(39%) of 5-nitro-7-cyano-3,3-dimethylbenzomorpholine, fluffy orange crystals, m.p. 176–181°. A sublimed sample (160°, 1 mm.) was used for analysis, m.p. 180–181.5°.

Anal. Calcd. for $C_{11}H_{11}N_3O_3$: C, 56.65; H, 4.76; N, 18.02. Found: C, 56.47; H, 4.92; N, 17.82.

By a procedure similar to that described for compound IIa above, the following dinitrobenzomorpholines were obtained:

3-Hydroxymethyl-3-ethyl-5,7-dinitrobenzomorpholine, IId, orange crystals, m.p. 139.5–141°, 37%.

Anal. Calcd. for $C_{11}H_{13}N_3O_6$: C, 46.64; H, 4.63; N, 14.84. Found: C, 46.51; H, 4.78; N, 14.90.

3-Hydroxymethyl-3-methyl-5,7-dinitrobenzomorpholine, IIe, orange crystals, m.p. 147.2–148.6°, 47%.

Anal. Calcd. for $C_{10}H_{11}N_3O_6$: C, 44.61; H, 4.12; N, 15.61. Found: C, 44.84; H, 3.95; N, 15.80.

3,3-Dihydroxymethyl-5,7-dinitrobenzomorpholine, IIf, yellow powder, m.p. 158.5–160 dec., 31%.

Anal. Calcd. for $C_{10}H_{11}N_3O_7$: C, 42.11; H, 3.89; N, 14.73. Found: C, 41.93; H, 4.05; N, 14.64.

5-Nitro-7-trifluoromethyl-3,3-dimethylbenzomorpholine, IIb. Two nitro groups are best introduced into 4-chlorobenzotrifluoride one at a time as described by Friedrich and Schniepp.[22] The first nitration gave 3-nitro-4-chlorobenzotrifluoride in 84% yield[23] and the second 3,5-dinitro-4-chlorobenzotrifluoride[24] in 85% yield. Seven grams (0.026 mole) of the dinitro compound was dissolved in 50 ml. of absolute methanol. The solution was refluxed with 4.65 g. (0.05 mole) of 2-amino-2-methyl-1-propanol for a few minutes, 4.0 g. of sodium methoxide was added in 50 ml. of methanol, and refluxing was continued 10 min. The product was precipitated by adding 50 ml. of water and recrystallized from 90% methanol to yield 4.8 g. (67%) of 5-nitro-7-trifluoromethyl-3,3-dimethylbenzomorpholine, golden needles, m.p. 107–109°. A sublimed analytical sample melted at 108–109.5°.

Anal. Calcd. for $C_{11}H_{11}N_2O_3F_3$: C, 47.83; H, 4.01; N, 10.14. Found: C, 48.09; H, 4.19; N, 10.13.

5-Amino-7-trifluoromethyl-3,3-dimethylbenzomorpholine, IIIb. In the presence of 0.30 g. of platinum oxide (prereduced) 1 g. of 5-nitro-7-trifluoromethylbenzomorpholine was reduced quantitatively in 40 ml. of absolute methanol at 1 atm. of hydrogen pressure in 1 hr. After removal of solvent the product was sublimed at 70° (1 mm.) to give 0.80 g. (90%) of white 5-amino-7-trifluoromethyl-3,3-dimethylbenzomorpholine, m.p. 80–82°.

Anal. Calcd. for $C_{11}H_{13}N_2OF_3$: C, 53.65; H, 5.37; N, 11.38. Found: C, 53.88; H, 5.43; N, 11.30.

8-Trifluoromethyl-4,4-dimethyltriazolo[1,5,4-d,e]benzomorpholine, IVb. A sublimed sample (0.27 g., 0.0011 mole) of 5-amino-7-trifluoro-3,3-dimethylbenzomorpholine, IIIb, was dissolved in 30 ml. of warm 50% sulfuric acid and then cooled in ice. An ice-cold solution of 0.12 g. (0.0017 mole) sodium nitrite in 10 ml. of water was added slowly over a 10-min. period with stirring. The reaction mixture was poured into 100 ml. of water and the white precipitate was collected. Recrystallization from dilute methanol gave 0.10 g. (35%) of short white needles, m.p. 101–102.5°.

