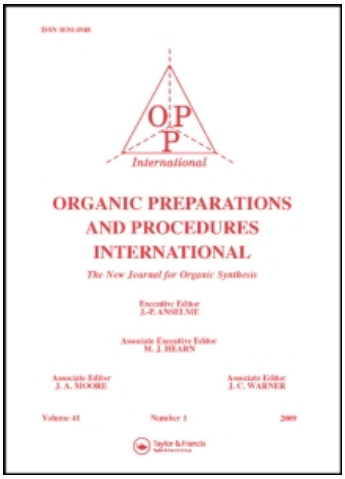

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SYNTHESIS OF JULOLIDINE DERIVATIVES

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SYNTHESIS OF JULOLIDINE DERIVATIVES

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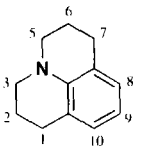
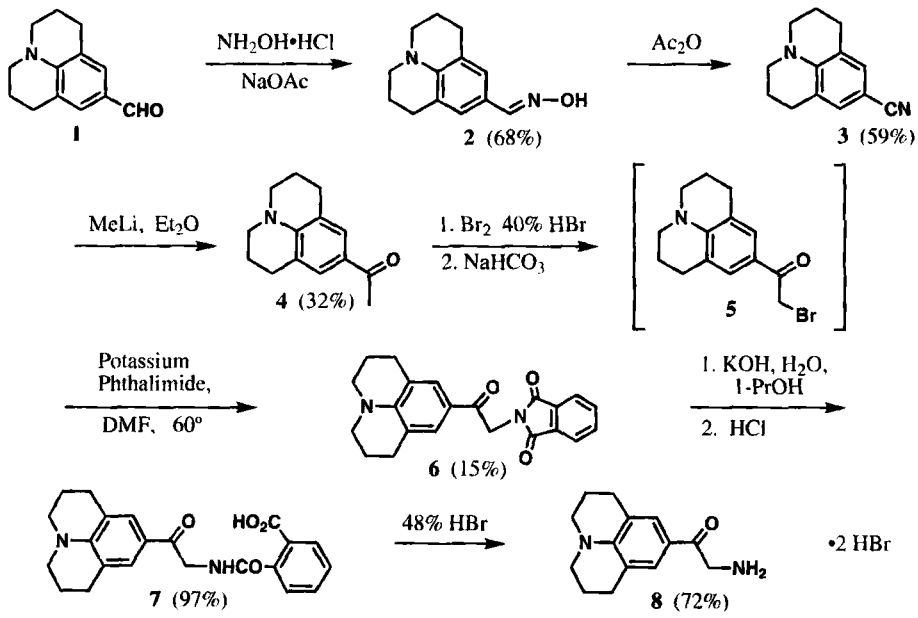
Julolidines are effective auxofluors in laser dyes[1,2] and biochemical stains.[3,4] They are among the strongest electron-releasing groups known, with a Hammett σ constant of -1.7 for the 9-julolidinyl group. This effect is the result of a combination of the electronic effects of two N-alkyl groups incorporated in rings and the concomitant steric effect that favors conjugation of the unshared pair of electrons on nitrogen with the benzene ring.[5] In an early study, Smith and Yu found that julolidine itself failed to undergo many common reactions such as nitrosation or Friedel-Crafts acylation. In addition, the Mannich reaction of julolidine with piperidine and formaldehyde gave only polymeric material. Sulfonation of julolidine by a method which succeeded on N,N-dimethylaniline did not give the 9-sulfonic acid.[6]



julolidine

Phenacylamines (as their salts) are the usual precusors of 5-phenyloxazoles, which are often valuable for their fluorescence properties. We wished to prepare a julolidine bearing the $COCH_2NH_2$ group at its 9-position (**8** in *Scheme 1*). The required intermediate, 9-acetyljulolidine (**4**), was mentioned in a patent, but apparently not prepared.[7] Another patent describes the conversion of 9-bromojulolidine to 9-lithiojulolidine, which upon treatment with N.N-dimethylacetamide gave a 40% conversion to **4**, which was not isolated.[8] In a study of the Vilsmeier reaction of N,N-dimethylaniline, Bosshard and Zollinger showed that the best yield of 4'-(dimethylamino)acetophenone (25%) was obtained with N-methylacetamide, and not with N,N-dimethylacetamide; the most commonly used formylating agent, N,N-dimethylformamide, also gave poor yields.[9] Our attempts to acetylate julolidine using N-methylacetamide gave no product at all.



