Preparation and Fluorescence of Substituted 2-Methyl-1-isoquinolones

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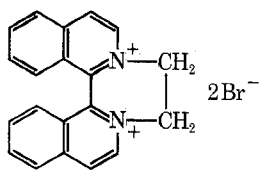
Various derivatives of 2-methyl-1-isoquinolone have been synthesized and their fluorescence examined to determine how the nature and position of the substituent affect the fluorescence maximum and quantum efficiency. An amino or dimethylamino group in the 4 position red-shifts the fluorescence maxima from 383 nm (methanol) to 530 or 505 nm, respectively, with some decrease in the quantum efficiency (5.4, 2.6, and 4.7%, respectively). An amino group in the 5 position improves the quantum efficiency (15%) but only red-shifts the fluorescence maximum about 23 nm. 2-Methyl-1-isoquinolone and the 4-amino compound undergo oxidation and/or oxidation–condensation reactions, some of which have been investigated.

The chemiluminescence, which results from the air oxidation of certain 1,1′-biisoquinolinium salts such as **1** in basic alcoholic or aqueous alcoholic systems, has been investigated recently.[1-3] The luminescing species are excited, fluorescent oxidation products, **2**, where X = H, OH, or



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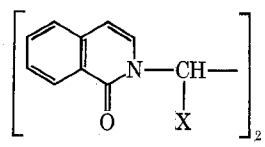
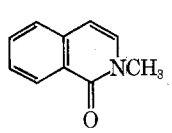


2

OR. These compounds fluoresce in the region 385–390 nm with fluorescent quantum efficiencies in the range 4–7%. Both of these factors are undesirable, however, if one wants to develop a practical chemiluminescent system. From the photopic standpoint, the fluorescence maximum should be in the region around 555 nm. Furthermore, since the overall chemiluminescence efficiency is a product of the chemical excitation efficiency and the fluorescence efficiency, the higher the latter, the easier it is to get bright systems with high light output. Finally, the chemical excitation efficiency should be larger for products with lower excitation energies if the Eyring–Rauhut effect holds in this case.[4] A study was undertaken, therefore, to determine whether and how the fluorescence maximum and quantum efficiency were affected by kind and position of substituents on either the hetero or benzo rings of the isoquinolone. The synthesis aspects were greatly simplified by making this study with derivatives of 2-methyl-1-isoquinolone (**3**). The fluorescence of the latter is essentially the same as that noted for the oxidation products from the 1,1′-biisoquinolinium salts, which are not easily accessible.

Synthesis and Chemistry. Most of the compounds were made by conventional procedures which are outlined in the Experimental Section. Several observations, however, are worthy of note and discussion.

(a) The preparation of **3** by the classical method of Decker,[5] namely, oxidation of 2-methylisoquinolinium iodide with potassium ferricyanide in basic medium, consistently gave a by-product (**4**) in low yield. Coupling at the 4,4′ positions is assigned on the basis of ^{1}H NMR evidence.



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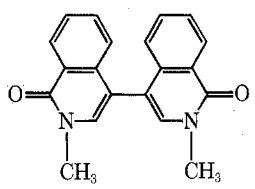

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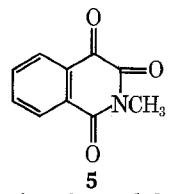
(b) Solid **3** is air oxidized at room temperature to the triketo compound **5**. The same compound has been previously reported as being formed by air oxidation of 2-methyl-3-isoquinolone[6] as well as by dichromate–sulfuric acid oxidation of 1,2,3,4-tetrahydro-2-methyl-4-isoquinolone.[7]



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(c) 2-Methyl-1-isoquinolone undergoes electrophilic attack in the 4 position with great ease, as previously observed by Horning, Lacasse, and Muchowski.[8] For example, it has been found that nitration can be effected rapidly and exothermically at 25° with 8 *N* nitric acid to yield 4-nitro-2-methyl-1-isoquinolone (**6**). On the other hand, nitration in 96% sulfuric acid at 5° with potassium nitrate yields approximately equal amounts of 5- and 7-nitro-2-methyl-1-isoquinolone (**7** and **8**) together with some of the 4 isomer (**6**) and a minor amount of 4,7-dinitro-2-methyl-1-isoquinolone (**9**). The species being nitrated in this case is probably the protonated amide rather than the neutral species as in the aqueous nitric acid systems. These results are consistent with those reported by Kawazoe and Yoshioka[9] for the nitration of isocarbostyril in sulfuric acid with potassium nitrate. Nitration at the 4 position is also rapid with 5-nitro-2-methyl-1-isoquinolone (**7**) in 16 *N* nitric acid at 30–35°.

(d) 2-Methyl-1-isoquinolone shows enamine character in that it can be alkylated in the 4 position (heating with benzyl bromide).

(e) Like other 1,2-dihydroisoquinoline derivatives,[10] 2-methyl-1-isoquinolone and benzaldehyde condense in the presence of concentrated hydrochloric acid; attack is again in the 4 position.

(f) Although both 5- and 7-nitro-2-methyl-1-isoquinolone (**7** and **8**) are catalytically hydrogenated (Adams' catalyst) in alcoholic hydrochloric acid to the corresponding amines without difficulty, the reduction of the 4 isomer (**6**) under similar conditions is more complicated, because of the reactivity of 4-amino-2-methyl-1-isoquinolone (**10**). The triketo compound (**5**) was consistently formed in 15–20% yield. Other evidence of the instability is the observation that 4-amino-2-methyl-1-isoquinolone hydrochloride (**11**) is no longer completely water soluble after being stored for a month in a desiccator. Samples in tightly stoppered bottles slowly lose their water solubility. The triketo compound (**5**) precipitates from aqueous solutions of the amine hydrochloride after several days at 25°.

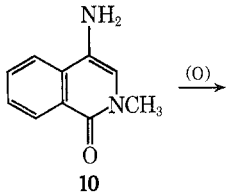
In addition to **5**, which is an oxidation–hydrolysis product, intermolecular condensation products such as the poorly soluble, high-melting pyridazine derivative (**12**) are

