"natural" adsorption and the "exchange" adsorption. The "natural" adsorption depends on the dilution and *P*H value of the solution. The "exchange" adsorption seems to depend on the mineral content of the original ash, principally on the amounts of calcium and iron present.

3. The mechanism of the hydrolysis of aluminum acetate is shown to be the same as for the chloride and sulfate solutions, while the adsorption increases with increasing hydrolysis, being highest for the acetate.

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[CONTRIBUTION NO. 66 FROM THE COBB CHEMICAL LABORATORY OF THE UNIVERSITY OF VIRGINIA]

RING ENLARGEMENT WITH DIAZOMETHANE IN THE HYDROAROMATIC SERIES[1]

BY ERICH MOSETTIG AND ALFRED BURGER

RECEIVED JUNE 9, 1930 PUBLISHED AUGUST 5, 1930

The present investigation was begun in a search for a preparative way to amino-alcohols of the type V, since compounds of this class may be expected to have interesting pharmacological properties. The oxide III appears to be the most convenient starting point for the synthesis of such substances; by simple addition of primary and secondary amines, with opening of the ethylene oxide ring, the oxide must be converted to amino-alcohols of the desired type. A method for the preparation of this hitherto unknown oxide lies in the action of diazomethane on cyclohexanone; the expected oxide represents, however, but one phase of the reaction.

The action of diazomethane on the carbonyl group in the aliphatic, aromatic, and heterocyclic series has been the subject of numerous recent investigations. Arndt and his co-workers[2] were the first to show that the reaction discovered by H. Meyer[3] and Schlotterbeck,[4] in which aldehydes are converted to the corresponding ketones by the action of diazomethane

$$\mathrm{RCHO} \xrightarrow{\mathrm{CH_2N_2}} \mathrm{RCOCH_3}$$

is not of general application. In some cases the reaction leads to the isomeric ethylene oxide derivative, while the ketone and a homolog are formed in small amounts as by-products. The mechanism postulated

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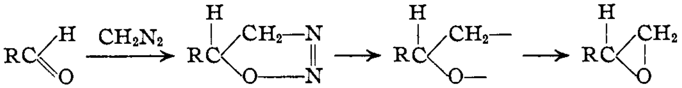
[1] This work was supported by funds from the Committee on Drug Addiction of the National Research Council.

[2] Arndt and Partale, *Ber.*, **60**, 446 (1927); Arndt, *Z. angew. Chem.*, **40**, 1099 (1927); Arndt and Eistert, *Ber.*, **61**, 1118 (1928); *cf.* Arndt, Eistert, and Amende, *ibid.*, **61**, 1952 (1928); Arndt, Eistert, and Ender, *ibid.*, **62**, 44 (1929).

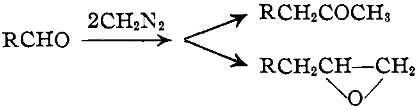
[3] H. Meyer, *Monatsh.*, **26**, 1300 (1905); *Ber.*, **40**, 847 (1907).

[4] Schlotterbeck, *ibid.*, **40**, 479 (1907); **42**, 2559 (1909).

by these authors, which also accounts for the occurrence of the by-products, expresses the formation of the oxide by the equation

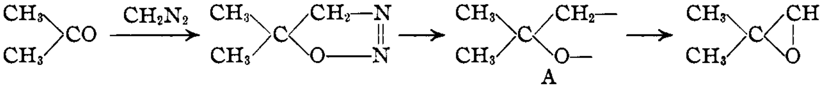


Mosettig[5] in an independent investigation of a special case—that of piperonal—obtained results differing from those of Arndt; from this aldehyde the chief products were substances which must have been formed by introduction of two CH_2 groups into the aldehyde



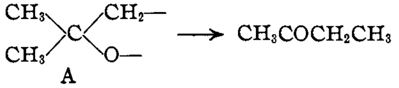
These results may easily be explained according to the Arndt mechanism; in this connection the influence of the methyl alcohol added to the reaction mixture has been emphasized.[6]

Meerwein and Burneleit[7] investigated at about the same time the action of diazomethane on acetone. Acetone alone is indifferent toward diazomethane, but reacts in the presence of catalysts, as water, alcohols or metal salts, to form asymmetric dimethyl ethylene oxide as the chief product, together with methyl ethyl ketone, and probably methyl *n*-propyl ketone and diethyl ketone. These authors formulated the reaction as proceeding to the oxide in the way already expressed by Arndt for aldehydes, in the equation



(1)

and postulated further that, through wandering of a CH_3 group in the hypothetical intermediate A, methyl ethyl ketone is formed



(2)

This ketone then reacts further with diazomethane to form in an analogous way the higher ketones, which were shown to be probably present.