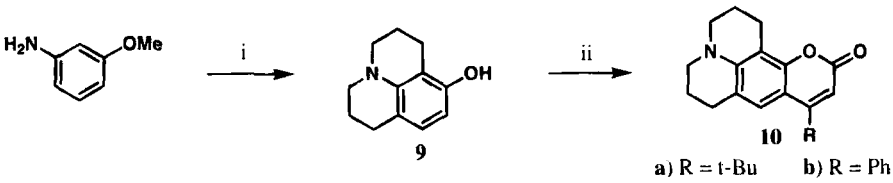
Scheme 1

Gilman and Kirby reported that although 4-(dimethylamino)benzonitrile does *not* react with methylmagnesium bromide, with methyllithium it afforded 4'-(dimethylamino)acetophenone in 45% yield.[10] We found that this route was applicable in the julolidine series. Accordingly, 9-formyljulolidine (**1**) was obtained by the typical Vismeier procedure, but in improved yield and purity by allowing the hydrolysis step to proceed overnight. The conversion of **1** directly to the nitrile (**3**) with sodium azide described by Smith and Yu was inferior to their oxime route (**1** to **2** to **3**).[6] Addition of methyllithium to **3** in ether at 0° gave 32% yield of the desired 9-acetyljulolidine (**4**) as clean yellow spars, mp 73°, with two preliminary phase changes of a type very common in julolidines.

The three commonly used methods to convert acetophenones to phenacylammonium compounds are (1) nitrosation and reduction; (2) the Delèpine reaction; and (3) the Gabriel synthesis.[11] We did not attempt the nitrosation and reduction route. Because of the presence of the amino function in julolidine, the diammonium dihalides, such as **8** in *Scheme 1*, formed on hydrolysis of the Delèpine product would have had about the same solubility as the ammonium halide by-product, and thus they would have been very difficult to purify; moreover, free phenacylamines are too unstable to handle. In contrast, the only by-product of the phthalimide method, after the second hydrolysis, with *acid* (**7** to **8**) is phthalic acid, which is easily removed. Thus bromination of the 9-acetyljulolidine (**4**) in 40% hydrobromic acid, followed by careful neutralization, gave the free base (**5**), which was condensed with potassium phthalimide in DMF to give the imide **6**; alkaline hydrolysis gave the phthalamic acid (**7**), and final

hydrolysis with 48% hydrobromic acid gave **8** as the dihydrobromide.

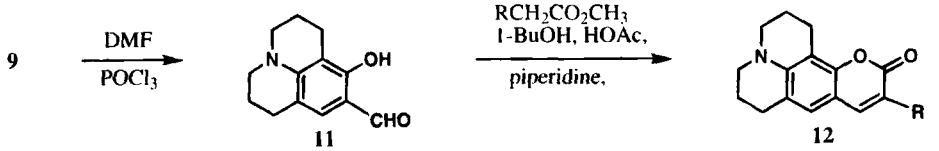
A number of coumarins (**10** and **12**), were prepared (*Schemes 2 and 3*) from 8-julolidinol (**9**)[12] [obtained in improved yield (52%) in the present work from the inexpensive 1-bromo-3-chloropropane and *m*-anisidine] as potential laser dyes, **10a-b** by the von Pechmann reaction and **12a-i** by the Knoevenagel condensation. Again, because of the unusual reactivity of julolidine, the most common catalyst for the von Pechmann reaction, zinc chloride, gave no product in the synthesis of the 4-t-butyl derivative **10a** from **9** and methyl 4,4-dimethylacetoacetate. A change from ethanol to 2-ethoxyethanol as solvent at 133° gave negligible amounts of coumarin. The use of polyphosphate ester (PPE) both as catalyst and medium at 130° gave up to 13% yield of the 4-t-butylcoumarin **10a**, whose identity as a coumarin and not a chromenone was shown by the location of its infrared band for carbonyl stretch at 1692 cm^{-1}. It was accompanied by large amount of a blue, water-soluble, solid by-product. Compound **10a** had a very strong fluorescence and was extremely solvatofluorochromic. It was found to be an unusually efficient laser dye (trade name Coumarin 487) when flashlamp-pumped in methanol.[13] Similarly, **9** and methyl benzoylacetate gave 27% of the 4-phenyl analog (**10b**), whose infrared band for carbonyl stretch at 1688 cm^{-1} showed it to be a coumarinas well. The 4-phenyl had only a weak fluorescence.