Table I
Substituted 2-Methyl-1-isoquinolones

Compd	Position and substituent(s)	Empirical formula	Mp, °C	Recrystn solvent
3	Unsubstituted	$C_{10}H_9NO$[g]	56.5–57.5[a]	3:1 cyclohexane–benzene
18	4-Cl	$C_{10}H_8ClNO$[h]	132–134	Cyclohexane
17	4-Br	$C_{10}H_8BrNO$[i]	129–130[b]	Cyclohexane
19	4-I	$C_{10}H_8INO$[i]	126.5–127.5	Ethanol
20	4-CN	$C_{11}H_8N_2O$[h]	197.5–198.5[c]	Ethanol
21	4-CO_2H	$C_{11}H_9NO_3$[h]	270.5–271.5 dec	Ethanol
6	4-NO_2	$C_{10}H_8N_2O_3$[h]	161.5–162.5[d]	7:3 cyclohexane–benzene
7	5-NO_2	$C_{10}H_8N_2O_3$[h]	116–117	Water
8	7-NO_2	$C_{10}H_8N_2O_3$[h]	214–216	Ethanol
25	4,5-Di-NO_2 • H_2O	$C_{10}H_9N_3O_6$[h]	220.5–221.5	Ethanol
9	4,7-Di-NO_2	$C_{10}H_7N_3O_5$[h]	294–296	DMF–ethanol
15	4-Br-7-NO_2	$C_{10}H_7BrN_2O_3$[i]	254–256 dec	Ethanol
10	4-NH_2	$C_{10}H_{10}N_2O$[g]	117–119	Benzene
11	4-NH_2 • HCl	$C_{10}H_{11}ClN_2O$[i]	235–237[e]	Ethanol–ether
	4-Salicylamino	$C_{17}H_{16}N_2O_2$[h]	155–156	Cyclohexane
23	5-NH_2	$C_{10}H_{10}N_2O$[g]	138–140	3:2 benzene–cyclohexane
22	5-NH_2 • HCl	$C_{10}H_{11}ClN_2O$[i]	261–263	2-Propanol–H_2O Ether
	5-$C_6H_5NHCSNH$	$C_{17}H_{15}N_3OS$[g]	208–209	Ethanol
16	7-NH_2 • HCl • H_2O	$C_{10}H_{13}ClN_2O_2$[g]	265–270 dec	Absolute Ethanol
	7-NH_2 • picrate	$C_{16}H_{13}N_5O_8$[g]	254–255 dec	Ethanol
26	4,5-Di-NH_2 • 2HCl • 2H_2O	$C_{10}H_{17}Cl_2N_3O_3$[i]	260–270	Ethanol–Ether
27	4-$(CH_3)_2N$ • HI	$C_{12}H_{15}IN_2O$[h]	209–211 dec	Absolute Ethanol
28	3-CH_3-4-NO_2	$C_{11}H_{10}N_2O_3$[g]	151	Ethanol
29	3-CH_3-4-NH_2-HCl • 0.5H_2O	$(C_{11}H_{14}ClN_2O)_2O$[i]	250–260 dec	Ethanol
30	4-$C_6H_5CH_2$	$C_{17}H_{15}NO$[h]	99.5–100.5	Cyclohexane
31	4-$C_6H_5C{\equiv}C$[f]	$C_{18}H_{13}NO$[h]	129.5–130.5	Cyclohexane

[a] Reported mp 57°: A. Albert and J. N. Phillips, *J. Chem. Soc.*, 1294 (1956). [b] E. Bamberger and W. Frew, *Ber.*, 27, 198 (1894), reported mp 132° for the product obtained when 2-methyl-1-isoquinolone was brominated in chloroform; the position of substitution was not established. Also see ref 8. [c] Reported mp 198°: G. Thuillier, B. Marcot, J. Cruanes, and P. Rumpf, *Bull. Soc. Chim. Fr.*, 4770 (1967); also reported in ref 8, 197–199°. [d] Reported (ref 8) 163–165°. [e] Resolidifies, then decomposes at 270–290°. [f] Both parent and base peak in the mass spectra were at *m/e* 259; calcd mol wt, 259. [g] Satisfactory analytical data (±0.4%) were reported for N. [h] Satisfactory analytical data (±0.4%) were reported for C, H, N, and Hal (if present). [i] Satisfactory analytical data (±0.4%) were reported for N and Hal.

recovered from reactions involving the free 4-amino-2-methyl-1-isoquinolone. One possible route to **12** involves an intermediate oxidation stage, analogous to **5**, which then condenses with another molecule of **10**, followed by oxidation to yield **12**.



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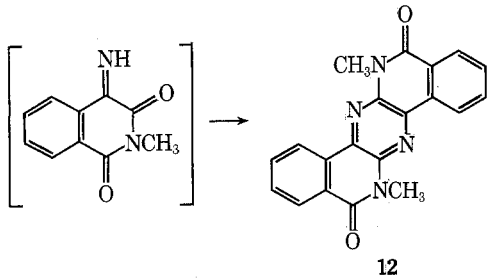
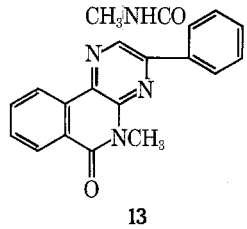


12

The structure of **12** is based on the elemental analysis, molecular weight determination, and ^1H NMR data. Another closely related product, **13**, which appears to have the following structure, was also isolated from reactions involving the free base. This structural assignment is made rather than the isomeric **14** (which is dihydro-**12**) largely because



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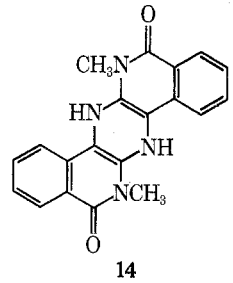

14

the ^1H NMR spectrum (two more protons than in **12**) shows (1) two kinds of methyl groups, one of which is a doublet that coalesces to a singlet when D_2O is added, rather than one type of methyl group as should be expected in **14**; (2) one exchangeable NH group rather than two; and (3) a singlet (one proton) at δ 8.77 which is similar to the chemical shift seen for the protons in the hetero ring of quinoxaline (δ 8.86). The infrared spectrum of **13** also shows two types of carbonyl absorption (**12** has only a single carbonyl stretch and one would expect **14** to behave similarly). In addition, the mass spectral fragmentation pattern for **13** is very complex when compared with that for

Table II
^{1}H NMR Spectral Data for Substituted 2-Methyl-1-isoquinolones

Compd	Solvent	Frequency, MHz	δ, ppm: NCH_3	H_3	H_4	H_5	H_6	H_7	H_8	Other data
3	$CDCl_3$	100	3.62 (s)	6.40 (d)	6.95 (d)		7.2–7.6 (m)		8.34 (m)	J_{34} = 7.0 Hz
17	$CDCl_3$	60	3.58 (s)	7.37 (s)			7.5–7.9 (m)		8.58 (m)	
20	$CDCl_3$	60	3.67 (s)	7.78 (s)			7.4–7.9 (m)		8.49 (m)	
6	$CDCl_3$	60	3.62 (s)	8.77 (s)		8.40 (m)	7.54 (dd)	7.80 (dd)	8.77 (m)	$J_{56} = J_{67} = J_{78}$ = 7.0, $J_{57} = J_{68}$ = 2.0 Hz
7	$CDCl_3$	60	3.64 (s)	7.25 (s)			8.70 (dd)	7.52 (t)	8.47 (dd)	$J_{67} = J_{78}$ = 8.0, J_{68} = 1.6 Hz
8	Polysol ($CDCl_3$ + DMSO-d_6)	60	3.57 (s)	6.62 (d)	7.55 (d)	7.75 (d)	8.33 (dd)		8.98 (d)	J_{34} = 7.5, J_{56} = 8.5, J_{68} = 2.3 Hz
25	DMSO-d_6	100	3.64 (s)	9.10 (s)			8.61 (dd)	7.85 (t)	8.47 (dd)	$J_{78} = J_{76}$ = 7.9, J_{68} = 1.4 Hz
9	$CF_3COCF_3 \cdot 1.6D_2O$	60	3.89 (s)	9.08 (s)		9.15 (d)	8.87 (m)		9.53 (dd)	J_{56} = 9, J_{68} = 2.3 Hz
15	$CDCl_3$	100	3.65 (s)	7.57 (s)		7.97 (d)	8.50 (dd)		9.28 (dd)	J_{56} = 8.7, J_{68} = 2.5 Hz
a	$CDCl_3$	100	3.53 (s)	7.30 (s)		7.60 (d)	7.76 (dd)		8.51 (d)	J_{56} = 8.7, J_{68} = 2.2 Hz
23	$CDCl_3$	60	3.65 (s)	6.42 (d)	7.07 (d)		6.7–7.5 (m)		7.93 (d)	δ 5.2 (NH)
16	CD_3COCD_3	100	3.56 (s)	6.40 (d)	7.02 (d)	7.34 (d)	7.08 (dd)		7.55 (d)	J_{34} = 7.3, J_{56} = 8.5, J_{68} = 2 Hz
27	D_2O	100	3.67 (s)	7.98 (s)			7.6–8.0 (m)		8.38 (dd)	δ 3.42 [$N(CH_3)_2$]
28	$CDCl_3$	60	3.68 (s)				7.3–7.9 (m)		8.45 (dd)	δ 2.52 (CCH_3)
30	$CDCl_3$	60	3.55 (s)	6.77 (s)			7.4–7.6 (m)		8.44 (m)	δ 4.01 (CH_2), 7.2 (C_6H_5)
31	$CDCl_3$	60	3.60 (s)				7.3–8.2 (m)		8.45 (dd)	

