1-Cinnamoyl-1,2-dihydroquinaldonitrile was prepared from 12 g. of freshly made cinnamoyl chloride in exactly the same manner as the benzoyl compound; needles from alcohol, m. p. 149–150°; yield, 16 g.

Anal. Calcd. for $C_{19}H_{14}ON_2$: C, 79.75; H, 4.93; N, 9.73. Found: C, 79.62; H, 5.02; N, 9.80.

CONVERSE MEMORIAL LABORATORY
HARVARD UNIVERSITY
CAMBRIDGE, MASS.

RECEIVED APRIL 17, 1940

COMMUNICATIONS TO THE EDITOR

ELECTROPHORETIC ISOLATION OF CONSTITUENTS OF RAGWEED POLLEN EXTRACTS*

Sir:

Dialyzed extracts of giant ragweed pollen were studied with the Tiselius[1] moving boundary technique at approximately *p*H 7.4 and 1.5°. Employing the Philpot–Svensson[2] cylindrical lens system to visualize the boundaries, we have found a major constituent which is negatively charged, unpigmented and migrates more slowly than the pigmented constituents. The latter are also negatively charged. The major unpigmented constituent may constitute as much as 75% of the material in fresh extracts when estimated by the criterion of the integration of the Philpot–Svensson curves. Similar Longsworth[3] diagrams have been obtained. The unpigmented fraction is highly skin reactive in individuals with ragweed hay fever. It may be introduced into the skin by electrophoresis in these cases by the positive pole even though the substance is negatively charged at the *p*H employed. The electrical mobility of the unpigmented constituent is 0.5×10^{-5} cm. sec.$^{-1}$ in 0.05 *M* phosphate buffer at *p*H 7.0.[4] Variations have been observed in the pigmented portions of the electrophoretic diagrams and apparently depend on the extent and nature of the dialysis as well as the age and treatment of the pollen grains.

COLUMBIA UNIVERSITY AND THE MOUNT SINAI HOSPITAL, NEW YORK CITY, AND THE BIOLOGICAL LABORATORIES, COLD SPRING HARBOR
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L. JENNINGS

RECEIVED MAY 17, 1940

* This investigation has been aided by a grant from the Josiah Macy, Jr., Foundation.

(1) A. Tiselius, *Trans. Faraday Soc.*, **33**, 524 (1937).

(2) H. Svensson, *Kolloid-Z.*, **87**, 190 (1939).

(3) L. G. Longsworth and D. A. MacInnes, *Chem. Rev.*, **24**, 271 (1939).

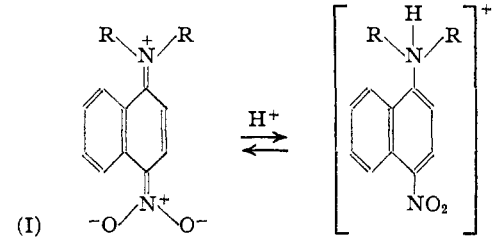
(4) H. A. Abramson, A. Sookne and L. S. Moyer, *J. Allergy*, **10**, 317 (1939); H. A. Abramson and M. H. Gorin, *Chem. Prod.*, **3**, 37 (1940).

THE STERIC INHIBITION OF RESONANCE

Sir:

It has been shown recently[1] that the concept of the steric inhibition of resonance offers an adequate explanation for the differences in acidity observed with trinitrotriphenylmethanes.

Using exactly the same reasoning, we have attacked this problem from a different point of view, *i. e.*, by a consideration of the basic strengths of substituted 4-nitro-1-naphthylamines.



The electron pair of the amino nitrogen atom (upon which depends the basicity of the molecule) is no longer present in the resonance isomer I. If the alkyl groups in I are large, they will inhibit the ability of the group R_2N- and the benzene ring to become coplanar. The result of this must be a diminution in resonance. This reduction in resonance by steric hindrance should result in an increase in the electron density at the amino nitrogen atom and thus lead to an increase in basicity. We have shown that the basicity of the substituted amine (I, R = CH_3) is much greater than that of the unsubstituted amine (I, R = H) and that this difference is far too great to be explained by an inductive effect of the methyl groups.

