NOTES

The Decomposition Voltage of Grignard Reagents in Ether Solution

By Elliot Q. Adams

Evans, Lee and Lee[1] have found decomposition voltages of Grignard reagents ranging from 0.86 volt for allylmagnesium bromide, to 2.17 volts for phenylmagnesium bromide. If the *differences* in the decomposition voltages of the saturated aliphatic derivatives produced by the introduction of one methyl group are taken, it is

α_1 -0.66 α_2 -0.21 α_3 -0.10
-0.18
β_1 $+0.14$
$+0.17$
γ_1 -0.10 (Evans, Lee and Lee)
$\Delta pK_A/pK_{A(subst.)}\alpha = -0.68$
β (Derick) $= -0.19$
γ $= -0.06$
δ $= -0.02$

α_1, α_2, α_3 represent the changes *in volts* in the decomposition potential of Grignard reagents in ether solution, produced by replacing, respectively, the first, second, and third α-hydrogen by methyl; β_1 and γ_1 represent similarly the changes *in volts* produced by the first methyl group in, respectively, the β and γ positions. α, β, γ and δ are the changes in Derick's function[3] produced by substituting chlorine for, respectively, the α-, β-, γ- or δ-hydrogens in butyric or valeric acid, or their chlorinated derivatives.

found that successive substitutions in the alpha position produce diminishing decreases in the decomposition potential, and that the effect of substitution in the beta position is opposite in sign to that of alpha or gamma substitution. Conant[2] has found that irreversible oxidation–reduction potentials are represented by equations similar in form to those for oxidation–reduction equilibrium potentials. Derick[3] has pointed out that the relative effects of substituents on the logarithms of the ionization constants of organic acids ($\Delta pK_A/pK_{A(substituted)}$ in present-day notation) are reduced approximately 3-fold by each additional carbon atom between the carboxyl and the substituent, without change in sign. The results of Evans, Lee and Lee agree within the error of measurement with the series

$$-0.63 :\mp 0.21 : -0.07 = 9 :\mp 3 : 1$$

that is, 3-fold reduction in the effect of successive alpha replacements, as well as with increasing distance from the MgBr radical. In the latter case, there is also an alternation in sign of the effect.

The results for phenyl- and allylmagnesium bromides indicate an effect of unsaturation alternating in sign, and less for the more distant double bond, in qualitative agreement with the rule for methyl groups.

Incandescent Lamp Department
General Electric Company
Nela Park
Cleveland, Ohio

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(1) W. V. Evans, F. H. Lee and C. H. Lee, This Journal, **57**, 489–490 (1935).

(2) J. B. Conant and M. F. Pratt, *ibid.* **48**, 3178–3192 (1926).

(3) C. G. Derick, *ibid.* **33**, 1182 (1911). The approximate numerical agreement between Evans, Lee and Lee's results in volts, and Derick's is, of course, a coincidence. Since pK_A for unsubstituted aliphatic acids is of the order of 5 and with a single strongly negative α-substituent becomes about 3, the unit of Derick's function for singly substituted acids will range from 3 to 5 pK units. (1 volt $\simeq$ 17 pK units.) The form of Derick's function provides for a diminishing effect on pK_A with successive substitutions, but the decrease even in the case of α-substitution is not as great as that shown in the results of Evans, Lee and Lee. Since the acid hydrogen in substituted acetic acids is separated by a carbon and an oxygen atom from the α-carbon of the chain, while in the Grignard reagents the magnesium atom is directly attached, a factor of the order of 9 is to be expected. There is, to be sure, no reason to expect the effect of a methyl group on the irreversible breaking of the bonding of magnesium to carbon in ether solution to be identical with the effect of chlorine on the equilibrium of the bonding of hydrogen to oxygen in aqueous solution.

Some Acyl Derivatives of *o*-Anisidine

By Lawrence H. Amundsen and C. B. Pollard

We have prepared a number of acyl derivatives of *o*-anisidine, the majority of which have not been described in the literature. The monoacyl derivatives were prepared by the action of the corresponding acyl chlorides upon 2 molecular proportions of *o*-anisidine.[1]

The diacyl derivatives were prepared by boiling a toluene solution of *o*-anisidine with 2.5 molecular proportions of acyl chlorides under reflux for twelve to eighteen hours. The dibenzoyl derivative precipitated upon cooling the solution and the dipropionyl derivative was obtained by evaporation of the toluene.

The first six compounds are very soluble in most organic solvents but only moderately soluble in pentane, hexane, etc. The next four compounds are very soluble in chloroform, dioxane and acetone, fairly soluble in alcohol, slightly

(1) Mühlhäuser, *Ann.*, **207**, 235 (1881); *Ber.*, **13**, 919 (1880).

