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Photochemical Synthesis of 1,2,3,4-Tetrahydroisoquinolin-3-ones and Oxindoles from N-Chloroacetyl Derivatives of Benzylamines and Anilines. Role of Intramolecular Exciplex Formation and *cis* Conformation of Amide Bonds[1)]

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Although *N*-chloroacetyl derivatives of benzylamines (**2**, **8**) and anilines (**21**, **25**, **29**) disappeared quite rapidly when irradiated with a high pressure mercury lamp, no photocyclization to six- and five-membered lactams occurred. Measurements of fluorescence quenching and disappearance quantum yields of *N*-chloroacetyl-(3,4-dimethoxylphenyl)-alkylamines having various lengths of alkyl chain revealed that the shorter the alkyl chain is, the more efficient the exciplex formation is. Therefore, the failure of photocyclization seemed to be due to *trans* conformation of amide bonds in the benzylamine and aniline derivatives. Introduction of an alkyl group on the amide nitrogen changed the stable conformation of amides from *trans* to *cis*, and hence *N*-alkyl-*N*-chloroacetylbenzylamines (**11**, **13**, **15**, **17**, **19**) readily gave the corresponding 1,2,3,4-tetrahydroisoquinolin-3-ones (**12**, **14**, **16**, **18**, **20**) on irradiation. Oxindoles (**36**, **38**, **40**, **41**, **43**, **46**) were similarly synthesized by photocyclization of *N*-alkyl-*N*-chloroacetylanilines (**35**, **37**, **39**, **42**, **45**).

Keywords——photocyclization; 1,2,3,4-tetrahydroisoquinolin-3-ones; oxindoles; fluorescence quenching; exciplex; quantum yield; *cis*-conformation of amide bond

Many heterocyclic compounds have been synthesized by photocyclization of *N*-chloroacetyl derivatives of pharmacodynamic amines and aromatic amino acids;[2)] a typical example is the synthesis of seven-membered lactams, benzazepinones, from *N*-chloroacetyl derivatives of phenethylamines having electron-donating substituents.[3)] Homologous compounds, eight-, nine-, and ten-membered lactams, have also been synthesized from phenylpropylamine, phenylbutylamine, and phenylpentylamine derivatives, respectively.[4)] On the other hand, the synthesis of five- and six-membered lactams from aniline and benzylamine derivatives, though expected to be easily achievable, has not been successful, except for the photocyclization of phenolic benzylamine derivatives.[5)] Many physicochemical and mechanistic studies have revealed a common mechanism in the photocyclizations of *N*-chloroacetylamines involving intramolecular electron transfer or exciplex formation between excited singlet states of electron-donating aromatic chromophores and electron-deficient chloroacetyl moieties.[6)] The failure to synthesize the five- and six-membered lactams, therefore, has been assumed to result from incomplete formation of the electron donor-acceptor pair or exciplex, which must require a perfectly overlapping sandwich conformation.[7)] In order to determine whether this assumption is correct and also to develop a synthetic method for five- and six-membered lactams, we have now examined the intramolecular fluorescence quenching and disappearance quantum yields of a series of amine derivatives. The above assumption was found to be incorrect.

Fluorescence Quenching and Disappearance Quantum Yield

Intermolecular quenching of the fluorescence of many electron-rich aromatics such as anisole, dimethoxybenzenes, and indole by methyl chloroacetate and chloroacetamide was found to involve exciplex formation,[6a)] whose efficiency is reflected in the extent of quenching.

The *N*-acetylphenethylamine (**1**) in 50% aqueous acetonitrile has strong fluorescence with a maximum at 310 nm (excitation at 282.5 nm), identical to that of 1,2-dimethoxybenzene.[8] The *N*-chloroacetylbenzylamine (**2**) also has the same emission, but with less than 1/20 of the intensity. This intramolecular quenching is clearly attributable to electron donor-acceptor pair or exciplex formation. The homologous *N*-chloroacetyl derivatives (**3**—**6**) exhibit similar behavior, and the relative fluorescence intensities of **2**—**6** with respect to that of **1** are plotted against the number of methylene groups (*n*) in Fig. 1, which indicates that the efficiency of exciplex formation depends only on the distance between the aromatic chromophore and the chloroacetyl moiety, and not on the geometrical restriction (sandwich conformation). Therefore, there must be a different reason for the failure to obtain the five- and six-membered lactams.

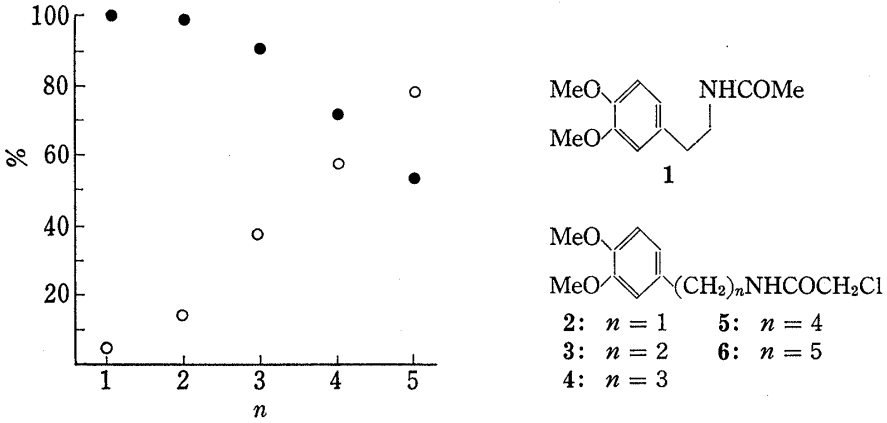


Fig. 1. a) The Ratio (%) of Fluorescence Intensities of **2**—**6** to that of **1** *vs.* *n* (○); b) The Ratio (%) of Disappearance Quantum Yields of **2**—**6** to that of **2** *vs.* *n* (●)

Quantum yield measurements for the disappearance of **2**—**6** supported this conclusion. Aqueous acetonitrile (50%) solutions of **2**—**6** and the 1,3-dimethyluracil actinometer[9] in quartz test tubes were irradiated with a 60 W low pressure mercury lamp on a "merry-go-round" apparatus. Disappearance of **2**—**6** was quantitatively followed by gas chromatography and the disappearance quantum yields were determined relative to the actinometer,[9] as also plotted in Fig. 1, which again indicates that **2** is photochemically most reactive, though no cyclization product has been isolated. Actually, on irradiation in aqueous ethanol **2** disappeared rapidly and **7** was the only isolable product. Under similar conditions, the isomeric *N*-chloroacetylbenzylamine (**8**) gave not a cyclization product, but the acetate (**9**), the dimer (**10**), and polymers.