The decrease in resonance reduces the polar character of these molecules[2] and should consequently lower the melting points (if other crystal

(1) Wheland and Danish, THIS JOURNAL, **62**, 1125 (1940).

(2) Birtles and Hampson, *J. Chem. Soc.*, 10 (1937).

structure factors remain essentially constant). The values in Table I show that the melting points decrease markedly with increasing size of the alkyl groups.

TABLE I

MELTING POINTS OF VARIOUS ALKYLATED AMINO NITRO COMPOUNDS

Substance	M. p., °C.
Nitroaminodurene	161
Nitrodimethylaminodurene	90
1-Amino-4-nitronaphthalene	191
1-Methylamino-4-nitronaphthalene	184
1-Ethylamino-4-nitronaphthalene	176
1-Benzylamino-4-nitronaphthalene	156
1-Dimethylamino-4-nitronaphthalene[a]	65
1-Diethylamino-4-nitronaphthalene[a]	Liquid

[a] There is no chance for a preferred position of the alkyl groups in this case.

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MINNEAPOLIS, MINNESOTA
RICHARD T. ARNOLD
GEO. PEIRCE
R. A. BARNES

RECEIVED MAY 16, 1940

THE BIOLOGICAL ACTIVITY OF SYNTHETIC PANTOTHENIC ACID

Sir:

The lactone of the "acid fragment" of pantothenic acid has been identified as α-hydroxy-β,β-dimethylbutyrolactone by Stiller, Keresztesy and Finkelstein.[1] The coupling of the synthetic *dl*-lactone with β-alanine in 50% yields, as determined by microbiological assay, and assuming the inactivity of one isomer, has been reported by Weinstock and co-workers.[2] In the present investigation the yield from the coupling reaction was 88%, and definite evidence was found for the inertness of the unnatural isomer.

When equimolecular amounts of 1 *N* sodium hydroxide, β-alanine and the lactone[3] are mixed at 0°, 50% coupling takes place almost immediately as determined by a Sörensen formol titration for free amino nitrogen. Upon standing no further coupling occurs. Instead, the remaining hydroxide ion disappears during the course of an hour, due probably to the saponification of the uncoupled lactone. If instead of equimolecular amounts, the ratio of lactone to β-alanine to 1 *N* sodium hydroxide is made 3:1:1, a 55% coupling occurs immediately, again followed by the disappearance of hydroxide ion. If now to this same solution an amount of 10 *N* sodium hydroxide equivalent to the amount of free β-alanine remaining is added, 51% of this remainder likewise couples. Upon repetition of the procedure, the % of the remainder of the β-alanine which couples falls off rapidly. The results of a typical experiment are summarized in Table I.

(1) As reported by Williams and Major, *Science*, **91**, 246 (1940).
(2) Weinstock, Arnold, May and Price, *ibid.*, **91**, 411 (1940).
(3) Prepared according to the directions of Kohn and Neustadter, *Monatsh.*, **39**, 295 (1918).

TABLE I

	Milliequivalents of β-alanine	Milliequivalents of hydroxide ion	Lactone	*dl*-pantothenic acid	Total % conversion
Present at start	540	540	1680	0	..
Present after 1 hr.	235[a]	< 1[b]	..	305[c]	55
Added at end of 1 hr.	0	235	0	0	..
Present at end of 2 hr.	115[a]	< 1[b]	..	425[c]	79
Added at end of 2 hr.	0	115	0	0	
Present at end of 3 hr.	78[a]	< 1[b]	..	462[c]	85
Added at end of 3 hr.	0	100	0	0	
Present at end of 4 hr.	68[a]	< 1[b]	..	472[c]	88

[a] By Sörensen formol titration. [b] Acid to phenolphthalein. [c] By difference.