[a] Unpurified 4,7-dibromo-2-methyl-1-isoquinolone.

12. It is not readily evident how one of the isoquinoline rings is reductively cleaved to furnish 13 unless a ring in an intermediate product is opened by a sequence analogous to that postulated by Gensler[11] to explain the products formed in the oxidation of substituted tetrahydroisoquinolines.

(g) Debromination occurs when 4-bromo-7-nitro-2-methyl-1-isoquinolone (15) is catalytically hydrogenated, the product being 7-amino-2-methyl-1-isoquinolone (as its hydrochloride), 16.

Experimental Section

Properties and analytical data for many of the compounds are summarized in Table I; ^{1}H NMR spectral data are given in Table II. Electronic spectral data are given in Table III.

[1] 2,2'-Dimethyl-1,1'-diketo-1,1',2,2'-tetrahydro-4,4'-biisoquinoline (6): This compound was always formed in low yield as a by-product in the preparation of 2-methyl-1-isoquinolone (3) by the oxidation of 2-methylisoquinolinium iodide with basic potassium ferricyanide.[5] It was recovered as follows: The crude (3) was dissolved in diethyl ether (3.6 g per 25 ml) and chilled at −68° until no more gummy material separated. The supernatant was decanted and the gum triturated with a small volume of ethanol. The white crystalline solid was filtered, washed with more solvent, and recrystallized from a large volume of ethanol. The compound did not melt up to 350° although sublimation occurred about 330–340°. ^{1}H nmr ($CF_3COCF_3 \cdot 1.6\ D_2O$, 100 MHz) δ 3.75 (s, 3H, NCH_3), 7.25(m, 1H, H_5), 7.29(m, 1H, H_3), 7.60(m, 2H, H_6, H_7) 8.25(m, 1H, H_8).

Anal. Calcd for $C_{20}H_{16}N_2O_2$: C, 75.93; H, 5.10; N, 8.86; mol wt, 316.3. Found: C, 75.70; H, 5.05; N, 8.95; mol wt (mass spectrum) 316 (both parent and base peak).

Trace amounts of this compound were found when equal weights of isoquinoline methiodide and sodium peroxide were allowed to stand for several months.

The same compound (identical ir spectrum) was made as follows: 0.77 g of 4-bromo-2-methyl-1-isoquinolone, 5 ml of ethanol, 6.5 ml of 5% ethanolic potassium hydroxide, 0.2 g of 3% Pd/$CaCO_3$, and 0.06 g of 95% hydrazine were stirred at 25° for 5 hrs. An additional 0.1 g of hydrazine was added and the stirring continued for 19 hrs. The solid mass was filtered and washed once with cold ethanol (nothing precipitated from the mother liquors and washings upon dilution with water).

[2] The cake was extracted with three 15-ml portions of boiling ethanol. Cooling the extracts at 5° furnished a white crystalline solid which was removed and washed with water. The compound melted above 320°.

1,2,3,4-Tetrahydro-2-methyl-1,3,4-trioxoisoquinoline (8): When (3) was allowed to stand at 50° exposed to air for several months, it gradually changed to an orange-red semi-solid mass. Recrystallization from absolute ethanol furnished orange needles, mp 186.5–188°. The infrared and ^{1}H nmr spectra are the same as those reported.[6]

Anal. Calcd for $C_{10}H_7NO_3$: C, 63.49; H, 3.73; N, 7.41. Found: C, 63.71; H, 3.72; N, 7.46.

The mono-tosylhydrazone was made by stirring 0.32 g of the above triketo compound, 0.7 g of tosylhydrazine, 11 ml of acetic acid and 18 ml of water for 66 hrs at room temperature. The product was filtered, washed well with water, dried, and recrystallized from absolute ethanol; 0.36 g. The orange-yellow, felted needles decomposed at 171.5–172.5°; reported,[12] 167.5–168°; ^{1}Hnmr (DMSO-d_6, 100 MHz) δ 2.36(s, NCH_3), 3.28 (s, CH_3 of tolyl), 7.74(m, H_7), 8.11 (dd, H_8).

Anal. Calcd for $C_{17}H_{15}N_3O_4S \cdot H_2O$: N, 11.18; S, 8.54. Found: N, 11.15; S, 8.32.

This tosylhydrazone was converted to 1,2,3,4-tetrahydro-4-diazo-1,3-dioxo-2-methyl-isoquinoline when a solution in DMSO was allowed to stand at 25° in the dark for 5 days. The product recovered by pouring into water, melted at 142–143°; reported,[12] 147–148°; ir(Nujol) 2120 cm^{-1} ($-N_2$), 1690, 1645 cm^{-1} (CO); ^{1}Hnmr (DMSO-d_6, 100 MHz) 3.30(s, 3H, NCH_3), 7.37 (m, 1H, H_6), 7.48 (m, 1H, H_5), 6.75 (m, 1H, H_7), 8.13 (dd, 1H, H_8).

[3] 4-Bromo-2-methyl-1-isoquinolone (17) was obtained in 80% yield by reacting equivalent amounts of N-bromosuccinimide and (3) in acetic acid at room temperature. The initial reaction was mildly exothermic. An identical material was prepared in 70% yield by oxidizing a basic aqueous solution of 4-bromo-2-methylisoquinolinium iodide with potassium ferricyanide at 35–40°.

The 4-chloro analog (18) was similarly made using N-chlorosuccinimide. 4-Iodo-2-methyl-1-isoquinolone (19). Iodine (2.5 g, 0.01 mole) was added portionwise to a stirred, cooled slurry of 1.6 g (0.01 mole) of (3) and 2.2 g (0.01 mole) of silver trifluoroacetate in 50 ml of ether. The iodine color was rapidly discharged after each addition. After removing the silver iodide, the ether solution was washed once with a small volume of 3% aqueous sodium bisulfite and once with water. Evaporation of the ether left 1.9 g (63%) of crude product. This procedure is an adaptation of one by Hennе and Zimmer.[13]

4-Cyano-2-methyl-1-isoquinolone (20) was made in 87% yield from the (17) and cuprous cyanide in DMF by the procedure of Friedman and Schechter.[14] Hydrolysis in 10% ethanolic potassium hydroxide followed by neutralization gave the 4-carboxy compound (22).

