as colorless crystals from ethyl alcohol; yield 1.1 g., m.p. 244°.

Anal. Calcd. for $C_{20}H_{15}NO_2$: C, 79.7; H, 5.0; N, 4.6; active H, 0.33. Found: C, 79.8; H, 5.1; N, 4.6; active H, 0.30.

XIa is insoluble in aqueous sodium hydroxide solution (10%), gives no color with ferric chloride solution and develops an orange color with concentrated sulfuric acid. It is easily soluble in benzene and hot alcohol, but difficulty soluble in ether and light petroleum.

(b) **3-Benzoyl-1,3-benzoxaz-2,4-dione (Xb).**—A solution of 1.5 g. of Xb[19] in 60 ml. of benzene was added to a solution of phenylmagnesium bromide. The reaction mixture was refluxed for 5 hours and kept overnight at room temperature. It was decomposed with dilute hydrochloric acid, extracted with ether and concentrated. The colorless crystals that separated were filtered, recrystallized from alcohol and identified as XIa by m.p., mixed m.p. and color reaction with sulfuric acid; yield 0.78 g., m.p. 244°.

Anal. Calcd. for $C_{20}H_{15}NO_2$: C, 79.7; H, 5.0; N, 4.6. Found: C, 79.6; H, 5.1; N, 4.4.

The ether–benzene mother liquor was evaporated and the oily residue washed twice with cold light petroleum. The resulting solid was crystallized from petroleum ether (b.p. 80–100°), containing a few ml. of benzene, as colorless crystals (yield 0.31 g., m.p. 163°) which were identified as triphenylcarbinol (m.p. and mixed m.p.).

(c) **2,3-Diphenylquinazolone-4 (XIIb).**—A solution of 1.5 g. of XIIb[20] in 50 ml. of benzene was added to a solution of phenylmagnesium bromide and the reaction mixture decomposed with 100 ml. of cold, dilute hydrochloric acid. The ethereal extract was evaporated and the oily residue, which solidified on cooling and scratching, was washed with cold light petroleum and crystallized from glacial acetic acid as colorless crystals (yield 0.68 g., m.p. 212°) identified as III (m.p. and mixed m.p.).

Anal. Calcd. for $C_{26}H_{19}NO$: C, 86.4; H, 5.3; N, 4.4. Found: C, 86.7; H, 5.3; N, 4.3.

Aniline was detected in the aqueous layer by diazotization and coupling with an alkaline solution of 2-naphthol, to form the scarlet phenyl-azo-2-naphthol dye which proved to be identical with an authentic specimen.

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[20] D. T. Zentmyer and E. C. Wagner, *J. Org. Chem.*, **14**, 967 (1949).

GIZA, CAIRO, EGYPT

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLLEGE OF ARTS AND SCIENCES, UNIVERSITY OF LOUISVILLE]

2-Pyrones. XIII.[1] The Chemistry of Coumalic Acid and its Derivatives

BY RICHARD H. WILEY AND LOUIS H. KNABESCHUH[2]

RECEIVED JULY 27, 1954

Coumalyl chloride has been converted to a variety of new compounds including four esters, ten amides and a ketone. It has been noted that the conversion of the chloride to the methyl ester is accompanied by formation of a previously unreported by-product—trimethyl trimesate. The amides are representative of a new class of such compounds and have been established as distinct from the isomeric pyridones, formed from methyl coumalate, by their chemical and physical (absorption) characteristics. The first successful Friedel–Crafts condensation of a 2-pyronecarboxylic acid chloride has provided the first known ketone in this series.

There is abundant evidence in the literature that coumalic acid and its derivatives undergo or fail to undergo reactions for reasons not always obvious from the accepted structural formula. We have commented previously on the difference in stability of the methyl esters of coumalic and isodehydroacetic acid toward pyridone formation.[3,4] Difficulties encountered in esterification of the acid are implied in the variety of reports on the preparation of the ester[5–7] and in the observation that the usual esterification procedure leads to ring fission.[8] Decarboxylation[9] likewise is not practical as it is with isodehydroacetic acid. For these reasons, additional information about the chemistry of coumalic acid and its derivatives is of particular interest.

