Mechanisms of the Wallach Rearrangement[1]

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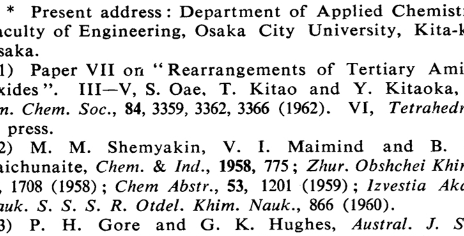
Recently, Shemyakin, Maimind and Vaichunaite[2] have shown, using ^{15}N-labeled azoxybenzene (I) that the rearrangement of the azoxybenzene (I) gave 4-hydroxyazobenzenes (III) and IV under various condition[3,4], where the two benzene rings were attacked with equal ease. They also observed that azoxybenzene recovered from these reactions remained practically unchanged in isotope distribution, and suggested that the rearrangement proceeds through a symmetrical intermediate II.

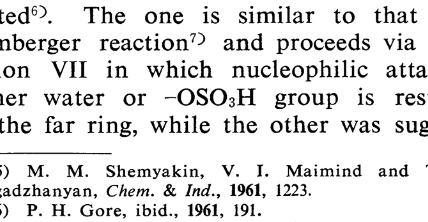


$$\underset{\text{(I)}}{C_6H_5\text{-}\underset{\overset{\downarrow}{O}}{N}={}^{15}N\text{-}C_6H_5} \rightarrow \underset{\text{(II)}}{C_6H_5\text{-}N\text{-}{}^{15}N\text{-}C_6H_5}$$

$$\rightarrow \underset{\text{(III)}}{C_6H_5\text{-}N={}^{15}N\text{-}C_6H_4OH\ (p)}$$

$$\underset{\text{(IV)}}{C_6H_5\text{-}{}^{15}N=N\text{-}C_6H_4OH\ (p)}$$

The prior formation of the *N*, *N*-oxide intermediate, II, in the rearrangement was further emphasized by the Russian workers[5] from their observations that there was no incorporation of ^{18}O into *p*-nitroazoxybenzene from ^{18}O-labeled sulfuric acid in the isomerization of β-*p*-nitroazoxybenzene (V) to α-*p*-nitroazoxybenzene (VI).



$$\underset{\text{(V)}}{C_6H_5\text{-}N=\underset{\overset{\downarrow}{O}}{N}\text{-}C_6H_4NO_2\ (p)} \xrightarrow{H_2S^{18}O_4} \underset{\text{(VI)}}{C_6H_5\text{-}\underset{\overset{\downarrow}{O}}{N}=N\text{-}C_6H_4NO_2\ (p)}$$

Meanwhile, two mechanisms have been suggested[6]. The one is similar to that of the Bamberger reaction[7] and proceeds via monocation VII in which nucleophilic attack by either water or $-OSO_3H$ group is restricted to the far ring, while the other was suggested

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[1] Paper VII on "Rearrangements of Tertiary Amine Oxides". III—V, S. Oae, T. Kitao and Y. Kitaoka, *J. Am. Chem. Soc.*, **84**, 3359, 3362, 3366 (1962). VI, *Tetrahedron* in press.

[2] M. M. Shemyakin, V. I. Maimind and B. K. Vaichunaite, *Chem. & Ind.*, **1958**, 775; *Zhur. Obshchei Khim.*, **28**, 1708 (1958); *Chem Abstr.*, **53**, 1201 (1959); *Izvestia Akad. Nauk. S. S. S. R. Otdel. Khim. Nauk.*, 866 (1960).

[3] P. H. Gore and G. K. Hughes, *Austral. J. Sci. Research*, **3A**, 136 (1950); *Chem. Abstr.*, **45**, 2889 (1951).

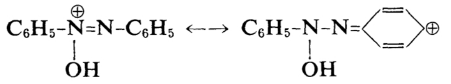
[4] V. O. Lukashurish and T. N. Khurdyumova, *Zhur. Obshchei Khim.*, **18**, 1961 (1948).

[5] M. M. Shemyakin, V. I. Maimind and Ts. E. Agadzhanyan, *Chem. & Ind.*, **1961**, 1223.

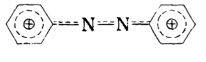
[6] P. H. Gore, ibid., **1961**, 191.

