The phthalhydrazide that formed was separated by filtration. The filtrate was concentrated to a small volume under reduced pressure and partitioned between methylene chloride and water. After drying the organic phase (Na_2SO_4), it was concentrated to dryness and the residue crystallized from a mixture of benzene and hexane to give 1.1 g of **11**, mp 47–51°. An additional 0.25 g (mp 51–54°) was obtained from the filtrate. Recrystallization of a sample from a mixture of ether and hexane gave colorless prisms: mp 51–54°; ir ($CHCl_3$) 3360 (NH), 1690 (amide CO), 1520 cm^{-1} (amide II).

Anal. Calcd for $C_{11}H_{14}N_2O_4$: C, 55.45; H, 5.92; N, 11.76. Found: C, 55.47; H, 6.14; N, 11.44.

2-(2-Aminobenzylideneaminoxy)acetic Acid (12).—To a solution of 13.6 g (0.1 mol) of 2-aminobenzaldoxime in 300 ml of ethanol containing 10.8 g (0.2 mol) of sodium methoxide, 9.5 g (0.1 mol) of chloroacetic acid was added. The mixture was stirred and heated to reflux for 2 hr and filtered to remove the solid that formed; the filtrate was concentrated to dryness under reduced pressure. On addition of water, **12** crystallized (2.0 g, mp 136–139°) and an additional 8.6 g (mp 134–138°, total yield 55%) was obtained on acidification of the mother liquor with acetic acid. Recrystallization from a mixture of methylene chloride and hexane gave a product melting at 137–139°: ir (KBr disk) 3460, 3450, 3340, 3360 (NH_2), 3200–2600 (associated COOH), 1710 cm^{-1} (carboxyl CO).

Anal. Calcd for $C_9H_{10}N_2O_3$: C, 55.66; H, 5.19; N, 14.43. Found: C, 55.46; H, 5.18; N, 14.49.

Cyclization of 11 to 13. A.—To a solution of 1 g (4 mmol) of **11** in 50 ml of ethanol, 16 ml of 1 *N* hydrochloric acid was added. Within 5 min, a white solid formed. After 16 hr at room temperature, the solid was separated by filtration (0.5 g, mp 263–266 dec). Recrystallization from a mixture of methanol and chloroform gave a product melting at 281–282°: ir (KBr) 3280 (NH), 1695 (amide CO), 1613, 1585, 1540 cm^{-1}; mass spectrum *m/e* 352, 176, 147, 118. The peak at *m/e* 176 could indicate the presence of the monomer.

Anal. Calcd for $(C_9H_8N_2O_2)_n$ C, 61.36; H, 4.58; N, 15.90. Found: C, 61.08; H, 4.77; N, 15.78.

B.—A solution of 2.35 g of **11** in 50 ml of pyridine was added during 1 hr to a refluxing solution of 2.35 g of pyridine hydrochloride in 200 ml of pyridine and the mixture refluxed for 4 more hr. Solvent was removed by distillation at reduced pressure and the residue was partitioned between methylene chloride and water. The organic phase was washed with water, dried (Na_2SO_4), and concentrated to dryness. Trituration of the residue with methylene chloride gave 200 mg of solid (mp 270–275°). Recrystallization from a mixture of methanol and chloroform gave a product melting at 269–270°: ir (KBr) 3270 (NH), 1690 (amide CO), 1660, 1620, 1580, 1540, 1500 cm^{-1}, mass spectrum *m/e* 352, 321, 305, 294, 176, 147, 131, 118.

Anal. Found: C, 61.13; H, 4.47; N, 15.83.

Registry No.—**2**, 16780-56-6; **3**, 16780-57-7; **4**, 16780-58-8; **5**, 1824-72-2; **6**, 16780-60-2; **7**, 16780-61-3; **8**, 16780-62-4; **9**, 16780-63-5; **10**, 16780-64-6; **11**, 16780-65-7; **12**, 16780-66-8; **13**, 16780-55-5.