Cyclohexanone, in ethereal solution, is practically indifferent toward diazomethane. When methyl alcohol is added, a rather vigorous reaction, with nitrogen evolution, begins. We were able to isolate as products cycloheptanone (suberone), cyclo-octanone (azelaone) and an oxide (III), isomeric with cycloheptanone. The chief product is cycloheptanone, while

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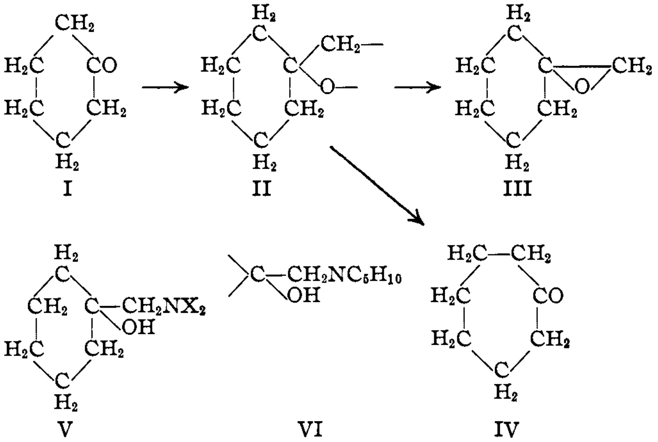
[5] Mosettig, *Ber.*, **61**, 1391 (1928); **62**, 1271 (1929).

[6] *Cf.* Mosettig and Jovanovič, *Monatsh.*, **53 and 54**, 430, footnote 6 (1929).

[7] Meerwein and Burneleit, *Ber.*, **61**, 1840 (1928). *Cf.* Meerwein, Bersin and Burneleit, *ibid.*, **62**, 999 (1929).

cyclo-octanone and the oxide in nearly equal amounts represent by-products. Following the Arndt–Meerwein scheme, the process may be represented



The conversion of II to III takes place parallel to that in Equation 1 for acetone, II to IV as in Equation 2; a ring CH_2 group adjacent to the carbonyl wanders to the open methylene group, which in this case must lead to expansion of the ring.[8] The transformation of cycloheptanone into cyclo-octanone takes place in an analogous way.

In order to exclude any possibility of error, the cyclohexanone employed was purified through the bisulfite compound and semicarbazone. The reaction products were separated by treating the ethereal solution with sodium bisulfite, which removed cycloheptanone. The cyclo-octanone, which forms no bisulfite compound,[9] could be separated from the oxide III in two ways: by precipitation as the semicarbazone, or by treating the mixture with piperidine, and making use of the basic properties of the resulting piperidino alcohol to separate it from the cyclo-octanone, which is obviously indifferent to piperidine under the conditions of the experiment.

The cycloheptanone was characterized as semicarbazone and dibenzylidene compound, which were compared by mixed melting point with the same derivatives of cycloheptanone from suberic acid.

Cyclo-octanone was likewise identified in the form of its semicarbazone and dibenzylidene compound; the semicarbazone was compared with a

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[8] Ring expansion with diazomethane was observed for the first time by Heller [*Ber.*, **52**, 741 (1919); **59**, 704 (1926)] in the change of isatin to dihydroxyquinoline. Arndt [Arndt, Eistert and Ender, *ibid.*, **62**, 44 (1929)], in the course of his investigations, revised and clarified the Heller formulation, in the light of his work. Very recently Hantzsch and Czapp have reported the conversion of oxindone-carboxylic ester into 1-hydroxy-4-methoxynaphthaline-2-carboxylic ester [*ibid.*, **63**, 566 (1930)]. *Cf.* Arndt, *ibid.*, **63**, 1180 (1930).

