# AN INTERPRETATION OF THE REARRANGEMENTS OF PINACONES AND TERTIARY AMINO-ALCOHOLS FROM THE ELECTRON THEORY OF VALENCY (THEORETICAL PART).

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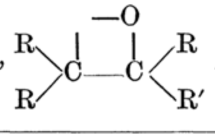
**Introduction.** Since the discovery of triphenyl-methyl by Gomberg, the theory of "Valenzbeanspruchung" has played an important rôle in the theoretical line of the organic chemistry. Consequently the comparison of firmness of attachment of organic radicals to an element affords one of the most interesting subjects. Thus, J. v. Braun⁽¹⁾ compared the firmness of attachment of organic radicals to nitrogen atom by the reaction products of tertiary amines and cyanogen bromide; and K. v. Auwers⁽²⁾ in his "quaternary indazolium salt method" by its thermal decomposition products.

As to the method to compare the "affinity requirement" of organic radicals to carbon atom Skraup and his co-workers proposed two methods, namely, "oxazol-⁽³⁾" and "carbinol method.⁽⁴⁾" In the former, the reaction velocity of ring rupture of substituted benzoxazoles is compared, and the latter is based on the assumption that basicity of various carbinols is due to the varying affinity of carbinol-carbon atom. Another method is given by Meerwein⁽⁵⁾ during studies on pinacoline-rearrangement. As is well known, pinacone, when dehydrated, easily yields pinacoline by intramolecular rearrangement. The mechanism of this transformation was the subject of discussion over twenty-five years, but finally Tiffeneau⁽⁶⁾ concluded that this rearrangement occurs together with elimination of water through a "fraction of a molecule,"  which cannot be isolated. Then in the

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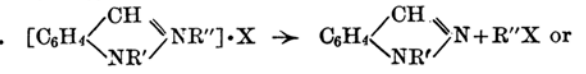
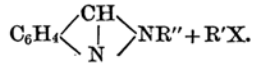
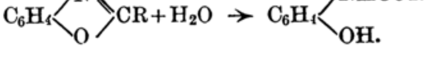
(1) *Ber.*, 55 (1922), 3165; 56 (1923), 1573. $R'R''R'''N + BrCN = R'R''N \cdot CN + R'''Br$.

(2) *Ber.*, 58 (1925), 1360. 



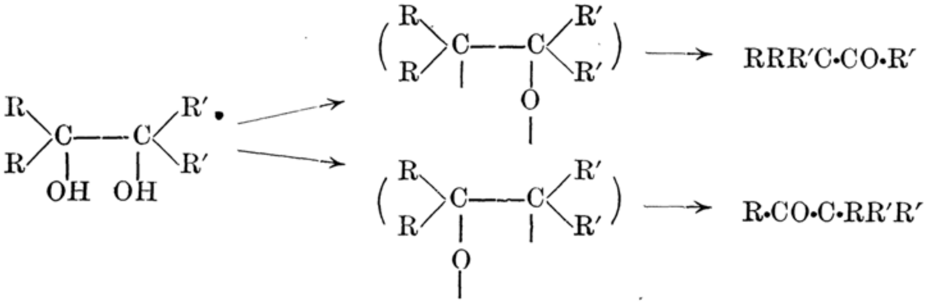
(3) *Ann.*, 419 (1919), 1; *Ber.*, 55 (1922), 1080. 

(4) *Ber.*, 55 (1922), 1074.

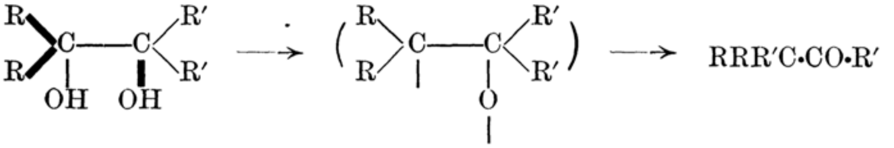
(5) *Ann.*, 419 (1919), 121.