4-Nitro-2-methyl-1-isoquinolone (6): 2-Methyl-1-isoquinolone (1.4 g) was added to 15 ml of 6N nitric acid at room temperature. The isoquinolone dissolved completely; the temperature rose slowly to 37° (some oxides of nitrogen were evolved) and soon the solution became turbid. After about 20 minutes the reaction mixture was filled with pale yellow, felted needles, which were filtered and washed well with cold water. The yield of crude product was 1.1 g (61%); mp 157–159°. An additional amount of less pure material separated from the diluted, cooled nitric acid solution.

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Catalytic hydrogenation in ethanol plus hydrochloric acid over platinum furnished the 4-amino derivative as its salt (11). The product was recovered just as soon as the hydrogenation was completed by removing the catalyst and precipitating the amine salt with excess diethyl ether. Evaporating the ether-alcohol mother liquors and adding water to the residue precipitated (8) (15-20% yield).

4-Nitro-, 7-Nitro-, and 4,7-Dinitro-2-methyl-1-isoquinolone (7, 8 and 9): 2-Methyl-1-isoquinolone (1.59 g, 0.01 mole) was added portionwise during 5 min to 15 ml of 96% sulfuric acid, stirred and cooled to 5°. Then 1.01 g of powdered potassium nitrate was added over 20 min, keeping the temperature 3-10°. After 30 min more, the dark red-brown solution was quenched on 50 g of ice. The orange-red product which crystallized after 16 hr at 5° was broken up, filtered, and washed well with cold water; 1.4 g, mp 90-150°. Extracting this mixture with 70 ml of boiling 95% ethanol left 0.08 g (3.2%) of insoluble, mp 280-285°, which was recrystallized by dissolving in a small volume of DMF and adding an equal volume of ethanol. The small plates melted at 296-296° after drying at 66°, 25 mm. The elemental analysis agrees with those required for a dinitro derivative; the ^{1}H nmr data are consistent with the 4,7-dinitro-2-methyl-1-isoquinolone (9) assignment.

Cooling the ethanolic solution to 5° gave orange needles (0.3 g, 14.7%), mp 214-216°. The nmr evidence supports 7-nitro-2-methyl-1-isoquinolone (8).

The ethanolic mother liquors were cooled to -15°, decanted from some amorphous material, and evaporated. By extracting the residue with boiling cyclohexane, filtering off insoluble (0.2 g, 9.8% more of 9), concentrating the extract and cooling, there was recovered 0.5 g (24.4%) of bright yellow felted needles, mp 102-105°. A tlc on Eastman silica gel chromatogram sheet using 95:5 benzene:ethanol to develop indicated three compounds: R_f = 0.63 (4-nitro), 0.51 (5-nitro) and 0.37 (7-nitro). The first and last were present in small amounts (< 15%). The mixture was then chromatographed on 2:1 silicic acid-celite with benzene-ethanol (95:5) to elute, and the main fraction recrystallized from water as bright yellow felted needles, mp 116-117°; reported[5] for 5-nitro-2-methyl-1-isoquinolone (7) about 120°.

The ^{1}H nmr also agrees with that required by (7). Catalytic reduction of the latter in ethanolic hydrochloric acid gave the 5-amino-2-methyl-1-isoquinolone as its salt (12). The free base (13) and derivatives were prepared by conventional methods.

4-Bromo-7-nitro-2-methyl-1-isoquinolone (14): Powdered potassium nitrate (0.9 g) was dissolved in 6 cc of 96% sulfuric acid with stirring and cooling in ice bath. Then 1.18 g of 17 was added portionwise over 5 min. The solution was stirred for 24 hr at ambient temperature before quenching over 20 g of ice. This acid solution was neutralized with cold conc. ammonium hydroxide, the solid product filtered and washed well with cold water. The still wet cake was recrystallized from 75 ml of 95% ethanol; 0.1 g (7%). Trace amounts more of the title compound were recovered by prolonged cooling of the recrystallization mother liquors at -15°. These mother liquors were heated to boiling and treated with an equal volume of water; the first material to separate upon cooling was amorphous. After removing the latter, a material melting 180-185° slowly crystallized (low yield). The infrared spectrum was significantly different than that of the above nitro compound.

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Elemental analysis (Found: Br, 42.88; Calcd: Br, 30.42), ^{1}H and ^{13}C nmr spectra suggested that this material was impure 4,7-dibromo-2-methyl-1-isoquinolone. It was not further purified.

4,5-Dinitro-2-methyl-1-isoquinolone (26): 5-Nitro-2-methyl-1-isoquinolone, 7, (0.6 g) was added all at once to 10 ml of 70% nitric acid. Complete solution was quickly attained. The temperature rose slowly from ambient to 35° and was then held at 30-35° by cooling in water bath. After standing for 45 min, the solution was poured over ice, the yellow solid filtered and washed with cold water. The yield of dried product was 0.32 g (44%), mp 210-215°. Recrystallization from 30 ml of ethanol raised the mp to 220.5-221.5°; small red-orange plates; ir (mull) 1680,1630 cm^{-1}. The same yield was obtained when the nitration was done in 12N nitric at ambient temperature (2 hr).

Reduction of 25 in ethanolic HCl was done catalytically over platinum. The solution of diamino dihydrochloride (28) so obtained was initially colorless but soon turned yellow, orange and finally red; addition of ether to turbidity and cooling gave the salt as a pale tan, crystalline powder; ir (mull) 3320 (NH), 1645 cm^{-1} (C=O).

From the reddish mother liquors there was recovered another salt, dec. 215-220 as a brown powder; ir (mull) 3360 (NH), 1670, 1650, 1635, 1610 cm^{-1} (C=O). This multiplicity of carbonyl absorptions suggests an amino triketone derivative, resulting from oxidation of the diamino compound.

4-Dimethylamino-2-methyl-1-isoquinolone Hydroiodide (27): 4-Amino-2-methyl-1-isoquinolone hydrochloride (11) (0.7 g) was dissolved in 8 ml of 60% ethanol, made basic with 20% aq. sodium hydroxide solution, diluted with 20 ml of 95% ethanol and 50 ml of ether. Excess methyl

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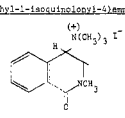
iodide was added to the solution, which had a strong green fluorescence and the flask tightly stoppered; after 6 days at ambient temperature, the solution was evaporated. The gummy residue was extracted with 20 ml of boiling absolute ethanol; cooling the extracts deposited a pale pink crystalline solid, decomposing 201-207°. One recrystallization from abs. ethanol raised the decomposition temperature to 209-211°. This salt was water soluble. The elemental analysis and ^{1}H nmr spectrum are in agreement with those required for the dimethylamino derivative, rather than the monomethylamino compound; ir (mull), 1650, 1670 cm^{-1} (C=O).