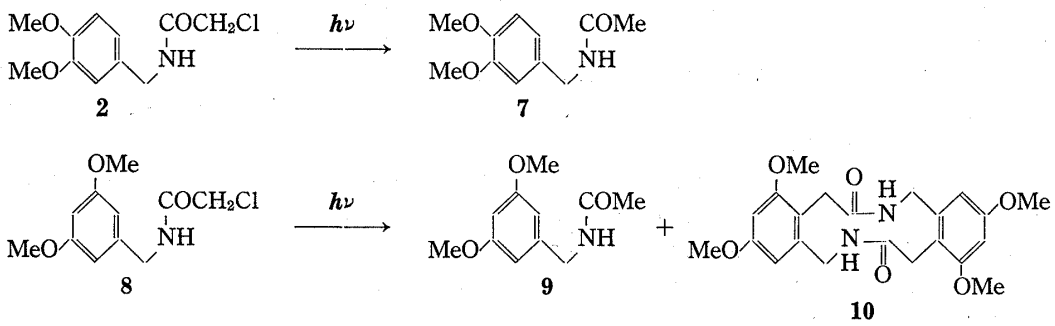
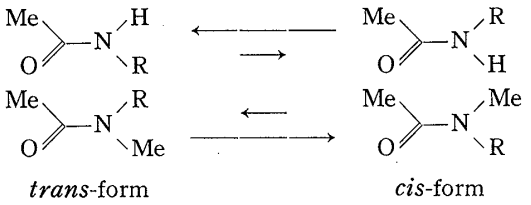


Chart 1

Synthesis of 1,2,3,4-Tetrahydroisoquinolin-3-ones

Extensive studies by nuclear magnetic resonance (NMR) spectroscopy have revealed that *N*-monosubstituted acetamides exist almost exclusively as *trans* isomers with a barrier to rotation around the amide bond.[10,11] Therefore, the short-lived biradical cationic intermediate (**i**) with the *trans* form cannot cyclize to a six-membered lactam unless it has a life-time long enough for rotation to the *cis* form.

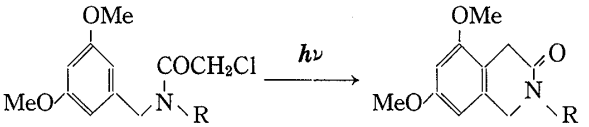
On the other hand, in unsymmetrical *N*,*N*-disubstituted acetamides the preferred isomer has the bulkier substituent *trans* to the methyl group on the carbonyl carbon,[12] because the most stable isomer is in general that in which steric repulsion between the alkyl group on the carbonyl carbon and the substituents on nitrogen is minimized. Therefore, introduction of a bulky substituent (R) on the nitrogen in **8** may lead to fixation of the amide group in the *cis* form between the chloromethyl group and the dimethoxybenzyl group; on irradiation, the *N*-alkylated compounds may then cyclize to isoquinoline derivatives.



trans-form *cis*-form

i

Chart 2



11: R=CH(C$_6$H$_5$)$_2$ **12** (17%)
13: R=CH$_2$C$_6$H$_5$ **14** (27%)
15: R=CH$_2$CH$_2$C$_6$H$_5$ **16** (31%)
17: R=Me **18** (40%)
19: R=CMe$_3$ **20** (63%)

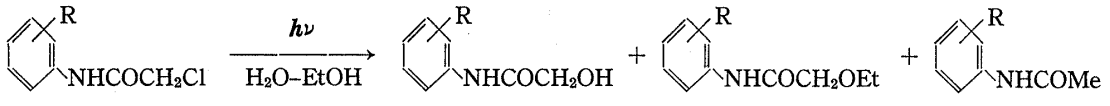
Chart 3

The *N*-tritylamine was first synthesized, but its N-chloroacetylation was unsuccessful, and hence photocyclization of the *N*-benzhydryl-*N*-chloroacetyl compound (**11**), synthesized easily from 3,5-dimethoxybenzylamine,[13] was examined. When a 50% aqueous acetonitrile solution of **11** was irradiated with a 100 W high pressure mercury lamp for 1 hr, the expected cyclization occurred to give the isoquinoline-3-one (**12**), though only in 17% yield. The presence of a highly reactive benzylic hydrogen in **11** presumably caused undesirable side reactions. *N*-Benzyl (**13**) and *N*-phenethyl derivatives (**15**) gave somewhat improved results. Under similar conditions, the *N*-methyl compound (**17**), which, though presumably present in both the *cis* and *trans* forms, has no benzylic hydrogen, also gave the corresponding cyclization product (**18**) in a better yield. Finally, the highly hindered *N*-*t*-butyl compound (**19**) cyclized more smoothly to the expected product (**20**) in 63% yield.

Synthesis of Oxindoles

These photocyclizations have been extended to the synthesis of oxindoles. By analogy with **2** and **8**, aniline derivatives gave only side-chain substitution products, and not cyclization products. Thus, on irradiation in aqueous ethanol, *N*-chloroacetyl derivatives of *o*- (**21**), *m*- (25), and *p*-anisidines (**29**) gave mainly the corresponding *N*-glycoloyl compounds (**22**, **26**, **30**) with an accompanying formation of *N*-ethoxyacteyl (**23**, **27**, **31**) and *N*-acetyl compounds (**24**, **28**, **32**), and no detectable formation of cyclization products was observed.

Acetanilide (**33**) is known to exist as the *trans* isomer almost exclusively,[14] and hence *N*-chloroacetylanisidines (**21**, **25**, **29**) could not cyclize to oxidoles. The formation of the *N*-glycoloyl compounds (**22**, **26**, **30**) can be explained as shown in Chart 5. The α-lactams (**iv**) must be transient species, which are subject to hydrolysis to the *N*-glycoloyl compounds, corresponding to alkyl-nitrogen bond fission.[15] Kumar *et al.* also obtained similar results in the photolysis of an *N*-chloroacetanilide derived from podocarpic acid.[16]



21: R=2-OMe
25: R=3-OMe
29: R=4-OMe

22 (47%)
26 (37%)
30 (37%)

23 (3%)
27 (2%)
31 (9%)

24 (10%)
28 (11%)
32 (11%)

Chart 4

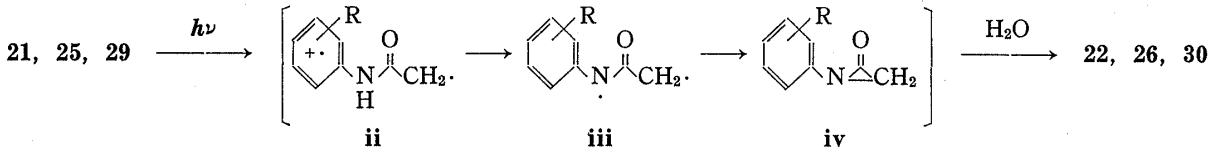


Chart 5

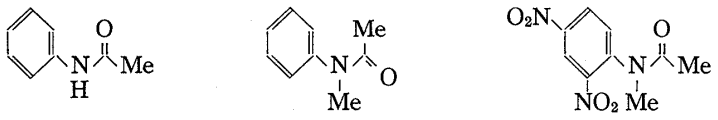
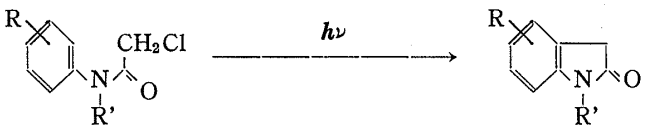


Chart 6

Introduction of a methyl group on the nitrogen in acetanilide is known to change dramatically the preferred conformation of the amide bond from the *trans* form to the *cis* form, whose content in the case of *N*-methylacetanilide (**34**) is 95%.[14] Therefore, *N*-methylchloroacetanilides are expected to give oxindole derivatives. On irradiation, *N*-chloroacetyl-*N*-methyl-*p*-anisidine (**35**) readily gave 5-methoxy-1-methyloxindole (**36**) in 55% yield. The 1-benzyloxindole (**38**) was similarly obtained in 67% yield. The *m*-anisidine derivative (**39**) cyclized more smoothly and gave 6-methoxy- (**40**) and 4-methoxy-1-methyloxindoles (**41**) in 66% and 6% yields, respectively. The *o*-anisidine derivative (**42**) also gave the corresponding product, 7-methoxy-1-methyloxindole (**43**), but the yield was only 20%. This may be explained in terms of a decrease in the content of the *cis* isomer. Actually, in *o*-substituted acetanilides the *cis* isomer fraction decreases because of steric interaction. For example, **44** is 37% *cis* and 63% *trans*.[17] Finally, even an aniline derivative (**45**) having no electrondonating methoxy group gave 1-methyloxindole (**46**), though in a poor yield.