[9] Ruzicka and Brugger, *Helv. Chim. Acta*, **9**, 339 (1926).

sample of cyclo-octanone semicarbazone generously supplied by Professor Ruzicka, with which it showed no depression in mixed melting point.

The oxide III was isomerized by distillation at atmospheric pressure over a trace of zinc chloride to hexahydrobenzaldehyde, which was characterized as the semicarbazone. This semicarbazone proved to be identical (mixed melting point) with the semicarbazone of hexahydrobenzaldehyde prepared according to Kon[10] from cyclohexylmagnesium chloride and ethyl orthoformate.

The oxide was also converted to a piperidino alcohol, which probably has the structure VI, assuming that the addition of the amine takes place in accordance with the general rule for addition of ammonia or amines to asymmetric ethylene oxides, the hydroxyl being formed on the carbon carrying the least hydrogen.

It is not excluded that the oxide III may have undergone some change, as isomerization, hydration or polymerization during the bisulfite treatment; this method of separation seemed, however, the most practicable. The cycloheptanone results from a primary reaction, as is shown by the simultaneous appearance of cyclo-octanone, which can hardly be explained except as a product of the further reaction of diazomethane on cycloheptanone formed in the original reaction mixture. The starting substance, cyclohexanone, could not be detected in the end-products.

Cyclopentanone was brought into reaction with diazomethane under the same conditions as in the case of cyclohexanone; for convenience in working up the product, an excess of diazomethane was used. The products of the completed reaction were worked up in the same manner as for the cyclohexanone reaction; cycloheptanone was found to be the chief product; cyclo-octanone was formed in smaller amount. Isomerization of the oxide fraction resulted in an aldehyde-containing distillate (fuchsin-sulfurous acid test) but separation of the mixture of semicarbazones (probably of cyclopentane aldehyde and hexahydrobenzaldehyde) failed. No crystalline products could be obtained from the action of piperidine. Cyclopentanone and cyclohexanone could not be detected.

The ring expansion described in this paper brings a new proof of the validity of the Meerwein assumption of radical wandering in the hypothetical intermediate A in Equation 2. It is possible that still higher homologs of the cyclic ketones or oxides are present among the reaction products from cyclopentanone and cyclohexanone. A systematic investigation carried out on large quantities of the homologous cyclic ketones might decide this, and at the same time make important contributions to our knowledge of ring strain and ring widening. A similar study of the action of diazo-ethane and its homologs would also be desirable in this connection, but lies outside the field of our researches.

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[10] Kon, *J. Chem. Soc.*, **128**, 1797 (1926).

Ketones of hydroaromatic nature which share two carbon atoms with one or more aromatic rings offer better prospects of success for the preparation of oxides of the desired type. We plan therefore to extend our studies of this reaction to tetralon (ketotetrahydronaphthalene) and its analogs.

In consideration of the relatively good yield, ease of preparation and purity of the cycloheptanone and cyclo-octanone obtained in the reaction described, and of the difficulty of the hitherto known preparative methods for these ketones, we believe that the action of diazomethane on cyclohexanone offers a practicable preparative way to these substances.

We take great pleasure in acknowledging our indebtedness to Professor Ruzicka for a sample of cyclo-octanone semicarbazone.

Experimental Part

Cyclohexanone and Diazomethane.—Cyclohexanone was converted into the bisulfite addition compound, and the ketone obtained from decomposition of this with alkali was fractionally distilled. The semicarbazone of the fraction boiling at 157° (corr.) was prepared and recrystallized from methyl alcohol (m. p. 167.5–169°), decomposed with hydrochloric acid, and the cyclohexanone obtained by steam distillation was finally again fractionally distilled.

The diazomethane was prepared from the action of methyl alcoholic potassium hydroxide on nitrosomethylurethan, and titrated with nitrobenzoic acid.