i) $Br(CH_2)_3Cl$, ; then 48 % HBr, ii) $RCOCH_2CO_2CH_3$, PPE,

Scheme 2

The Vilsmeier reaction on **9** to give the 9-formyl-8-hydroxyjulolidine **11** also benefited from prolonged hydrolysis. Condensation of **11** with various active esters gave the coumarins**12a-i**. While the lasing properties of these compounds have been reported, along with longwave absorption peaks, fluorescence peaks and quantum yields (mostly near unity),[1] this is the first report of their syntheses, along with more complete spectral data including extinction coefficients. These 3-substituted coumarins (**12a-i**) were much less solvatofluorochromic than **10a**.



a) R = 2-benzothiazolyl b) R = 2-benzoxazolyl c) R = methylsulfonyl d) R = phenyl
e) R = phenylsulfonyl f) R = 2-pyridyl g) R = 3-pyridyl h) R = 4-pyridyl i) R = ethoxycarbonyl

Scheme 3

Coumarins **10a**, **12a-c**, **f**, **i** are commercially available from Exciton, Inc., of Dayton, OH, USA.

EXPERIMENTAL SECTION

Commercial reagents and solvents were used as received unless indicated otherwise. All melting points were determined in unsealed capillary tubes in a heated oil bath (Thomas-Hoover Unimelt, Arthur H. Thomas Co.) using 76 mm immersion thermometers, and they needed no correction. Most stirring in round-bottomed flasks was done with teflon-coated magnets of prolate spheroid shape. **All evaporations were carried out with a rotary evaporator at a final pressure of 15-30 torr.** Most solids were dried in a vacuum oven at 15-30 torr. Chromatographic purification by extraction from an "Ace-Kau" means that boiling solvent was allowed to fall on a solid sample and pass through a column of adsorbent in a special apparatus,[14] (an Ace-Kauffman Column, Ace Glass Co., Cat. No. 5879). Alumina was neutral, Br. I, Aldrich 19,997-4. Thin-layer chromatography was carried out with Whatman MK6F silica 1 x 3 inch plates visualized with short- and long-wave ultraviolet light. Elemental analyses were done by either Desert Analytics, Tucson AZ, Microanalysis, Wilmington DE, or Oneida Research Services, Rensselaer, NY. Infrared spectra were determined as potassium bromide pellets (unless noted otherwise) with either a Perkin-Elmer 283 grating instrument or with a Perkin-Elmer 1600 series FTIR using a diffuse reflectance cell. Ultraviolet spectra were determined with a Shimadzu UV 265 (unless noted otherwise). PMR spectra were carried out on a number of different instruments; the field strength and presence of FT are indicated. Fluorescence peaks were obtained with a Farrand Mk. II spectrofluorimeter and the wavelengths are corrected.