35: R=4-OMe, R'=Me
37: R=4-OMe, R'=$CH_2C_6H_5$
39: R=3-OMe, R'=Me
42: R=2-OMe, R'=Me
45: R=H, R'=Me

36: R=5-OMe, R'=Me (55%)
38: R=5-OMe, R'=$CH_2C_6H_5$ (67%)
40: R=6-OMe, R'=Me (66%)
41: R=4-OMe, R'=Me (6%)
43: R=7-OMe, R'=Me (20%)
46: R=H, R'=Me (15.4%)

Chart 7

Experimental

***N*-Chloroacetyl-3-(3,4-dimethoxyphenyl)propylamine** (**4**)——A THF (250 ml) solution of $LiAlH_4$ (5 g, 0.13 mol) in a 1 l flask equipped with a Soxhlet extractor and containing 3-(3,4-dimethoxyphenyl)propionamide[18] (13.7 g, 65.5 mmol) in its thimble was heated under reflux for 3.5 hr. The flask was cooled in an ice bath and water (5 ml) was then added dropwise to decompose excess hydride. After removal of the

precipitate by filtration, the filtrate was concentrated to leave an oil, which was dissolved in acetone (70 ml) and mixed with 40% aqueous K_2CO_3 (25 ml). The mixture was cooled on an ice bath and chloroacetyl chloride (9.85 g, 87 mmol) was then added dropwise with vigorous stirring. The stirring was continued for 40 min at 0° and then for 30 min at room temperature. The acetone was removed *in vacuo* and the resulting mixture was extracted with benzene. The extracts were washed with saturated NaCl solution, dried (Na_2SO_4), and concentrated to leave a solid, which was recrystallized from benzene–ether–hexane to give **4** (11.07 g, 62%), mp 88.5—90°. IR ν_{max}^{Nujol} cm^{-1}: 3360, 1650. MS *m/e* (%): 273 (28), 271 (M^+, 80), 178 (38), 165 (32), 151 (100). NMR ($CDCl_3$) δ: 1.88 (2H, quintet, $J=7$ Hz), 2.63 (2H, t, $J=7$ Hz), 3.35 (2H, q, $J=7$ Hz), 3.86 (3H, s), 3.88 (3H, s), 4.03 (2H, s), 6.52 (1H, br. s), 6.72 (1H, d, $J=2$ Hz), 6.73 (1H, dd, $J=2$, 8 Hz), 6.80 (1H, d, $J=8$ Hz). *Anal.* Calcd for $C_{13}H_{18}ClNO_3$: C, 57.46; H, 6.68; N, 5.15; Cl, 13.05. Found: C, 57.65; H, 6.60; N, 5.24; Cl, 13.08.

***N*-Chloroacetyl-4-(3,4-dimethoxyphenyl)butylamine (5)**——A THF (300 ml) solution of 4-(3,4-dimethoxyphenyl)butyramide[19] (10 g, 42.2 mmol) was added dropwise to a boiling, stirred ether (100 ml) solution of $LiAlH_4$ (5 g, 0.132 mol) for 40 min. After a further 1.5 hr, the mixture was cooled in an ice bath, and 2 N NaOH (35 ml) was then added dropwise for 15 min to decompose excess hydride. After removal of the precipitate by filtration, the filtrate was concentrated to leave an oil, which was dissolved in benzene (200 ml), and the benzene solution was extracted with 10% HCl. The HCl extracts were made alkaline with 25% NaOH and extracted with CH_2Cl_2. After concentration of the extracts to *ca.* 300 ml, 10% Na_2CO_3 solution (100 ml) and then chloroacetyl chloride (4.4 ml, 46 mmol) were added dropwise with stirring and cooling at 0°. The stirring was continued for 30 min at room temperature, and the CH_2Cl_2 layer was separated, combined with CH_2Cl_2 extracts of the aqueous layer, dried (Na_2SO_4), and then concentrated to leave a solid, which was recrystallized from hexane to give **5** (7.1 g, 56%), mp 85—86°, or mp 88° after sublimation. IR ν_{max}^{Nujol} cm^{-1}: 3270, 1660. MS *m/e* (%): 287 (8), 285 (M^+, 25), 164 (13), 151 (100). NMR ($CDCl_3$) δ: 1.4—1.8 (4H, m), 2.60 (2H, t, $J=7$ Hz), 3.33 (2H, q, $J=7$ Hz), 3.86 (3H, s), 3.88 (3H, s), 4.05 (2H, s), 6.55 (1H, br. s), 6.71 (1H, d, $J=2$ Hz), 6.72 (1H, dd, $J=2$, 8 Hz), 6.80 (1H, d, $J=8$ Hz). *Anal.* Calcd for $C_{14}H_{20}ClNO_3$: C, 58.84; H, 7.05; N, 4.90; Cl, 12.41. Found: C, 58.71; H, 7.09; N, 4.93; Cl, 12.61.

***N*-Chloroacetyl-5-(3,4-dimethoxyphenyl)pentylamine (6)**——The compound **6** was synthesized from 5-(3,4-dimethoxyphenyl)valeramide (mp 106°; 5 g, 21 mmol), prepared from the corresponding chloride[20] and NH_3, as described in the foregoing experiment. Yield 4.744 g (75%), mp 75—76° (EtOH–H_2O), or mp 76° after sublimation. IR ν_{max}^{Nujol} cm^{-1}: 3290, 1660. MS *m/e* (%): 301 (13), 299 (M^+, 30), 151 (100). NMR ($CDCl_3$) δ: 1.28—1.46 (2H, m), 1.50—1.78. (4H m), 2.56 (2H, t, $J=7$ Hz), 3.30 (2H, q, $J=7$ Hz), 3.86 (3H, s), 3.87 (3H, s), 4.04 (2H, s), 6.54 (1H, br. s), 6.68 (1H, d, $J=2$ Hz), 6.69 (1H, dd, $J=2$, 8 Hz), 6.78 (1H, d, $J=8$ Hz). *Anal.* Calcd for $C_{15}H_{22}ClNO_3$: C, 60.09; H, 7.40; N, 4.67; Cl, 11.83. Found: C, 60.02; H, 7.49; N, 4.73; Cl, 12.11.

Measurement of Fluorescence Intensities of 2—6——Sample solutions for fluorescence measurements (Hitachi MPF-2A fluorescence spectrometer) were prepared by dissolving **1**—**6** (*ca.* 1 mg, purified by both recrystallization and sublimation) in spectro-grade 50% aqueous MeCN (100 ml). Fluorescence intensities of the sample solutions were determined by dividing the peak heights at the wavelength (310 nm) of maximum emission by the optical densities of the corresponding samples at the excitation wavelength (282.5 nm). Relative fluorescence intensities of **2**—**6** with respect to that of **1** were as follows: **2**, 4%; **3**, 13.4%; **4**, 37.1%; **5**, 58.7%; **6**, 76.9%; **1**, 100%).