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5-Aroyl- (or -Acyl-) 4-hydroxycoumarins

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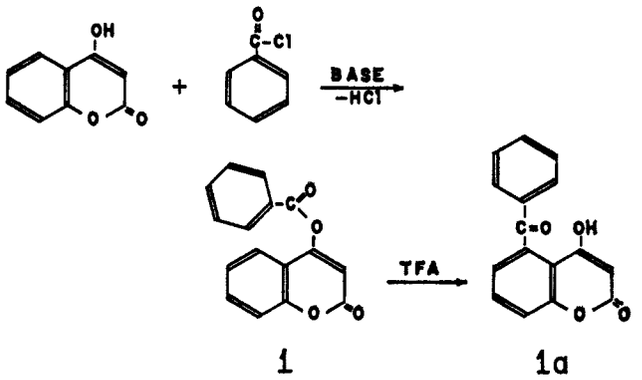
In this Note we present a novel rearrangement of 4-acyloxy- or 4-aroyloxycoumarins (see Table I) given as the **1–5** series, to give 5-aroyl- (or -acyl-) 4-hydroxy coumarin in good yield. This is the only rearrangement, to our knowledge, involving oxygen heterocycles in which a group has migrated from one ring to another and in this respect is quite different from the recorded instances of the Fries reaction[2] involving coumarins.

The rearranged compounds described in Table II as **1a–5a**, are considered by us to be produced by the reaction for **1a** given in Chart I and may be visualized as the general course of the reaction for the production of all the other members of the series.

CHART I

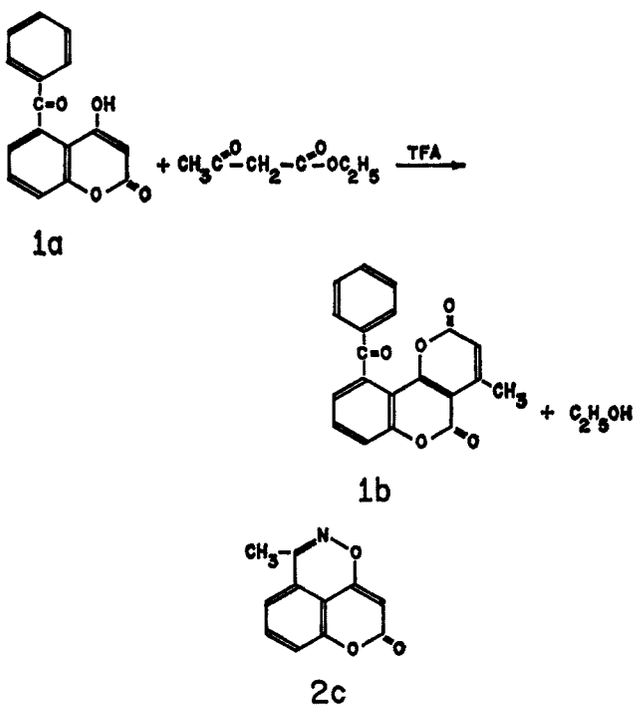


Compound **2a** is the only member of the series which formed a 2,4-dinitrophenylhydrazone.

The failure of the compounds to form dinitrophenyl hydrazones showed that the ketones were hindered and the infrared spectra showed that they were hydrogen bonded. Therefore, the migrating aroyl or acyl group must have taken up positions 3 or 5 on the ring system.

A comparison of the properties of **2a** with 3-acetyl-4-hydroxycoumarin, which had been very carefully

CHART II



(1) Address all inquiries to this author.

(2) R. C. Elderfield, "Heterocyclic Compounds," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1951, p 195.