Anal. Calcd. for $C_{11}H_{10}N_3OF_3$: C, 51.36; H, 3.92; N, 16.34. Found: C, 51.16; H, 4.09; N, 16.01.

Azo Dyes from 8-Amino-4,4-dimethyltriazolo[1,5,4-d,e]-benzomorpholine, IVg. Standard procedures for diazotization of 8-amino-4,4-dimethyltriazolo[1,5,4-d,e]benzomorpholine and coupling with various compounds in sodium acetate solution were employed to obtain the dyes described in Table I. The dyes were all recrystallized from 95% ethanol.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, M. S. UNIVERSITY]

Chloromethylation of Some Coumarin Derivatives

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Several coumarin derivatives have been chloromethylated and the structures of the chloromethyl derivatives established by direct comparison of the methyl derivatives, obtained on reduction, with the known compounds or authentic specimens synthesized for this purpose.

The chloromethylation of coumarins has not been studied so far. As chloromethyl derivatives are useful for the synthesis of a variety of compounds, the present work was undertaken. Coumarin, 4-methylcoumarin, 4′-methyl-1,2-naphtha-α-pyrone, and 7,8-dimethoxy-4-methylcoumarin on chloromethylation with paraformaldehyde and hydrogen chloride gave the corresponding 3-chloromethyl derivatives. Higher chloromethyl derivatives could not be obtained. The chloromethyl derivatives were reduced to the corresponding 3-methylcoumarin derivatives and directly compared with the authentic specimens.

7-Methoxy-4-methylcoumarin with one mole of paraformaldehyde gave a mixture from which only the 6-chloromethyl derivative could be isolated in a pure state. This was reduced to 7-methoxy-4,6-dimethylcoumarin. With 2.3 moles of paraformaldehyde a mixture was obtained from which both the 3,6- and the 3,8-dichloromethyl derivatives were isolated. These were reduced to the corresponding 3,4,6-trimethyl- and 3,4,8-trimethylcoumarin, which were synthesized for comparison by the Pechmann condensation of ethyl-α-methyl acetoacetate with 4-methyl- and 2-methylresorcinol respectively and subsequent methylation of the hydroxycoumarins formed. The 3,6,8-trichloromethyl derivative was obtained by the further chloromethylation of the above dichloromethyl derivatives and by the chloromethylation of 7-methoxy-4-methylcoumarin in ethylene dichloride in presence of zinc chloride.