Measurement of Disappearance Quantum Yields of 2—6——Sample solutions (0.01 M, 5 ml) in 50% aqueous MeCN containing $NaHCO_3$ (5 mg) and an aqueous solution (0.939 mM, 5 ml) of dimethyluracil as an actinometer[9] were irradiated simultaneously in quartz test tubes with 253.7 nm light from a 60 W low pressure mercury lamp (EL-J-60, Eiko-sha, Osaka) for 15 min on a "merry-go-round" apparatus. After being mixed with an EtOAc solution (0.01 M, 1 ml) of ethyl 3-(3,4-dimethoxyphenyl)propionate as an internal standard for GLC, aliquots (1 ml) of sample solutions were concentrated to dryness *in vacuo*, and then the residues were dissolved in EtOAc (0.5 ml) and analyzed quantitatively by GLC (Shimadzu GC-4A gas chromatograph with FID detector; column, 1.5% OV-17, 2 m; column temperature, 170—250° (15°/min); N_2 (carrier gas) flow rate, 60 ml/min). Disappearance quantum yields of **2**—**6** were determined relative to the dimethyluracil actinometer ($\phi=0.013$),[9] and the results were as follows: **2**, 0.37; **3**, 0.37; **4**, 0.33; **5**, 0.27; **6**, 0.21.

Photolysis of 2——An H_2O–EtOH (9: 1) solution (300 ml) of *N*-chloroacetyl-3,4-dimethoxybenzylamine (**2**)[21] (730.5 mg, 3 mmol) was irradiated with a 100 W high pressure lamp (EHB-WU-100, Eiko-sha, Osaka) for 5 hr under nitrogen. The solution was stirred with excess Ag_2CO_3 to remove chloride ions and the silver salts were then removed by filtration through a Büchner funnel containing a matting of Celite filter aid. The filtrate was concentrated *in vacuo*, and extracted with EtOAc. The extracts were dried (Na_2SO_4) and concentrated to leave an oil, which was chromatographed on a silica gel column to give recovered **2** (35 mg) and *N*-acetyl-3,4-dimethoxybenzylamine (**7**; 120 mg, 19%).[22] Recrystallization from benzene–hexane gave colorless needles, mp 89—90°. IR ν_{max}^{Nujol} cm^{-1}: 3300, 1635. NMR ($CDCl_3$) δ: 2.10 (3H, s), 3.95 (6H, s), 4.40 (2H, d, $J=6$ Hz), 6.85 (3H, s). *Anal.* Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69. Found: C, 63.24; H, 7.25; N, 7.04.

***N*-Chloroacetyl-3,5-dimethoxybenzylamine (8)**——Chloroacetyl chloride (2.26 g, 20 mmol) in CH_2Cl_2

(10 ml) was added dropwise over a 20 min period to a stirred and cooled (0°) solution of 3,5-dimethoxybenzylamine[13] (1.67 g, 10 mmol) in a mixture of CH_2Cl_2 (30 ml) and saturated $NaHCO_3$ solution (50 ml). Stirring was continued for 2 hr at room temperature, then the CH_2Cl_2 layer was separated, combined with CH_2Cl_2 extracts of the aqueous layer, washed with 10% HCl and saturated $NaHCO_3$ and NaCl solutions, dried (Na_2SO_4), and concentrated to leave a solid (2.5 g). Recrystallization from hexane–EtOAc gave **8** (2.1 g, 86%), mp 112—113°. IR ν_{max}^{Nujol} cm^{-1}: 3230, 1650, 1600. MS *m/e* (%): 245 (26), 243 (M^+, 77), 218 (100), 167 (29), 166 (67), 165 (27), 151 (30), 139 (33). NMR ($CDCl_3$) δ: 3.79 (6H, s), 4.11 (2H, s), 4.43 (2H, d, J=6 Hz), 6.43 (3H, br. s), 6.84 (1H, br. s). *Anal.* Calcd for $C_{11}H_{14}ClNO_3$: C, 54.22; H, 5.79; N, 5.75; Cl, 14.55. Found: C, 54.44; H, 5.72; N, 5.87; Cl, 14.28.

Photolysis of 8——A solution of **8** (1 g, 4.1 mmol) and $NaHCO_3$ (1 g, 12 mmol) in MeCN (150 ml) and H_2O (200 ml) was irradiated with the 100 W lamp for 1 hr under nitrogen. The resulting precipitate was a colorless powder: 2,4,10,12-tetramethoxy-5,6,7,8,13,14,15,16-octahydrodibenzo[*c*,*i*]-1,7-diazacyclododecine-6,17-dione (**10**; 74 mg, 9%), mp >320°. IR ν_{max}^{Nujol} cm^{-1}: 3260, 1650. MS *m/e* (%): 414 (M^+, 16), 207 (55), 206 (29), 164 (100), 151 (13).[23]

The filtrate was concentrated to *ca.* 50 ml and extracted with EtOAc. The extracts were washed with saturated NaCl solution, dried (Na_2SO_4), and concentrated to leave an oil, which was chromatographed on a silica gel column with EtOAc–CH_2Cl_2 (1: 1) to give *N*-acetyl-3,5-dimethoxybenzylamine (**9**; 43 mg, 5%), mp 105—105.5° (benzene). IR ν_{max}^{Nujol} cm^{-1}: 3250, 1625, 1595. MS *m/e* (%): 209 (M^+, 60), 166 (100), 152 (20), 151 (20), 150 (15), 139 (34), 124 (30). NMR ($CDCl_3$) δ: 2.03 (3H, s), 3.78 (6H, s), 4.36 (2H, d, J=6 Hz), 5.72 (1H, br. s), 6.32—6.48 (3H, m). *Anal.* Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69. Found: C, 63.00; H, 7.21; N, 6.72.

***N*-Benzhydryl-*N*-chloroacetyl-3,5-dimethoxybenzylamine** (**11**)——An anhydrous MeCN (30 ml) solution of 3,5-dimethoxybenzylamine[13] (2 g, 12 mmol), benzhydryl chloride (3.3 g, 16 mmol), and Et_3N (1.6 g, 16 mmol) was heated under reflux for 15 hr. After removal of the solvent, the residue was dissolved in CH_2Cl_2 (70 ml) and mixed with Na_2CO_3 (8 g) in H_2O (70 ml), then chloroacetyl chloride (2.1 ml, 26 mmol) was added with stirring and cooling at 0°. Stirring was continued for 1 hr at room temperature, then the CH_2Cl_2 layer was separated, combined with CH_2Cl_2 extracts of the aqueous layer, washed with 10% HCl and saturated $NaHCO_3$ and NaCl solutions, dried (Na_2SO_4), and concentrated. The residue was purified by passage through a silica gel column. Elution with hexane–EtOAc (5: 1) and recrystallization of the product from hexane–EtOAc gave colorless prisms of **11** (2.35 g, 48%), mp 107—108°. IR ν_{max}^{Nujol} cm^{-1}: 1650. MS *m/e* (%): 409 (M^+, 3), 257 (45), 242 (30), 151 (100). NMR ($CDCl_3$) δ: 3.60 (6H, s), 3.98 (2H, s), 4.66 (2H, s), 5.89 (2H, br. s), 6.81 (1H, t, J=2 Hz), 7.26 (11H, br. s). *Anal.* Calcd for $C_{24}H_{24}ClNO_3$: C, 70.32; H, 5.90; N, 3.42; Cl, 8.65. Found: C, 70.37; H, 5.85; N, 3.49; Cl, 8.87.