By evaporating the ethanolic mother liquors used for the extraction step and triturating the residue with water there was obtained about 40 mg of a yellow solid, melting above 300°. It could be recrystallized from DMF; a solution in conc. sulfuric acid had a pale green fluorescence; ir (mull), 3260 (NH or OH), 1630 (sh), 1615 cm^{-1} (C=O). It was not further investigated.

In another experiment the free-base, 10, in absolute ethanol plus sodium hydroxide (1.5 molar equivalent) was treated with excess methyl iodide and allowed to stand several days at ambient temperature. Addition of ether to turbidity gave a tan solid which melted 193-194° after recrystallization from 1:1 abs. ethanol-2-propanol. This compound showed only a sharp, single carbonyl absorption at 1660 cm^{-1} and no OH or NH. The ^{1}H nmr spectrum and the analyses suggest that this material is trimethyl(3,4-dihydro-2-methyl-1-isoquinolonyl-4)ammonium iodide:



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^{1}H nmr (100 MHz, DMSO-d_6) 3.18 (s, 12H, NCH_3), 4.26 (m, 2H, CH_2), 5.16 (m, 1H, CH), 7.81 (m, 3H, H_5, H_6, H_7), 8.07 (m, 1H, H_8).

Anal. Calcd for $C_{13}H_{19}IN_2O$: C, 45.10; H, 5.53; I, 36.66; N, 8.09. Found: C, 44.97; H, 5.99; I, 36.61; N, 8.06. The picrate of the latter compound melted 206.5-207.5° after recrystallization from ethanol; yellow plates.

Anal. Calcd for $C_{19}H_{21}N_5O_8$: C, 51.00; H, 4.73; N, 15.65. Found: C, 50.94; H, 4.80; N, 15.58.

The condensation products 12 and 13 were also recovered in another attempt to methylate 10. The free base from 1.4 g of 11 in 100 ml of benzene, 50 ml of ether and 10 ml of abs. ethanol was treated with 2 ml of methyl iodide and stored in a tightly stoppered flask in the dark for several days. The initial green fluorescence gradually changed to a blue-purple fluorescence and an orange solid slowly crystallized. After cooling to 5°, the solid was filtered. The solid was first extracted several times with warm water to remove the hydroiodide salts (extracts contained iodide), then with three 15 ml portions of hot ethanol (these extracts were saved - see below). There was left 0.24 g of yellow-orange solid; recrystallization from DMF yielded orange, felted needles, mp 394° (dta, 5°/min). (This compound can also be recrystallized from ethanol, in which it is only sparingly soluble; the solution has a bright blue fluorescence.) Solutions in conc. sulfuric acid have an intense blue-green fluorescence. The spectral and analytical evidence agree with those required for 12: ^{1}H nmr (100 MHz, 96% H_2SO_4) 54.19 (s, 3H, NCH_3), 7.6-8.1 (m, 2H, H_6, H_7), 8.25 (d, J = 7 Hz, 1H, H_5), 8.92 (d, J = 7 Hz, 1H, H_8); ir (mull), 1665 cm^{-1} (C=O).

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Anal. Calcd for $C_{20}H_{14}N_4O_2$: C, 70.16; H, 4.12; N, 16.37; mol wt 342.3. Found: C, 69.88, 69.65, 69.34; H, 4.53, 4.47, 3.98; N, 16.25, 16.08; mol wt (mass spec. parent) 342.

The 45 ml of ethanolic extracts were cooled to 5°, filtered from a trace of 12 and evap. to about 10 ml; cooling gave very pale yellow to white, felted needles of 13, mp 263-264°: ^{1}H nmr (100 MHz, $CDCl_3$) 62.93 (d, 3H, $NHCH_3$, J = 5 Hz, doublet collapses to a singlet in presence of D_2O), 3.90 (s, 2H, NCH_2), 5.84 (broad singlet, 1H, NH, exchanges in D_2O), 7.5-7.9 (m, 6H, $H_{aromatic}$), 8.52 (m, 1H, H_8), 8.77 (s, 1H, pyrazine ring), 8.80 (m, 1H, $H_{8'}$); ir (mull), 3230 (sharp, narrow absorption NH); 1665, 1645 cm^{-1} (C=O).

Anal. Calcd for $C_{20}H_{16}N_4O_2$: C, 69.75; H, 4.68; N, 16.27; mol wt 344.4. Found: C, 69.26; H, 4.71; N, 16.34; mol wt (mass spec. parent), 344.

Additional amounts of both 12 and 13 could be recovered by reworking the original reaction mother liquors.

2,3-Dimethyl-4-nitro-1-isoquinolone (22): 2,3-Dimethylisoquinolinium iodide was oxidized in basic solution with potassium ferricyanide using the usual procedure; much ether-insoluble tar was formed. The ether-soluble 2,3-dimethyl-1-isoquinolone was obtained in 30% yield; the mp of the off-white crude product was 95-98°. Attempts to recrystallize were unsuccessful, the compound always becoming dark and tarry. Nitration at 25° with 8N nitric acid proceeded rapidly to furnish the more stable 4-nitro derivative which was readily recrystallized from 95% ethanol as orange crystals.

Reduction to the corresponding amino compound (23) was done catalytically.

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4-Benzyl-2-methyl-1-isoquinolone: 2-Methyl-1-isoquinolone (0.8 g) and benzyl bromide[15] (0.9 g) was heated at 160-180° for 3 hr. The dark viscous product was cooled, slurried with 15 ml of ethanol, and chilled to -15°. The yellow solid was removed, washed with cold ethanol and dried; 23 mg; mp above 320°. It was recrystallized by dissolving in warm DMF adding water to incipient turbidity and cooling. The bright yellow powder was filtered, washed well with water, and dried at 100°, 25 mm, for 1 day. Solutions in DMF or chloroform had an intense blue fluorescence. The analyses correspond to those required for tris-(2-methyl-1-isoquinolonyl-4)-phenylmethane.

Anal. Calcd for $C_{37}H_{29}N_3O_3$: C, 78.84; H, 5.19; N, 7.46; mol wt, 563.6. Found: C, 78.87; H, 4.93; N, 7.40; mol wt, 564.

The original ethanolic mother liquors were evaporated to dryness and the gummy residue extracted with two 20 ml portions of boiling cyclohexane. Evaporation of the latter furnished the crude 4-benzyl-2-methyl-1-isoquinolone (30), as an oil that crystallized. Two wasteful recrystallizations from cyclohexane finally gave sparkling, colorless prisms. The yield was not determined.

Bis-(2-methyl-1-isoquinolonyl-4)phenylmethane: 2-Methyl-1-isoquinolone (0.8 g, 0.005 mole), 1.1 g of benzaldehyde, 12.5 ml of 95% ethanol and 12.5 ml of conc. hydrochloric acid were refluxed for 2 hr. The cooled solution was diluted with 50 ml of water and chilled at 5° for several days. When the oil which separated had crystallized, the supernatant phase was decanted and the crystals washed with a small volume of alcohol; 0.7 g, mp 280-282°. The compound can be recrystallized from either benzene or ethanol; mp 281-282.5°. Two strong carbonyl absorptions are present at 1630 and 1655 cm^{-1}.

