D$ 1.4379, d^{20}_4 1.135, b.p. 78–80° (0.3 mm.), m.p. 26–27°; lit.[9] b.p. 126° (12 mm.), m.p. 27–28°) and **ethyl N-carbethoxyalanate (Vb)**[10] ($n^{12}D$ 1.4391, d^{20}_4 1.080, b.p. 65–70° (0.1 mm.), m.p. 24–25°; lit.[11] b.p. 123° (10 mm.), m.p. 25°) were prepared in 50–80% yields by the method of Fisher and Otto.[9] **Ethyl carbethoxymethyl carbonate (VIIIa)** and **ethyl 1-carbethoxyethyl carbonate (VIIIb)** were prepared by the method of Rehberg, Dixon, and Fisher.[12]

Ethyl N-Carbethoxy-N-nitrosoglycinate (VIa).[13]—Anhydrous sodium acetate (13 g., 0.16 mole) was added to a solution of 10 g. (0.11 mole) of nitrogen tetroxide in 50 ml. of methylene chloride.[14] The solution was cooled to −70° at which time 10 g. (0.057 mole) of carbamate Va was added dropwise while the solution was being stirred. The solution was warmed to 0° and the reaction was allowed to proceed for 20 min. after which most of the nitrogen tetroxide and methylene chloride were evaporated *in vacuo*. The residue was extracted with ether and the extract was washed with sodium carbonate solution and water. After the extract was dried over sodium sulfate, the ether was evaporated *in vacuo* to give nitrosocarbamate VIa which was distilled to yield 11 g. (0.054 mole, 95%) of the yellowish pink nitrosocarbamate, b.p. 60–62° (0.1 mm.), $n^{14}D$ 1.4456, λ_{max} 242 mμ (ϵ 6.0×10^3). Compound VIa was also prepared by the aqueous method of White[14] and by the method of Hantzsch and Metcalf.[15]

Ethyl N-Carbethoxy-N-nitrosoalanate (VIb).[13]—The nitrogen tetroxide and nitrous acid methods of White[14] were used to obtain nitrosocarbamate VIb in 55–90% yields [$n^{13}D$ 1.4446, b.p. 38–40° (0.01 mm.), λ_{max} 243 mμ (ϵ 4.01×10^3)]. Compound VIb was unstable and decomposed slowly at room temperature.

Pyrolysis of Ethyl N-Carbethoxy-N-nitrosoglycinate (VIa).—Nitrosocarbamate VIa (290 mg., 1.42 mmoles) was heated for 10 hr. at 125–140° (50–100 mm.) in a 2-ml. pear-shaped flask equipped with a fractionating column and a receiver cooled by a Dry Ice–acetone bath. The yellow liquid product was collected in three fractions, and the ethanol was removed from the product by evaporation at 20 mm. The yield of ethyl diazoacetate (VIIa) was 120 mg. (1.05 mmoles, 74%), $n^{21}D$ 1.4611, lit.[6] $n^{25}D$ 1.4616. The infrared spectrum of this sample was identical with the spectrum of ethyl diazoacetate prepared by the reaction of nitrous acid with ethyl glycinate.[6] Treatment of the entire distillate with 3,5-dinitrobenzoic acid yielded 69 mole % of the ester IXa. The infrared spectrum of the brown residue in the distillation flask (60 mg., 0.34 mmole, 24%) was identical with the infrared spectrum of the carbamate Va.

Runs were also made at pressures ranging from atmospheric to 0.2 mm. and at temperatures ranging from 90 to 145°; however, the conditions reported above were optimum. At high pressures and temperatures, the yields were lower, and at pressures less than 1 mm., the reactant distilled.

(9) E. Fisher and E. Otto, *Ber.*, **36**, 2107 (1903).
(10) We wish to thank Donald E. Schmelz for preparing this compound.
(11) E. Fisher and W. Axhausen, *Ann.*, **340**, 139 (1905).
(12) C. E. Rehberg, M. B. Dixon, and C. H. Fisher, *J. Org. Chem.*, **13**, 261 (1948).
(13) Repeated contact with these nitroso compounds led to skin rashes.
(14) E. H. White, *J. Am. Chem. Soc.*, **77**, 6008 (1955); see also ref. 3.
(15) A. Hantzsch and W. V. Metcalf, *Ber.*, **29**, 1682 (1896).