TABLE I. CHLOROMETHYLCOUMARINS

No.	Substance	Product Obtained	M.P.	Yield, %	Formula	C, %		H, %		Cl, %	
						Found	Calcd.	Found	Calcd.	Found	Calcd.
1	Coumarin	3-Chloromethyl-	111	33	$C_{10}H_7O_2Cl$	61.51	61.69	3.51	3.59	17.99	18.30
2	4-Methylcoumarin	3-Chloromethyl-	139–140	73	$C_{11}H_9O_2Cl$	63.18	63.30	4.02	4.31	16.61	17.00
3	7-Methoxy-4-methylcoumarin	6-Chloromethyl-	246	10[a]	$C_{12}H_{11}O_3Cl$	60.81	60.37	4.73	4.61	14.52	14.88
		3,6-Dichloromethyl-	195	Poor[a]	$C_{13}H_{12}O_3Cl_2$	54.28	54.35	3.92	4.18	24.60	24.73
		3,8-Dichloromethyl-	199–200	Poor[a]	$C_{13}H_{12}O_3Cl_2$	54.36	54.35	4.06	4.18	24.79	24.73
		3,6,8-Trichloromethyl-	168	22	$C_{14}H_{13}O_3Cl_3$	50.13	50.06	3.82	3.87	32.02	31.74
4	Methyl 7-hydroxy-4-methyl-coumarin-6-carboxylate	3,8-Dichloromethyl-	202	80	$C_{14}H_{12}O_5Cl_2$	51.26	50.75	3.63	3.62	21.41	21.45
5	7-Hydroxy-4-methylcoumarin-6-carboxylic acid	3,8-Dichloromethyl-	[b]	71	$C_{13}H_{10}O_5Cl_2$	49.70	49.21	3.12	3.15	22.16	22.39
6	Methyl 7-methoxy-4-methyl-coumarin-6-carboxylate	3-Chloromethyl-coumarin-6-carboxylic acid	188–190	72	$C_{13}H_{11}O_5Cl$	55.64	55.22	4.01	3.88	12.07	12.56
7	7,8-Dimethoxy-4-methyl coumarin	3-Chloromethyl-	140–141	36	$C_{13}H_{13}O_4Cl$	58.48	58.10	5.16	4.84	13.68	13.22
8	4′-Methyl-1,2-naphtha-α-pyrone	3′-Chloromethyl-	205–206	33	$C_{15}H_{11}O_2Cl$	70.02	69.63	4.29	4.25	13.99	13.73

[a] Mixture of various products formed; hence the yield of the isolated product is poor. [b] The product decomposes at about 210° and swells up. The resulting solid does not melt even on strong heating.

On reduction 7-methoxy-3,4,6,8-tetramethylcoumarin was obtained as seen by direct comparison with the methyl ether of the product from the Pechmann condensation of 2,4-dimethylresorcinol and ethyl-α-methyl acetoacetate. Attempts to chloromethylate 7-hydroxy-4-methyl-, 7,8-dihydroxy-4-methyl-, and 5,7-dihydroxy-4-methylcoumarin and its dimethyl ether resulted in the formation of polymeric products from which it was difficult to isolate a product with definite melting point.

7-Hydroxy-4-methylcoumarin-6-carboxylic acid and its methyl ester could not be chloromethylated in aqueous solution but in glacial acetic acid using anhydrous zinc chloride the 3,8-dichloromethyl derivatives were obtained. These were reduced and the products compared with the authentic specimens. Methyl-7-hydroxy-3,4,8-trimethylcoumarin-6-carboxylate required for comparison was synthesized by the Pechmann condensation of methyl 2,4-dihydroxy-3-methylbenzoate with ethyl-α-methyl acetoacetate. This was hydrolyzed to the corresponding acid which on decarboxylation gave 7-hydroxy-3,4,8-trimethylcoumarin.

Methyl-7-methoxy-4-methylcoumarin-6-carboxylate on chloromethylation gave only 7-methoxy-3-chloromethyl-4-methylcoumarin-6-carboxylic acid, which was reduced to the corresponding 3,4-dimethyl derivative and compared with an authentic specimen.

All the chloromethylcoumarins have been converted into the acetoxymethyl and methoxymethylcoumarins.

EXPERIMENTAL

All melting points are uncorrected.

Chloromethylations. (a) 4-Methyl-, 7-methoxy-4-methyl-, and 7,8-dimethoxy-4-methylcoumarin, and 4′-methyl-1,2-naphtha-α-pyrone have been chloromethylated as follows: A mixture of the coumarin derivative (0.02 mole) in minimum quantity of acetic acid (80%) and paraformaldehyde (0.02 mole) was treated with hydrogen chloride at 60–70° for 1 hr. and the mixture was left overnight. Next day the product which separated as such or on dilution with water was filtered, washed with alcohol, and crystallized from benzene. When only monochloromethylation takes place, better yields of the products are obtained by using 2 to 3 moles of paraformaldehyde. 7-Methoxy-4-methylcoumarin on chloromethylation with 2.3 moles of paraformaldehyde gave a mixture which was separated by dissolving it in excess of hot benzene and allowing it to cool. The 3,8-dichloromethyl derivative started separating in the form of needles. After a time when the other isomer, which crystallized in the form of buds, started separating, the solution was filtered. The residue on further crystallization from benzene yielded the pure 3,8-dichloromethyl derivative. The filtrate on further cooling yielded the 3,6-isomer in a pure form.