TABLE I

ACYL DERIVATIVES OF *o*-ANISIDINE

Acyl groups	Solvent used in crystn.	Yield, %	M. p., °C.	Formula	Nitrogen % Calcd.	Found
Propionyl	Ether[a]	73	33.5–34.5	$C_{10}H_{13}NO_2$	7.82	7.80
Butyryl	Ether[a]	78	24.5–25.5	$C_{11}H_{15}NO_2$	7.25	7.11
Valeryl	Ether[a]	91	25.5–26.5	$C_{12}H_{17}NO_2$	6.76	6.45
Isovaleryl	Ether[a]	94	49–49.5	$C_{12}H_{17}NO_2$	6.76	6.59
Caproyl	Ether[a]	61	33–33.5	$C_{13}H_{19}NO_2$	6.33	6.38
Heptanoyl	Pet. ether	67	42–43	$C_{14}H_{21}NO_2$	5.96	5.73
Phenylacetyl[b]	Dilute alc.	88	82.5–83			
Hydrocinnamyl	Isopropyl ether or benzene and heptane	100	59.5–60	$C_{16}H_{17}NO_2$	5.49	5.50
m-Bromobenzoyl		86	112.5–113	$C_{14}H_{12}BrNO_2$	4.58	4.59
					Br, 26.11	25.60
p-Anisoyl		100	96.5–97.5	$C_{15}H_{15}NO_3$	5.45	5.42
Benzoyl[c]			66–67			
Acetyl[d]			85–85.5			
Dibenzoyl	Alc. or toluene	60	149.5–150	$C_{21}H_{17}NO_3$	4.23	4.25
Dipropionyl	Hexane	85	62.5–63.5	$C_{13}H_{17}NO_3$	5.96	5.98

[a] By cooling with solid carbon dioxide.

[b] Aggarwal, Das and Rây[2] prepared this compound from *o*-anisidine and phenylacetic acid and reported a melting point of 84°.

[c] Prepared by Mühlhäuser,[1] who reported a melting point of 59.5°.

[d] Mühlhäuser[1] reported a melting point of 78°. Our melting point agrees with the one given in Mulliken's "Identification of Pure Organic Compounds," Vol. II, p. 151.

soluble in ether, and almost insoluble in hexane. *o*-Dibenzoylanisidine is difficultly soluble in toluene and alcohol but readily soluble in chloroform. *o*-Dipropionylanisidine is soluble in practically all organic solvents.

One additional compound was prepared during this investigation. Its properties are given below.

***o*-Benzoylmethylaminophenyl Benzoate.**—This compound was prepared by the Schotten–Baumann method in 40% yield. It was crystallized from alcohol. It is soluble in dioxane, acetone, chloroform and benzene; somewhat soluble in alcohol and ether; and almost insoluble in petroleum solvents, m. p. 114–115°.

Anal. Calcd. for $C_{21}H_{17}NO_3$: N, 4.25. Found: N, 4.12.

(2) Aggarwal, Das and Rây, *J. Ind. Chem. Soc.*, **6**, 717 (1929).

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF FLORIDA
GAINESVILLE, FLORIDA

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Addition of Methyl Alcohol to Dialkylacetylenes

BY G. F. HENNION AND J. A. NIEUWLAND

The many well-known reactions of acetylene and its homologs with hydroxylated compounds (alcohols, carboxylic acids, etc.) are characterized by the fact that they proceed quite readily in an appropriate acid medium in the presence of a small amount of a suitable mercuric salt. The mechanism of this catalysis has engaged our attention for some time. There is little doubt but what the reaction of an acetylene with methyl alcohol, for example, produces first a vinyl ether which in turn immediately adds a second molecule of alcohol to form the ketal or acetal. There is evidence to indicate that the mercuric salts function only in the first of these reactions.

In attempting to determine whether the catalytic mercuric salt forms an intermediate with the acetylene by addition or substitution (or both) we have succeeded in adding methyl alcohol to two dialkylacetylenes in the usual way.[1] This indicates quite clearly that an intermediate of the mercury acetylide type is not essential to the mechanism of catalysis.

Preparation of 2-Octyne.—This compound was obtained by the action of methyl iodide on sodium amylacetylide in liquid ammonia: b. p. 132–136°; d^{32} 0.751; $n^{32}D$ 1.4227.