[7] a) "Name Reaction in Organic Chemistry" (Jinmei-Yuki-Hannoshu), Vol. II, Ed. by M. Murakami and Y. Yukawa, Asakura Book Publ. Co., Tokyo (1954), p. 228; b) C. K. Ingold, "Structure and Mechanism in Organic Chemistry", Cornell Univ. Press, New York (1953), p. 621.

to involve the symmetrical dication VIII, which may be attacked at either ring.



(VII)



(VIII)

We have reported in the earlier communication[8] that no excess of ^{18}O was incorporated from the medium in *p*-hydroxyazobenzene obtained when the rearrangement of azoxybenzene was carried out with 83% sulfuric acid, labeled by 0.67 atom % of ^{18}O. However, we have found later that a part of our experiments were in error and hence presented a new interpretation with a new set of data[9]. Since then, we have learned that the Russian workers[10] have also worked out a similar problem and presented much the same interpretation from the Wallach rearrangement.

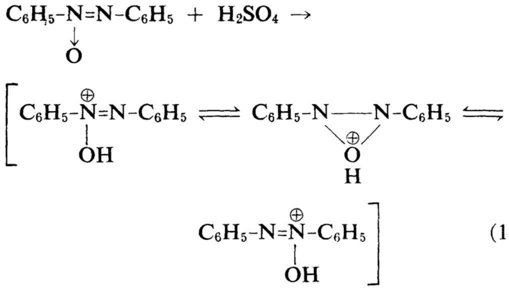
In this paper, we would like to correct a part of the published results and to summarize all the results of our studies hitherto being made on the Wallach rearrangement.

Azoxybenzene-^{18}O was prepared from ^{18}O-labeled nitrobenzene which was made by reacting benzene with the mixture of ^{18}O-labeled potassium nitrate and ^{18}O-labeled sulfuric acid. Then the rearrangement of this ^{18}O-labeled azoxybenzene was performed in 83% ordinary sulfuric acid. The resulting *p*-hydroxyazobenzene was found to have lost almost all the excess of ^{18}O, and only very small amount of excess of ^{18}O (about 10%) was found to be remaining. When an equivalent mixture of azoxybenzene-^{18}O and *o*-methylazoxybenzene was treated in the same medium, both *p*-hydroxyazobenzene and 4-hydroxy-2′-methylazobenzene obtained were also found to have lost most of the excess ^{18}O originally present in the starting azoxybenzene-^{18}O.

We also repeated the rearrangement of azoxybenzene in 83% sulfuric acid enriched with ^{18}O and found that the resulting *p*-hydroxyazobenzene was incorporated with ^{18}O from the medium, but the ^{18}O value was roughly 15~20% less than that of the medium used.

These observations suggest that the main portion of the Wallach rearrangement is an intermolecular process similar to Bamberger type where solvent water attack nucleophilically para position of benzene ring.

Combining with the observations of Russian workers on the prior isomerization, the overall mechanism of the main reaction may be depicted as follows;



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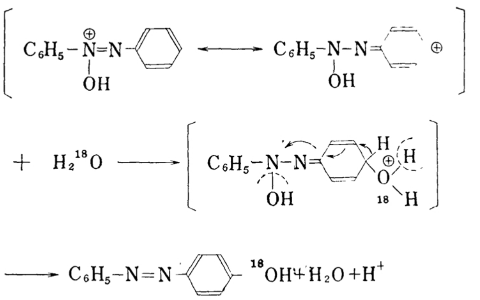
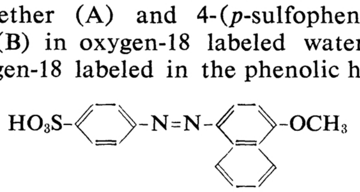
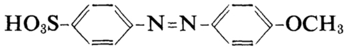


(2)

Recently, Bunnet, Buncel and Nahahedian[11] have shown that the phenolic products of hydrolysis of 4-(*p*-sulfophenylazo)-1-naphthyl methyl ether (A) and 4-(*p*-sulfophenylazo)-anisole (B) in oxygen-18 labeled water carry the oxygen-18 labeled in the phenolic hydroxy



(A)



(B)

group, and they suggested the following similar mechanism.