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Anal. Calcd for $C_{27}H_{22}N_2O_2$: C, 79.78; H, 5.46; N, 6.89; mol wt, 406.5. Found: C, 80.01; H, 5.62; N, 6.89; mol wt (mass spectrum), 406.

Bis-(2-Methyl-1-isoquinolonyl-4) methane: This compound was obtained in 5% yield during an attempted Mannich reaction on 2-methyl-1-isoquinolone with piperidinium chloride and paraformaldehyde. After recrystallization from 98% ethanol the mp was 299-301° (dec); reported,[6] 302-303°; ^{1}H nmr (60 MHz, $CDCl_3$), 63.30 (s, 3H, NCH_3), 4.06 (s, 2H, CH_2), 6.73 (s, 1H, H_3), 7.63 (m, 3H, H_5,H_6,H_7), 8.53 (m, 1H, H_8).

Anal. Calcd for $C_{21}H_{18}N_2O_2$: C, 76.35; H, 5.49; N, 8.48; mol wt, 330. Found: C, 76.51; H, 5.73; N, 8.16; mol wt, 330 (mass spectrum).

4-Phenylethynyl-2-methyl-1-isoquinolone (31). Equivalent amounts of 19 and cuprous phenylacetylide in dry pyridine were refluxed and stirred for 16 hrs under nitrogen. The product was separated from the cuprous iodide by evaporating the pyridine under reduced pressure, extracting the residue several times with boiling cyclohexane and evaporating the latter; the yield was quantitative.

Use of the 17 was much less satisfactory; even after 52 hr refluxing unreacted cuprous phenylacetylide was present. Isolation and purification of the phenylethynyl compound were also more difficult.

N-Methylnaphthostyril (33) was prepared from naphthostyril by the procedure of Roshinskii and Mostoslavskii;[16] recrystallization per their instructions gave the reported melting point (> 80°). However, it was immediately evident when the fluorescence was examined that this material was a mixture of two compounds (emission$_{max}$, 395 and 525 nm). This result was confirmed by ^{1}H nmr ($CDCl_3$) which revealed both N-methyl (63.45) and O-methyl (63.71). The latter was present to the extent of 20-25%. Chromatographic separation on 2:1 silicic acid-Celite, using

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ethylene dichloride as the eluent (the O-methyl isomer moved slightly faster), gave a fraction which melted 86-87° after recrystallization from n-hexane. The ^{1}H nmr now showed essentially no O-methyl peak; the fluorescence peak at 395 nm was absent. The O-methyl isomer was not obtained in pure form.

N-Methylphenanthridone (23) melted at 107° after recrystallization from 50% ethanol; reported,[17] 108°.

Photoluminescence Measurements. All measurements were made with a Turner Model 210 Spectrofluorometer; this instrument automatically corrects the emission spectra and the excitation energy.[18] Spectra from this instrument appear to agree well with those from other corrected spectrum instruments.[19]

The absorbences were typically measured in solutions of about 10^{-3} M, the emission and excitation from solutions of about 10^{-5} M.

Quantum yields were made using the comparison technique versus quinine sulfate as q = 0.55. The details have been discussed elsewhere.[19] The results, summarized in Table 3, were obtained on solutions under 700 torr of air. Stern-Volmer quenching constants for O_2 are given for three compounds as K in units of torr^{-1}.

Phosphorescence was examined by cooling solutions to -196° in test tubes and irradiating with a filtered ultraviolet lamp. All the isoquinolones examined phosphoresced yellow with lifetimes, by eye, of a few to several tenths of seconds. The reported colors of fluorescence and phosphorescence were observed, respectively, during and immediately after irradiation by a near uv lamp.

Table III
Electronic Spectra of Compounds

Compd	Substituent	Solvent	Absorption[a] peaks λ, nm	ε × 10⁻³	λ, nm	ε × 10⁻³	Excitation peaks, nm 1st	2nd	Emission peaks, nm 1st	2nd	Quantum yield[b]	K 10⁻³/Torr
			A. 2-Methyl-1-isoquinolones									
3		CH_3OH	325	3.2	288	6.2	325	288	368	383	0.054	0.07
17	4-Br	CH_3OH	326	5.4	294	9.8	322	291	395			
	4-HO	CH_3OH	313	2.1	254	9.2			(355)[c]	415		
	4-C_6H_5CO	CH_3OH							359	403	Low	
11	4-NH_2 · HCl	CH_3OH	318	6.3	290.5	8.1	310		513	530	0.027	0.26
11	4-NH_2 · HCl	H_2O	305	3.9			310		530		0.026	
11	4-NH_2 · HCl	H_2O + NaOH	305		295		310		529			
11	4-NH_2 · HCl	CH_3CN	322		295				410	428		
11	4-NH_2 · HCl	C_6H_6					317		500			
22	5-NH_2 · HCl	CH_3OH	346	8.7	300	12.2	345	304	406		0.15	0.27
16	7-NH_2 · HCl	CH_3OH	332	2.5	292	8.0	344	298	456		0.076	
26	4,5-DiNH_2 · HCl	CH_3OH	326	4.0	255		325	255	427		0.068	
27	4-$(CH_3)_2N$ · HI	CH_3OH	305	11.8	265	5.5	310		505			
27	4-$(CH_3)_2N$ · HI	CH_3OH + NaOH							502		0.047	
27	4-$(CH_3)_2N$ · HI	CH_3CN					314		525			
27	4-$(CH_3)_2N$ · HI	CH_3CN + 2%CH_3OH					314		525			
27	4-$(CH_3)_2N$ · HI	C_6H_6					316		490			
31	$C_6H_5C{\equiv}C$	CH_3OH	309	18.2	257	16.2	310	257	420			
			B. Related Compounds									
Isocarbostyril		CH_3OH					318		367[d]	382		
Isocarbostyril		0.01 *M* $NaOCH_3$ in CH_3OH	318		268		320	281				
5		CH_3OH		1.3					417			
32	*N*-Methylnaphthostyril	CH_3OH	367		337	1.7	340		506	525	0.086	
32	*N*-Methylnaphthostyril	H_2O	367						506	525		
33	*N*-Methylphenanthridone	CH_3OH					325		362	378		

[a] Molar absorbance, ε, in l. mol^{-1} cm^{-1}. [b] Under air (700 Torr) vs. quinine as 0.55. [c] It seems likely that this emission is due to an impurity. [d] Reported[21] 369 mm (95% ethanol).

Table IV
Phosphorescence Relative to Fluorescence of Certain Isoquinolones

Compd	In benzene 25° Fluor	−196° Fluor	−196° Phos	In methanol 25° Fluor	−196° Fluor	−196° Phos
3	Violet	Violet	Yellow-green	Violet		Blue-green
11	Blue-violet	Blue	Yellow-green	Yellow		Yellow-green
22	Blue-violet	Blue-violet	Yellow-green			
27				Yellow-green	Yellow-green	Yellow-green

Discussion

Fluorescence Theories. The enhancement of molecular fluorescence has mainly been a pragmatic procedure. A few general ideas have been developed and are presented in a recent book on laser dyes.[20] Certainly the amino group is the major substituent for enhancing fluorescence. Schäfer[20] discusses molecular fluorescence in terms of the length L of a π electron cloud associated with a chain of conjugated double bonds. The absorption maximum wavelength is given by

$$\lambda = \frac{8mc_0}{h}\,\frac{L^2}{N+1} \qquad (1)$$

where N is the number of π electrons. Adding amino groups at the ends of the chain increases L without increasing N, thus increasing λ substantially.