Reaction of 2-Octyne with Methyl Alcohol.—The catalyst was prepared by heating together momentarily 3 g. of red mercuric oxide, 1 ml. of $(C_2H_5)_2O{\cdot}BF_3$, 0.5 g. of trichloroacetic acid, and 3 ml. of methyl alcohol. The reaction was carried out and the product purified as previously described.[1] From 55 g. of 2-octyne there was obtained 48 g. of 3,3-dimethoxyoctane: yield, 55%; b. p. 90–92° at 26 mm.; d^{25} 0.8552; $n^{25}D$ 1.4171; MR calcd. 51.67, found 51.22.

(1) Hennion, Killian, *et al.*, THIS JOURNAL, **56**, 1130 (1934), and subsequent papers.

Anal. Calcd. for $C_{10}H_{22}O_3$: C, 68.89; H, 12.73. Found: C, 69.00; H, 12.79.

Hydrolysis of a 1-ml. sample yielded a ketone which was in turn converted to the semicarbazone. The latter melted at 112–113° which agrees with the value of 112° given by Pickard and Kenyon[2] for the semicarbazone of 3-octanone.

Reaction of Methoxy-4-butyne-2 with Methyl Alcohol.—A sample of this acetylene[3] was obtained through the courtesy of Dr. Wallace H. Carothers of E. I. du Pont de Nemours & Company to whom our sincere thanks are extended.

The catalyst was prepared as described above and the reaction carried out in the usual way. Forty-two grams of the acetylene yielded 42 g. of 2,2,4-trimethoxybutane, b. p. 67–69° at 30 mm.; yield, 57%. This compound has been obtained previously from vinylacetylene.[4]

(2) Pickard and Kenyon, *J. Chem. Soc.*, **103**, 1936 (1913).

(3) Jacobson, Dykstra and Carothers, THIS JOURNAL, **56**, 1169 (1934).

(4) Killian, Hennion and Nieuwland, *ibid.*, **56**, 1786 (1934).

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p-Bromophenacyl Formate, a Solid Derivative of Formic Acid

BY CHARLES D. HURD AND ROBERT E. CHRIST

It was found by Judefind and Reid[1] that many aliphatic acids could be identified easily as their *p*-bromophenacyl esters. These solid esters made excellent derivatives for the acids. According to these authors, however, formic acid gave negative results. In contrast to this statement, we have found that formic acid behaves regularly. The preparation of *p*-bromophenacyl formate is a simple matter and the compound makes an admirable derivative. It melts at 140°.

One gram of sodium formate (solid) was dissolved in 5 cc. of water and 10 cc. of 95% alcohol. Then 1 g. of *p*-bromophenacyl bromide was added. The solution was boiled until nearly all the solvent had disappeared. More alcohol was added and it was boiled another half hour until the solvent had nearly disappeared. Finally, the product was dissolved in dilute alcohol and then cooled. The crystalline product was filtered and recrystallized from dilute alcohol. A total of 0.38 g. of product was obtained which possessed a melting point of 140°.

Equally good results were obtained by refluxing instead of boiling away the solvents. Then, the first amount of alcohol is sufficient.

(1) Judefind and Reid, THIS JOURNAL, **42**, 1052 (1920).

Anal. Subs., 0.2027; AgBr, 0.1551. Calcd. for $C_9H_7O_3Br$: Br, 32.89. Found: Br, 32.56.

CONTRIBUTION FROM THE
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Optical Rotation Study of the New Orally Effective Principle of Ergot

BY E. C. KLEIDERER

Commercial production of the orally effective principle recently isolated from ergot has provided an adequate source for an intensive study of its properties.

The free base, called ergotocin by Kharasch and Legault, was crystallized from benzene and dried *in vacuo* for about eight hours. It melted at 157–158° (corr., bath at 150° when sample was introduced). The maleate salt was prepared from the crystalline base, and dried *in vacuo*.

The initial specific rotations of the free base in various solvents are given below. All rotations in this investigation were made in a one-decimeter tube at 28° unless otherwise stated. Due

TABLE I

Solvent	Wt. and vol. of solvent	α_D	$[\alpha]_D$
Distilled water	0.0276 g. in 10 cc.	+0.21°	+76.1°
Abs. methyl alcohol	.0485 g. in 15 cc. tube, 2 dm.	+ .26°	+40.2°
Cyclohexanol	.00659 g. in 1 cc. (micro)	+ .21°	+31.6°
Chloroform	.0179 g. in 10 cc.	− .08° at 50°	−44.7° at 50°
Benzene	.0164 g. in 10 cc.	− .10° at 75°	−61.0° at 75°

to the slight solubility of the base in cold chloroform and benzene, the rotations in these solvents were taken in a Landolt heating chamber.