The esterification of coumalyl chloride, prepared by a useful modification of previously described processes,[10–12] is the most satisfactory, and, in our hands, the only reproducible method of all those reported in the literature[5–8] for the preparation of methyl coumalate. The ester, which can be recrystallized from ligroin to give white crystals, m.p. 67–71°, is not stable and decomposes on attempted fractionation and on standing. The sodium bicarbonate washings of the crude ester, after acidification, slowly deposit a white crystalline solid, m.p. 145–146°, identified as trimethyl trimesate, reported m.p. 144°.[10] We also have isolated this compound as a by-product from the direct esterification of coumalic acid. Presumably the acid conditions result in partial decomposition of the methyl coumalate to methyl formylacetate which is trimerized or is extracted by bicarbonate from the crude ester and on acidification and standing is converted to trimethyl trimesate. This decomposition constitutes a reversal of the reaction by which the acid is formed and the condensation constitutes a reaction similar to mesitylene formation from acetone.

Coumalyl chloride reacts readily at 0° in ether solution to form coumalamide from ammonia or N-substituted coumalamides from primary amines. This reaction is unusual in view of the known ease with which methyl coumalate is converted to pyridones at room temperature and perhaps overemphasis of this possibility may account for the absence of previous descriptions of such amides. Aside from an early ambiguous report by von Pechmann,[12] the only previous[13] report on coumalamides

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[1] Previous paper in this series, R. H. Wiley and C. H. Jarboe, THIS JOURNAL, **77**, 403 (1955).

[2] The authors wish to acknowledge support of this research through a grant NSF-G55 from the National Science Foundation.

[3] R. H. Wiley, Patricia Beasley and L. H. Knabeschuh, THIS JOURNAL, **76**, 311 (1954).

[4] R. H. Wiley, L. H. Knabeschuh, LaVerne Duckwall and N. R. Smith, *ibid.*, **76**, 625 (1954).

[5] L. Ruzicka, *Helv. Chim. Acta*, **4**, 504 (1921).

[6] W. T. Caldwell, F. T. Tyson and L. Lauer, THIS JOURNAL, **66**, 1483 (1944).

[7] N. R. Campbell and J. H. Hunt, *J. Chem. Soc.*, 1176 (1947).

[8] H. von Pechmann, *Ann.*, **273**, 171 (1893).

[9] J. Fried and R. C. Elderfield, *J. Org. Chem.*, **6**, 566, 577 (1941).

[10] H. von Pechmann, *Ann.*, **264**, 261 (1891).

[11] H. Meyer, *Monatsh.*, **25**, 487 (1904).

[12] H. von Pechmann, *Ber.*, **34**, 1406 (1901).

[13] H. M. Basel, U. S. Patent 2,364,304, December, 1944.

describes some N,N-disubstituted amides. The secondary amines, from which these amides were made, structurally prohibit pyridone formation. The amides reported herein are physically distinct on the basis of chemical properties, absorption characteristics and melting points (where both isomers are known) from the pyridones. For example, N-(benzyl)-coumalamide is a neutral compound which melts at 177–178.5°. The isomeric N-(benzyl)-2-pyridone-5-carboxylic acid titrates as a monobasic acid and melts at 206–208°.[4] The ultraviolet absorption characteristics of the two types of compounds also are distinct. The coumalamides as a group show a principal absorption maximum between 330 and 375 mμ (log ε 4.24–4.57) with, in some compounds (N-thiazolyl and N-pyridyl), a secondary maximum at 280 mμ (log ε 3.7). This serves to distinguish the coumalamides from the N-substituted pyridones which show maxima at 260 mμ (log ε 4.1–4.2) and at 290–300 mμ (log ε 3.7–3.9).[4] Coumalamide absorbs at much longer wave lengths than does either coumalic acid or its methyl ester and does not show the double maxima observed with the latter.