***N*-Benzyl-*N*-chloroacetyl-3,5-dimethoxybenzylamine** (**13**)——*N*-Benzyl-3,5-dimethoxybenzylamine hydrochloride[24] (4.3 g, 14.7 mmol) was converted to **13** (4.39 g, 90%) as described above. Colorless oil. IR ν_{max}^{neat} cm^{-1}: 1660. MS *m/e* (%): 335 (7), 333 (M^+, 20), 257 (45), 242 (30), 151 (100). NMR ($CDCl_3$) at 60° δ: 4.11 (6H, s), 4.12 (2H, s), 4.49 (2H, br. s), 4.58 (2H, br. s), 6.3—6.4 (3H, m), 7.2—7.4 (5H, m).

***N*-Phenethyl-3,5-dimethoxybenzamide**——A solution of 3,5-dimethoxybenzoyl chloride[25] (10 g, 50 mmol) in CH_2Cl_2 (20 ml) was added dropwise to a stirred and cooled (0°) mixture of phenethylamine (6.1 g, 50 mmol) in CH_2Cl_2 and Na_2CO_3 (3.2 g, 30 mmol) in H_2O (15 ml). The CH_2Cl_2 layer was separated, combined with CH_2Cl_2 extracts of the aqueous layer, washed with 10% HCl and saturated $NaHCO_3$ and NaCl solutions, dried (Na_2SO_4), and concentrated to leave a solid (14.2 g, 98%), mp 75—77° (CH_2Cl_2–CCl_4). IR ν_{max}^{Nujol} cm^{-1}: 3290, 1635, 1550, 1535. MS *m/e* (%): 285 (M^+, 90), 194 (15), 181 (40), 165 (100). NMR ($CDCl_3$) δ: 2.91 (2H, t, J=6.5 Hz), 3.66 (2H, t, J=6.5 Hz), 3.79 (6H, s), 6.08 (1H, br. s), 6.55 (1H, t, J=2 Hz), 6.80 (2H, d, J=2 Hz), 7.1—7.5 (5H, m). *Anal.* Calcd for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71; N, 4.91. Found: C, 71.25; H, 6.69; N, 4.81.

Phenethyl-3,5-dimethoxybenzylamine——The foregoing amide (1 g, 3.5 mmol) in THF (10 ml) was added dropwise to a boiling, stirred solution of $LiAlH_4$ (0.4 g, 10.5 mmol) in THF (20 ml). The solution was stirred and refluxed for 2 hr after the addition, and then cooled at 0° in an ice bath. 2 N NaOH (1.3 ml) was added dropwise over a period of 15 min to the cooled solution, and the precipitated inorganic salts were removed by filtration. The filtrate was concentrated to leave an oil, which was dissolved in ether and treated by the dropwise addition of saturated methanolic HCl to precipitate the hydrochloride (829 mg, 78%), colorless needles, mp 155—156° (H_2O). IR ν_{max}^{Nujol} cm^{-1}: 1610, 1595. MS *m/e* (%): 271 (M^+—HCl, 5), 180 (55), 151 (100). NMR (D_2O) δ: 3.08 (2H, t, J=6.5 Hz), 3.30 (2H, t, J=6.5 Hz), 3.80 (6H, s), 4.15 (2H, s), 6.62 (3H, s), 7.1—7.5 (5H, m). *Anal.* Calcd for $C_{17}H_{22}ClNO_2$: C, 66.33; H, 7.20; N, 4.55; Cl, 11.52. Found: C, 66.67; H, 7.13; N, 4.66; Cl, 11.63.

***N*-Chloroacetyl-*N*-phenethyl-3,5-dimethoxybenzylamine** (**15**)——The hydrochloride (1.5 g, 4.9 mmol) was converted to **15** (1.5 g, 87%) as described above.

Colorless oil, IR ν_{max}^{neat} cm^{-1}: 1660. MS *m/e* (%): 349 (5), 347 (M^+, 16), 243 (20), 151 (100). NMR (DMSO-d_6) at 70° δ: 2.83 (2H, t, J=7 Hz), 3.50 (2H, t, J=7 Hz), 3.73 (6H, s), 4.25 (2H, s), 4.49 (2H, s), 6.41 (3H, s), 7.24 (5H, s).

***N*-Chloroacetyl-*N*-methyl-3,5-dimethoxybenzylamine** (**17**)——An EtOH (50 ml) solution of 3,5-dimethoxybenzaldehyde[26] (2 g, 12 mmol) and a 40% aqueous $MeNH_2$ solution (4.7 ml) were mixed and allowed

to stand at room temperature overnight. $NaBH_4$ (460 mg, 12 mmol) was added to the solution with stirring, and after 1 hr, the solvent was evaporated off to leave an oil which was dissolved in 10% HCl (130 ml). The solution was washed with CH_2Cl_2, then made alkaline with 10% NaOH, and extracted with CH_2Cl_2. The extracts were concentrated to leave *N*-methyl-3,5-dimethoxybenzylamine as an oil, which was chloroacetylated as described above to yield **17** (2.7 g, 87%). Colorless oil, IR ν_{max}^{neat} cm^{-1}: 1660. MS *m/e* (%): 259 (30), 257 (M^+, 95), 222 (100), 180 (58), 165 (47), 151 (80). NMR ($CDCl_3$) at 60° δ: 2.99 (3H, s), 3.77 (6H, s), 4.10 (2H, s), 4.52 (2H, s), 6.37 (3H, s).

***N*-*t*-Butyl-*N*-chloroacetyl-3,5-dimethoxybenzylamine (19)**——A benzene (5 ml) solution of 3,5-dimethoxybenzaldehyde[27] (0.5 g, 3 mmol) and *t*-butylamine (1 g, 13.7 mmol) was refluxed continuously, while H_2O was removed with a water-separator. After 2 hr, the benzene was evaporated off, MeOH (5 ml) and $NaBH_4$ (200 mg, 5.26 mmol) were added to the residue, and the solution was allowed to stand at room temperature overnight. Removal of the MeOH by evaporation left *N*-*t*-butyl-3,5-dimethoxybenzylamine, which was converted to **19** (0.703 g, 78%) as described above, mp 59—60° (aq MeOH). IR ν_{max}^{Nujol} cm^{-1}: 1660. MS *m/e* (%): 301 (8), 299 (M^+, 27), 244 (29), 242 (79), 208 (19), 166 (100), 151 (96). NMR ($CDCl_3$) δ: 1.49 (9H, s), 3.80 (6H, s), 4.00 (2H, s), 4.62 (2H, s), 6.36 (3H, s). *Anal.* Calcd for $C_{15}H_{22}ClNO_3$: C, 60.09; H, 7.40; N, 4.67; Cl, 11.83. Found: C, 60.06; H, 7.35; N, 4.70; Cl, 11.81.