(b) Coumarin, 7-hydroxy-4-methylcoumarin-6-carboxylic acid, its methyl ester and methoxy methyl ester were chloromethylated as follows: A mixture of coumarin derivative (0.01 mole) in glacial acetic acid (50 ml.), paraformaldehyde (excess) and zinc chloride (0.01 mole) was heated on a steam bath and dry hydrogen chloride passed through it for 1 hr. The chloromethyl derivative which separated on cooling as such or on dilution with water was further crystallized from benzene.

TABLE II

REDUCTION PRODUCTS FROM CHLOROMETHYLCOUMARINS DESCRIBED IN TABLE I

No.	Coumarin[a]	M.P.	Formula	C, % Found	C, % Calcd.	H, % Found	H, % Calcd.
1	3-Methyl-[a]	92	—	—	—	—	—
2	3,4-Dimethyl-[b]	115	—	—	—	—	—
3	7-Methoxy-4,6-dimethyl-[c]	181	$C_{12}H_{12}O_3$	70.08	70.58	5.68	5.88
	7-Methoxy-3,4,6-trimethyl-[d]	190	$C_{13}H_{14}O_3$	70.95	71.55	6.68	6.42
	7-Methoxy-3,4,8-trimethyl-[d]	188–190	$C_{13}H_{14}O_3$	71.15	71.55	6.06	6.42
	7-Methoxy-3,4,6,8-tetramethyl-[d]	131	$C_{14}H_{16}O_3$	72.40	72.39	6.51	6.94
4	7-Hydroxy-3,4,8-trimethyl-6-carbomethoxy-[e]	187	$C_{14}H_{14}O_5$	64.30	64.12	5.28	5.34
5	7-Hydroxy-3,4,8-trimethyl-6-carboxy-[f]	280	$C_{13}H_{12}O_5$	62.80	62.90	4.62	4.83
6	7-Methoxy-3,4-dimethyl-6-carboxy-[g]	248	$C_{14}H_{14}O_5$	64.22	64.12	5.38	5.34
7	7,8-Dimethoxy-3,4-dimethyl-[h]	109	$C_{13}H_{14}O_4$	66.85	66.60	5.96	6.00
8	3′,4′-Dimethyl-1,2-naphtha-α-pyrone-[i]	199–200	—	—	—	—	—

[a] The products described here have been directly compared with the authentic specimens synthesized as indicated for each product. C. Mentzer and P. Meunier, *Bull. Soc. Chim.*, **10**, 356 (1943) [*Chem. Abstr.*, **38**, 2649 (1944)]. [b] Peters and Simonis, *Ber.*, **41**, 830 (1908). [c] Methylation of 7-hydroxy-4,6-dimethylcoumarin prepared according to Yanagita, *Ber.*, **71**, 2269 (1938). [d] Methylation of the corresponding hydroxy derivative described in Table IV. [e] Pechmann condensation of methyl 2,4-dihydroxy-3-methylbenzoate with ethyl-α-methyl acetoacetate (described in Table IV). [f] Hydrolysis of 4. [g] Hydrolysis of methyl 7-methoxy-3,4-dimethylcoumarin-6-carboxylate prepared according to Sethna and Shah, *J. Indian Chem. Soc.*, **15**, 383 (1938). [h] Methylation of 7,8-dihydroxy-3,4-dimethylcoumarin prepared according to Canter, Martin and Robertson, *J. Chem. Soc.*, 1877 (1931). [i] Chakravarti, *J. Indian Chem. Soc.*, **8**, (407 1931).