Okazaki and Okumura also have shown that the rearrangement of ^{18}O-labeled hydroxylamine in aqueous acid media gave *p*-aminophenol which have lost almost all the excess ^{18}O originally present in the starting material[12].

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[8] S. Oae, T. Fukumoto and M. Yamagami, This Bulletin, 34, 1873 (1961).

[9] S. Oae, T. Fukumoto and M. Yamagami, the 15th Annual Meeting of The Chemical Society of Japan, Kyoto, April, 1962.

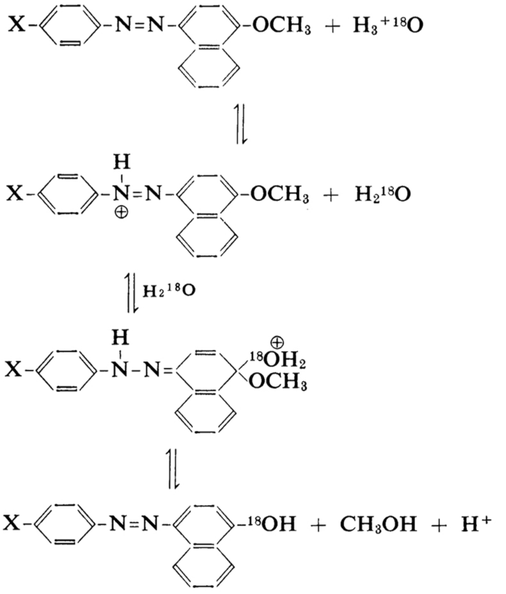
[10] M. M. Shemyakin, Ts. E. Agadzhanyan, V. I. Maimind, R. V. Kudryavtsev and D. N. Kursanov (Inst. Heteroörg. Compds., Moscow). *Doklady Akad. Nauk. S. S. S. R.*, 135, 346-349 (1960); *Chem. Abstr.*, 55, 11337 (1961).

[11] J. F. Bunnet, E. Buncel and K. V. Nahahedian, *J. Am. Chem. Soc.*, 84, 4136 (1962).

[12] S. Okazaki and M. Okumura, the 15th Annual Meeting of The Chemical Society of Japan, Kyoto, April, 1962.

TABLE I. ^{18}O STUDY OF REARRANGEMENT OF AZOXY COMPOUNDS

No.	Azoxy compound	Rearrangement conditions	Resultant hydroxyazo compound	Excess ^{18}O (at %)		
				Initial azoxy compound	Medium	Hydroxyl of hydroxyazo compound
1	Azoxybenzene (1 g.)	83% H_2SO_4 (90°C, 10 min.)	*p*-Hydroxyazobenzene (0.5 g.)	0	0.32	0.25
2	Azoxybenzene (1 g.)	83% H_2SO_4 (90°C, 10 min.)	*p*-Hydroxyazobenzene (0.5 g.)	0.49	0	0.06
3	α-4-Methylazoxybenzene (20 g.)	83% H_2SO_4 (90°C, 2 min.)	4-Hydroxy-4′-methylazobenzene (14 g.) +	0	0.38	0.27
			2-Hydroxy-4′-methylazobenzene (80 mg.)			0.05
4	Azoxybenzene (0.5 g.) +	83% H_2SO_4 (90°C, 10 min.)	*p*-Hydroxyazobenzene (0.15 g.) +	0.28	0	0.03
	α-2-Methylazoxybenzene (0.5 g.)		4-Hydroxy-2′-methylazobenzene (0.15 g.)	0		0.04
5	Azoxybenzene (1 g.)	UV light (40～45°C, 65 hr.)	*o*-Hydroxyazobenzene (0.45 g.)	0	0.47	0.01
6	Azoxybenzene (1 g.)	UV light (40～45°C, 25 days)	*o*-Hydroxyazobenzene (0.92 g.)	0.38	0	0.35
7	α-4-Methylazoxybenzene (3 g.)	UV light (40～45°C, 7 days)	2-Hydroxy-4′-methylazobenzene (1.6 g.)	—	—	—
8	*p*-Hydroxyazobenzene (1 g.)	83% H_2SO_4 (90°C, 10 min.)	*p*-Hydroxyazobenzene (0.9 g.)	0	0.30	0

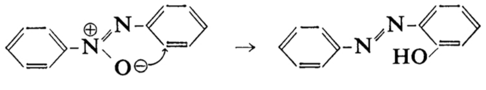


In both our experiments and the Russians, one finds that a small, but noticeable amount of oxygen appeared to be coming directly from the original azoxy-oxygen. Whether or not this is due to the direct oxidation we proposed earlier, one needs further experiments with a little higher concentration of ^{18}O before making any final comment.