Pyrolysis of Ethyl N-Carbethoxy-N-nitrosoalanate (VIb).—Nitrosocarbamate VIb (2.12 g., 9.72 mmoles) was heated for 8 hr. at 125–135° (50–100 mm.) in the same apparatus used in the pyrolysis of the nitrosocarbamate VIa. The yield of yellow ethyl α-diazopropionate (VIIb) (n^{18}D 1.4489, lit.[16] n^{18}D 1.4472) was 0.89 g. (6.9 mmoles, 71%); the infrared spectrum was consistent with the structure assigned. Treatment with 3,5-dinitrobenzoic acid yielded the ester IXb, m.p. 74.5–76°. An infrared spectrum of the dark residue (0.45 g., 2.4 mmoles, 25%) was identical with the spectrum of carbamate Vb; distillation of the brown residue gave the carbamate Vb (n^{14}D 1.4397). Pyrolyses in the presence of solid sodium carbonate led to essentially the same results. For optimum yields in the pyrolyses, temperatures between 115 and 140° and pressures between 50 and 150 mm. should be used.

Reaction of Ethyl Diazoacetate (VIIa) with 3,5-Dinitrobenzoic Acid.—Ethyl diazoacetate (0.101 g., 0.89 mmole) was mixed with 0.188 g. (0.89 mmole) of 3,5-dinitrobenzoic acid and the stirred mixture was kept at 0°. After 1 day, 10 ml. of ether was added and the mixture was stirred at 25–30° for 1 day. Ether was added to a total volume of 50 ml. and the solution was washed with cold sodium bicarbonate solution and water, and then dried. When the ether was evaporated *in vacuo*, 0.249 g. (0.84 mmole, 94%) of light yellow crystals was obtained, m.p. 59–60°. The infrared spectrum of this ester (IXa) was identical with the spectrum of ester prepared from ethyl chloroacetate (*vide infra*).

Reaction of Ethyl α-Diazopropionate (VIIb) with 3,5-Dinitrobenzoic Acid.—Compound VIIb (0.50 g., 3.9 mmoles) and 3,5-dinitrobenzoic acid (0.83 g., 3.9 mmoles) were dissolved in 25 ml. of dry dioxane and the solution was kept at 25–30° for 2 days. The volatiles were evaporated *in vacuo* to give 0.17 g. (0.54 mmole 14%) of ester IXb, m.p. 74.5–76°. The infrared spectrum was identical with that of a sample of the ester prepared from ethyl lactate (*vide infra*).

Carbethoxymethyl 3,5-Dinitrobenzoate (IXa).—Sodium 3,5-dinitrobenzoate (2.8 g., 12 mmoles) was dissolved in 50 ml. of 50% aqueous ethanol. After 1.2 g. (9.8 mmoles) of ethyl chloroacetate and 1.5 g. (10 mmoles) of sodium iodide were added, the mixture was heated on the steam bath for 4 hr. Most of the solvent was removed *in vacuo*, after which the residue was extracted with ether. The ether was removed to give 1.4 g. (4.7 mmoles, 48%) of yellow crystalline ester, m.p. 48–51°. After three recrystallizations from methylene chloride–hexane, 0.13 g. (0.44 mmole) of very light yellow needles of ester IXa was isolated, m.p. 59–60°.

Anal. Calcd. for $C_{11}H_{10}N_2O_8$: C, 44.30; H, 3.38; N, 9.40. Found: C, 44.36; H, 3.65; N, 9.46.

1-Carbethoxyethyl 3,5-Dinitrobenzoate (IXb).—Ethyl lactate (3.5 g., 0.030 mole) and 4.0 g. (0.020 mole) of 3,5-dinitrobenzoyl chloride were added to 25 ml. of dry pyridine. The reaction was allowed to proceed with stirring at room temperature for 2 hr. after which the pyridine was removed *in vacuo* to give a highly viscous residue. This residue was dissolved in methylene chloride and washed successively with dilute hydrochloric acid, sodium bicarbonate solution, and water. The solution was then dried and evaporated to a yellow-brown solid (4.1 g., 0.013 mole, 65%; m.p. 66–70°) which was fractionally crystallized from methylene chloride–hexane at 0°. White needles of ester IXb were obtained, m.p. 75–76° (0.80 g., 2.6 mmoles, 13.0%).