TABLE I

AROYLOXY OR ACYLOXY DERIVATIVES OF 4-HYDROXYCOUMARIN

Compd[a]	Aroyl halide or anhydride used	Mp, °C	Yield, %	Empirical formula	Calcd, % C	Calcd, % H	Calcd, % Other	Found, % C	Found, % H	Found, % Other
1	Benzoyl chloride	126.5–127.5	88	$C_{16}H_{10}O_4$	72.17	3.78		72.13	3.94	
2	Acetic anhydride	112–113[b]	92	$C_{11}H_8O_4$	64.70	3.94		64.94	4.17	
3	*p*-Chlorobenzoyl chloride	174–174.5	100	$C_{16}H_9ClO_4$	63.90	3.01	11.79 (Cl)	63.62	3.18	11.94 (Cl)
4	*o*-Chlorobenzoyl chloride	130–132	85	$C_{16}H_9ClO_4$	63.90	3.01	11.79 (Cl)	63.68	3.11	11.87 (Cl)
5	*p*-Nitrobenzoyl chloride	195.5–197	100	$C_{16}H_9NO_6$	61.74	2.91	4.50 (N)	61.49	3.04	4.57 (N)

[a] Registry no. for these compounds are given in descending order: 16709-58-3, 15059-36-6, 16709-66-3, 16709-68-5, and 16709-70-9. [b] Lit. mp 103°, according to I. Heilbron, "Dictionary of Organic Compounds," Vol. 3, 4th ed, Oxford Press, New York, N. Y., p 1666.

TABLE II

5-AROYL- (OR -ACYL-) 4-HYDROXYCOUMARINS

Compound	Yield, %	Mp, °C	Empirical formula	Calcd, % C	Calcd, % H	Calcd, % Other	Found, % C	Found, % H	Found, % Other
5-Benzoyl-4-hydroxycoumarin (**1a**)	85	217	$C_{16}H_{10}O_4$	72.17	3.78		72.24	3.84	
5-Acetyl-4-hydroxycoumarin (**2a**)	88	213–213.5	$C_{11}H_8O_4$	64.70	3.94		64.83	4.04	
5-(4-Chlorobenzoyl)-4-hydroxycoumarin (**3a**)	70	232–233	$C_{16}H_9ClO_4$	63.90	3.01	11.79 (Cl)	63.75	3.20	11.98 (Cl)
5-(2-Chlorobenzoyl)-4-hydroxycoumarin (**4a**)	98	218.5–219	$C_{16}H_9ClO_4$	63.90	3.01	11.79 (Cl)	63.74	3.08	11.90 (Cl)
5-(4-Nitrobenzoyl)-4-hydroxycoumarin (**5a**)	55	215–216	$C_{16}H_9NO_6$	61.74	2.91	4.50 (N)	61.45	3.18	4.73 (N)

TABLE III

SPECTRAL CHARACTERISTICS OF MEMBERS OF **1a–5a** SERIES

Compd[d]	Infrared absorption[a,b] bands at 4000–1500 cm^{-1}	Ultraviolet absorption maxima,[c] mμ (log ε)
1a	3400, 2950 b, 2710, 2570, 1695, 1603, 1550, 1502	232 (4.27), 282 (4.30), 306 (4.30)
2a	3375, 2900, 2720, 2580, 1695 vb, 1558	230 (4.18), 281 (4.21), 305 (4.21)
3a	3450, 2960, 2825, 2550, 1673, 1587	210 (4.29), 243 (4.41)
4a	3370 b, 2900, 2720, 2550, 1610, 1593, 1547	225 (4.31), 280 (4.31) pl, 303 (4.32)
5a	3120, 2840 vb, 2660, 2547, 1686, 1601, 1535	230 (4.02), 281 (4.04), 305 (4.03)

[a] Abbreviations used are b = broad, vb = very broad, sh = shoulder. [b] Spectra were taken on Beckman IR-8 spectrometer using KBr pellets. [c] Spectra were taken on Bausch and Lomb Spectronic-505 spectrometer in Spectrograde methanol; pl = plateau. [d] Registry no. are given in descending order: 16709-59-4, 16709-63-0, 16709-66-3, 16709-69-6, and 16709-71-0.

studied[3,4] previously, shows that the migration had not involved position 3; therefore, the migration of the aroyl or acyl group must have been to position 5. The presence of a free 3 position in these products was confirmed by conversion of the 5-benzoyl compound **1a** into **1b** on condensation with acetoacetic ester in the usual way.[5] Reaction of **1a** and **2a** with hydroxylamine under forcing conditions gave products considered to be oxazines **2c** (Chart II).