The molar absorbance is generally increased by the addition of amino group auxochromes. This is often paralleled by an increase in the fluorescence quantum yield. In long-chain compounds the direction of L is simple to determine. In polycyclics, there seem to be more than one axis, each with its own L and λ. Furthermore, linear polycyclics like anthracene act longer than phenanthrene where the rings are angular.

In heterocyclics and compounds with carbonyl groups the π electron clouds are skewed in relation to the geometric axes. One way to find the ends of the axes might be to place amino groups in various positions and note the effect.

However, with heterocyclic compounds there is another effect having to do with n,π^* and π,π^* transitions in the singlet manifold. The former is much more likely to give intersystem crossing to the triplet. Any molecular change which lowers the relative energy of the (π,π^*) S_1^* state will

therefore enhance the fluorescence while decreasing the phosphorescence.

Although our results can be explained by the "theories" stated, there is really not enough data and too much leeway in the theories to make a real test. The pertinent possibilities will be pointed out below.

Phosphorescence and Fluorescence. Visual examination of the phosphorescence in a few of the isoquinolones was made by freezing methanolic solutions in liquid nitrogen. Table IV shows the results. The phosphorescence was quite long lived and could generally be distinguished from fluorescence by moving a solution away from the exciting uv lamp.

Compound 3 shows the expected red shift of phosphorescence from fluorescence. The shift was larger in benzene than in methanol.

Compound 11 acts much like 3 in benzene, showing a red shift of phosphorescence. However, in methanol it fluoresces in the yellow. The phosphorescence is then to the blue side of the fluorescence. This surely means that the excited singlet either forms some sort of exciplex or is protonated before emitting. The triplet in solid methanol presumably cannot form a similar exciplex. The fluorescence from the solid could not be seen since the phosphorescence competed with it in brightness.

Compound 22 was much like 3, while 27 was much like 11. Both 22 and 27 decomposed before the measurements were completed.

The large phosphorescence of all these compounds indicated that the fluorescence quantum efficiency was not very high.

Impurities and Decomposition. The fluorescence studies showed the presence of fluorescent impurities in some of the isoquinolones and of instability (oxidation or decomposition) in their solutions. For the important compounds it was necessary to repurify and to resynthesize samples just prior to use in order to repeat results. Impurities which show up in fluorescence spectra can be maximized or minimized by shifting the excitation wavelength. The size of an impurity peak depends not only upon its concentration, but upon its quantum yield and absorbance relative to the major compound.

Compound 3 was pure and relatively stable as a solid and in alcohols or water for weeks. Eventually it air oxidizes to give 5.

Compound 11 showed a small extraneous fluorescence at 315 nm when excited at 290 nm. It decomposed as a solid within a few months and in alcoholic solution within several days. In acetonitrile (AN) it seemed to react very rapidly. Upon dissolution in O_2-free AN there were two fluorescent bands around 420 and 490 nm. These bands then disappeared within hours. Oxygenated AN caused a different pattern which was not further examined.

Compound 22 showed a fluorescent impurity at 493 nm when excited at 300 nm. This impurity peak did not show during excitation at 347 nm. Solutions were stable for a few days and the solid decomposed slowly.

The 7-amino isomer, 16, was pure and stable in solution for short periods. The excitation peaks are inaccurate since they were measured in a concentrated solution.

The 4,5-diamino compound, 26, had a very small fluorescent impurity peak at 350 nm. The 4-dimethylamino derivative, 27, was initially pure, but it decomposed before measurements were completed.

Like the amino compound, 4-hydroxy-2-methyl-1-isoquinolone was unstable (and hence impure). The 4-benzoyl derivative also appeared to contain small amounts of fluorescent impurities. Hence the results for these are uncertain.

By way of contrast, derivatives such as the 4-bromo (17) or 4-phenylethynyl (31) were both pure and stable from a fluorescence standpoint.

Fluorescence Results. Table III shows the data gathered on fluorescence. A spectrum of the parent compound 3 has been published earlier.[2] Here only the peaks of absorption and emission are given. The molar absorbance, ϵ, is given at the peaks where

$$A = \epsilon c = \log I_0/I$$

and A is the optical density read on the Turner used as a double beam spectrometer.[18]

The quantum yields were calculated using the formula

$$q = q_{std}\frac{A_{std}\theta n^2\lambda_{std}}{A\theta_{std}n_{std}^2\lambda}$$

The general procedure has been described before.[19] With the unstable compounds all the measurements were made within a few hours of preparing the solutions.

Quenching studies with O_2 were done by deaerating the solutions in a N_2 box and running a spectrum in cuvettes sealed with Teflon caps. Then spectra were run with the caps removed from the cuvettes and finally with oxygenated solutions. This gave us points at 0, 147, and 700 Torr of O_2. The Stern–Volmer equation

$$F = \frac{F_0}{1 + KP_{O_2}}$$

was used to calculate the quenching constant K from the emission peak heights without oxygen, F_0, and with oxygen, F.

Examination of the fluorescence results in Table III shows that every substitution on the parent, 3, caused some red shift of the emission with the possible exception of benzoyl. However, the effect was relatively small with the groups 4-bromo, 5-amino, 4-benzoyl, and 4-hydroxy. Other amino groups had a much more pronounced effect. For example, the 4-amino compound 11 had a Stokes shift of 203 nm in methanol. Part of this may be due to a different mechanism in the excited state. That is, excited 11 probably forms an exciplex, which may also account for the lower quantum yield. A similar Stokes shift is observed with the 4-dimethylamino group in compound 27 but the quantum yields are not lowered as much with this methylated amine.

Amino groups on the 5 or 7 position show much less effect on the Stokes shift, but do increase the quantum yield of fluorescence. 3-Amino-2-methyl-1-isoquinolone was previously reported[21] to fluoresce at 456.5 nm in 95% ethanol.

Compound 26, 4,5-diamino-2-methyl-1-isoquinolone, was prepared to see whether it would show both a large Stokes shift *and* a large quantum yield increase. The result was a moderate shift and a moderate increase. Clearly the groups on the 4 and 5 position interact and as a consequence the effects are not additive.

Several compounds related to 3 were also examined. Isocarbostyril or isoquinolone has the same emission peaks as 3, showing that the *N*-methyl group has little effect. The main air oxidation product of 3, namely 1,2,3,4-tetrahydro-2-methyl-1,3,4-trioxoisoquinoline (5), fluoresces at 417 nm; 5 does not appear to be an impurity in the sample of 3 while fluorescence was measured. *N*-Methylphenanthridone (33) can be viewed as 3 with a longer group fused onto the 3,4 position. As such it is the only substituted isoquinolone examined which showed a blue shift of the emission peaks. On the other hand, *N*-methylnaphthostyril (32) fluoresced in about the same region as the 4-amino-2-methyl-1-isoquinolone.

One hope for increasing the fluorescence quantum yield

is to lower the energy of the π,π^* transition below that of the n,π^* transition. This would decrease singlet–triplet crossover and decrease phosphorescence. Since strong phosphorescence was always observed, none of the substitutions examined accomplished this energy inversion.

