

NOTES

A Note on the Use of Methoxyacetic Anhydride for the Determination of Hydroxyl Groups

BY DOUGLAS W. HILL

The standard procedures for the determination of the presence and number of hydroxyl groups in organic compounds are methylation, followed by estimation of the methoxyl value, and acetylation, followed by estimation of the acetyl value. With the increasing use of micro-analysis the former is the better method since all who are familiar with the various methods of micro acetyl determination realize their unsatisfactory nature. The methoxyl determination, on the other hand, is readily performed but it suffers from the disadvantage that some compounds contain hydroxyl groups which are easily acetylated but which cannot easily be methylated. Into this group falls quercetin which readily yields a pentaacetyl derivative but gives a pentamethoxy derivative only with difficulty.¹ Penta-(methoxyacetyl)-quercetin is described later.

It appeared likely that the difficulties and uncertainties attending the acetyl determination might be eliminated largely by substituting the methoxy derivative for acetic anhydride in the acetylation reaction. The number of hydroxyl groups present in the original compound would then be determined from the methoxyacetyl derivative by estimating the methoxyl value. Up to the present time methoxyacetic anhydride has been difficult to obtain but it has now become commercially available² and the possibility of its use in place of acetic anhydride has therefore been realized. It appears to behave in the same manner as acetic anhydride and the methoxyacetyl derivatives described in the experimental part were all prepared in good yield by procedures in general use with acetic anhydride. In general, as might be expected, the compounds have lower melting points than the corresponding acetyl derivatives.

Experimental

Di-(methoxyacetyl)-hydroquinone (I).—This compound was prepared by heating hydroquinone with methoxyacetic anhydride in pyridine solution for 0.75 hour. The solid precipitated by pouring into water was crystal-

(1) See Gomm and Nierenstein, *THIS JOURNAL*, **53**, 4408 (1931).

(2) A part of the anhydride used in this investigation was supplied by the firm of Dr. Fraenkel and Dr. Landau of Berlin, Oberschönweide, Germany.

lized first from alcohol and finally from petroleum ether (b. p. 60–80°) as fine colorless needles melting at 89.5–90°.

***p*-Methoxyacetoxybenzoic Acid (II).**—This was prepared in aqueous alkaline solution by the method of Chattaway.³ It was crystallized first from aqueous alcohol and finally from alcohol as glistening colorless needles melting at 164–165°.

Methoxyacetylchalcone (III).—Prepared in ethereal solution with addition of anhydrous potassium carbonate according to the method of Malkin and Nierenstein.⁴ After crystallizing from aqueous alcohol it was obtained from petroleum ether (b. p. 60–80°) as pale yellow needles which melted at 93°.

***p*-Methoxyacetoxyacetophenone (IV).**—Prepared by the method of Malkin and Nierenstein⁴ and crystallized first from dilute acetone and then from petroleum ether (b. p. 40–60°) as colorless needles melting at 56–57°.

Penta-(methoxyacetyl)-quercetin (V).—This compound was obtained by gently boiling a solution of quercetin in methoxyacetic anhydride for four hours. The solution was then poured into water and the precipitated solid crystallized several times from a mixture of alcohol and acetone and finally from benzene. It was thus obtained as colorless needles melting at 97–98°.

ANALYTICAL DATA

Subs.	Formula	Found, % (micro)			Calculated, %		
		C	H	OCH ₃	C	H	OCH ₃
I	C ₁₂ H ₁₄ O ₆	56.89	5.56	23.70	56.69	5.51	24.30
II	C ₁₀ H ₁₀ O ₅	57.26	4.74	14.40	57.14	4.76	14.76
III	C ₁₅ H ₁₆ O ₄	72.82	5.43	10.15	72.90	5.40	9.81
IV	C ₁₁ H ₁₂ O ₄	63.72	5.86	14.40	63.46	5.77	14.90
V	C ₃₀ H ₃₀ O ₁₇	54.26	4.62	22.60	54.38	4.53	23.31

The author wishes to express his appreciation to Dr. M. Nierenstein for his suggestions and to the Colston Research Society of the University of Bristol for a grant which has defrayed the expenses of this investigation.

Summary.—Methoxyacetic anhydride is suggested as a substitute for acetic anhydride in the estimation of hydroxyl groups. Some methoxyacetyl compounds are described.

(3) Chattaway, *J. Chem. Soc.*, 3495 (1931).(4) Malkin and Nierenstein, *THIS JOURNAL*, **53**, 239 (1931).