(6) *Compt. rend.*, 143 (1906), 687.

case of unsymmetrically substituted pinacones, we may have:



and the direction of the rearrangement may be determined by the firmness of the union of the two hydroxyl radicals. Now, Meerwein considered that the carbon atom combined to hydrocarbon radicals which possess greater "affinity requirement" leaves less affinity to combine with hydroxyl group, consequently it is this hydroxyl radical which is removed on dehydration. The scheme of the rearrangement is as follows:

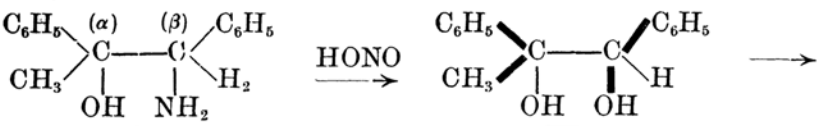


where thick bar denotes the greater "affinity requirement." By the studies on various pinacones he determined the relative "affinity requirement" of several radicals. In addition to his result, taking in consideration those given by Skraup,⁽¹⁾ we have the following series:

$$C_6H_5{\cdot}CH_2- < C_2H_5- < CH_3- < C_6H_5- < p\text{-}CH_3{\cdot}C_6H_4- < p\text{-}CH_3O{\cdot}C_6H_4- < C_{10}H_7-.$$

*Action of nitrous acid on tertiary amino-alcohols.* Few years ago Mc Kenzie⁽²⁾ found that tertiary amino-alcohols, when acted by nitrous acid, do not give normally glycols but they perform a kind of pinacoline rearrangement which he proposed to call *semipinacolinic deamination.* Now, if we attempt to predict the result of this transformation by the theory of "affinity requirement" as in the case of pinacones, we will be surprised at unexpected results (see Table below).

For example, in the case of $\beta$-amino-$\alpha$ $\beta$-diphenyl-$\alpha$-methyl-ethyl-alcohol (I), we expect the following course of reaction:



(I) (II)

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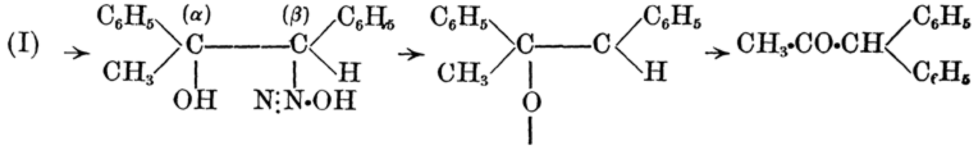
(1) Loc. cit.

(2) McKenzie and Richardson, *J. Chem. Soc.*, 123 (1923), 79.

(III) (IV)

The transformation from (III) to (IV) is explained thus: out of the two substituents attached to β-carbon atom the less firmly combined hydrogen atom migrates to α-carbon atom, giving phenyl-methyl-acetophenone (IV). But the product actually obtained is diphenyl-acetone $(C_6H_5)_2CH \cdot CO \cdot CH_3$. In order to explain this contradiction, McKenzie supposed that the transformation occurs in the following manner:



(V) (VI) (VII)

Owing to the easiness with which nitrogen is eliminated, the hydroxyl group attached to α-carbon atom is more firmly bound than is the nitrogen atom attached to β-carbon atom, so that the linkage $-N_2OH$ would be severed first. Though this assumption accounts for the mode of dehydration in all the semipinacolinic deamination of amino-alcohols, it can not explain why certain tertiary amino-alcohols such as γ-amino-ααγ-triphenyl-propyl alcohol,(1) $(C_6H_5)_2C(OH) \cdot CH_2 \cdot CH(NH_2) \cdot C_6H_5$ and β-amino-β-phenyl-αα-diethyl-ethyl alcohol,(2) $(C_2H_5)_2C(OH) \cdot CH(NH_2) \cdot C_6H_5$ behave normally toward nitrous acid, giving corresponding glycols. Moreover, as the theory of "affinity requirement" can not explain why in the above example, phenyl group which is to be considered more firmly bound than methyl group migrates in the last stage of the reaction (VI)→(VII), we must admit the provision that a certain migrational aptitude is conceded to each radical, this property being not necessarily concomitant with its saturation capacity.(3) This means that the theory of "affinity requirement" can not foretell the products of semipinacolinic deamination of tertiary amino-alcohols, except those of the type $R_2C(OH) \cdot CHR'(NH_2)$.