Hahn and Jaffé[13] have recently shown that the rearrangement of 4-substituted azoxybenzene gives 2-hydroxy-4′-methylazobenzene as byproduct of 4-hydroxy-4′-methylazobenzene. We have allowed 4-methylazoxybenzene to react in 83% sulfuric acid, labeled by 0.58 atom % of ^{18}O at 60～70°C for 10 min. and found that resulting 4-hydroxy-4′-methylazobenzene, the main product, incorporated ^{18}O in 80～90% from the medium, while 2-hydroxy-4′-methylazobenzene obtained as red crystals, m. p. 100～101°C, in a very small yield, incorporated very little excess ^{18}O from the medium.

While the rearrangement to para position followed the Bamberger type intermolecular process, the rearrangement to ortho position apparently proceeded via intramolecular oxygen shift.

Since the oxygen migrated to the far ring in this case just as was shown by the Russian workers previously by the ^{15}N tracer studies[2], they adopted following Badger and Buttery's scheme[16] for the ortho rearrangement. Another alternative and probably more likely



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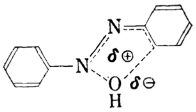
[13] Chi-Sun Hahn and H. H. Jaffé, *J. Am. Chem. Soc.*, **84**, 946 (1962).

path for the ortho rearrangement is via the following "intimate ion pair", similar to the one suggested for the formation of 4-tosyloxyisoquinoline by the reaction of isoquinoline *N*-oxide and *p*-toluenesulfonyl chloride[14].



A similar rearrangement of azoxybenzene to *o*-hydroxyazobenzene by ultraviolet light has been known[15,16]. The Russian workers[2] found that the original excess of ^{15}N was in the nitrogen group attached to the hydroxylated benzene when carried out the reaction in 85% ethanol for 65 hr. at 30∼40°C. We have performed the reaction in 85% ethanol containing 15% $H_2{}^{18}O$ (enriched by 0.67 atom % of ^{18}O) and found that the resulting *o*-hydroxyazobenzene incorporated very little excess ^{18}O from the medium. We favor that the reaction proceed through an intramolecular oxygen radical shift from *N*-oxide. A similar free radical shift is known in the reaction of dimethylaniline-*N*-oxide with acetic anhydride[17a]. 2-Picoline *N*-oxide was also known to rearrange to 2-pyridinemethanol by ultraviolet irradiation[17b].

Experimental

Azoxybenzene was prepared by refluxing methanol solution containing both nitrobenzene and sodium hydroxide; m. p. 35∼36°C.

^{18}O-Labeled Sulfuric Acid.—This preparation was described elsewhere[18].

^{18}O-Labeled Potassium Nitrate was prepared by Anbar's method[19].

^{18}O-Labeled Nitrobenzene was prepared by first dissolving ^{18}O-labeled potassium nitrate (5 g.) in $H_2S^{18}O_4$ (5 g., 0.75 atom % of ^{18}O) and then adding benzene (2 g.) dropwise in the mixture with vigorous stirring. Stirring was continued for 20 min. at 50∼55°C after the benzene was added. The reaction mixture was then poured into water (20 ml.) and oily precipitate separated out was extracted with 30 ml. benzene. After drying and removing benzene, the remaining oil was distilled and the fraction of b. p. 93∼95°C/17 mmHg was collected. The yield was 2.7 g. (83%).

^{18}O-Labeled Azoxybenzene was prepared by heating ^{18}O-labeled nitrobenzene (8 g., 0.84 atom % of ^{18}O) with sodium hydroxide (8 g.) in methanol (8 g.), m. p. 35∼36°C, 0.69 atom % of ^{18}O.

Found: C, 72.60; H, 4.99. Calcd. for $C_{12}H_{10}N_2O$: C, 72.73; H, 5.05%.