9-Formyl-2,3,6,7-tetrahydro-*1H,5H*-benzo[ij]quinolizine (**1**).- The Vilsmeier reaction on 2,3,6,7-tetrahydro-*1H,5H*-benzo[ij]quinolizine (julolidine) was carried out by the method of Cai *et al.*[15a] with the modification of allowing the hydrolysis of the ionic intermediate with sodium acetate to proceed overnight; this modification raised the yield of water-washed product to 87-92% of **1** as yellow crystals, mp 84-84.5°, *lit.* mp 77-79°,[5] 85%, mp 79-81°.[15b]

9-Formyl-2,3,6,7-tetrahydro-*1H,5H*-benzo[ij]quinolizine Oxime (**2**).- A mixture of 9-julolidinecarboxaldehyde (20.95 g, 104 mmoles, **1**), 300 mL of 95% ethanol, hydroxylamine hydrochloride (7.75 g, 112 mmoles) in 22.3 mL of water (5M solution), and sodium acetate trihydrate (15.18 g, 112 mmoles, Acros) in 22.3 mL of water (5M solution), was heated to 70° and stirred for 24 hours at this temperature, and was quenched in 100 g of ice and left at –20° for 48 hours. The pale orange solid was collected and dried at 65°/30 torr/ 24 hours to yield 14.31 g of solid, mp 120-130°. The filtrate was stored at –20° for 48 hours to give 3.41 g of second crop, mp 120-130°, and an identical mixture melting point; and the crops were combined to total 17.72 g (79%) of solid, *lit.* mp 127-128°,[6] 126-128°.[15a]

9-Cyano-2,3,6,7-tetrahydro-*1H,5H*-benzo[ij]quinolizine (**3**).- With stirring, 9-julolidinecarboxaldehyde oxime (**2**, 17.41 g, 81 mmoles) and 124 mL of acetic anhydride were heated to reflux for 3 hours, after which the dark mixture was poured into 200 g of ice. The mixture was stirred, neutralized (pH ~ 7 to 8) with aqueous ammonia and allowed to stand overnight at

room temperature to obtain a black solid which was collected, dried at 60°/30 torr/24 hours to give 14.7 g of dark solid, mp 100-110°. Similarly, 1.54 g of material with the same melting point was obtained from 9-julolidinecarboxaldehyde oxime (**2**, 2.05 g, 9.4 mmoles). The crude batches from 2 runs (16.20 g) were blended and placed in a medium Ace-Kau over 4 cm Florisil (Aldrich 22,074-4) and extracted with 250 mL of benzene for 30 minutes. Once all the material had been extracted, the pot was cooled to room temperature, evaporated, and the colored solid was dried at 60°/30 torr/18 hours. The material was again placed in a medium Ace-Kau over 4 cm of Florisil (Aldrich 22,074-4) and extracted with 250 mL of cyclohexane for 3 hours. Once all the material had been collected, the pot was cooled to room temperature, the light yellow crystals were isolated by decantation, and dried at 60°/30 torr/18 hours to yield 10.27 g (58%) of **3,** mp 118.5°–120°, *lit.* mp 119°.[6]

