PERTINENT NMR DATA

	Values						
	a	*b*	*c*	*d*	*e*	*f,f'*	*g*
III	7.85	—	4.18, 3.91	3.41, 3.24 3.14, 2.98	7.58, 7.41	9.14, 9.10	5.50, 5.27
IV	—	7.69, 7.59 7.46, 7.33	4.14, 3.89	3.37, 3.20 3.11, 2.93	7.61, 7.42	9.12, 9.08	5.49, 5.27

mer, 30 minutes; column temperature, 180°; flow rate 50 ml./min. at an inlet pressure of 46 p.s.i.

Unequivocal evidence for the ionone skeleton of IV was obtained by the following: On atmospheric hydrogenation with platinum oxide in glacial acetic acid, three mole equivalents of hydrogen were absorbed; chromic acid oxidation (12 hr.) of the tetrahydroionol thus formed gave, on work-up, a ketone whose semicarbazone melted at 172–174°. Admixture of the latter with the semicarbazone of authentic tetrahydroionone,[8] m.p. 175–177°, prepared from α-ionone, showed no melting point depression.

Anal.[9,10] Calcd. for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.53; H, 10.47; mol. wt., 192; n_D^{20} 1.5003; $\lambda_{max}^{C_2H_5OH}$ 226 mμ, ϵ 12,620. γ_{max}^{liq} 1682 cm.$^{-1}$ (conjugated carbonyl), 892 cm.$^{-1}$ (vinylidene methylene).

γ-*n*-*Methylionone.* Vapor phase chromatography trapping of the distillate richest in γ-*n*-methylionone gave the pure compound; for this purpose, a Celite packing, impregnated with Dow Corning Silicone No. 710 (25% w./w.) in a $^3/_{16}$-in. ten-foot column, with a flow rate of 50 ml./min. (inlet pressure of 26 p.s.i.) at 180°, was used. Support for the *n*-methylionone skeleton of IV was obtained as follows: On hydrogenation, as described above, three moles of hydrogen were absorbed; chromic acid oxidation of the *n*-methyltetrahydroionol gave a ketone whose semicarbazone melted at 116–118° after repeated recrystallizations. The melting point of the latter was undepressed upon admixture with the semicarbazone of authentic *n*-methyltetrahydroionone, m.p. 116–118°.

Anal. Calcd. for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.81; H, 10.65; mol. wt., 206, n_D^{20} 1.4969; b.p. 76°/0.3 mm.; $\lambda_{max}^{C_2H_5OH}$ 227 mμ, ϵ 12,430. γ_{max}^{liq} 1682 cm.$^{-1}$ (conjugated carbonyl), 892 cm.$^{-1}$ (vinylidene methylene).

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(9) Microanalyses by the Schwarzkopf Microanalytical Laboratory, Woodside 77, N. Y.

(10) Molecular weights were determined by the low-ionization, parent-ion technique on a Consolidated Electrodynamics Model 21-103C mass spectrometer. See, for example, F. H. Field and S. H. Hastings, *Anal. Chem.*, **28**, 1248 (1956).

Cyanocoumarins

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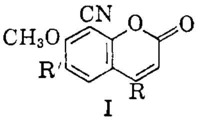
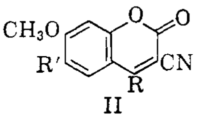
A few cyanocoumarins have been previously synthesized[1–5] but no attempt appears to have been made so far to prepare them by the Rosenmund-von Braun reaction on the halogenated coumarins or to study their hydrolysis. The present work deals with these aspects.

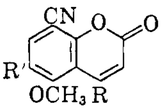
Methyl 7-methoxy-8-iodocoumarin-6-carboxylate, methyl 7-methoxy-8-iodo-4-methylcoumarin-6-carboxylate, and methyl 5-methoxy-8-iodo-4-methylcoumarin-6-carboxylate, when heated with anhydrous cuprous cyanide at temperatures mentioned in Table I, yielded the corresponding 8-cyano derivatives (Ia and b) and (IIIb). With hot 10% alkali the cyano group of these coumarins remained intact, but the esters were hydrolyzed to the corresponding carboxylic acids which on decarboxylation gave the cyanocoumarins (Ic and d) and (IIId), respectively, identical with those obtained by the Rosenmund-von Braun reaction on 7 - methoxy - 8 - iodocoumarin, 7 - methoxy - 8-iodo-4-methylcoumarin and 5-methoxy-8-iodo-4-methylcoumarin. These cyanocoumarins also remained unaffected on boiling with 10% potassium hydroxide solution.