Twenty-four grams of cyclohexanone was added to a solution of 13.6 g. of diazomethane in 900 cc. of dry ether, cooled in ice. No significant evolution of nitrogen took place, even on long standing at 0°; on addition of 200 cc. of absolute methyl alcohol, a vigorous evolution of nitrogen began. When this began to diminish, after several hours, the reaction mixture was removed from the ice-bath, and allowed to stand at room temperature. On the next day the solution was noticeably lighter in color but became completely colorless only after three days. The colorless solution was filtered free of a slight flocculent precipitate (polymethylenes), the ether evaporated and the methyl alcohol removed in vacuum at 22° with a fractionating column. It is here unavoidable that small amounts of volatile substances from the reaction product distil off with the methyl alcohol or ether. For this reason the methyl alcohol was again distilled in vacuum with a fractionating column. The combined distillation residues were dissolved in about 100 cc. of ether and shaken for two to three hours with saturated sodium bisulfite solution. The crystallized bisulfite compound which separated was filtered out and washed many times with ether. The filtrate, consisting of a bisulfite and an ethereal layer, was separated, the bisulfite layer shaken out several times with ether and the ethereal extract combined with the ether layer above mentioned.

The combined ether was washed several times with dilute sodium carbonate solution and dried over sodium sulfate. It contained the oxide and the cyclo-octanone. After evaporation of the ether, the residue was distilled at 20 mm. pressure and the following fractions were collected: Fraction 1, b. p. 35–60°, 2 g.; Fraction 2, b. p. 61–95°, 6.5 g.; Fraction 3, b. p. 95–105°, 2.6 g.

Fraction 1, which consisted chiefly of the oxide, and gave no color with fuchsin-sulfurous acid, was distilled twice at atmospheric pressure over a trace of freshly fused zinc chloride. A drop of the distillate gave with fuchsin-sulfurous acid an intense red-violet color, showing that the isomerization to the aldehyde had taken place. On addition of an aqueous solution of semicarbazide hydrochloride and sodium acetate, a semicarbazone precipitated out immediately; crystallized three times from methyl alcohol, it formed shining leaflets or needles of m. p. 171–172° (sintering at 170°).

Anal. Subs., 4.216 mg.: 0.931 cc. of N (24°, 749 mm.). Calcd. for $C_8H_{15}ON_3$: N, 24.85. Found: N, 25.01.

To confirm the assumption that this was the semicarbazone of hexahydrobenzaldehyde, hexahydrobenzaldehyde was prepared by the method of Kon[10] from cyclohexylmagnesium chloride and ethyl orthoformate. The semicarbazone of this melted at 172.5–173°, sintering at 171°; the mixed melting point with the semicarbazone of the product from isomerization of the oxide was 171–172°.[11]

Fraction 3 consisted chiefly of cyclo-octanone. It crystallized to a thick paste when cooled in a freezing mixture. It was converted to a semicarbazone in the same manner as Fraction 1, which had the melting point 167.5–169° after one recrystallization from methyl alcohol.

Anal. Subs., 3.586 mg.: 0.739 cc. of N (23°, 744 mm.), 3.680 mg.; CO_2, 7.955 mg.; H_2O, 3.100 mg. Calcd. for $C_9H_{17}ON_3$: C, 58.96; H, 9.36; N, 22.94. Found: C, 58.95; H, 9.43; N, 23.26.

The mixed melting point with Ruzicka's sample of cyclo-octanone semicarbazone of m. p. 168–169° lay at 168–169°.

The colorless dibenzylidene compound of cyclo-octanone, which was obtained in analogy with the Wallach[12] dibenzylidene compound from suberone by condensation with two moles of freshly distilled benzaldehyde in the presence of sodium methylate, melted after recrystallization from slightly diluted methyl alcohol at 107.5–109° (the mixed melting point with the dibenzylidene compound of the same melting point from suberone lay at 85–95°).

Anal. Subs., 0.0876: CO_2, 0.2791; H_2O, 0.0572. Calcd. for $C_{22}H_{22}O$: C, 87.37; H, 7.33. Found: C, 86.89; H, 7.31.