At the end of the experiment, the solution was biologically assayed with chicks,[4] and found to contain 3,680,000 chick filtrate factor units, corresponding to 36 units per mg. of *dl*-pantothenic acid. Natural pantothenic acid has been stated to contain 71 chick units per mg.[5] This points to the inactivity of one enantiomorph in the synthetic preparation.

At the same time a mixture of 10 g. of the *dl*-lactone and 7 g. of β-alanine was incorporated in 1000 g. of heated diet and biologically assayed. Slight but definite activity was observed, calculated to correspond roughly to a coupling *in vivo* of 0.06% of the mixture. This indicates that none of the activity of the pantothenic acid solution at the level fed (corresponding to 2.1 mg. of *dl*-pantothenic acid per 100 g. of diet) may be attributed to the presence of unchanged starting materials.

(4) Jukes, *J. Biol. Chem.*, **117**, 11 (1937).
(5) Jukes, *ibid.*, **129**, 225 (1939).

DIVISIONS OF CHEMISTRY AND POULTRY HUSBANDRY
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S. H. BABCOCK, JR.
T. H. JUKES

RECEIVED MAY 20, 1940

NAPHTHOQUINONE OXIDES

Sir:

Since 2-methyl-1,4-naphthoquinone oxide can be converted very easily and efficiently [Fieser, *J. Biol. Chem.*, **133**, 391 (1940)] into the isomer phthiocol, it was somewhat surprising to discover

that the substance surpasses phthiocol by far in vitamin K activity. The observation that the pure oxide [Fieser, Campbell, Fry and Gates, THIS JOURNAL, **61**, 3216 (1939)] is fully effective in the chick assay at a dosage of 5 γ prompted the investigation of other oxides of 2-alkyl and 2,3-dialkyl 1,4-naphthoquinones, and it was found that the hydrogen peroxide procedure [Fieser, *et al.*, *loc. cit.*] provides a convenient route to a number of substances of both types. Farnesylnaphthoquinone oxide [found: C, 78.88; H, 8.16] and phytylnaphthoquinone oxide [found: C, 79.91; H, 9.76] were obtained as nearly colorless oils showing, respectively, very weak and weak (500 γ) antihemorrhagic activity. These substances are cleaved by alkali to a mixture of 2-hydroxy-1,4-naphthoquinone and its 3-alkyl derivative. Crystalline oxides were obtained from 2,3-dimethyl-1,4-naphthoquinone [m. p. 104–104.5°, found: C, 71.26; H, 5.09; active at 25 γ] and 2-methyl-3-cinnamyl-1,4-naphthoquinone [m. p. 85–86°, found: C, 78.94; H, 5.47].

Vitamin K_1 was converted in nearly quantitative yield into the 2,3-oxide, which was obtained as an almost colorless oil [found: C, 79.85; H, 9.69]. Any uncertainty as to the structure is eliminated by the observation that the absorption spectrum corresponds closely with that of 2,3-dimethyl-1,4-naphthoquinone oxide. The K_1 oxide shows antihemorrhagic activity of about the same order as the vitamin (1.5 γ) and gives no purple-blue color with alcoholic alkali. The properties of the oxide are of interest in connection with the reports of Fernholz, Ansbacher and coworkers [THIS JOURNAL, **61**, 1613 (1939); *Proc. Soc. Exptl. Biol. Med.*, **42**, 655 (1939)] stating that they have isolated from alfalfa concentrates a nearly colorless substance of high potency which does not give the Dam–Karrer color test characteristic of vitamins K_1 and K_2. However, in our hands, there is no great difference in the ratio of the effective dose of the oxide and of vitamin K_1 when assayed by the six and eighteen hour method.