The compound which constitutes an exception to the above general characterization of the N-substituted coumalamides is N-(2-thiazolyl)-coumalamide. The ultraviolet absorption spectrum is nearly identical with that of N-(2-pyridyl)-coumalamide with two maxima, but the compound is distinctly acidic. It is soluble in hot, dilute sodium bicarbonate and can be reprecipitated therefrom with dilute acid. It can be titrated in ethanol and shows a strong acid type curve. The only structural possibilities consistent with the available data are those of tautomeric structures. The acidity can be related to the resonance stabilization of the anion formed on removal of a proton. There is nothing in these structures to indicate why the thiazolyl, as compared to the pyridyl or pyrimidyl, amide should be acidic except an empirical distinction which may be assigned to the resonance stabilization of the thiazole ring. Although the pyridonecarboxylic acid structure is not rigorously excluded for this thiazolyl amide, it is not thought to be a likely possibility because the absorption data are totally unlike those for the pyridones and because 2-aminothiazole gives no pyridone under the usual conditions[4] used for pyridone formation from methyl coumalate.

The Friedel–Crafts condensation of coumalyl chloride with anisole has provided the first known 2-pyrone ketone: 5-(*p*-methoxybenzoyl)-2-pyrone, m.p. 153–154.5°. The reaction was carried out in carbon disulfide at 40° with an excess of aluminum chloride as catalyst to give 7–10% yield of product. The ketone gives a precipitate with 2,4-dinitrophenylhydrazine which appears to be a mixture of products resulting in part from ring cleavage. Permanganate oxidation of the ketone gives anisic acid. The ultraviolet absorption spectrum shows a maximum of high intensity (log ε 4.28) at 290 mμ and a maximum of less intensity (log ε 3.85) at 226 mμ. The maximum at 290 mμ occurs in both the ketone and esters of coumalic acid, but the second maximum at 226 mμ in the ketone is shifted from the maximum at 245 mμ observed with the esters.

We wish to record at this time the data characterizing four new esters of coumalic acid. These were prepared from *m*-methoxyphenol, *o*-methoxyphenol, triethylene glycol and pentamethylene glycol by the reaction of coumalyl chloride with the appropriate phenol or glycol.

Experimental[14]

Coumalyl Chloride.—The method for preparing this compound was essentially that of Fried and Elderfield[9]; however, in place of extracting the acid chloride from the crude mixture with high boiling ligroin, it was found that a purer product could be obtained in 87% yields by distilling the product *in vacuo*.

Methyl Coumalate.—This ester was prepared by warming coumalyl chloride with excess methanol at 60° for one hour. The reaction mixture was poured onto water and taken up in ether. The ether solution was washed with aqueous bicarbonate and evaporated to give 93% yield of crude ester. Distillation gave a fraction, b.p. 123–150° (3 mm.), m.p. 67–71°, in 50% yield. The bicarbonate washings after acidification and standing gave 2.0 g. (5.6% of the theoretical amount) of trimethyl trimesate, m.p. 140–154°. Recrystallization gave 0.6 g. of product, m.p. 145–146°, reported 144°.[12] Saponification of the trimethyl trimesate gave trimesic acid, m.p. 368–369°, reported m.p.'s 345–350°,[10] 375–380°,[15] 380°.[16]

Anal. Calcd. for $C_9H_6O_6$: neut. equiv., 70. Found: neut. equiv., 71.7.

***m*-Methoxyphenyl Coumalate.**—This ester was prepared from coumalyl chloride and *m*-methoxyphenol. A mixture of 0.6 g. (0.013 mole) of *m*-methoxyphenol and 2.0 g. (0.013 mole) of coumalyl chloride was heated at 140° for 1.5 hours. The mixture was poured onto ice, extracted with ethyl ether and the ether solution washed with cold 1% sodium hydroxide solution to remove the contaminating methoxyphenol. The crude product obtained on evaporating the ether was recrystallized from benzene–ligroin to give 0.8 g. (25.0% of the theoretical amount) of *m*-methoxyphenyl coumalate, m.p. 71–72.5° after drying *in vacuo* over paraffin chips.

Anal. Calcd. for $C_{13}H_{10}O_5$: C, 63.41; H, 4.07. Found: C, 63.34, 63.64; H, 4.11, 4.24.