Compounds **11** and **27** in particular show large red shifts, which suggest that the axis of L in eq 1 goes near the 4 position. This axis must be for an n,π^* transition based on the argument in the foregoing paragraph. There should be another axis for the π,π^* transition which presumably goes near the 6 position. It is unfortunate that a 6-amino compound was not available for testing this idea.

These two amino compounds, **11** and **27**, are much more strongly quenched by oxygen than is **3**. The Stern–Volmer constant $K = k_q\tau$, where k_q is the quenching rate constant and τ the excited-state lifetime. It is possible that the amino compounds have a longer lifetime, τ, than **3**. However, it would be expected that they would form stronger charge transfer complexes with O_2 and thus have a larger k_q and no change of τ.

There are some differences between **11** and **27**. For example, the dimethylamino group in **27** effects a smaller red shift in fluorescence than does the amino group in **11** (both compared with **3**) but at the same time causes less of a decrease in quantum yield.

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Registry No.—**3**, 4594-71-2; **4**, 54931-49-6; **5**, 21640-33-5; **5** monotosylhydrozone, 54931-50-9; **6**, 33930-79-9; **7**, 42792-96-1; **8**, 54931-51-0; **9**, 54931-52-1; **10**, 54931-53-2; **11**, 54931-54-3; **11** salicyl derivative, 54931-55-4; **12**, 54931-56-5; **13**, 54931-57-6; **16** HCl, 54931-58-7; **16** picrate, 54931-60-1; **17**, 33930-63-1; **18**, 27187-01-5; **19**, 54931-61-2; **20**, 20334-97-8; **21**, 54931-62-3; **22**, 54931-63-4; **22** phenylthiourea derivative, 54931-64-5; **23**, 42792-97-2; **24**, 54931-65-6; **25**, 54931-66-7; **26**, 54931-67-8; **27**, 54931-68-9; **28**, 54931-69-0; **29**, 54931-70-3; **30**, 54931-71-4; **31**, 54931-72-5; **32**, 1710-20-9; **33**, 4594-73-4; 2-methylisoquinolinium iodide, 3947-77-1; 1,2,3,4-tetrahydro-4-diazo-1,3-dioxo-2-methylisoquinoline, 6075-60-1; *N*-bromosuccinimide, 128-08-5; 4-bromo-2-methylisoquinolinium iodide, 54931-73-6; *N*-chlorosuccinimide, 128-09-6; trimethyl(3,4-dihydro-2-methyl-1-isoquinolonyl-4)ammonium iodide, 54931-74-7; trimethyl(3,4-dihydro-2-methyl-1-isoquinolonyl-4)ammonium picrate, 54931-76-9; 2,3-dimethylisoquinolinium iodide, 32431-36-0; 2,3-dimethyl-1-isoquinolone, 7114-78-5; tris(2-methyl-1-isoquinolonyl-4)phenylmethane, 54931-77-0; bis(2-methyl-1-isoquinolonyl-4)phenylmethane, 17054-56-7; bis(2-methyl-1-isoquinolonyl-4)methane, 27330-16-1

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References and Notes

(1) S. F. Mason and D. R. Roberts, *Chem. Commun.*, 476 (1967).
(2) R. A. Henry and C. A. Heller, *J. Lumin.*, **4**, 105 (1971).
(3) C. A. Heller, R. A. Henry, and J. M. Fritsch, "Chemiluminescence and Bioluminescence", M. J. Cormier, D. M. Hercules, and J. Lee, Ed., Plenum Press, New York, N.Y., 1973, p 249.
(4) Reference 3, p 244.
(5) H. Decker, *J. Pract. Chem.*, **47**, 28 (1893).
(6) N. J. Mruk and H. Tieckelmann, *Tetrahedron Lett.*, 1209 (1970).
(7) I. G. Hinton and F. G. Mann, *J. Chem. Soc.*, 599 (1959).
(8) D. E. Horning, G. Lacasse, and J. M. Muchowski, *Can. J. Chem.*, **49**, 2785 (1971).
(9) Y. Kawazoe and Y. Yoshioka, *Chem. Pharm. Bull.*, **8**, 24 (1960).
(10) S. F. Dyke, *Adv. Heterocycl. Chem.*, **14**, 279 (1972).
(11) W. J. Gensler, "Heterocyclic Compounds", Vol. 4, R. C. Elderfield, Ed., Wiley, New York, N.Y., 1952, p 405.
(12) J. M. Muchowski, *Tetrahedron Lett.*, 1773 (1966).
(13) A. L. Henne and W. F. Zimmer, *J. Am. Chem. Soc.*, **73**, 1362 (1951).
(14) L. Friedman and H. Schecter, *J. Org. Chem.*, **26**, 2522 (1961).
(15) A GLC on the benzyl bromide, after this experiment had been performed, indicated a mixture.
(16) Y. I. Rozhinskii and M. A. Mostoslavskii, *Zh. Org. Khim.*, **8**, 2177 (1972).
(17) A. Pictet and E. Patry, *Ber.*, **26**, 1962 (1893).
(18) G. K. Turner, *Science*, **146**, 183 (1964).
(19) C. A. Heller, R. A. Henry, B. A. McLaughlin, and D. E. Bliss, *J. Chem. Eng. Data*, **19**, 214 (1974).
(20) F. P. Schäfer, Ed., "Dye Laser", Springer-Verlag New York, New York, N.Y., 1973.
(21) T. Okano and H. Matsumoto, *Yakugaku Zasshi*, **89**, 510 (1969).

Lithium Aluminum Hydride Reduction of Terpene Sultones

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Lithium aluminum hydride reduction of camphene sultone, 10-isobornyl sultone, and 6-bornyl sultone yield, depending on exact conditions, sulfinate esters, mercapto alcohols, or sulfur-free alcohols. Mercaptans are slowly, and sulfides even more slowly, converted to hydrocarbons by lithium aluminum hydride at 100°.

During an investigation of the chemistry of camphene sultone (**1**)[2] it was discovered that desulfurization to camphene hydrate (**5**) took place on reduction with lithium aluminum hydride. The desulfurization reaction not only provided a powerful method for structural and stereochemical elucidation,[2] but also permitted the facile synthesis of bornane derivatives[3] and the selective introduction of a deuterium atom into the bornane and camphane ring systems.[2] We have now examined the lithium aluminum hydride reduction of terpene sultones in greater detail and wish to report that in addition to the sulfur-free alcohol, cyclic sulfinate esters and mercapto alcohols are also produced.

Camphene Sultone. Treatment of camphene sultone (**1**) with an excess of lithium aluminum hydride in THF at reflux for 6 hr, followed by work-up with aqueous hydrochloric acid, gave 33% of camphene sulfinate ester (**2**), 18% 9-mercaptocamphene hydrate (**3**), 45% of 9-mercaptocamphene (**4**), 1% of camphene hydrate (**5**), and 3% of camphene. Camphene and 9-mercaptocamphene (**4**) were not present to any appreciable extent in the crude product, but were formed in varying amounts by dehydration of **3** and **5** during GLC isolation.

The structure assigned camphene sulfinate **2** was based on elemental and mass spectral analysis, which confirmed a