Photocyclization of 11, 13, 15, 17, and 19——A 50% aqueous MeCN (300 ml) solution of a chloroacetamide (**11**, **13**, **15**, **17**, **19**; 10 mM) and $NaHCO_3$ (10 mM) was irradiated with the 100 W lamp for 1.5 hr. After removal of the MeCN, the aqueous layer was saturated with NaCl and extracted with CH_2Cl_2 or EtOAc. The extracts were dried (Na_2SO_4) and concentrated to leave a solid, which was chromatographed on a silica gel column. Elution with hexane–EtOAc (5: 2) for **12**, hexane–EtOAc (2: 1) for **14**, hexane–EtOAc (1: 1) for **16**, benzene–EtOAc (1: 2) for **18**, or CH_2Cl_2 for **20** gave a tetrahydroisoquinolin-3-one; yields and physical data are as follows:

2-Benzhydryl-5,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-3-one (12)——Yield 18.4%, mp 77—78° (benzene–hexane). IR ν_{max}^{Nujol} cm^{-1}: 1650. MS *m/e* (%): 373 (M^+, 24), 182 (12), 167 (21), 166 (20), 165 (100). NMR ($CDCl_3$) δ: 3.61 (2H, s), 3.72 (3H, s), 3.89 (3H, s), 4.11 (2H, s), 6.16 (1H, d, J=2 Hz), 6.36 (1H, d, J=2 Hz), 7.1—7.4 (11H, m). *Anal.* Calcd for $C_{24}H_{23}NO_3$: C, 77.19; H, 6.21; N, 3.75. Found: C, 77.10; H, 6.15; N, 3.55.

2-Benzyl-5,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-3-one (14)——Yield 27.2%, colorless prisms, mp 138° (hexane–EtOAc). IR ν_{max}^{Nujol} cm^{-1}: 1640. MS *m/e* (%): 297 (M^+, 76), 206 (28), 178 (18), 164 (100). NMR ($CDCl_3$) δ: 3.54 (2H, t, J=2 Hz), 3.70 (3H, s), 3.78 (3H, s), 4.34 (2H, t, J=2 Hz), 4.72 (2H, s), 6.10 (1H, d, J=2 Hz), 6.30 (1H, d, J=2 Hz), 7.20 (5H, s). *Anal.* Calcd for $C_{18}H_{19}NO_3$: C, 72.70; H, 6.44; N, 4.71. Found: C, 72.66; H, 6.51; N, 4.71.

5,7-Dimethoxy-2-phenethyl-1,2,3,4-tetrahydroisoquinolin-3-one (16)——Yield 33.0%, colorless needles, mp 115—116° (EtOAc). IR ν_{max}^{Nujol} cm^{-1}: 1650. MS *m/e* (%): 311 (M^+, 38), 220 (20), 207 (26), 192 (100), 164 (15). NMR ($CDCl_3$) δ: 2.96 (2H, t, J=8 Hz), 3.49 (2H, t, J=2 Hz), 3.73 (2H, t, J=8 Hz), 3.78 (3H, s), 3.81 (3H, s), 4.28 (2H, t, J=2 Hz), 6.16 (1H, d, J=2 Hz), 6.35 (1H, d, J=2 Hz), 7.25 (5H, s). *Anal.* Calcd for $C_{19}H_{21}NO_3$: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.09; H, 6.73; N, 4.40.

5,7-Dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinolin-3-one (18)——Yield 44.4%, colorless needles, mp 121—122° (hexane–EtOAc). IR ν_{max}^{Nujol} cm^{-1}: 1640. MS *m/e* (%): 221 (M^+, 78), 164 (100). NMR ($CDCl_3$) δ: 3.09 (3H, s), 3.47 (2H, t, J=2 Hz), 3.76 (6H, s), 4.47 (2H, t, J=2 Hz), 6.25 (1H, d, J=2 Hz), 6.35 (1H, d, J=2 Hz). *Anal.* Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 64.99; H, 6.85; N, 6.32.

2-*t*-Butyl-5,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-3-one (20)——Yield 71.3%, colorless oil. IR ν_{max}^{neat} cm^{-1}: 1640. MS *m/e* (%): 263 (M^+, 37), 220 (15), 207 (31), 164 (100). NMR ($CDCl_3$) δ: 1.50 (9H, s), 3.40 (2H, t, J=2 Hz), 3.76 (6H, s), 4.40 (2H, t, J=2 Hz), 6.28 (2H, s).

Photolysis of 21, 25, and 29——An H_2O–EtOH (9: 1—4: 1) solution (360 ml) of **21**,[27] **25**,[27] or **29**[28] (798 mg, 4 mmol) was irradiated with the 100 W lamp for 7 hr under nitrogen. The solution was stirred with excess Ag_2CO_3 and the silver salts were then removed by filtration. The filtrate was concentrated *in vacuo*, and extracted with EtOAc. The extracts were dried (Na_2SO_4) and concentrated *in vacuo*, and the residue was subjected to preparative TLC with CH_2Cl_2–EtOAc (10: 1) to give the *N*-glycoloyl- (**22**, **26**, **30**), *N*-ethoxyacetyl- (**23**, **27**, **31**), and *N*-acetylanisidines (**24**,[29] **28**,[30] **32**[31]). The yields are shown in Chart 4, and physical data for the products are given below.

***N*-Glycoloyl-*o*-anisidine (22)**——mp 108—109.5° (benzene). IR ν_{max}^{Nujol} cm^{-1}: 3380, 3180, 1650. NMR ($CDCl_3$) δ: 3.87 (3H, s), 4.23 (2H, s), 6.70—7.08 (3H, m), 8.14 (1H, dd, J=2, 7.5 Hz), 8.75 (1H, br. s). MS *m/e* (%): 182 (57), 181 (M^+, 100), 150 (89), 135 (75), 123 (97), 108 (95). *Anal.* Calcd for $C_9H_{11}NO_3$: C, 59.66; H, 6.12; N, 7.73. Found: C, 59.75; H, 6.03; N, 7.65.

***N*-Ethoxyacetyl-*o*-anisidine (23)**——Colorless oil. IR ν_{max}^{neat} cm^{-1}: 3390, 1690. MS *m/e* (%): 209 (M^+, 100), 164 (65), 150 (70), 135 (89), 108 (56). NMR ($CDCl_3$) δ: 1.30 (3H, t, J=7 Hz), 3.64 (2H, q, J=7 Hz), 3.87 (3H, s), 4.04 (2H, s), 6.84—7.24 (3H, m), 8.40 (1H, dd, J=3, 7 Hz), 9.0 (1H, br. s).

***N*-Glycoloyl-*m*-anisidine (26)**——mp 67.5—69° (benzene–hexane). IR ν_{max}^{Nujol} cm^{-1}: 3360, 2900, 1665. MS *m/e* (%): 181 (M^+, 100), 150 (49), 123 (88), 107 (38). NMR ($CDCl_3$) δ: 3.79 (3H, s), 4.19 (2H, s), 6.69 (1H, dd, J=2, 8 Hz), 7.03 (1H, d, J=8 Hz), 7.23 (1H, t, J=8 Hz), 7.28 (1H, d, J=2 Hz). *Anal.* Calcd for $C_9H_{11}NO_3$: C, 59.66; H, 6.12; N, 7.73. Found: C, 59.55; H, 5.96; N, 7.87.