I



II



III

	a	b	c	d	e
R =	H	CH_3	H	CH_3	CH_2COOCH_3
R′ =	$COOCH_3$	$COOCH_3$	H	H	H

7-Methoxy-3-iodocoumarin, 7-methoxy-3-iodo-4-methylcoumarin, and methyl 7-methoxy-3-iodo-4-methylcoumarin-6-carboxylate on similar reaction with anhydrous cuprous cyanide yielded the corresponding 3-cyano derivatives (IIc, d, and b). The cyanocoumarin (IIc) was previously prepared by Baker[3] by the condensation of 2-hydroxy-4-methoxybenzaldehyde with malononitrile in presence of piperidine. With hot 10% alkali these 3-cyanocoumarins yielded the corresponding coumarin-3-carboxylic acids.

Methyl 7-methoxy-8-iodocoumarin-4-acetate on a similar Rosenmund-von Braun reaction gave a mixture of 7-methoxy-8-cyano-4-methylcoumarin (Id) and methyl 7-methoxy-8-cyanocoumarin-4-acetate (Ie).

On hydrolysis with sulfuric acid (90% by volume)

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(1) B. B. Dey and A. Kutti, *Proc. Indian Acad. Sci., India*. **6**, 641 (1940).

(2) C. H. Schroeder and K. P. Link, *J. Am. Chem. Soc.*, **75**, 1886 (1953).

(3) W. Baker and C. S. Howes, *J. Chem. Soc.*, 119 (1953).

(4) M. Crawford and J. W. Rasburn, *J. Chem. Soc.*, 2155 (1956).

(5) C. Wiener, C. H. Schroeder, and K. P. Link, *J. Am. Chem. Soc.*, **79**, 5301 (1957).

TABLE I

CYANOCOUMARINS[a]

No.	Coumarin	Rosenmund-von Braun Reaction Temperature	M.P.	Yield, %	Formula	C, %		H, %		N, %	
						Found	Calcd.	Found	Calcd.	Found	Calcd.
1	7-Methoxy-8-cyano-	180–190	269–270	60	$C_{11}H_7O_3N$	65.7	65.7	3.4	3.5	6.7	7.0
2	7-Methoxy-3-cyano-	180–190	225–226	40	$C_{11}H_7O_3N$	65.7	65.7	3.2	3.5	7.0	7.0
3	7-Methoxy-8-cyano-6-carbomethoxy-	210–220	192	54	$C_{13}H_9O_5N$	60.2	60.2	3.7	3.5	5.5	5.4
4	7-Methoxy-8-cyano-4-carbomethoxymethyl-	190–210	192	22	$C_{14}H_{11}O_5N$	61.8	61.5	4.0	4.0	5.3	5.1
5	7-Methoxy-8-cyano-4-methyl-	220–230	289–291	55	$C_{12}H_9O_3N$	67.0	67.0	4.3	4.2	6.5	6.5
6	7-Methoxy-3-cyano-4-methyl-	180–185	223	75	$C_{12}H_9O_3N$	67.0	67.0	4.2	4.2	6.2	6.5
7	7-Methoxy-8-cyano-4-methyl-6-carbomethoxy-	240–245	276	70	$C_{14}H_{11}O_5N$	61.3	61.5	4.4	4.1	5.3	5.1
8	7-Methoxy-3-cyano-4-methyl-6-carbomethoxy-	250–255	249	70	$C_{14}H_{11}O_5N$	61.8	61.5	4.4	4.1	4.8	5.1
9	5-Methoxy-8-cyano-4-methyl-	260–270	227–230	46	$C_{12}H_9O_3N$	67.3	67.0	4.2	4.2	6.8	6.5
10	5-Methoxy-8-cyano-4-methyl-6-carbomethoxy-	225–230	236	44	$C_{14}H_{11}O_5N$	61.9	61.5	4.2	4.1	4.9	5.1

[a] Obtained on Rosenmund-von Braun reaction from the corresponding iodocoumarins described by S. S. Lele and S. Sethna [*J. Org. Chem.*, **23,** 1731 (1958)] and S. S. Lele, M. G. Patel, and S. Sethna [*J. Indian Chem. Soc.*, **37,** 775 (1960)].