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Preparation of Picolinic Acid Amide from α -BromopyridineBY WALLACE R. BRODE AND CLARENCE BREMER¹

In a recent article Craig² has described the preparation of α -pyridyl cyanide from α -bromopyridine. Attempts on our part to prepare this

(1) An abstract of a portion of a thesis presented by Clarence Bremer in partial fulfillment for the degree of Doctor of Philosophy in Chemistry at The Ohio State University, June, 1933.

(2) Craig, *THIS JOURNAL*, **56**, 231 (1934).

compound, using practically the same quantities of α -bromopyridine and anhydrous cyanide resulted in decomposition with a considerable yield of pyridine. As Craig has pointed out, this decomposition results from prolonged heating before vacuum distillation of the reaction mixture. Failure to obtain the desired product by this method led to an attempted preparation by a bomb tube method.

Fifteen grams of 2-bromopyridine, prepared according to the method of Wibaut,³ together with 15 g. of potassium cyanide, 20 cc. of water and 2 g. of $\text{Cu}(\text{CN})_2$ (catalyst) were placed in a bomb tube and heated at a temperature of 175° for eighteen hours. Considerable pressure was developed due to the evolution of ammonia, so that the tube had to be cooled in ice water before opening. The layer of α -bromopyridine had disappeared and an oily layer was floating on top of the aqueous solution. Extraction of the reaction mass with ether and evaporation of the solvent yielded a thick sirup which had an odor resembling acetamide and which yielded a crystalline mass on standing for a few days. Recrystallization yielded picolinic amide as a pure compound, m. p. 106.3–106.8° (corr.) (litt.⁴ 103.5°). *Anal.* 3.635 mg. picolinic amide gave 0.756 of N at 743 mm. and 29°. Percentage N (found), 22.97; calcd., 22.95. Yield of purified product 3 g. (25%). The aqueous layer on evaporation and neutralization with sulfuric acid (care is necessary due to hydrogen cyanide fumes) yielded a small quantity of picolinic acid.

(3) Wibaut and Overhoff, *Rec. trav. chim.*, **51**, 385 (1932).

(4) Meyer, *Monatsh.*, **15**, 173 (1894).

CONTRIBUTION FROM THE
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Crystalline Lead and Strontium Salts of *d*-Xyonic Acid and a Crystalline Triacetate of *d*-Threose¹

BY ROBERT C. HOCKETT

The description by Hasenfratz² of crystalline lead xyloate prompts us to communicate our own data concerning this and the strontium salt of the same acid. According to our notes, we first isolated the lead xyloate on August 31, 1932,

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Hasenfratz, *Compt. rend.*, **196**, 350 (1933).

from a xyloic acid solution which had been treated with basic lead carbonate to remove bromides, as "colorless, well-formed prisms with nearly rectangular corners." These crystals showed efflorescence quickly on standing in air and accordingly were recrystallized from water, filtered, washed with water-alcohol mixtures, with absolute alcohol, and finally with ether, and then dried in air until there was a sharp break in the rate of loss of weight indicating the nearly complete removal of ether. They then showed $[\alpha]_D^{20} - 6.8^\circ$ (0.7571 g. in 25 cc. of soln. in water; 2-dm. tube; $\alpha = 0.41^\circ$ to the left) and m. p. 58–59°. We have confirmed Hasenfratz's observation that the precipitation of lead from this salt by hydrogen sulfide is an advantageous method of preparing xyloic acid for conversion into the difficultly crystallizable xyloic lactone.

Anal. Subs. 0.2288, 0.2008: cc. *N*/10 $\text{Na}_2\text{S}_2\text{O}_3$,³ 10.86, 9.50. Calcd. for $(\text{C}_5\text{H}_9\text{O}_6)_2\text{Pb} \cdot 5\text{H}_2\text{O}$: Pb, 33.03. Found: 32.72, 32.68.

The various data confirm those of Hasenfratz.

Having observed in January, 1931, that amorphous strontium xyloate was better adapted for degradation to a tetrose by Ruff's method than amorphous calcium xyloate, we have made many preparations of the strontium salt within the last two years. This substance was eventually obtained in a crystalline form whose properties and analyses are fully in accord with the description made by Kiliani⁴ and confirm his observation that it is a pentahydrate. Allen and Tollens's⁵ description of the hydrated salt as containing 8.5 molecules of water leaves it doubtful whether they had in hand the pure crystalline salt. Since our first crystals formed, the salt has crystallized with great readiness, even without seeding; on account of its sparing solubility in cold water it should be useful in identifying and purifying xyloic acid. When heated very rapidly this hydrate melts unsharply at 65–75° but drying to constant weight at 55° converts it within twenty-four hours to an anhydrous powder, $[\alpha]_D^{20} + 13.2^\circ$ (0.4266 g. in 25 cc. of soln. in water; 2-dm. tube; $\alpha = 0.45^\circ$ to the right). This salt is now very readily prepared from xylose in a yield of 96% of the theoretical by an application of the electrolytic method of Isbell and Frush.⁶

(3) Scott, "Standard Methods of Chemical Analysis," D. Van Nostrand Co., New York, 1925, 4th ed., Vol. I, p. 278.