***N*-Ethoxyacetyl-*m*-anisidine (27)**——Colorless oil. IR ν_{max}^{neat} cm^{-1}: 3390, 1680. MS *m/e* (%): 209 (M$^+$, 91), 186 (36), 165 (52), 149 (97), 136 (94), 123 (100). NMR ($CDCl_3$) δ: 1.30 (3H, t, J=7.5 Hz), 3.66 (2H, q, J=7.5 Hz), 3.80 (3H, s), 4.04 (2H, s), 6.67 (1H, ddd, J=1.3, 2.5, 8.0 Hz), 7.04 (1H, ddd, J=1.3, 2.5, 8.0 Hz), 7.15 (1H, t, J=8 Hz), 7.34 (1H, t, J=2.5 Hz).

***N*-Glycoloyl-*p*-anisidine (30)**——mp 95—96° (benzene–hexane). IR ν_{max}^{Nujol} cm^{-1}: 3400, 3320, 1650. MS *m/e* (%): 181 (M$^+$, 100), 123 (91), 122 (87), 108 (89). NMR ($CDCl_3$) δ: 3.78 (3H, s), 4.17 (2H, s), 6.85 (2H, d, J=9 Hz), 7.43 (2H, d, J=9 Hz), 8.35 (1H, br. s). *Anal.* Calcd for $C_9H_{11}NO_3$: C, 59.66; H, 6.12; N, 7.73. Found: C, 59.62; H, 5.95; N, 7.71.

***N*-Ethoxyacetyl-*p*-anisidine (31)**——Colorless oil. IR ν_{max}^{neat} cm^{-1}: 3320, 2970, 2900, 1680. MS *m/e* (%): 209 (M$^+$, 100), 165 (52), 149 (46), 136 (90), 122 (71), 108 (41). NMR ($CDCl_3$) δ: 1.30 (3H, t, J=7 Hz), 3.66 (2H, q, J=7 Hz), 3.80 (3H, s), 4.04 (2H, s), 6.88 (2H, d, J=9 Hz), 7.48 (2H, d, J=9 Hz).

***N*-Chloroacetylation of *N*-Alkylanisidines**——Chloroacetyl chloride (25—30 mmol) was added dropwise to a stirred mixture of *N*-alkylanisidine (10 mmol) (*N*-methyl-*p*-anisidine,[32] *N*-benzyl-*p*-anisidine,[33] *N*-methyl-*m*-anisidine,[32] or *N*-methyl-*o*-anisidine[32]) in CH_2Cl_2 (25—40 ml) and saturated $NaHCO_3$ solution (50—80 ml) at room temperature. After 1.5—2 hr, the solution was diluted with CH_2Cl_2 (50 ml), washed with 2 N HCl and saturated $NaHCO_3$ and NaCl solutions, dried (Na_2SO_4), and concentrated to leave the *N*-alkyl-*N*-chloroacetylanisidine (**35**, **37**, **39**, **42**) as a solid. Physical data are given below.

***N*-Chloroacetyl-*N*-methyl-*p*-anisidine (35)**——Yield 99%, mp 55° (EtOH–H_2O).[34] IR ν_{max}^{Nujol} cm^{-1}: 1680. MS *m/e* (%): 215 (19), 213 (M$^+$, 57), 137 (100), 122 (62), 90 (95) NMR ($CDCl_3$) δ: 3.28 (3H, s), 3.82 (3H, s), 3.84 (2H, s), 6.92 (2H, d, J=9 Hz), 7.06 (2H, d, J=9 Hz).

***N*-Benzyl-*N*-chloroacetyl-*p*-anisidine (37)**——Yield 81%, mp 69—70° (MeOH–H_2O). IR ν_{max}^{Nujol} cm^{-1}: 1665. MS *m/e* (%): 291 (13), 289 (M$^+$, 39), 154 (29), 91 (100). NMR ($CDCl_3$) δ: 3.20 (3H, s), 3.80 (2H, s), 4.82 (2H, s), 6.84 (4H, s), 7.20 (5H, s). *Anal.* Calcd for $C_{16}H_{16}ClNO_2$: C, 66.32; H, 5.57; N, 4.83; Cl, 12.22. Found: C, 66.22; H, 5.49; N, 4.93; Cl, 11.94.

***N*-Chloroacetyl-*N*-methyl-*m*-anisidine (39)**——Yield 80%, mp 98—100° (benzene). IR ν_{max}^{Nujol} cm^{-1}: 1670. MS *m/e* (%): 215 (22), 213 (M$^+$, 70), 178 (40), 177 (35), 164 (40), 137 (53), 136 (100), 108 (49), 92 (65), 90 (95), 77 (68). NMR ($CDCl_3$) δ: 3.30 (3H, s), 3.84 (3H, s), 3.91 (2H, s), 6.8—7.0 (3H, m), 7.34 (1H, t, J=8 Hz). *Anal.* Calcd for $C_{10}H_{12}ClNO_2$: C, 56.21; H, 5.66; N, 6.56; Cl, 16.59. Found: C, 56.11; H, 5.63; N, 6.49; Cl, 16.55.

***N*-Chloroacetyl-*N*-methyl-*o*-anisidine (42)**——Yield 82%, mp 49—50° (hexane). IR ν_{max}^{Nujol} cm^{-1}: 1680. MS *m/e* (%): 215 (31), 213 (M$^+$, 91), 184 (24), 182 (71), 164 (42), 122 (63), 90 (100). NMR ($CDCl_3$) δ: 3.18 (3H, s), 3.79 (2H, s), 3.81 (3H, s), 6.8—7.5 (4H, m). *Anal.* Calcd for $C_{10}H_{12}ClNO_2$: C, 56.21; H, 5.66; N, 6.56; Cl, 16.59. Found: C, 56.37; H, 5.61; N, 6.59; Cl, 16.32.

Photocyclization of 35, 37, 39, 42, and 45——A 10 mM solution (500 ml) of **35**, **37**, **39**, or **42**, and *N*-chloroacetyl-*N*-methylaniline (**45**)[35] in MeCN–H_2O (3: 4—1: 6) containing $NaHCO_3$ (1 g) was irradiated with the 100 W lamp under N_2 for 3—5 hr. MeCN was removed by evaporation and the residue was extracted with CH_2Cl_2. The extracts were washed with saturated NaCl solution, dried (Na_2SO_4), and concentrated to leave an oil, whith was chromatographed on a silica gel column with CH_2Cl_2–EtOAc (20: 1) for **36**, **40**, **41**, and **43**, CH_2Cl_2–hexane (1: 1) for **38**, and CH_2Cl_2 for **46**. Yields and physical data are as follows:

5-Methoxy-1-methyloxindole (36)[32]——Yield 55%, mp 96—97° (petroleum ether). IR ν_{max}^{Nujol} cm^{-1}: 1690. MS *m/e* (%): 177 (M$^+$, 89), 162 (100), 144 (26). NMR ($CDCl_3$) δ: 3.18 (3H, s), 3.49 (2H, s), 3.79 (3H, s), 6.69 (1H, dd, J=1, 7.5 Hz), 6.83 (1H, dd, J=2.5, 7.5 Hz), 6.87 (1H, dd, J=1, 2.5 Hz).

1-Benzyl-5-methoxyoxindole (38)——Yield 67%, colorless oil. IR ν_{max}^{neat} cm^{-1}: 1705. MS *m/e* (%): 253 (M$^+$, 42), 152 (20), 91 (100). NMR ($CDCl_3$) δ: 3.44 (2H, s), 3.60 (3H, s), 4.74 (2H, s), 6.44 (1H, d, J=8.5 Hz), 6.60 (1H, dd, J=2.5, 8.5 Hz), 6.72 (1H, d, J=2.5 Hz).