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(1) McKenzie and Richardson, *J. Chem. Soc.*, **123** (1923), 85.

(2) Ibid., **1927**, 571.

(3) Tiffeneau and Lévy, *Compt. rend.*, **176** (1923), 312.

TABLE 1.

The Products of Semipinacolinic Deamination of Tertiary Amino-alcohols.

| No. | Tert. amino-alcohol. | Actual product. | Product expected from | |
|---|---|---|---|---|
| | | | Electron theory | Affinity-requirement |
| 1. | $Ph_2C(OH)\cdot CHPh(NH_2)$ | $Ph_2CH\cdot CO\cdot Ph$ | The same. | The same. |
| 2. | $PhMeC(OH)\cdot CHPh(NH_2)$ | $Ph_2CH\cdot CO\cdot Me$ | The same. | The same. |
| 3. | $PhEtC(OH)\cdot CHPh(NH_2)$ | $Ph_2CH\cdot CO\cdot Et$ | The same. | $PhEtCH\cdot CO\cdot Ph$ |
| 4. | $PhNapC(OH)\cdot CHPh(NH_2)$ | $Ph_2CH\cdot CO\cdot Nap$ | $PhNapCH\cdot CO\cdot Ph$ | $PhNaCH\cdot CO\cdot Ph$ |
| 5. | $Ph_2C(OH)\cdot CHMe(NH_2)$ | $PhMeCH\cdot CO\cdot Ph$ | The same. | $Ph_2CH\cdot CO\cdot Me$ |
| 6 | $Ph_2C(OH)\cdot CHBzl(NH_2)$ | $PhBzlCH\cdot CO\cdot Ph$ | The same. | $Ph_2CH\cdot CO\cdot Bzl$ |
| 7. | $Ph_2C(OH)\cdot CH_2(NH_2)$ | $PhCH_2\cdot CO\cdot Ph$ | The same. | $Ph_2CH\cdot CHO$ |
| 8. | $PhAnisC(OH)\cdot CH_2(NH_2)$ | $AnisCH_2\cdot CO\cdot Ph$ | The same. | $PhAnisCH\cdot CHO$ |
| 9. | $PhNapC(OH)\cdot CH_2(NH_2)$ | $NapCH_2\cdot CO\cdot Ph$ | The same. | $PhNapCH\cdot CHO$ |
| 10. | $Bzl_2C(OH)\cdot CHMe(NH_2)$ | $BzlMeCH\cdot CO\cdot Bzl$ | The same. | — * |
| 11. | $Bzl_2C(OH)\cdot CHPh(NH_2)$ | $BzlPhCH\cdot CO\cdot Bzl$ | The same. | — * |

Ph = Phenyl, Me = Methyl, Et = Ethyl, Nap = Naphthyl, Bzl = Benzyl, Anis = *p*-Anisyl.

* As the difference of the "affinity requirement" between two benzyl groups and hydrogen atom plus phenyl (or methyl) group is not known, we can say nothing about the products of the rearrangement in these cases.

*Literatures.*

1. McKenzie and Richardson, *J. Chem. Soc.*, **123** (1923), 79; McKenzie and Wills, ibid., **127** (1925), 283.
2. McKenzie and Richardson, loc. cit.; McKenzie and Roger, ibid., **125** (1924), 844.
3. McKenzie and Roger, ibid., **1927**, 574.
4. McKenzie and Dennler, ibid., **125** (1924), 2105; Orékhov and Tiffeneau, *Compt. rend.*, **178** (1924), 1619.

5 and 6. McKenzie and Wills, loc. cit.

7. Bettzieche, *Z. physiol.* **140** (1924), 273.
8. Orékhov and Tiffeneau, *Compt. rend.*, **180** (1925), 70.
9. Luce, ibid., 145.

10 and 11. Bettzieche and Ehrlich, *Z. physiol.*, **150** (1925), 197.

11. McKenzie and Roger (*J. Chem. Soc.*, **1927**, 574) obtained further the corresponding glycol as a by-product

## Interpretation from the Electron Theory.

In order to deduce a more reliable theory which interprets without a provision all the rearrangements similar to pinacoline transformation, I have determined the standpoint of the interpretation in the modern electron theory which has been developed by Lapworth(1) and by Kermack and Robinson.(2) This theory has great possibility to explain clearly the

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(1) *J. Chem. Soc.*, **121** (1922), 461.