Fraction 2 consists apparently of the oxide and cyclo-octanone. Since the small quantity of material put fractional distillation out of consideration, the cyclo-octanone was separated from a sample of the mixture with semicarbazide hydrochloride and sodium acetate. The well-pressed semicarbazone was recrystallized from methyl alcohol and melted at 167–169°. The main portion of Fraction 2 was heated with an equal weight of water and of piperidine in a sealed tube for six hours at 95–100°. The reaction mixture was taken up in ether and water, and the ether layer washed with water to remove most of the unreacted piperidine. The piperidino alcohol was now extracted out of the ether with dilute hydrochloric acid; in the ether remained the unaffected cyclo-octanone, which was characterized as the semicarbazone. The acid layer was made alkaline and extracted with ether. The brown oily residue from evaporation of the ether was freed from piperidine by standing for many days over phosphorus pentoxide in a vacuum desiccator. It was then brought into dry ethereal solution, and the base precipitated as the hydrochloride by addition of ethereal hydrochloric acid. The hydrochloride was dissolved in alcohol and ether added to the point where the solution barely remained clear; on standing, crystals separated, m. p. 194.5–195°.

Anal. Subs., 0.2073: AgCl, 0.1262; 5.476 mg, 0.286 cc. of N (25°, 752 mm.). Calcd. for $C_{12}H_{24}ONCl$: Cl, 15.18; N, 6.00. Found: Cl, 15.06; N, 5.92.

The piperidino alcohol gave no crystalline picrate.

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[11] The melting points of semicarbazones in general depend upon the mode of heating. Perhaps the considerable differences in melting point of this semicarbazone to be found in the literature may be due to this fact. Wallach, *Ann.*, **347**, 333 (1906), m. p. 167–168°; Zelinsky, *Ber.*, **40**, 3051 (1907), m. p. 173–174°; Bouveault, *Bull. soc. chim.*, [3] **29**, 1050 (1903), m. p. 176°; Sircar, *J. Chem. Soc.*, 55 (1928), m. p. 175°; Danilow and Danilowa, *Ber.*, **62**, 2668 (1929), m. p. 173°.

[12] Wallach, *ibid.*, **29**, 1600 (1896).

Suberone.—The bisulfite compound separated from the original reaction mixture was combined with the bisulfite mother liquor, made alkaline with sodium carbonate, and the ketone which separated distilled out with steam. The distillate was extracted with ether, this evaporated and the residue distilled in vacuum. At 15 mm. the boiling point was 68–70°, yield 9.6 g. of a colorless oil which proved to be nearly pure suberone. The semicarbazone prepared from it melted after one crystallization from methyl alcohol at 163–163.5°, sintering at 162°.

Anal. Subs., 2.455 mg.: 0.549 cc. of N (24°, 743 mm.), 0.0771 g.; CO_2, 0.1611; H_2O, 0.0641. Calcd. for $C_8H_{15}ON_3$: C, 56.76; H, 8.94; N, 24.85. Found: C, 56.99; H, 9.30; N, 25.13.

The mixed melting point with the semicarbazone of suberone (m. p. 163–163.5°) which we prepared by dry distillation of barium suberate according to the directions of Day, Kon and Stevenson,[13] lay at 163–163.5°. The dibenzylidene compound melted at 107–108.5°.[12]

Anal. Subs., 0.1147: CO_2, 0.3670; H_2O, 0.0728. Calcd. for $C_{21}H_{20}O$: C, 87.45; H, 7.00. Found: C, 87.27; H, 7.10.

The mixed melting point with dibenzylidene suberone (from suberic acid) lay at 107–108.5°.

A second experiment, carried out with the same proportions of reagents and under the same conditions, gave the same products, but in slightly different ratio: 20 g. of cyclohexanone yielded in Fraction 1 (oxide), 1 g., Fractions 2 and 3 combined, 4.9 g., and from the bisulfite compound 11.9 g. of suberone.

Cyclopentanone and Diazomethane.—Twenty-three grams of cyclopentanone, purified through the semicarbazone (m. p. 212°), was treated with 22.5 g. of diazomethane under the conditions described in the cyclohexanone experiment. The product was worked up in an analogous way; from the bisulfite compound 14 g. of a ketone (suberone) of b. p. 69–70° (15 mm.) was obtained. The semicarbazone melted at 162–163°.

Anal. Subs., 0.1177: CO_2, 0.2458; H_2O, 0.0972; 2.792 mg. by 0.620 cc. of N (23°, 743 mm.). Calcd. for $C_8H_{15}ON_3$: C, 56.76; H, 8.94; N, 24.85. Found: C, 56.96; H, 9.24; N, 25.04.

The mixed melting point with suberone semicarbazone lay at 161–163°; the dibenzylidene compound melted at 107–108.5°, and showed no depression in melting point with that of suberone from suberic acid.