(4) Kiliani, *Ber.*, **59**, 2464 (1926).

(5) Allen and Tollens, *Ann.*, **260**, 312 (1890).

(6) Isbell and Frush, *Bur. Standards J. Research*, **6**, 1145 (1931); **8**, 571 (1932).

The preparation of crystalline *d*-threose triacetate (well-built prisms, m. p. 113–114°, $[\alpha]_D^{20}$ in $\text{CHCl}_3 + 35.5^\circ$) by the degradation of strontium *d*-xylostate was described before the Division of Organic Chemistry of the American

Chemical Society in Chicago, September, 1933, and with additional data will form the subject of an early communication.

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COMMUNICATIONS TO THE EDITOR

NON-ELECTROLYTE SOLUTIONS

Sir:

The author's equation for certain non-electrolyte solutions¹ has recently been seriously misinterpreted, doubtless because of the extremely brief form in which it was presented. For binary solutions the final equations may be expressed in the form

$$\Delta H = \Delta F - RT (n_1 \ln x_1 + n_2 \ln x_2) = \frac{A V_1 V_2 n_1 n_2}{n_1 V_1 + n_2 V_2}$$

$$\Delta \bar{F}_2 - RT \ln x_2 = \frac{A V_2 V_1^2 n_1^2}{(n_1 V_1 + n_2 V_2)^2}$$

where $\Delta \bar{F}_2$, ΔF and ΔH are the changes of the chemical potential per mole of the second component, of the free energy, and of the heat content of the system, respectively, n_1 and n_2 the mole numbers of the components, V_1 and V_2 their molal volumes and x_1 and x_2 their mole fractions. A is independent of the composition at constant temperature and pressure.

The relation of A to the temperature was not explicitly stated, but, recalling the Gibbs-Helmholtz relations, we see that, at constant composition, the second member of the first equation, and therefore the third, must be independent of the temperature. This can be true for all compositions only when the coefficient of expansion, α , is the same for the two components, and then only if $A V_1$ and $A V_2$ are independent of the temperature. Negishi, Donnally and Hildebrand² apparently failed to see this necessity, consider it "implied in Scatchard's treatment" that A is independent of the temperature, and discuss "the applicability of an equation derived by Scatchard" on this basis. The variation they find is very largely that of $1/V_2$.

When the two components do not have the same α and, as in the case discussed, the tempera-

ture and composition cannot be varied independently, the applicability of the equation as an approximation may be tested in either of two ways. The isothermal equation may be taken as exact and any change in $A V_2$ attributed to changing temperature by measuring the volumes at the temperatures in question; or the constant-composition equation taken as exact and any change in $A V_2$ attributed to changing composition by measuring all the volumes at some standard temperature. The author has used the second method.^{1,3} The results of the two methods differ very little in the present case, and the mean deviation from the average varies only from 0.9 to 1.8% for the four solvents. The corresponding deviation of k in Hildebrand's equation is about the same in two cases, much better in the case of TiCl_4 , which may be considered a coincidence, and very much poorer for $\text{C}_2\text{H}_4\text{Br}_2$, which is very likely not a fair test. These measurements add very little to the comparison of the two equations. There is no significant change in the relation of A to the value calculated from the energies of evaporation of the components.

Negishi, Donnally and Hildebrand state that "it would be preferable to substitute for" my expression of A an expression which seems to me ambiguous. If the a 's in their equation (8) are the same as in the equation immediately preceding, the method they suggest is identical with mine; if the a 's are the same as in equation (7), the substitution seems to me undesirable. A more detailed justification of the method I used is given by Hildebrand and Wood.⁴

These authors derive the second equation above and say, "The same equation has been given by Scatchard by the aid of some of the same assumptions as here employed, plus the arbitrary one

(1) G. Scatchard, *Chem. Rev.*, **8**, 321 (1931).

(2) G. R. Negishi, L. H. Donnally and J. H. Hildebrand, *This Journal*, **55**, 4793 (1933).

(3) G. Scatchard, *ibid.*, **53**, 3186 (1931).

(4) J. H. Hildebrand and S. E. Wood, *J. Chem. Physics*, **1**, 817 (1933).