6-Methoxy-1-methyloxindole (40)[32]——Yield 66%, mp 99—100° (petroleum ether). IR ν_{max}^{Nujol} cm^{-1}: 1705, 1625. MS *m/e* (%): 177 (M$^+$, 100), 162 (22), 148 (80). NMR ($CDCl_3$) δ: 3.18 (3H, s), 3.45 (2H, s), 3.82 (3H, s), 6.40 (1H, d, J=2 Hz), 6.54 (1H, dd, J=2, 8 Hz), 7.11 (1H, d, J=8 Hz).

4-Methoxy-1-methyloxindole (41)[32]——Yield 6%, mp 137° (H_2O). IR ν_{max}^{Nujol} cm^{-1}: 1700. MS *m/e* (%): 177 (M$^+$, 100), 162 (20), 148 (71). NMR ($CDCl_3$) δ: 3.20 (3H, s), 3.45 (2H, s), 3.86 (3H, s), 6.49 (1H, d, J=8 Hz), 6.61 (1H, d, J=8 Hz), 7.26 (1H, t, J=8 Hz).

7-Methoxy-1-methyloxindole (43)[32]——Yield 20%, mp 101—102° (hexane). IR ν_{max}^{Nujol} cm^{-1}: 1690. MS *m/e* (%): 177 (M$^+$, 100), 162 (15), 134 (48). NMR ($CDCl_3$) δ: 3.46 (5H, s), 3.84 (3H, s), 6.7—7.1 (3H, m).

1-Methyloxindole (46)[36]——Yield 15.4%, mp 88—89° (hexane). IR ν_{max}^{Nujol} cm^{-1}: 1710. MS *m/e* (%): 147 (M$^+$, 100), 118 (85). NMR ($CDCl_3$) δ: 3.12 (3H, s), 3.40 (2H, s), 6.1—7.3 (4H, m).

References and Notes

1) A part of this work has been reported in a preliminary form: T. Hamada, Y. Okuno, M. Ohmori, T. Nishi, and O. Yonemitsu, *Heterocycles*, **8**, 251 (1977).
2) S. Naruto and O. Yonemitsu, *Chem. Pharm. Bull.*, **28**, 900 (1980), and references cited therein.
3) O. Yonemitsu, T. Tokuyama, M. Chaykovsky, and B. Witkop, *J. Am. Chem. Soc.*, **90**, 776 (1968).

4) Y. Okuno, K. Hemmi, and O. Yonemitsu, *Chem. Commun.*, **1971**, 745; T. Hamada, M. Ohmori, and O. Yonemitsu, *Tetrahedron Lett.*, **1977**, 1519.
5) M. Ikeda, K. Hirao, Y. Okuno, N. Numao, and O. Yonemitsu, *Tetrahedron*, **33**, 489 (1977).
6) *a*) M.T. McCall, G.S. Hammond, O. Yonemitsu, and B. Witkop, *J. Am. Chem. Soc.*, **92**, 6991 (1970); *b*) S. Naruto, O. Yonemitsu, N. Kanamaru, and K. Kimura, *ibid.*, **93**, 4053 (1971); *c*) O. Yonemitsu, H. Nakai, Y. Okuno, S. Naruto, K. Hemmi, and B. Witkop, *Photochem. Photobiol.*, **15**, 509 (1972); *d*) S. Naruto and O. Yonemitsu, *Tetrahedron Lett.*, **1975**, 3399; *e*) N. Numao, T. Hamada, and O. Yonemitsu, *Tetrahedron*, **43**, 1889 (1978).
7) T. Okada, T. Fujita, M. Kubota, S. Masaki, and N. Mataga, *Chem. Phys. Lett.*, **14**, 563 (1972).
8) *Cf.* T. Hamada, A. Nishida, and O. Yonemitsu, *Heterocycles*, **12**, 647 (1979).
9) N. Numao, T. Hamada, and O. Yonemitsu, *Tetrahedron Lett.*, **1977**, 1661.
10) W.E. Stewart and T.H. Siddall, III, *Chem. Rev.*, **70**, 517 (1970).
11) L.A. LaPlanche and M.T. Rogers, *J. Am. Chem. Soc.*, **86**, 337 (1964).
12) L.A. LaPlanche and M.T. Rogers, *J. Am. Chem. Soc.*, **85**, 3728 (1963).
13) M.E. Kuehne and B.F. Lambert, *J. Am. Chem. Soc.*, **81**, 4278 (1959).
14) B.F. Pedersen and B. Pedersen, *Tetrahedron Lett.*, **1965**, 2995.
15) I. Lengyel and J.C. Sheehan, *Angew. Chem. Int. Ed. Engl.*, **7**, 25 (1968).
16) B. Kumar, R.M. Mehta, S.C. Kalra, and G.S. Manku, *J. Chem. Soc. Chem. Comm.*, **1976**, 971.
17) J.A. Weil, A. Blum, A.H. Heiss, and J.K. Kinnaird, *J. Chem. Phys.*, **46**, 3132 (1967).
18) A. Pictet and M. Finkelstein, *Chem. Ber.*, **42**, 1985 (1909).
19) R.B. Moffett, *J. Med. Chem.*, **7**, 319 (1964).
20) J.A. Barltrop, A.J. Johnson, and G.D. Meakins, *J. Chem. Soc.*, **1951**, 181.
21) E.C.S. Jones and F.L. Pyman, *J. Chem. Soc.*, **127**, 2588 (1925).
22) P. Borgna, L. Vicarini, and G. Calderara, *Farmaco. Ed. Sci.*, **32**, 813 (1977); *C. A.*, **88**, 190339e (1978).
23) Since **10** is completely insoluble in all usual solvents, no NMR spectrum is available. The structure was established on the basis of the mass fragmentation pattern.
24) S. Teitel and A. Brossi, *J. Heterocycl. Chem.*, **7**, 1401 (1970).
25) J.E. Davies, F.E. King, and J.C. Roberts, *J. Chem. Soc.*, **1955**, 2782.
26) F. Mauthner, *J. Prak. Chem.*, **100**, 176 (1919).
27) M. Heiderberger and W.A. Jacobs, *J. Am. Chem. Soc.*, **41**, 1450 (1919).
28) F. Reverdin, *Helv. Chim. Acta*, **6**, 88 (1923).
29) A. Kaufmen, *Chem. Ber.*, **42**, 3482 (1909).
30) F. Reverdin and K. Nidmer, *Chem. Ber.*, **46**, 4066 (1913).
31) F. Reverdin and A. Bucky, *Chem. Ber.*, **39**, 2679 (1906).
32) A.H. Beckett, R.W. Daisley, and J. Walker, *Tetrahedron*, **24**, 6093 (1968).
33) E. Fröhlich and E. Wedekind, *Chem. Ber.*, **40**, 1010 (1907).
34) H. Plieninger and C.E. Castro, *Chem. Ber.*, **87**, 1760 (1954).
35) C.A. Bischoff, *Chem. Ber.*, **34**, 2125 (1901).
36) R. Stolle, *Ger.* 335673 [*C.A.*, **17**, 1802[9] (1923)].