***o*-Methoxyphenyl Coumalate.**—This ester was prepared from coumalyl chloride and *o*-methoxyphenol by the procedure described for the *m*-methoxyphenyl ester. There was obtained a 15.6% yield of crystals, m.p. 87–89.5°.

Anal. Calcd. for $C_{13}H_{10}O_5$: C, 63.41; H, 4.07. Found: C, 63.93, 64.03; H, 4.20, 4.24.

Triethylene Glycol Dicoumalate.—This ester was prepared from coumalyl chloride and triethylene glycol. A mixture of 1.5 g. (0.01 mole) of triethylene glycol and 3.16 g. (0.02 mole) of coumalyl chloride was heated at 90° for 2 hours. The white, crystalline product was recrystallized twice from benzene–ligroin to give 0.1 g. (2.5% of the theoretical amount) of triethylene dicoumalate, m.p. 99–100.5°.

Anal. Calcd. for $C_{18}H_{18}O_{10}$: C, 54.82; H, 4.60. Found: C, 54.84, 54.97; H, 4.85, 4.77.

Pentamethylene Glycol Dicoumalate.—This ester was prepared from coumalyl chloride and pentamethylene glycol by the procedure described for the triethylene glycol ester. There was obtained a 5.5% yield of crystals, m.p. 80–83.5°.

Anal. Calcd. for $C_{17}H_{16}O_8$: C, 58.62; H, 4.60. Found: C, 58.40; H, 4.80.

Coumalamide.—A solution of 0.5 g. (0.0032 mole) of coumalyl chloride in 50 ml. of absolute ethyl ether was added to 10 ml. of ammonium hydroxide at 0.4°. The ether was decanted and the solid was collected on a filter and washed thoroughly with water. Recrystallization of the orange product from water and from aqueous ethanol gave 0.3 g. (67.4% of the theoretical amount) of yellow needles of coumalamide, m.p. 244–245° dec.

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(14) Carbon, hydrogen and nitrogen analyses by Micro-Tech., Skokie, Ill. All melting points are corrected.

(15) C. Graebe and H. Krafft, *Ber.*, **39**, 2509 (1906).

(16) F. Ullmann and J. B. Uzbachian, *ibid.*, **36**, 1799 (1903)

Anal. Calcd. for $C_6H_5O_3N$: N, 10.07. Found: N, 10.17, 10.22.

N-Substituted Coumalamides.—These compounds, described elsewhere, were prepared from the appropriate amine and coumalyl chloride by the procedure given above for coumalamide. Often the gummy solid obtained as the crude reaction product was washed by decantation prior to filtration. Most of the products were recrystallized from two different solvents or solvent pairs indicated. The N-(2-thiazolyl) amide also was purified by solution and reprecipitation from alkali.

5-(*p*-Methoxybenzoyl)-2-pyrone.—To a solution of 6.0 g. (0.038 mole) of coumalic acid chloride in 150 ml. of carbon disulfide was added 5.8 g. (0.054 mole) of anisole and 17.6 g. (0.132 mole) of aluminum chloride. The reaction mixture was warmed on a water-bath and held at 40° for 8 hours with stirring. Following the usual procedures, there was obtained 0.9 g. (10.3% of the theoretical amount) of crystals which after two recrystallizations from ethanol as white, needle-like crystals melted at 153–154.5°.

Anal. Calcd. for $C_{13}H_{10}O_4$: C, 67.83; H, 4.35. Found: C, 67.94, 67.68; H, 4.31, 4.51.

The ketone gives a solid derivative with 2,4-dinitrophenylhydrazine, m.p. 259–260°, which was not crystalline in appearance and was insoluble in the usual recrystallizing solvents. Oxidation of 0.1 g. (0.00043 mole) of the ketone with aqueous, alkaline potassium permanganate gave about 0.05 g. of crystals, m.p. 179–181°. A mixed melting point with an authentic sample of anisic acid showed no depression.