2-Methylazoxybenzene was prepared by an improved method. Five grams of 2-methylazobenzene prepared by Parsons's method[20] was dissolved in 40 ml. of glacial acetic acid then, 15 ml. of 30% hydrogen peroxide was added and the mixture was heated for 1 hr. at 85∼90°C. As the reaction progressed, the color of reaction mixture changed from brown to orange-yellow finally giving clear yellow solution. Then, the reaction mixture was poured into water. Oily layer separated was washed several times with water and was distilled and the fraction of b. p. 127∼129°C/2 mmHg was collected. The yield was 5.2 g. (97%).

Found: C, 73.94; H, 5.77. Calcd. for $C_{13}H_{12}N_2O$: C, 73.58; H, 5.66%.

4-Methylazoxybenzene was prepared from 4-methylazobenzene by similar method as 2-methylazoxybenzene, m. p. 46∼47°C.

Found: C, 73.80; H, 5.49. Calcd. for $C_{13}H_{12}N_2O$: C, 73.58; H, 5.66%.

Rearrangement Reaction of Azoxybenzene in ^{18}O-Labeled Sulfuric Acid.—A mixture of 1 g. of azoxybenzene and 4 g. of 83% sulfuric acid (0.50 atom % of ^{18}O) was heated for 10 min. at 90°C and then the reaction mixture was poured into ice water. A tarry product appeared was collected by filtration and this was refluxed for 10 min. with 50 ml. 3% potassium hydroxide solution. Insoluble material was removed by filtration and the black colored filtrate was refluxed with charcoal for 5 min. and filtered while hot. The filtrate was neutralized with 6 N hydrochloric acid solution. The precipitate appeared was collected by filtration and recrystallized from benzene. *p*-Hydroxyazobenzene was thus obtained, m. p. 151∼152°C (lit.[21] 152°C), 0.45 atom % of ^{18}O. The yield was 0.5 g. (50%).

Found: C, 72.08; H, 4.96. Calcd. for $C_{12}H_{10}N_2O$: C, 72.73; H, 5.05%.

Rearrangement Reaction of ^{18}O-Labeled Azoxybenzene in Sulfuric Acid.—A mixture of 1 g. of ^{18}O-labeled azoxybenzene (0.69 atom % of ^{18}O) and 4 g. of 83% sulfuric acid was heated for 10 min. at 90°C and treated similarly as described above. *p*-Hydroxyazobenzene was obtained, m. p. 151∼152°C, 0.26 atom % of ^{18}O. The yield was 0.5 g. (50%).

Reaction of a Mixture of ^{18}O-Labeled Azoxybenzene and 2-Methylazoxybenzene in Sulfuric Acid.—A mixture of 0.5 g. of ^{18}O-labeled azoxybenzene (0.69 atom % of ^{18}O) and 0.5 g. of 2-methylazoxybenzene was heated in 4 g. of 83% sulfuric acid for 10 min. at 90°C and treated similarly as described above. Crude product (0.5 g.) obtained was recrystallized from 2 ml. benzene. Crystalline powder appeared rapidly was collected by filtration and the filtrate was kept standing overnight. Rhombic crystals came out from the filtrate. The former crystals were recrystallized from benzene and the

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[14] S. Oae, T. Kitao and Y. Kitaoka, *Tetrahedron*, in press.

[15] W. M. Cumming and C. S. Ferier, *J. Chem. Soc.*, **127**, 2374 (1925).

[16] G. M. Badger and R. G. Buttery, ibid., **1954**, 2243.

[17] a) S. Oae, T. Kitao and Y. Kitaoka, *J. Am. Chem. Soc.*, **84**, 3366 (1962); b) N. Hata, This Bulletin, **34**, 1440 (1961).

[18] S. Oae, T. Kitao and Y. Kitaoka, Annual Report of the Radiation Center of Osaka Prefecture, Vol. I, 33 (1960).

[19] M. Anbar, M. Halman and S. Pinchas, *J. Chem. Soc.*, **1960**, 1242.

[20] T. Parsons, Jr., and J. Ballar, Jr., *J. Am. Chem. Soc.*, **58**, 268 (1936).