Anal. Calcd. for $C_{12}H_{12}N_2O_8$: C, 46.16; H, 3.38; N, 8.97. Found: C, 46.02; H, 3.66; N, 8.95.

An attempt to prepare ester IXb from excess ethyl lactate and 3,5-dinitrobenzoyl chloride in the absence of pyridine at 70° yielded mainly ethyl 3,5-dinitrobenzoate.

Ethyl N-(3,5-Dinitrobenzoyl)glycinate.—This compound (light yellow needles from methylene chloride–hexane, m.p. 152–154°) was prepared in 56% yield from ethyl glycinate hydrochloride and 3,5-dinitrobenzoyl chloride in dry pyridine (4-hr. reaction time).

Anal. Calcd. for $C_{11}H_{11}N_3O_7$: C, 44.45; eq. H, 3.73; eq. N, 14.13. Found: C, 44.51; H, 3.71; N, 13.97.

Ethyl N-(3,5-Dinitrobenzoyl)-N-nitrosoglycinate (Xc).—This compound was prepared in 73% yield by the nitrogen tetroxide nitrosation of the corresponding amide (see above) in methylene chloride.[14] Recrystallization from ether–hexane mixtures yielded light yellow crystals of Xc, m.p. 68–70° (followed by gas evolution at 78°). This compound was unstable, and samples showed signs of decomposition (NO_2) after several days.

(16) T. Curtius and E. Müller, *Ber.*, **37**, 1269 (1904).

Anal. Calcd. for $C_{11}H_{10}N_4O_8$: C, 40.50; H, 3.10; N, 17.17. Found: C, 40.42; H, 3.04; N, 16.28.

Pyrolysis of this compound at 75° (100 mμ) yielded principally the parent amide. Recrystallization of the product yielded pure amide, m.p. 151–154°.

The Nitrosoacetamide and Benzamide of Ethyl Alanate.[13]—These compounds were prepared by the nitrogen tetroxide nitrosation of the acetyl and benzoyl derivatives of methyl alanate. Pyrolyses at 50–90° (100–200 mm.) yielded a mixture of ethyl diazopropionate and the carboxylic acids; the acid could be removed with dilute solutions of sodium carbonate.

Ethyl Diazoacetate (VIIa).—In addition to the pyrolytic methods outlined above, this compound can be prepared in 50–75% yields by the dropwise addition of ethyl N-nitroso-N-acetylglycinate to an excess of tetraethylenepentamine under high vacuum. The mixture is stirred vigorously and the product collected in a cooled receiver; about 4–8 hr. are required for the reaction.

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Action of Nitrous Acid on Osazone Acetates. A New Synthesis of Osotriazoles

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Osazones are known[1] to react with nitrous acid to give first the aldosulose ("osone") 1-hydrazone (II) and then with excess reagent to yield the aldosulose (IV) in yields up to 65%. We have now carried out this reaction with the tetra-*O*-acetylphenylosazones from D-galactose, D-glucose, and L-sorbose, but, instead of the expected aldosulose tetraacetates, we obtained the corresponding phenylosotriazole tetraacetates in about 80% yields. The D-galactose derivative crystallized from the crude reaction mixture and the D-glucose and L-sorbose derivatives were identified by deacetylation to the free osotriazoles. The different course followed by the reaction with osazone acetates seems to be due to the absence in the molecule of free hydroxyl groups which allow the formation of cyclic modifications. Osazone acetates have been shown[2] to possess acyclic bis(hydrazone) structures (V), whereas the unacetylated derivatives may form in solution some of the cyclic hydrazino hydrazone forms (I). If we now assume that nitrous acid reacts more rapidly with the labile and highly reactive hydrazino group,[3] than with a true hydrazone residue, we would expect the unacetylated osazones to undergo a series of cyclizations and eliminations of hydrazino groups leading first to the aldosulose hydrazone (II) and finally to the aldosulose (IV). Scission of the hydrazino groups is probably achieved through the intermediate

(1) H. Ohle, G. Henseke, and A. Czyzewski, *Ber.*, **86**, 316 (1953); G. Henseke and M. Winter, *ibid.*, **89**, 956 (1956).

(2) M. L. Wolfrom, M. Konigsberg, and S. Soltzberg, *J. Am. Chem. Soc.*, **58**, 490 (1936).

(3) H. S. Isbell, *Ann. Rev. Biochem.*, **12**, 205 (1943); F. Weygand, *Ber.*, **73**, 1284 (1940).