Experimental Section[6]

4-Acyloxycoumarins.—To a mixture consisting of 0.05 mol of 4-hydroxycoumarin, 0.05 mol of the aroyl halide, and 0.05 mol of pyridine was added 200 ml of benzene. The mixture was gradually brought to its boiling point on a hot plate.

The benzene layer was decanted from the bottom layer, and the solvent was evaporated; the resulting solid was combined with any residue which did not dissolve in the benzene, and the solids were thoroughly washed with warm water to give the aroyloxy compound.

In the case of compound **2** theoretical amounts (0.05 mol) each of acetic anhydride and 4-hydroxycoumarin were heated together in the presence of one drop of concentrated sulfuric acid. The resulting liquid was poured into 150 ml of cold water to give the crude yield.

Compounds **1** and **2** were recrystallized twice from heptane. Compound **3** was purified by dissolving the compound in ethyl acetate and precipitating out the substance with heptane. The process was repeated for a second precipitation.

Compounds **4** and **5** were recrystallized twice from ethyl acetate. Other data on these compounds are given in Table I.

5-Acyl-4-hydroxycoumarins.—A 10-g sample of each of the compounds of the **1–5** series was heated for 15 hr in 30 ml of trifluoroacetic acid. The mixtures were poured into water, chilled, and filtered, and the precipitates were dried in air. The compounds were purified by taking them up in ethyl acetate and precipitating them with heptane. The process was repeated for a second or third recrystallization.

The analytical data for the compounds are given in Table II and the optical characteristics are recorded in Table III.

10-Benzoyl-4-methyl-2H,5H-pyrano[3,2-*c*][1]benzopyran-2,5-dione (1b).—A mixture of 2.2 g of **1a**, 2 g of ethyl acetoacetate, and 5 ml of trifluoroacetic acid was refluxed for 24 hr. The solution was poured into water, filtered, and dried in air. The yield was 2.5 g. The compound was extracted with cold ethyl acetate and the residue was taken up in tetrahydrofuran and precipitated with heptane, mp 255–256°.

Anal. Calcd for $C_{20}H_{12}O_5$: C, 72.28; H, 3.63. Found: C, 72.02; H, 3.47.

The **2,4-dinitrophenylhydrazone of compound 2a** was prepared in the usual way and then recrystallized once from absolute ethanol, mp 273°.

Anal. Calcd for $C_{17}H_{12}N_4O_7$: C, 52.13; H, 3.14; N, 14.57. Found: C, 53.29; H, 3.01; N, 14.78.

Preparation of 3-phenyl-8H-pyrano[2,3,4-*ij*][2,3]benzoxazin-8-one (1c) and 3-methyl-8H-pyrano[2,3,4,-*ij*][2,3]benzoxazin-8-one (2c).—A 3-g sample of each of the compounds (**1a** and **2a**) and 3 g of hydroxylamine hydrochloride were ground together, placed in a flask, and heated in a Fisher Hi-Temp oil bath at 180° for 2 hr. The melt was treated with 100 ml of water, thoroughly extracted with ethyl acetate, and then precipitated with heptane. This process was repeated additionally so that no solid was observed upon taking the melting point of compound **1c** (decomposition above 232°).

Anal. Calcd for $C_{16}H_9NO_3 \cdot HCl$: N, 4.67. Found: N, 4.67.

Since compound **1c** consistently gave correct analyses for the hydrochloride, the purification for **2c** was modified by adding sodium bicarbonate to the water solution and then extracting with ethyl acetate as above for **1c**, finally purified the product to give the salt free **2c**, mp 221–223°.

Anal. Calcd for $C_{11}H_7NO_3$: C, 65.57; H, 3.50; N, 6.96. Found: C, 65.39; H, 3.44; N, 6.84.