[21] R. Paganini, *Ber.*, **24**, 366 (1891).

latter were recrystallized from ligroin several times, respectively. The former, m. p. 150~151°C, 0.23 atom % of ^{18}O, 0.15 g. and the latter, m. p. 99~100°C, 0.24 atom % of ^{18}O, 0.15 g. were obtained. Both crystals did not depress the melting point of the two authentic samples, 4-hydroxyazobenzene and 4'-hydroxy-2-methylazobenzene[21] upon admixture.

Rearrangement Reaction of Azoxybenzene under Ultraviolet Irradiation.—In a sealed tube is placed a mixture of 1 g. of azoxybenzene and 20 ml. of 85% ethanol (consisted of 3 ml. of ^{18}O enriched water (0.67 atom % of ^{18}O) and 17 ml. absolute ethanol), and the mixture was irradiated for 65 hr. at 40~45°C under ultraviolet. After removing water and ethanol under reduced pressure, the remaining solid was added 50 ml. 3% potassium hydroxide aquous solution and was refluxed for 10 min. After cooling and removing unreacted azoxybenzene by filtration, the filtrate was neutralized with hydrchloric acid. Brown crystals appeared were recrystallized from ethanol and violet needles, m. p. 82.5°C, 0.21 atom % of ^{18}O, was obtained. The yield was 0.45 g. (45%). (*o*-Hydroxyazobenzene (lit.[22] m. p. 82.5°C)).

Rearrangement Reaction of ^{18}O-Labeled Azoxybenzene under Ultraviolet Irradiation.—In a sealed tube is placed a mixture of 1 g. of ^{18}O-labeled azoxybenzene (0.58 atom % of ^{18}O) and 20 ml. of absolute ethanol, and the mixture was irradiated for 25 days at 40~45°C and was treated similarly as described above. The product, m. p. 82.5°C, 0.55 atom % of ^{18}O, was obtained. The yield was 0.92 g. (92%).

Rearrangement Reaction of α-4-Methylazoxybenzene.—In a three-necked flask was placed a mixture of 20 g. of α-4-methylazoxybenzene and 80 g. of 83% ^{18}O-labeled sulfuric acid (0.58 atom % of ^{18}O) and the mixture was heated at 60~70°C for 10 min. and was treated similarly. The crude product, m. p. 147~150°C, 14 g. was obtained (70%). The separation of the *o*-isomer, 2-hydroxy-4'-methylazobenzene from the *p*-isomer was achieved by the following method. The product (14 g.) was dissolved in 20 ml. hot benzene and then allowed to stand for 5~6 hr. at room temperature. Yellow needles formed were separated and were recrystallized from benzene repeatedly. 4-Hydroxy-4'-methylazobenzene, m. p. 150~151°C, 0.54 atom % of ^{18}O, was thus obtained.

Found: C, 72.61; H, 5.78. Calcd. for $C_{13}H_{12}N_2O$: C, 73.58; H, 5.66%.

The filtrate was evaporated under reduced pressure, and the residue (ca. 5 g.) was distilled by steam distillation, then red crystals, m. p. 98~101°C, 80 mg. were obtained. The red crystals were converted to copper salt by precipitation with 50% alcoholic copper acetate solution. This copper salt contained 0.25 atom % of ^{18}O and was identified with authentic sample, which was prepared by ultraviolet irradiation of α-4-methylazoxybenzene, by infrared spectrophotometric method.

Found: C, 57.53; H, 3.99. Calcd. for $C_{13}H_{11}N_2 \cdot OCu$: C, 56.83; H, 4.01%.

2-Hydroxy-4'-methylazobenzene.—In a sealed tube is placed a mixture of 3 g. of α-4-methylazoxybenzene and 20 ml. of ethanol, and the mixture was irradiated under ultraviolet light for 7 days at 40~45°C. After removing ethanol, the solid was distilled by steam distillation and red crystals, m. p.; 100~101°C (1.6 g.) was obtained in 54% yield.

Found: C, 72.80; H, 5.11. Calcd. for $C_{12}H_{12}N_2O$: C, 73.58; H, 5.66%.

Determination of ^{18}O is described elsewhere[15].

The results of ^{18}O distribution of all the ^{18}O tracer experiments for this rearrangement are tabulated in Table. I.

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[22] E. Bamberger, ibid., 33, 1950 (1900).