We have found that the oxides of vitamin K_1 and of methylnaphthoquinone can be reduced smoothly to vitamin K_1 hydroquinone and methylnaphthohydroquinone with sodium hydrosulfite in aqueous alcohol, even at room temperature. This lends plausibility to the hypothesis that the high potency of the oxides is due to a reduction in the organism to the corresponding quinones or hydroquinones; possibly the 2-methyl oxide is converted in part into the comparatively inactive phthiocol.

CONVERSE MEMORIAL LABORATORY L. F. FIESER
HARVARD UNIVERSITY
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RESEARCH LABORATORIES,
MERCK AND CO., INC., AND M. TISHLER
MERCK INSTITUTE FOR THERAPEUTIC RESEARCH
RAHWAY, NEW JERSEY W. L. SAMPSON

RECEIVED APRIL 20, 1940

MISCIBILITY OF CARBON DIOXIDE AND WATER UNDER HIGH PRESSURE

Sir:

Wiebe and Gaddy [THIS JOURNAL, **62**, 815 (1940)] report the solubility of carbon dioxide in water and make the following statement: "The compositions of the gas and liquid phases at 12° and 600 atm. were identical." My understanding of the behavior of carbon dioxide–water systems is that compression at 12° to about 47.7 atm. will change the phases from a gas (predominantly carbon dioxide) and liquid (mostly water) to a gas (mostly carbon dioxide), a liquid (mostly carbon dioxide), and a liquid (mostly water). Further attempts to compress the system will cause the gas phase to change to a liquid (mostly carbon dioxide) phase and leave at its disappearance two liquids, one predominantly water and the other predominantly carbon dioxide.

Their data show that compression of the two phases increases the carbon dioxide content of the water phase only from 0.03 mole fraction to less than 0.04 mole fraction. Lowry and Erickson [*ibid.*, **49**, 2729 (1927)] indicated that the water concentration in the liquid carbon dioxide was much lower than the above concentration of carbon dioxide in the water phase. Wiebe and Gaddy [*ibid.*, **61**, 315 (1939)] state the mutual solubility of water and carbon dioxide as liquid–liquid system is affected by pressure to only a slight extent.

These statements appear contradictory to the above quotation of identical phases. Any critical phenomena in this region would be of the liquid–liquid critical solution type and not of the type reported by Kuenen [*Commun. Phys. Lab. Univ. Leiden*, **4** (1892)] for the carbon dioxide–methyl chloride system. To become mutually soluble, it is normally expected that the two phases approach each other in composition. A consideration of the probable behavior of these two phases upon compression indicates a possible explanation of the above contradictions. At 10 to 20°,

carbon dioxide is relatively close to its critical temperature and is more compressible than water. At low pressures the predominantly water phase is the more dense but the increase of pressure to about 200 atm. and about 500 atm. at 10 and 20°, respectively, would cause the two immiscible fluids to reach the same density.

I know no reason to believe that the same density makes the two phases miscible but the formation of a relatively uniform suspension of the two phases might occur. Unless the possibility of this reversal in the positions of the two phases in the equilibrium cell were recognized, experimental results might indicate a critical state had been reached. Details of the manipulation of the equilibrium cell and quantitative results at the high pressures in the reported region of complete miscibility should show whether the proposed explanation of the unusual results is tenable.

DEPARTMENT OF CHEMICAL ENGINEERING
UNIVERSITY OF MICHIGAN
ANN ARBOR, MICHIGAN D. L. KATZ

RECEIVED APRIL 18, 1940

REDISTRIBUTION REACTIONS

Sir:

Recently Calingaert and co-workers[1] have described a "hitherto unrecognized type of intermolecular exchange of organic radicals" which they term "redistribution reactions." These reactions are characterized by equilibrium constants which are independent of temperature through the temperature range employed, and which have values that agree with the idea of a random distribution of the exchanging radicals to within the precision of the data obtained.