(2) Ibid., 427.

mechanism of the most essential parts of these transformations, that is (i) elimination of water from a molecule, and (ii) migration of a group.

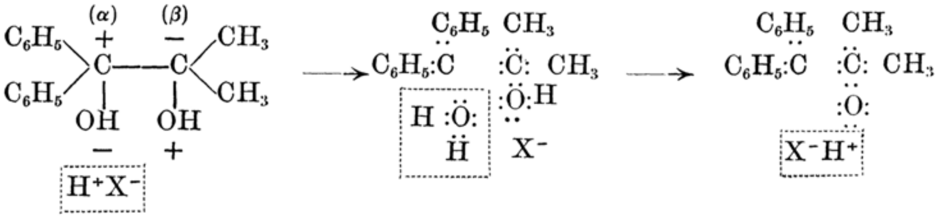
In the discussion of the mechanism of a reaction of organic compounds, especially of those which contain various hydrocarbon radicals as in our case, we must first determine the relative electro-negativity of these radicals. This question has already been solved by Kharasch and Marker,(1) from the studies of the reaction between unsymmetrical dialkylmercuric compounds and hydrogen chloride. The reaction runs as follows:

$$R.Hg.R' + HCl = RH + R'.HgCl,$$

where the relatively electro-negative radical combines with hydrogen atom. In this way the electro-negativity of hydrocarbon radicals are found to be $\alpha{-}C_{10}H_7{-} > p\text{-}CH_3O{\cdot}C_6H_4{-} > o,p\text{-}CH_3{\cdot}C_6H_4{-} > C_6H_5{-} > CH_3{-} > C_2H_5{-},\ C_3H_7{-} > C_6H_5{\cdot}CH_2{-}$(2)

**1. The Mechanism of Pinacoline Rearrangement.** From the fact that the pinacoline rearrangement occurs only in the presence of acid and that pinacone remains unchanged when boiled with soda-solution or when heated with water at 120°–130°, it may be assumed that *acid behaves in this case not only as dehydrating agent but also as a catalyst* as in the case of the rearrangement of phenyl-chlor-amine into *p*-chlor-aniline ($C_6H_5{\cdot}NH{\cdot}Cl \rightarrow Cl{\cdot}C_6H_4{\cdot}NH_2$). This assumtion may be considered probable since the rearrangement of tertiary amino-alcohols occurs in the presence of nitrous acid only, without ordinary dehydrating agent.

Then the mechanism of the rearrangement of unsym. diphenyl-pinacone may be formulated as follows:



(VIII) (IX) (X)

$$\longrightarrow (C_6H_5)_2CH_3C{\cdot}CO{\cdot}OH_3$$

(XI)

As $\alpha$- and $\beta$-carbon atoms are induced respectively positive and negative, the former by the influence of phenyl and the latter by methyl group; the

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(1) *J. Am. Chem. Soc.*, 48 (1926), 3130.

(2) This result shows a good agreement with the order of "affinity requirement" given above. But this concordance is not merely accidental, as the electron theory involves in itself the principle of "affinity requirement."

theory of induced alternate polarity demands that hydroxyl group attached to $\alpha$-carbon atom has negative polarity (VIII). Consequently it is this hydroxyl group that is attracted by hydrogen ion of the acid, when an acid $H^+X^-$ is acted on this pinacone. This attraction weakens the linkage between this hydroxyl group and $\alpha$-carbon atom and increases the positive character of this carbon atom. In other words, the octet around this carbon atom becomes more and more unstable, and this causes, on the other hand, the increase of the stability of the octet of the adjacent carbon atom($\beta$) (IX). As the results of this, hydrogen atom of the hydroxyl group bound to this negative carbon atom ($\beta$) will be brought into very free state and can combine with anion $X^-$ of the acid (X). Then the disturbance of the distribution of electrons is restored by the migration of one of the methyl groups to $\alpha$-carbon atom and by sharing four electrons between $\beta$-carbon- and oxygen atoms (XI). This final product is the same as that derived by Meerwein from the theory of "affinity requirement." The rearrangement of pinacones, $R_2C(OH)$. $CR'_2(OH)$, where R and R′ are alkyl or aryl radicals, can be likewise interpreted. When the polarity difference between the two carbon atoms ($\alpha$ and $\beta$) is not marked, as is in the cases of pinacones with different R and R′, the homologous aliphatic radicals, the rearrangement takes its course in two directions, giving two isomeric ketones in different quantities, where the proportion of the two ketones formed is dependent on the polarity difference between the $\alpha$- and $\beta$-carbon atoms.