9-Acetyl-2,3,6,7-tetrahydro-*1H,5H*-benzo[ij]quinolizine (**4**).- Into a 500 mL, 3-necked round-bottomed flask equipped with magnetic stirring, nitrogen inlet, a thermometer dipping into the solution, a pressure equalizing addition funnel fitted with a septum, and a reflux condenser with Drierite tube, were placed 9-cyanojulolidine (10.27 g, 51.8 mmoles, **3**) and 300 mL of dry ether (Fisher F-138-1), and the suspension was stirred vigorously; the solid did not dissolve completely. Methyllithium solution in ether (1.2 g, 34.2 mL of 1.6M, 55 mmoles, Acros) was transferred *via* double-ended needle to the addition funnel and added dropwise over 1 hour, keeping the temperature below 25°. An orange color developed just after addition of a few mL of the methyllithium and intensified steadily. Once all of the methyllithium had been added, hot water was added to the bath to raise the temperature of reaction mixture to reflux for two hours; the mixture was then allowed to cool to room temperature during 17 hours, then was chilled to 5° in an ice bath. The pressure-equalizing funnel was replaced by another funnel, and 10 mL of water was added dropwise, producing an exothermic reaction to 20°, after which the mixture was again cooled to 10°. Then 28 mL of 6M hydrochloric acid was added dropwise over 15 minutes (exothermic reaction to 18°), and the mixture was allowed to stand at room temperature for 4 hours, after which 150 mL of water was added; the whole allowed to stand overnight and neutralized (pH ~ 8) with sodium carbonate. The resulting orange solid was collected and air-dried for two days to yield 7.07 g of material, mp 57-61°; it was placed in a medium Ace-Kau over 4 cm Silica Gel (Merck 10181) and extracted with 125 mL of 1,1,2-trichlorotrifluoroethane. All material showing a weak blue fluorescence was extracted quickly. The extract was cooled to –20° to deposit 3.67 g (32%) of nice yellow spars, mp 72-73.5° (phase changes at 65° and 69°). IR (Perkin-Elmer 283, 10% in chloroform): 3020 (Ar-H), 2945 (CH_3O), 2845 (R-H), 1650 (C=O), 1592 (C=C), 1569, 1514, 1436, 1358 (CH_3C=O def), 1314 & 1300 (C—N), 1191 (C—N), 1109 (w), 975 (w), 896 (w). ^{1}HNMR (Anasazi Eft-90, $CDCl_3$): δ 1.955 (4H, dd, J: see below, H2,H6), 2.468 (3H, s, -COC$\underline{H}_3$), 2.771 (4H, t, $J_{H1\text{-}H2,H6\text{-}H7}$= 6.3 Hz, H1,H7), 3.273 (4H, t, $J_{H2\text{-}H3,H6\text{-}H6}$= 5.5 Hz, H3,H5), 7.455 (2H, s, H8,H10).

Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 77.97; H, 7.75; N, 6.41.

1-(2,3,6,7-tetrahydro-*1H,5H*-benzo[ij]quinolizine-9-yl)-2-phthalamidoethanone (**6**).- In a 100 mL flask with a stir bar were placed 9-acetyljulolidine (**4**, 3.60 g, 0.0167 mole) and 10 mL of 40% hydrobromic acid. After all base had dissolved, its hydrobromide salt precipitated. To this suspension was added dropwise bromine (0.86 mL, 2.68 g, 0.0167 mol) in 5 mL of 40% hydrobromic acid over 2 hrs. The resulting solution was kept overnite at 20°, treated with 35 mL of water, and the solution was transferred to a 200 mL tall beaker, and diluted with water to 75 mL, then neutralized with excess sodium bicarbonate. The free base was extracted with 35 mL of chloroform, the extract dried over 5 g sodium sulfate, and then evaporated to 4.4 g of a black tar (**5**) at bath temp. 20°.

To this was added 25 mL of DMF and potassium phthalimide (3.49 g, 0.0188 mol). The mixture was heated at 60° for 4 days utilizing a Therm-O-Watch relay, and then quenched in 45 mL of water to give a solid. The reactor was rinsed with 5 mL of methanol, and the combined mixture was stirred 30 min, filtered, the solid washed with a large amount of water, and dried at 100°/20 torr/2 hrs to give 2.93 g of dark rust-colored solid, which was extracted from 2 cm of basic alumina in a medium Ace-Kau with 55 mL of benzene overnight. The dark extract was diluted while hot with 50 mL of heptane and kept at 0°, decanted, and air-dried to give 1.3 g, mp 217-230°. This was recrystallized from 25 mL of 1-butanol, then 50 mL of 1-butanol to give 1.02 g (15%) of **6** as yellow needles, mp 235-237°. ^{1}HNMR on Anaszi Eft-90, 1.7% $CDCl_3$: 1.952 (4H, dd, J: see below, 2xH2", 2xH6"); 2.765 (4H, t, $J_{H1"-H2",H6"-H7"}$ = 6.3 Hz, 2xH1", 2xH6"); 3.286 (4H, t, $J_{H2"-H3",H5"-H6"}$ = 5.67 Hz, 2xH3",2xH5"); 5.018 (2H, s, 2xH1'); 7.468 (2H, s, H8",H10"); 7.7-7.9 (4H, m, AA'BB', H4,H5,H6,H7).