The rotation of the methyl alcoholic solution of the free base on standing at room temperature became more dextro as shown in Table II, while no change was observed on a water solution of the free base after standing at room temperature for one hundred hours.

TABLE II

Time, hr.	Initial	17	30	71.5	95.5
$[\alpha]^{28}D$	+40.2°	+48.0°	+53.1°	+59.6°	+61.8°

The methyl alcohol was evaporated from the sample which had stood ninety-five and one-half hours, the residue recrystallized from benzene and the dried (*in vacuo*) product dissolved in

water giving $[\alpha]^{28}D$ +95.4°. The melting point of the initial sample was 157–158° (dec.) and of the sample obtained from the 95.5-hour solution was 160–161° (dec.).

By the isolated rabbit uterus method,[1] the physiologic activity of the base obtained from the 95.5-hour sample was about 90% of that of the initial sample.

Initial rotations of the maleate salt of the new base were as follows.

TABLE III

Solvent	Wt. and vol. of solution	$\alpha^{28}D$	$[\alpha]^{28}D$
Distilled water	0.1042 g. in 10 cc.	+0.48°	+46.2°
Abs. methyl alcohol	.1017 g. in 25 cc.	+ .308°	+37.9°

Rotations were again made on these same solutions after standing at room temperature for forty-eight hours, and were found to be as follows: on the water solution $\alpha^{28}D$ +0.56°, $[\alpha]^{28}D$ +53.7°; on the methyl alcohol $\alpha^{28}D$ +0.20°, $[\alpha]^{28}D$ 24.6°. The forty-eight-hour methyl alcohol solution was evaporated *in vacuo* to dryness at room temperature, water was added to bring the solution up to the original methyl alcohol volume. The rotation was $\alpha^{28}D$ 0.214°, $[\alpha]^{28}D$ 52.9°. The physiologic activity of these forty-eight-hour samples as determined by the isolated rabbit uterus method was approximately the same as that of an initial sample.

The explanation of these results is not clear at present; evidently some change is occurring in the molecule which affects the optical rotation, but which does not greatly affect the physiologic activity. Changes of rotation have been noted in the cases of ergotinine and ergotamine which have been ascribed to a change into ergotoxine in the former case and into ergotaminine in the latter case. This explanation does not appear to be a logical one for the changes occurring here, since the physiologic activity seems to be practically unchanged and since the product obtained from a solution of the salt of the new base in methyl alcohol and the product obtained from a solution in water appear to be the same.

The author wishes to express his thanks to Dr. K. K. Chen and to Mr. E. E. Swanson of the Lilly Research Laboratories for their aid in determining the physiologic potency.

THE LILLY RESEARCH LABORATORIES
INDIANAPOLIS, INDIANA RECEIVED JULY 24, 1935

(1) Davis, Adair, Chen and Swanson, *J. Pharmacol.*, **54**, 398 (1935); Swanson, Hargreaves and Chen, *J. Am. Pharm. Assoc.*, in press.

An Improved Method of Extraction

BY CHARLES A. MARLIES AND VICTOR K. LA MER

In an investigation on the acid and salt catalysis of nitramide,[1] NH_2NO_2, a novel method of extraction was employed in the final stage of the preparation of this interesting compound. In the customary method[2] the compound is extracted from its aqueous solution, some forty extractions with ether being necessary on account of the exceedingly unfavorable distribution ratio. The improvement consists of immersing the flask containing the nitramide solution and supernatant ether layer into a "dry ice" freezing mixture and swirling until the water layer solidifies completely. The nitramide passes into the ether layer which is decanted through a filter. Complete extraction was achieved by repeating the process three times. The yield obtained on evaporation of the four combined ether extracts was 80%, whereas the maximum yield by the previous method was but 25%, in agreement with the experience of Brönsted's laboratory.[3]

The low yields by the previous[2] method are probably due to decomposition during the prolonged evaporation of the large volume of ether. Nitramide is an extremely unstable substance and the catalytic action resulting from the concentration of the ever-present impurities (including water) during the evaporation probably causes considerable loss by decomposition.

This method of freezing the solvent during extraction should prove generally useful not only in cases where the distribution ratio is unfavorable but also to remove small amounts of material from large volumes of solution, provided, of course, that solid solution is not an important complication.

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COLUMBIA UNIVERSITY
NEW YORK, N. Y. RECEIVED JUNE 3, 1935

(1) Marlies and La Mer, THIS JOURNAL, **57**, 1812 (1935).
(2) Thiele and Lachman, *Ann.*, **288**, 267 (1895).
(3) Brönsted and Pedersen, *Z. physik. Chem.*, **108**, 185 (1924); and a later private communication.