In view of the large amount of experimental work done by these authors already, it seems justifiable to point out that, while such reactions have not hitherto been recognized as a type, their existence need not surprise one; and, furthermore, given any of the reactions so far studied, the *equilibrium* results obtained could have been predicted about as closely as the experiments justify the idea of random exchange of radicals.

The significance of these reactions lies, first, in the fact that, to the precision to which a modified Redgrove[2] rule would apply, values of ΔH would be zero in all cases. Thus in every type of exchange studied certain bonds are broken and others are formed, but the latter are always identical with the former except for slight steric effects. For $\Delta H = 0$, $K = e^{\Delta S^0/R}$, and ΔS^0 for random distribution should be measured by the relative external symmetry numbers of the molecules involved in the equilibrium; *e. g.*, in the type reaction

$$\underset{\sigma = 12}{R_4M} + \underset{12}{R'_4M} \rightleftarrows \underset{2}{2R_2R'_2M} \qquad (1)$$

$$\Delta S^0_\sigma = R \ln \frac{12^2}{2^2} = 7.11 \text{ units or } K = 36$$

where σ is the external symmetry number. By the nature of the reactions studied, the only remaining appreciable contributions to ΔS^0 would lie in the effect of the redistribution of mass on the translational entropies, and on the redistribution of principal moments of inertia on the possible rotational entropies. Based on six specific redistributions from systems typified by the left-hand side of equation 1, the former of the two mentioned contributions (*i. e.*, mass redistribution) averages 0.076 entropy unit (a heat effect of about 27 small calories at 350°K.); and, assuming stretched molecules and free rotation, the average of the upper limit of the second contribution to ΔS^0 mentioned above is, for the same six reactions, 0.86 entropy units (a heat effect of about 300 small calories at 350°K.).

It is therefore not surprising that the controlling factor in determining the equilibrium state for such reactions is the value of ΔS^0_σ, or randomness of distribution.

UNIVERSITY OF MISSOURI
COLUMBIA, MISSOURI ALLEN E. STEARN

RECEIVED MARCH 11, 1940

THE ISOMERIZATION EQUILIBRIUM OF *n*-BUTANE AND *i*-BUTANE AND THE THIRD LAW OF THERMODYNAMICS

Sir:

Recently complete measurements in this Laboratory of the thermal properties of the two butanes from 11°K. to their respective boiling points furnish values for the entropies of the gases at their normal boiling points. For *n*-butane $S^\circ_{272.66°K.} = 72.05 \pm 0.2$ e. u.; for *i*-butane $S^\circ_{261.44°K.} = 67.54 \pm 0.2$ e. u. These values, together with available heat capacity data on the gas, yield a value of $\Delta S^\circ_{298.1} = -3.7 \pm 0.3$ e. u. for the reaction

n-butane(g) ⟶ *i*-butane(g)

(1) Calingaert and Beatty, THIS JOURNAL, **61**, 2748 (1939); Calingaert, Beatty and Neal, *ibid.*, **61**, 2755 (1939); Calingaert and Soroos, *ibid.*, **61**, 2758 (1939); Calingaert Beatty and Hess, *ibid.*, **61**, 3300 (1939).

(2) Redgrove, *Chem. News*, **116**, 37 (1917).

The work of Moldavskii and Nizovdima[1] upon the equilibrium constant for this reaction from 70–150°, combined with the measurement of Montgomery, McAteer and Franke[2] at 27° furnishes an independent value for the entropy difference of the two isomers. Two of these equilibrium measurements, at 27° (Montgomery) and at 70° (Moldavskii) were made in the liquid phase at pressures of about 3 and 10 atmospheres, respectively. The constants were calculated to the gas phase with fugacity data for *n*-butane[3] and *i*-butane[4] reported by Sage, Webster and Lacey. The assumption that the liquid follows Raoult's law is in accord with the results of Montgomery, *et al.*[2] The other equilibrium measurements were made in the gas phase by a flow method. The heat of isomerization -2200 ± 200 cal./mole was obtained from the slope of a $\log K - \frac{1}{T}$ plot. Essentially a straight line was obtained, which indicates that over the temperature range in question ΔH is constant to within a small fraction of the experimental error in the equilibrium values. This constancy of ΔH has been confirmed by statistical mechanical calculation.