Anal. Calcd for $C_{22}H_{20}N_2O_3$: C, 73.31; H, 5.59; N, 7.77. Found: C, 73.54; H, 5.44; N, 7.84.

2-Amino-1-(2,3,6,7-tetrahydro-*1H,5H*-benzo[ij]quinolizine-9-yl)ethanone Dihydrobromide (**8**).- To a solution of potassium hydroxide (0.192 g of 85%, 0.163 g, 0.00291 mole) in 10 mL of water was added **6** (0.94 g, 0.00261 mole), then 3 mL of 1-propanol, and the mixture was boiled under reflux overnight. The solution was transferred to a beaker, allowed to cool to 20°, and neutralized to pH 4.7 (barely acid to Congo Red) with 6 M hydrochloric acid. The product crystallized slowly; it was collected, washed several times with water and dried at 100°/20 torr/2 hrs to give 0.96g (97%) of tan solid, assumed to be 1-(2,3,6,7-tetrahydro-1H,5H-benzo[ijquinolizine-9-yl)-2-(2-carboxybenzamido)ethanone (**7**), mp 143-146° (dec.).

This solid with 15 mL of 48% hydrobromic acid was boiled under reflux with magnetic stirring overnight. The mixture was cooled to 20° and the precipitated phthalic acid was filtered off, and the filtrate was evaporated to afford a solid, to which 10 mL of toluene was added, and again evaporated. The solid residue was triturated with 25 mL of acetone, collected, washed with acetone and dried as above to yield **8** as a purplish solid, mp 233-237° (dec), 0.72 g (72%). ^{1}HNMR (Anasazi Eft-90, 2.3% in trifluoroacetic acid): 2.505 (4H, br s, H2',H6'); 3.232 (4H, br t, $J_{H1"-H2",\ H6"-H7"}$ = 6 Hz, H1',H6'); 3.778 (4H, br s, H3',H5'); 4.985 (2H, br d, H1); 7.553 (3H, br s, $N\underline{H}_3$); 7.916 (2H, s, H8', H10').

Anal. Calcd for $C_{14}H_{20}Br_2N_2O$: C, 42.88; H, 5.14; N, 7.15. Found: C, 42.78; H, 5.38; N, 7.56

8-Hydroxy-2,3,6,7-tetrahydro-*1H,5H*-benzo[ij]quinolizine (**9**).- A mixture of *m*-anisidine (2.40 moles, 296 g, 270 mL) and 1-bromo-3-chloropropane (9.11 moles, 1433 g, 900 mL.) was heated strongly with magnetic stirring until the first sign of exotherm at 95°. The heating mantle was turned off until the exotherm peaked at 140°, then turned on again for 23 hours, to attain a tempertaure of 142°, then higher voltage was applied for another 21 hours, when the temperature reached 153°. The voltage was reduced and the mixture was allowed to cool overnight to ~ 80° at which point 450 mL of 48% hydrobromic acid was added; then the mixture was boiled under reflux for 3.5 hours, once again allowed to cool to 80°; then 600 mL of toluene was added, and after 5 minutes of stirring, transferred hot to a separatory funnel, and the lower layer was removed, diluted with 1500 mL of water and mechanically stirred while ice was added until the temperature reached 10°; then portions of 500 mL of 50% w/w sodium hydroxide and ice were added alternately below 20°, followed by 600 mL of toluene. The lower aqueous layer was brought to pH 7 with acetic acid, then the sticky solid was collected, air-dried overnight and further at 90°/20 torr/5 hours to give 242 g of crude **9**, mp 129-132°. It was purified by extraction from a 10-cm high column of Davison Grade 62 Silica Gel in a large Ace-Kau with 2 L of 1,1,2-trichlorotrifluoroethane to yield, after cooling at 0°, filtration and drying, 214 g (52%) of **9** as a white solid, mp 132-134°, *lit.* mp 135°.[16]