The portion of the reaction product which gave no bisulfite compound was distilled at 20 mm.; the oxide-containing fraction, boiling up to 45° (1 g.) was isomerized with zinc chloride as described. The distillate from this gave an intense color with fuchsin–sulfurous acid; with semicarbazide a mixture of semicarbazones was formed, probably those of cyclopentane aldehyde, hexahydrobenzaldehyde and cyclo-octanone. The separation of these was unsuccessful. The main portion of distillate, 6.5 g. of boiling point 45–110° (20 mm.), was in part treated with piperidine (see below), and in part converted to semicarbazone (cyclo-octanone), which melted at 165–166.5°.

Anal. Subs., 0.0834: H_2O, 0.0712; CO_2, 0.1805; 4.152 mg., 0.846 cc. of N (23°, 748 mm.). Calcd. for $C_9H_{17}ON_3$: C, 58.96; H, 9.36; N, 22.94. Found: C, 59.03; H, 9.55; N, 23.13.

It was not possible, even after repeated crystallization, to raise the melting point of this semicarbazone; that it consisted of nearly pure cyclo-octanone semicarbazone is shown both by the analysis and by the mixed melting point of 167.5–169° with the

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[13] Day, Kon and Stevenson, *J. Chem. Soc.*, **117**, 642 (1920).

semicarbazone prepared from our cyclo-octanone out of cyclohexanone and diazomethane as well as that obtained from Professor Ruzicka.

The reaction of the main portion of this fraction with piperidine did not yield homogeneous derivatives of the piperidino alcohol.

Summary

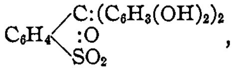
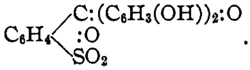
The action of diazomethane on cyclohexanone in the presence of methyl alcohol yields as the main product cycloheptanone, and in smaller quantities cyclo-octanone and an oxide isomeric with cycloheptanone.

Diazomethane with cyclopentanone leads (through cyclohexanone) to cycloheptanone as chief product, and cyclo-octanone as by-product. In this case, the oxide formed was not identified.

The reaction may be advantageously applied to the preparation of cycloheptanone and cyclo-octanone.

University, Virginia

NOTES

Note on Catechol Sulfonephthalein.—Catechol sulfonephthalein, first mentioned by Moir,[1] was prepared by substantially the method of Lubs and Clark,[2] condensing at temperatures under 100 two moles of catechol with one mole of symmetrical dichloro derivative of *o*-sulfobenzoic acid, but omitting the use of zinc chloride as condensing agent. The resulting product was analyzed for sulfur, giving 95.71 and 95.76% of the calcd. for the formula  $C_6H_4\left\langle\begin{matrix}C:(C_6H_3(OH)_2)_2\\ :O\\ SO_2\end{matrix}\right.$, or 100.40 and 100.45% of the calcd. for the formula  $C_6H_4\left\langle\begin{matrix}C:(C_6H_3(OH))_2:O\\ :O\\ SO_2\end{matrix}\right.$. The product is amorphous, of a very deep purple color (practically black), solid but not brittle at ordinary temperatures, and moderately hygroscopic. When warmed to about 60° it is softened sufficiently to drop from a small stirring rod. Its solubilities are: miscible in all proportions with water; readily soluble in methanol, ethanol, acetone, glacial acetic acid and ethyl acetate; slightly soluble in ethyl acetoacetate, acetic aldehyde and ethyl ether; insoluble in benzene, toluene, xylene, petroleum ether, carbon disulfide, carbon tetrachloride, chloroform and acetic anhydride. Attempts at crystallization, using the first-named solvents, have been unsuccessful.

The aqueous solution of this product is found to give colors of but a fraction, about one-tenth, of the intensities of colors of other sulfonephthaleins. A noteworthy feature of several of these colors, and one not mentioned by Moir, is their tendency to change, in some cases in only a

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[1] J. Moir, *J. So. Afr. Assoc. Anal. Chem.*, **3**, 6 (1920); *C. A.*, **14**, 3607 (1920).

[2] H. A. Lubs and W. M. Clark, *J. Wash. Acad. Sci.*, **5**, 609 (1915).