From the equilibrium data two values of ΔS°_{298} for the isomerization reaction may be obtained, one using the measured heat[5] (A), the other using the heat of isomerization from the slope of the plot (B). These two values are compared with our experimental value of ΔS°_{298} (C) in Table I.

TABLE I

$n\text{-}C_4H_{10}\ (g) = i\text{-}C_4H_{10}\ (g)$

ΔS°_{298} cal./deg./mole	Source of data
-2.1 ± 0.6	Equilibrium measurement (Montgomery, *et al.*[2])
	Heats of combustion (Rossini[6])
-3.7 ± 0.3	Thermal data to 11 °K. *n*-butane submitted for publication in THIS JOURNAL
	i-butane, unpublished data
-4.0 ± 0.8	Temperature coefficient of equilibrium constant. Montgomery *et al.*,[2] and Moldavskii and Nizovdima.[1]

The agreement between (B) and (C) is well within experimental error. There is thus at present no reason to doubt[6] the practical applicability of the third law of thermodynamics to these compounds.

The assistance of the Standard Oil Development Company in portions of this work is gratefully acknowledged.

(1) Moldavskii and Nizovdima, *Compt. rend. acad. sci. U. R. S. S.*, **23**, 919–20 (1939); *Chem. Abs.*, **34**, 931 (1940).

(2) Montgomery, McAteer and Franke, THIS JOURNAL, **59**, 1768 (1937).

(3) Sage, Webster and Lacey, *Ind. Eng. Chem.*, **29**, 1188 (1937).

(4) Sage and Lacey, *ibid.*, **30**, 673 (1938).

(5) Rossini, *J. Chem. Phys.*, **3**, 438 (1935).

(6) Kassel, THIS JOURNAL, **59**, 2745 (1937).

SCHOOL OF CHEMISTRY AND PHYSICS G. H. MESSERLY
THE PENNSYLVANIA STATE COLLEGE J. G. ASTON
STATE COLLEGE, PENNSYLVANIA R. M. KENNEDY

RECEIVED MAY 6, 1940

NEW BOOKS

Die exakten Methoden der Mikromassanalyse. (The Exact Methods of Titrimetric Microanalysis.) By Dipl.-Ing. JOSEF MIKA. (Die chemische Analyse. Edited by WILHELM BÖTTGER, Hannover. XLII. Band.) Ferdinand Enke Verlag, Hasenbergsteige 3, Stuttgart W, Germany, 1939. xii + 180 pp. 19 figs. 16.5 × 25 cm. Price, RM. 18; bound, RM. 19.60.

The author limits himself to a discussion of such titrimetric methods as can be applied to samples of approximately 10 microequivalents, *i. e.*, 1 to 10 milligrams of material. As a rule it is tried to attain a relative precision of 1 part in a thousand. Methods giving a relative precision of 10 parts in a thousand are included, however, if they offer practical advantages. Hundredth normal standard solutions are suggested for the use with burets of approximately 1 ml. total capacity, which permit delivery and determination of volume with a precision o 0.001 to 0.0001 ml.

In the general part are discussed: the recognition of the end-point with the use of colorimetric, potentiometric, and conductometric methods; the concentration of the standard solutions and the determination and accuracy of their titer; burets, pipets, and aliquot partition; storing of standard solutions; containers for the titrated solutions, stands for titration; apparatus for potentiometric and conductometric titrations; and the testing for purity of the reagents and the water used as solvent. The special part comprises: neutralimetry with the use of dyestuff indicators and of potentiometric and conductometric indication of the end-point; oxidimetry, redox indicators, and electrometric indication; titrations based on the formation of precipitates or complexes with the use of colori-