TABLE II

HYDROLYSIS PRODUCTS FROM THE CYANOCOUMARINS MENTIONED IN COLUMN 2, TABLE I

No.	Hydrolysis with[a]	Product Obtained Coumarin	M.P.	Formula	C, %		H, %		N, %	
					Found	Calcd.	Found	Calcd.	Found	Calcd.
1	A	7-Methoxy-8-carbamoyl-	277–279	$C_{11}H_9O_4N$	60.7	60.3	3.9	4.1	6.8	6.4
3	A	7-Methoxy-8-carbamoyl-6-carboxy-	267–268	$C_{12}H_9O_6N$	54.8	54.8	3.3	3.5	5.7	5.3
	B	7-Methoxy-8-cyano-6-carboxy-	228	$C_{12}H_7O_6N$	59.0	58.8	2.6	2.9	5.9	5.7
4	A	7-Methoxy-8-carbamoyl-4-acetic acid-	235–236	$C_{13}H_{11}O_6N$	56.3	56.3	3.8	4.0	5.1	5.0
	B	7-Methoxy-8-cyano-4-acetic acid-	274–275	$C_{13}H_9O_5N$	60.3	60.2	3.5	3.5	5.6	5.4
		7-Methoxy-8-cyano-4-methyl-			(See Table I)					
5	A	7-Methoxy-8-carbamoyl-4-methyl-	278	$C_{12}H_{11}O_4N$	61.7	61.8	4.5	4.8	6.1	6.0
6	A, B	7-Methoxy-4-methyl-3-carboxy-[b]	184–185	$C_{12}H_{10}O_5$	61.2	61.5	4.3	4.3	—	—
7	A	7-Methoxy-8-carbamoyl-4-methyl-6-carboxy-	272	$C_{13}H_{11}O_6N$	56.0	56.3	3.7	4.0	4.9	5.1
	B	7-Methoxy-8-cyano-4-methyl-6-carboxy-	283	$C_{13}H_9O_5N$	60.2	60.2	3.6	3.5	5.6	5.4
8	A	7-Methoxy-4-methyl-3,6-dicarboxy-	208–210	$C_{13}H_{10}O_7$	55.9	56.1	3.4	3.6	—	—
	B	7-Methoxy-3-cyano-4-methyl-6-carboxy-[c]	248	$C_{13}H_9O_5N$	60.2	60.2	3.5	3.5	5.8	5.4
9	A	5-Methoxy-8-carbamoyl-4-methyl-	286	$C_{12}H_{11}O_4N$	61.5	61.8	4.7	4.8	6.0	6.0
10	A	5-Methoxy-8-carbamoyl-4-methyl-6-carboxy-	272	$C_{13}H_{11}O_6N$	56.2	56.3	4.0	4.0	4.9	5.0
	B	5-Methoxy-8-cyano-4-methyl-6-carboxy-	248	$C_{13}H_9O_5N$	60.1	60.2	3.9	3.5	5.5	5.4

[a] A = Sulfuric acid (90% by volume); B = Potassium hydroxide (10%). [b] Baker *et al.* [*J. Chem. Soc.*, *S* 12 (1949)]. [c] Hydrolysis was carried out by keeping with cold alkali (10%) for 48 hr.

TABLE III

HYDROLYSIS OF 8-CARBAMOYL DERIVATIVES MENTIONED IN COLUMN 3, TABLE II

S. No.	Method of Hydrolysis	Product Obtained Coumarin	M.P.	Formula	C, %		H, %	
					Found	Calcd.	Found	Calcd.
1	Hydriodic acid[a]	7-Hydroxy-8-carboxy-	230	$C_{10}H_6O_5$	58.2	58.3	3.1	2.9
3	Alkali (10%) or Sulfuric acid (50%)	7-Methoxy-6-carboxy-[b]	—	—	—	—	—	—
4	"	7-Methoxy-4-methyl-[c]	—	—	—	—	—	—
5	"	7-Methoxy-4-methyl-8-carboxy-[d]	—	—	—	—	—	—
7	"	7-Methoxy-4-methyl-6-carboxy-[e]	—	—	—	—	—	—
9	Sulfuric acid (50%)	5-Methoxy-4-methyl-8-carboxy-	286	$C_{12}H_{10}O_5$	61.2	61.5	4.6	4.3
10	"	5-Methoxy-4-methyl-6,8-dicarboxy-	284	$C_{13}H_{10}O_7$	56.2	56.1	3.6	3.6