TABLE III

ACETOXY AND METHOXYMETHYLCOUMARINS FROM THE CHLOROMETHYLCOUMARINS DESCRIBED IN TABLE I

S No.	Derivative Prepared	M.P.	Formula	C, % Found	C, % Calcd.	H, % Found	H, % Calcd.
1	A[a]	105–107	$C_{12}H_{10}O_4$	66.17	66.05	4.19	4.58
	B[a]	126	$C_{11}H_{10}O_3$	69.11	69.47	5.20	5.26
2	A	128	$C_{13}H_{12}O_4$	67.72	67.24	5.07	5.17
	B	72	$C_{12}H_{12}O_3$	70.80	70.58	5.76	5.88
3	A	191	$C_{14}H_{14}O_5$	63.86	64.12	5.47	5.34
	B	136	$C_{13}H_{14}O_4$	66.42	66.65	5.91	6.02
	A	180	$C_{17}H_{18}O_7$	60.72	61.07	5.67	5.38
	B	169	$C_{15}H_{18}O_5$	64.32	64.73	6.48	6.52
	A	174	$C_{17}H_{18}O_7$	61.40	61.07	4.98	5.38
	B	174	$C_{15}H_{18}O_5$	64.50	64.73	6.58	6.52
	A	203	$C_{30}H_{22}O_9$	59.02	59.11	5.22	5.46
	B	182	$C_{17}H_{22}O_6$	63.80	64.34	6.48	6.88
4	A	198	$C_{18}H_{18}O_9$	57.29	57.14	4.36	4.76
	B	138	$C_{16}H_{18}O_7$	59.42	59.62	5.48	5.59
5	B	138	$C_{16}H_{18}O_7$		Same as 4 B		
6	B[b]	175	$C_{15}H_{16}O_6$	61.37	61.64	5.13	5.47
7	A	148	$C_{15}H_{16}O_6$	61.48	61.50	5.16	5.48
	B	96	$C_{14}H_{16}O_5$	63.46	63.63	5.75	6.06
8	A	172	$C_{17}H_{14}O_4$	71.85	72.30	5.10	4.96
	B	116	$C_{16}H_{14}O_3$	75.83	75.59	5.37	5.51

[a] A = Acetoxymethyl; B = Methoxymethyl. [b] The product obtained is methyl 7-methoxy-3-methoxymethyl-4-methylcoumarin-6-carboxylate.

TABLE IV

COUMARINS SYNTHESIZED BY THE PECHMANN CONDENSATION OF ETHYL-α-METHYL ACETOACETATE WITH VARIOUS PHENOLS

No.	Phenol	Coumarin Obtained	M.P.	Formula	C, % Found	C, % Calcd.	H, % Found	H, % Calcd.
1	4-Methylresorcinol	7-Hydroxy-3,4,6-trimethyl-	266	$C_{12}H_{12}O_3$	70.27	70.58	5.39	5.88
2	2-Methylresorcinol	7-Hydroxy-3,4,8-trimethyl-	274	$C_{12}H_{12}O_3$	70.54	70.58	5.71	5.88
3	2,4-Dimethylresorcinol	7-Hydroxy-3,4,6,8-tetramethyl-	232	$C_{13}H_{14}O_3$	71.20	71.54	6.12	6.47
4	Methyl 2,4-dihydroxy-3-methylbenzoate	7-Hydroxy-3,4,8-trimethyl-6-carbomethoxy-	187			See Table II, No. 4		

The chloromethyl derivatives deteriorate when heated in aqueous or aqueous acetic acid solutions.

General reduction procedure. The chloromethyl derivative (0.5 g.) in acetic acid (8 ml.) and water (2 ml.) was treated during 0.5 hr. with zinc dust (0.5 g.) and the reaction mixture heated on a steam bath for 2 hr. in all. The reaction mixture was then filtered and poured into cold water. The methyl derivative which separated was crystallized from dilute acetic acid. It was necessary to add hydrochloric acid (0.5 ml.) in the case of 7-methoxy-3,6-dichloromethyl-4-methylcoumarin to prevent the formation of the diacetoxymethyl derivative, and in the case of 7-hydroxy-3,8-dichloromethylcoumarin and 7-methoxy-3-chloromethyl-4-methylcoumarin-6-carboxylic acid to precipitate the product.