(3) H. R. Eisenhauer and K. P. Link, *J. Amer. Chem. Soc.*, **75**, 2046 (1953).
(4) F. D. Chattaway, *J. Chem. Soc.*, 2495 (1931).
(5) L. L. Woods and J. Sterling, *Texas J. Sci.*, **15**, 200 (1963).
(6) Analyses were all performed by Dr. C. Tiedcke, Teaneck, N. J., except for compound **1c** which was done by Galbraith Laboratories, Knoxville, Tenn. All melting points were taken on paired Fisher-Johns melting point blocks.

Registry No.—1b, 16709-60-7; 1c, 16709-61-8; 2a 2,4-dinitrophenylhydrazone, 16709-64-1; 2c, 16709-65-2.

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Synthesis of 6-Benzyl-3-oxo-6-azabicyclo[3.2.1]octane[1]

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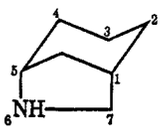
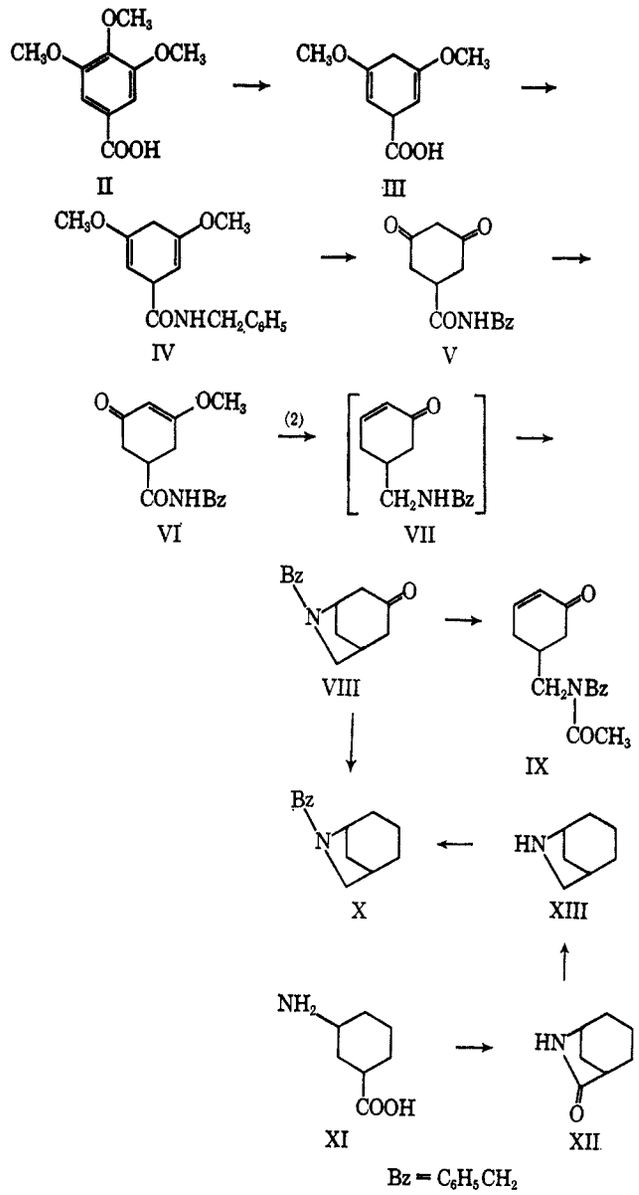
The literature reports only few syntheses of the 6-azabicyclo[3.2.1]octane system (I),[2-4] and only four syntheses of derivatives with a useful function on the three-membered bridge.[5,6] Our interest in this system as well as in other related azabicyclo compounds led us to investigate the sequence described below, which makes the 3-oxo derivative VIII readily available.