[a] Hydrolysis with hydriodic acid was carried out by heating the 8-carbamoyl derivative with hydriodic acid at 130° in an oil bath for 3 hr. [b] S. Kumar, L. Ram, and J. N. Ray [*J. Indian Chem. Soc.*, **23**, 365 (1946)]. [c] Pechmann and Duisberg [*Ber.*, **16**, 2122 (1883)]. [d] Limaye and Kulkarni [*Rasayanam*, **1**, 251 (1943)]; *Chem. Abstr.*, **38**, 4264 (1944). [e] Dalvi and Sethna [*J. Indian Chem. Soc.*, **26**, 405 (1949)].

the 8-cyanocoumarins gave the corresponding 8-carbamoyl derivatives, while the 3-cyanocoumarins yielded the corresponding coumarin-3-carboxylic acids (Table II). The 8-carbamoylcoumarin derivatives on further hydrolysis with sulfuric acid (50%) or alkali gave the 8-carboxylic acids. However, in the case of 7-methoxy-8-carbamoylcoumarin-4-acetate only 7-methoxy-4-methylcoumarin was obtained and in the cases of methyl 7-methoxy-8-carbamoylcoumarin-6-carboxylate and its 4-methyl analog, the carbamoyl group was eliminated during the hydrolysis (Table III).

The cyanocoumarins (Ic and d), (IId), and (IIId) were demethylated to the corresponding hydroxy derivatives.

EXPERIMENTAL

All melting points are uncorrected.

Rosenmund-von Braun synthesis (see Table I). The iodo derivative (0.01 mole) was mixed with anhydrous cuprous cyanide (0.02 mole) and heated with stirring at the specified temperature for 10 minutes. The mixture was powdered and extracted with either acetone or acetic acid. The residue from the extract recrystallized from acetic acid in needles. Addition of cyano derivative from a previous run as recommended by Koelsch and Whitney[6] to the reaction mixture improved the yield.

A. Sulfuric acid hydrolysis (see Table II). The cyano compound (0.5 g.) was heated with sulfuric acid (90% by volume) on a steam bath for 2 to 3 hr. The solid obtained on pouring the reaction mixture on crushed ice was extracted with sodium hydrogen carbonate to separate the acid wherever formed. The product obtained was crystallized from acetic acid.

B. Alkaline hydrolysis (see Table II). The cyanocoumarin (0.5 g.) was heated with aqueous alcoholic potassium hydroxide solution (10%) on a steam bath for 2 to 3 hr. The product obtained on acidification was purified through sodium hydrogen carbonate and crystallized from acetic acid.

Hydrolysis with sulfuric acid (50%) (see Table III). The carbamoyl derivative (0.5 g.) was heated with sulfuric acid (18 ml.; 50%) in an oil bath at 120° for 3 hours. The product obtained on pouring the reaction mixture on crushed ice crystallized from acetic acid. Sulfuric acid (50%) was prepared by adding concentrated sulfuric acid (6 ml.) to a mixture of acetic acid (8 ml.) and water (4 ml.).

Demethylations (see Table IV). The methoxycyanocoumarin was dissolved in acetic anhydride and then heated with hydriodic acid at 120° in an oil bath for 3 hours. The product obtained crystallized from acetic acid.

Acknowledgment. One of us (M.G.P.) thanks the Government of India for the award of a research scholarship.

TABLE IV

HYDROXYCYANOCOUMARINS[a]

S. No.	Coumarin	M.P.	Formula	C, %		H, %		N, %	
				Found	Calcd.	Found	Calcd.	Found	Calcd.
1	7-Hydroxy-8-cyano-	305	$C_{10}H_5O_3N$	64.2	64.2	2.6	2.7	7.8	7.5
5	7-Hydroxy-8-cyano-4-methyl-	272	$C_{11}H_7O_3N$	65.4	65.7	3.2	3.5	7.3	7.0
6	7-Hydroxy-3-cyano-4-methyl-	298	$C_{11}H_7O_3N$	65.4	65.7	3.8	3.5	6.8	7.0
9	5-Hydroxy-8-cyano-4-methyl-	276	$C_{11}H_7O_3N$	65.9	65.7	3.6	3.5	7.2	7.0

[a] Obtained by demethylation of the corresponding methoxycyano derivatives described in Table I.

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(6) C. F. Koelsch and A. G. Whitney, *J. Org. Chem.*, **6**, 795 (1941).