**2. The Mechanism of Semipinacolinic Deamination of Tertiary Amimo-alcohols.** Now taking again $\beta$-amino-$\alpha\beta$-diphenyl-$\alpha$-methyl-ethyl alcohol as an example, the "key stom" which causes the polarity in this molecule, when placed in an activated state, may be assumed to be the most negative and reactive amino group. In consequence of the induced alternate polarity caused by this negative key atom, $\beta$-carbon atom is induced strongly positive, $\alpha$-carbon atom negative and the hydroxyl group positive in its turn (XII). Then the corresponding glycol, which is assumed to be formed when amino-alcohol is treated with nitrous acid, will have strongly negative hydroxyl group bound to $\beta$-carbon atom (XIII), therefore, according to the mechanism described in the last section, it must give such a "fraction of molecule" as (XIV). Further, if one of the group attached to $\alpha$-carbon atom migrates to $\beta$-carbon atom in order to restore the disturbance of the affinity, the group that wanders must be the one that is more negative, since $\beta$-carbon atom has positive polarity. Thus in this case it is the phenyl group that wanders, and the final product must be diphenyl acetone (XV). This interpretation is proved by the actual product of the rearrangement.

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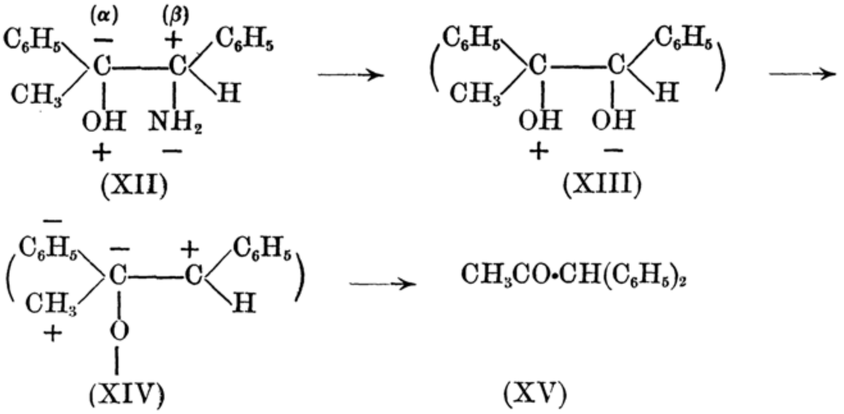
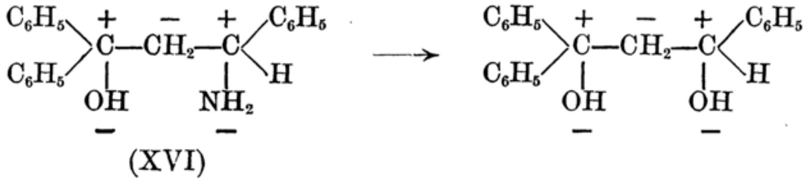
(1) Vorländer, *Ber.*, 30 (1897), 2766.