I

The starting point (see Scheme I) is trimethylgallic acid (II), which can be converted smoothly by Birch reduction into 3,5-dimethoxy-1,4-dihydrobenzoic acid (III).[7] Treatment of this acid with benzylamine and N,N-dicyclohexylcarbodiimide furnished the N-benzylamide IV. Acid hydrolysis of the enol ether groupings of IV gave diketo compound V which is probably largely enolic. With methanol in the presence of acid, diketo compound V was converted into the β-methoxy-α,β-unsaturated ketone VI. Reduction with lithium aluminum hydride followed by exposure to aqueous sulfuric acid gave rise to the α,β-unsaturated ketone VII,

SCHEME I



which cyclized spontaneously to the desired 6-benzyl-3-oxo-6-azabicyclo[3.2.1]octane (VIII). Interestingly, compound VII with hydroxyl in place of benzylamino appears not to cyclize to the corresponding 6-oxo-6-oxabicyclo[3.2.1]octane.[8] Although the α,β-unsaturated ketone VII could not be obtained, treatment of bicyclo compound VIII with acetic anhydride opened the ring by acyl cleavage to give the N-acetyl derivative IX of VII. The assigned structure for bicyclo ketone VIII was confirmed when its Wolff–Kishner reduction product X proved to be the same as the product obtained by benzylating the known 6-azabicyclo[3.2.1]-octane (XIII). The latter was prepared from 3-aminocyclohexanecarboxylic acid (XI) by cyclization to XII and reduction.[2,3]

Ethylenimine derivatives similar to XVIII have been found to react readily with nucleophiles to give both 6-azabicyclo[3.2.1]octanes (as in XVII) and 2-azabicyclo[2.2.2]octanes (*i.e.*, isoquinuclidines, as in XIX).[6] The possibility of reaching isoquinuclidine XIX was attractive, and the series of reactions V →

(1) This investigation was supported by Public Health Service Research Grant No. CA 08386 from the National Cancer Institute.

(2) F. R. Hewgill and P. R. Jefferies, *J. Chem. Soc.*, 2767 (1955); H. Najer, R. Giudicelli, and J. Sette, *Bull. Soc. Chim. Fr.*, 1593 (1962).

(3) H. K. Ball, Jr., *J. Amer. Chem. Soc.*, **80**, 6412, 6420 (1958); **82**, 1209 (1960).

(4) W. J. Sullivan, *Dissertation Abstr.*, **19**, 682 (1958) (Doctoral Dissertation, University of Michigan, Ann Arbor, Mich., 1957); E. N. Skiest, *ibid.*, **22**, 1021 (1961) (Doctoral Dissertation, University of Michigan, Ann Arbor, Mich., 1961); B. E. Betts and W. Davey, *J. Chem. Soc.*, 1683, 3333 (1961); P. G. Gassman and B. L. Fox, *J. Org. Chem.*, **32**, 3679 (1967). Also *cf.* R. K. Blackwood and C. R. Stephens, *Can. J. Chem.*, **43**, 1382 (1965).

(5) H. R. Snyder, R. B. Hasbrouck, and J. F. Richardson, *J. Amer. Chem. Soc.*, **61**, 3558 (1939); W. A. M. Davies, A. R. Pinder, and I. G. Morris, *Tetrahedron*, **18**, 405 (1962). Actinobolamine, a degradation product from actinobolin, has been described as a 3-oxo-6-azabicyclo[3.2.1]octane derivative by M. E. Munk, C. S. Sodano, R. L. McLean, and T. H. Haskell, *J. Amer. Chem. Soc.*, **89**, 4158 (1967).

(6) W. Nagata, S. Hirai, K. Kawata, and T. Aoki, *ibid.*, **89**, 5045 (1967); W. Nagata, S. Hirai, K. Kawata, and T. Okumura, *ibid.*, 5047; J. W. Huffman and T. Kamiya, *Tetrahedron Lett.*, 1857 (1966).

(7) M. E. Kuehne and B. F. Lambert, *ibid.*, **81**, 4278 (1959); A. J. Birch, P. Hextall, and S. Sternhell, *Aust. J. Chem.*, **7**, 256 (1954); O. L. Chapman and P. Fitton, *J. Amer. Chem. Soc.*, **85**, 41 (1963).

(8) E. E. van Tamelen and G. T. Hildahl, *ibid.*, **75**, 5451 (1953); **78**, 4405 (1956).