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[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF THE BROOKHAVEN NATIONAL LABORATORY AND CORNELL UNIVERSITY]

The Acid-catalyzed Rearrangement of Cinenic Acid[1]

BY J. MEINWALD[2]

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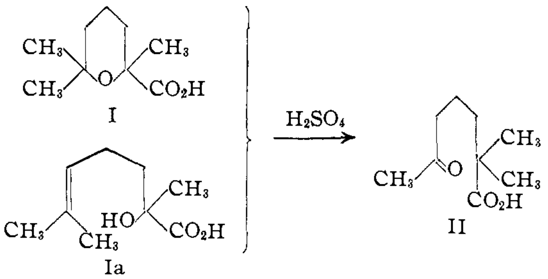
Tracer studies reveal that the isomerization of α-cinenic acid (I) to geronic acid (II) involves carboxyl transfer rather than methyl migration. Some mechanistic implications of this finding are discussed.

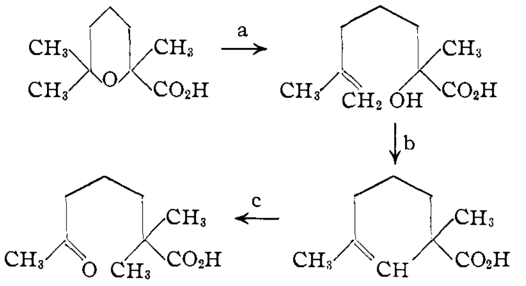
The concept of the "1,2-shift" as the underlying mechanism of organic molecular rearrangements has been remarkably powerful. From its formulation in the 1920's to the present, it has shown itself capable of accommodating an astounding variety of molecular changes.[3] Although recent theoretical developments have led to a considerable refinement of detail, no fundamental modification of the concept has been necessary. In this context, those rearrangements which *cannot* be rationalized in terms of a 1,2-shift, or a short sequence of such shifts, are of special significance. One example of this type of reaction is the benzidine rearrangement; the large effort expended on this transformation[4] reflects the unusual interest in rearrangements of a "non-Whitmore" type.

A less well known and less understood rearrangement has been mechanistically paradoxical for over forty years. This is the isomerization of α-cinenic acid (I) or β-cinenic acid (Ia) to geronic acid (II) represented in equation 1, which Rupe reported to occur in concentrated sulfuric acid solution.[5] In a fascinating summary of Rupe's life work, Dahn and Reichstein called attention to this mysterious observation, and pointed out that it seems to be *without analogy* in organic chemistry.[6,7] Rupe himself was concerned with the novelty of the rearrangement and offered two different explanations of the experimental facts. The first of these is represented in equation 2.[5] Since neither the cyclodehydration step (b) nor the hydration step (c) have any reasonable precedent, this series must be viewed with considerable doubt.

(1)



(2)



Rupe's second suggestion, transcribed into currently acceptable notation in equation 3, deserves more serious consideration.[8] Here the key step is visualized as a *direct transfer of one of the C_6-methyl groups to a site five atoms removed.* Once more this type of change is totally without analogy. Besides the unprecedented 1,5-shift of methyl, the initial cleavage of the tetrahydropyran ring is in a direction which would be unexpected, since it results in placing a formal positive charge adjacent to an

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[1] Research carried out in part under the auspices of the U. S. Atomic Energy Commission.

[2] All work involving radioactivity was carried out during the tenure of an appointment as Associate in Chemistry at the Brookhaven National Laboratory.

[3] For an intersting historical survey of the development of this concept, as well as a review of its scope, see C. K. Ingold," Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 473–529.

[4] Reference 3, pp. 631–642.

[5] H. Rupe and C. Liechtenhan, *Ber.*, **41**, 1278 (1908).

[6] H. Dahn and T. Reichstein, *Helv. Chim. Acta*, **35**, 1 (1952).

[7] In a preliminary investigation of this reaction, carried out at Cornell University, Mr. Richard Burrows was able to confirm Rupe's findings in detail. The 2,4-dinitrophenylhydrazone of the rearrangement product was identical with an authentic sample of geronic acid 2,4-dinitrophenylhydrazone.

[8] H. Rupe and H. Hirschmann, *Helv. Chim. Acta*, **16**, 505 (1933).