9-t-Butyl-2,3,6,7-tetrahydro-*1H,5H,11H[1]*-benzo[6,7,8-ij]quinolizin-11-one (**10a**).- To magnetically stirred polyphosphate ester (PPE, 1027 g)[17] at 60° was added a hot solution of 8-julolidinol (**9**, 165 mol, 312 g) in methyl 4,4-dimethylacetoacetate (1.65 mol, 260 g). When the exotherm to 90° subsided, the mixture was heated at 130° for 3 hrs, allowing volatiles to distill, then, after it had cooled to 120°, the mixture was quenched in 2.1 L each of ice and methanol, collected, washed with 1 L of 1:1 v/v methanol:water and dried at 60°/30 torr/18 hrs with a final 2 hrs at 100° to give 71 g (14.5% crude). Crude **10a** dissolved in 350 mL of chloroform was stirred with 5 g of carbon (Fisher C-170), filtered, and the filtrate was poured through a column of 71 g of Davison Grade 62 Silica Gel, followed by 2x350 mL of chloroform. All eluate was evaporated and the yellow solid was recrystallized from a mixture of 300 mL of methanol and 100 mL of abs. ethanol at -20°. The supernatant liquor was decanted, and the large spars were washed with 300 mL of methanol and dried as before to give 60.8 g (12.4%), mp 186-189° (phase-change at 179°). The liquor and washings were concentrated to give a second crop which was recrystallized twice from 125 mL portions of methanol to yield 5.1 g (1%) of product with a similar mp. UV (95% ethanol) 218 nm (e = 34,000), 249 (11,000), 388 (20,000); IR (KBr) 2920, 2870, 2820, 1692, 1603, 1350, 1315, 1155 cm^{-1}. Fluorescence at 10^{-5} M: in hexane, exc 359, 375 nm, emission 411 nm; in ethyl acetate, exc 375, emission 442; in DMF, exc 390, emission 460; in 95% ethanol, exc 390, emission 473; all emission very strong. *Anal.* Calcd for $C_{19}H_{23}NO_2$: C, 76.73; H, 7.79; N, 4.71. Found: C, 76.71; H, 7.95; N, 4.86

9-Phenyl-2,3,6,7-tetrahydro-*1H,5H,11H[1]*-benzo[6,7,8-ij]quinolizin-11-one (10b).- The procedure for **10a** was followed with 8-julolidinol (**9**) and methyl benzoylacetate to give 33% of crude **10b**, mp 141-143°. Extraction from alumina and silica gel in an Ace-Kau with dichloromethane, evaporation, and recrystallization of the residue from methanol at 0° gave 27% as dark yellow prisms, mp 143.5-145°. UV (95% ethanol) 218 nm (e = 36,100), 271 (18,200), 406 (21,400); IR (KBr) 2930, 2830, 1688, 1600, 1360, 1310, 1137 cm^{-1}. Fluorescence (10^{-5} M, 95% ethanol), exc 397 nm, emission 526 nm, weak.

9-Formyl-8-hydroxy-2,3,6,7-tetrahydro-*1H,5H*-benzo[ij]quinolizine (11).- The procedure above for the deshydroxy analog **1** was followed, including a 2-hour period on a steam bath and an overnight hydrolysis period with sodium acetate, to give 89-90% of **11** as yellow granules, mp 68-70°. Recrystallization from a small volume of methanol at –17° raised the mp to 70.5-71.5°, *lit.* mp 70-72°.[18] ^{1}HNMR (60 MHz, 10% in $CHCl_3$): 1.92 (4H, dd, $NCH_2C\underline{H}_2CH_2$), 2.63 (4H, t, J = 6 Hz, $NCH_2CH_2C\underline{H}_2$), 3.23 (4H, t, J = 6 Hz, $NC\underline{H}_2CH_2CH_2$), 6.78 (1H, s, H10), 9.34 (1H, s, C<u>H</u>O), 11.71 (1H, s, O<u>H</u>).

Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.86; H, 6.96; N, 6.45. Found: C, 71.39; H, 6.68; N, 6.15

Active Esters.- Ethyl 2-benzothiazoleacetate was prepared as described,[19] but using mechanical stirring, in up to 94% yield. Ethyl 2-benzoxazoleacetate could not be prepared by the methods of van Dormael,[20] Barnikow *et al.*,[21] or Gorbatov;[22] but the method of Wamhoff *et al.*[23] gave a quantitative yield of oily product, which could be used when crude, and which crystallized after 8 months, mp 55-59° (*lit.* mp 56-57°).[23] Methyl methylsulfonylacetate was prepared as described.[24] Ethyl phenylacetate was was redistilled before use. Methyl phenylsulfonylacetate was prepared as described[25] except that 2-methoxyethanol at reflux for 2 hours was substituted for DMF based on a study.[26] The crude amber oil was used directly. Methyl 2-pyridylacetate was obtained from K & K Labs. and redistilled, bp 98-118°/30 torr. Ethyl 3-pyridylacetate, Aldrich E4,725-5, was used as received. Diethyl malonate was used as received from MC&B.

10-Substituted-2,3,6,7-tetrahydro-*1H,5H,11H[1]*-benzo[6,7,8-ij]quinolizin-11-ones (12a-i).- The reported procedure for the 10-nitro analog[27] gave crude products which were purified, and whose solvents, yields, assays, and UV spectral data are shown in **Table 1**.

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TABLE 1. Yields and Physical Constants of Coumarins **12a-i**

Cmpd	Solvent[a]	Yield (%)	mp (°C)	Elemental Analyses: Calc/(Found) C	H	N	Absorption λ max in nm (e x 10^{-3})[b]
12a	DMF	77	251-254	70.57 (70.82)	4.85 (4.62)	7.48 (7.59)	214 (64.8); 306 (16.5); 480 (87.0)
b	1-BuOH	80	276-278	73.73 (73.88)	5.06 (4.91)	7.82 (7.90)	203 (37.1); 302 (12.2); 465 (56.8)
c	2-PrOH	75	191.5-193	60.17 (60.07)	5.37 (5.27)	4.39 (4.43)	217 (31.9); 264 (8.7); 433 (43.4)
d	MeOH	10	172-173.5	79.47 (79.77)	6.03 (5.75)	4.41 (4.49)	216 (33.8); 277 (11.4); 416 (32.5)
e	MeCN[d]	41	270-273 dec	66.16 (66.12)	5.02 (4.94)	3.67 (3.64)	211 (50.6); 439 (50.7)
f	EtOAc[d]	31	214-216 dec	75.45 (75.91)	5.70 (5.25)	8.80 (8.88)	212 (33.2); 279 (10.2) 436 (39.0)
g	1-PrOH	61	164-165	75.45 (75.68)	5.70 (5.45)	8.80 (9.01)	210 (46.4); 276 (11.7); 426 (35.8)
h	EtOAc[c]	23	255-258 dec	75.45 (75.56)	5.70 (5.49)	8.80 (9.13)	211 (35.1); 277 (8.5); 438 (39.6)
i	Freon TF[f,g]	42	146.5-147	68.99 (68.99)	6.11 (5.95)	4.47 (4.25)	216 (31.5); 267 (8.5); 433 (47.0)g

a) Recrystallization solvent. b) In 95% ethanol. c) Extracted using Soxhlet extractor. d) Extracted from Davison Grade 62 Silica Gel in an Ace-Kau. e) Extracted from neutral alumina in an Ace-Kau. f) Extracted from Davison Grade 62 Silica Gel and neutral alumina in an Ace-Kau with 1,1,2-trichlorotrifluoroethane. g) ^{1}H NMR (60 MHz, 10% in $CHCl_3$): 1.36 (3H, t, J = 6 Hz, $C\underline{H}_3CH_2$-), 1.98 (4H, dd, $NCH_2C\underline{H}_2CH_2$), 2.80 (4H, t, J = 6 Hz, $NCH_2CH_2C\underline{H}_2$), 3.31 (4H, t, J = 6 Hz, $NC\underline{H}_2CH_2CH_2$), 4.33 (2H, q, $CH_3C\underline{H}_2$-),6.86 (1H, s, H8), 8.24 (1H, s, H9). h) Ref. 28.

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