Pechmann condensations. Equimolar proportions of ethyl-α-methyl acetoacetate and the required phenol were treated with sulfuric acid (80%) and kept for 24 hr. The next day the mixture was poured into water and the product obtained crystallized from rectified spirit (see Table IV).

Acetoxy methylcoumarins were prepared by refluxing the chloromethylcoumarin in glacial acetic acid with fused sodium acetate for 2 hr. (see Table III).

Methoxymethylcoumarins were prepared by refluxing the chloromethylcoumarin with methyl alcohol in the presence of fused potassium carbonate for 6 hr. (Table III).

BARODA, INDIA

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

Pyridine 1-Oxides. VII. 3-Nitropyridine 1-Oxide[1a]

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3-Aminopyridine was converted to 3-nitropyridine 1-oxide by three different routes, the preferable one being preliminary oxidation with peroxysulfuric acid to 3-nitropyridine, followed by *N*-oxidation with 40% peracetic acid. In agreement with expectation, the nitro group of 3-nitropyridine 1-oxide could not be displaced by nucleophilic reagents such as methoxide ion and was inert toward acetyl chloride. Treatment of 3-nitropyridine 1-oxide with phosphorus oxychloride gave a mixture of 2-chloro-3-nitropyridine and 6-chloro-3-nitropyridine, and treatment with acetic anhydride gave 3-nitro-2-pyridone.

The usefulness and versatility of pyridine-1-oxides as synthetic intermediates is due both to the facility with which the *N*-oxide grouping can be introduced and selectively removed and to its unique amphoteric ability to facilitate both nucleophilic substitution and displacement reactions and electrophilic substitution reactions.[2] For example, the ready accessibility of 4-nitropyridine 1-oxides by direct nitration of the *N*-oxides,[3,4] and the ease with which such intermediates can be converted into other 4-substituted pyridine derivatives by reductive and nucleophilic displacement reactions of the 4-nitro group have been extensively exploited by organic chemists concerned with synthetic manipulations in the pyridine field.[2] The versatility of 4- (or 2-) nitropyridine-1-oxides as synthetic intermediates is due in part to conjugation of the nitro group with the *N*-oxide function, and a consequent ready displacement of the nitro group by attacking nucleophiles. With the unconjugated isomer, 3-nitropyridine 1-oxide, however, such nucleophilic displacements of the nitro group would not be expected, but facilitation of nucleophilic substitution in the 2-,4- and 6-positions should be observed. Preference for the 2-position would be anticipated by analogy, as nicotinamide-1-oxide upon treatment with phosphorus oxychloride and phosphorus pentachloride yields exclusively 2-chloronicotinonitrile,[5] and 3-halopyridine 1-oxides upon treatment with acetic anhydride give only 3-halo-2-pyridones.[6] An investigation of the chemistry of 3-nitropyridine 1-oxide thus appeared to be of both theoretical and possible synthetic interest.

3-Nitropyridine 1-oxide (III) has previously been prepared by the action of benzoyl nitrate on pyridine 1-oxide (very low yield)[7] and by direct oxidation of 3-nitropyridine with hydrogen peroxide in acetic acid (34% yield[7] and 40% yield[8]). The use of commercially available 40% peracetic acid is a convenient alternative to the above conditions and affords comparable yields (40.5%). Alternative routes were investigated but were much less satisfactory. For example, direct oxidation of 3-aminopyridine with peroxytrifluoroacetic acid gave a mixture of 3-nitropyridine (II) (21%) and 3-nitropyridine 1-oxide (III) (22%). An adaptation (I→IV→V→VI→III) of the procedure previously described by Brown[9] for the preparation of 2-nitropyridine 1-oxide from 2-

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