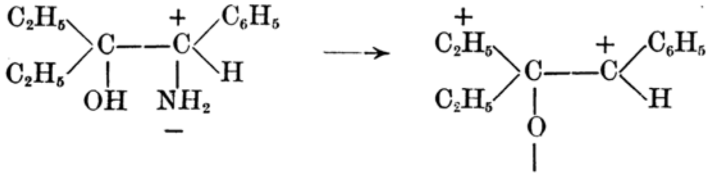


It is obvious from Table 1 that this interpretation in the prediction of the product of the semipinacolinic deamination is not only applicable in this one example, but also gives satisfactory results in many other cases. Out of a dozen examples the case which stands against this interpretation is only one, that is, that of $\beta$-amino-$\alpha$ $\beta$-diphenyl-$\alpha$-naphthyl-ethyl alcohol (No. 4 in the Table) in which phenyl group which is more positive than naphthyl group wanders to $\beta$-carbon atom. This might be considered due to some steric influence of the phenyl group attached to $\beta$-carbon atom, since in the case of the $\beta$-amino-$\alpha$-phenyl-$\alpha$-naphthyl-ethyl alcohol (No. 9) the rearrangement takes the normal course.

**3. Behaviour of Tertiary Amino-Alcohols towards Nitrous Acid.** The electronic interpretation can explain why tertiary amino-alcohols generally undergo semipinacolinic deamination by nitrous acid, whereas in few cases normal displacement of amino group takes place. In the former, the state of marked polarity developed in the molecule due to the presence of a strongly negative group such as amino radical may be sufficient to cause the molecular transformation by mere catalytic action of the acid present. This may account at the same time, for the normal displacement of amino group in the cases of $\gamma$-amino-$\alpha\alpha\gamma$-triphenyl-propyl alcohol (XVI) and of $\beta$-amino-$\beta$-phenyl-$\alpha\alpha$-diethyl-ethyl alcohol (XVII). Because in the former, the fact that two hydroxyl groups in the corresponding glycol are induced in the same sence, may be considered to play an important rôle, and in the latter, the ethyl group cannot easily migrate to the positively polarised $\beta$-carbon atom in consequence of its positive character.



(XVI)



(XVII)

**4. The Rearrangements of Trisubstituted α-Glycols.** Which afford an interesting problem by the variety of their modes of transformation, will be discussed in another paper.

## Conclusion.

Hitherto the rearrangements of pinacones and their closely related compounds have been interpreted from the theory of "affinity requirement." But as this theory is compelled to admit the provision that the migrational aptitude of a certain group is not necessarily concordant with its "affinity requirement," it cannot generally foretell the rearrangement product.

An interpretation based on the theory of induced alternate polarity and on the assumption that acid behaves in these rearrangements not only as dehydrating agent but also as a catalyst, has following advantages:

(1) The products of rearrangements of pinacones and tertiary amino-alcohols are reliably predicted by one and the same reasoning.

(2) We can also explain why tertiary amino-alcohols generally behave abnormally toward nitrous acid, whereas in certain cases normal displacement of amino group takes place.

Of course, this electronic interpretation is by no means perfect, on the contrary, there remains a fundamental problem undissolved. That is a question of the steric influence. The steric influence is an important, but an unknown factor, which, as well as the general and alternate effects due to a key atom, has a directive influence on a chemical reaction. It must be the most important task given on the electron theory to bring the nature of this influence to light. Besides this fundamental problem, the above electronic interpretation has some contradictory facts:

(1) The rearrangements of alkyl-trimethyl pinacones propose a strong objection to this interpretation, for they give ketones, $CH_3 \cdot CO \cdot CR(CH_3)_2$, by the migration of the more positive group.(1)

(2) When β-amino-β-phenyl-αα-diethyl-ethyl alcohol is treated with nitrous acid, the main product is the corresponding glycol, as already

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(1) R=$C_2H_5$, Meerwein, *Ann.*, 396 (1896), 255; R=n- and iso-$C_3H_7$, Locquin and Leers, *Bull. Soc. chim.*, 39 (1926), 426.

described, while according to the above explanation in the case of β-amino-β-phenyl-αα-dibenzyl-ethyl alcohol the normal displacement of amino group should take place at least as easily as in the former case, since as benzyl is more positive than ethyl, it should migrate more difficultly to positively polarized β-carbon atom. But the actual products betray this prediction, for it gives the glycol only as a by-product.(1)

These contradictions will be discussed again when a sufficient number of new experimental materials are obtained.

I with to express my hearty thanks to Prof. K. Matsubara for his kind inspection of this paper.

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Tokyo Imperial University.

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(1) McKenzie and Roger, *J. Chem. Soc.*, 1927, 574.