LACTAM AND AMIDE ACETALS. 69.* SYNTHESIS AND PROPERTIES OF 3-(AMINOMETHYLENE)-2-INDOLINONE DERIVATIVES

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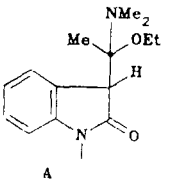
Oxindole derivatives reacted with the diethyl acetals of dimethylformamide and dimethylacetamide to give the corresponding derivatives of 3-(aminomethylene)-, (aminoethylidene)-, and (ethoxyethylidene)-2-indolinone. These products were then easily converted to N-aryl- and N-alkylaminomethyleneoxindoles upon treatment with aryl or alkyl amines. The alkylation of N,N-dimethylaminomethylene-2-indolinones by dimethyl sulfate and triethyloxonium tetrafluoroborate, and the reactions of the resulting methyl sulfates and tetrafluoroborates with nucleophilic reagents were studied. The configuration of the 3-(aminomethylene)-2-indolinone derivatives prepared at the enamine C=C double bond was investigated by NMR. The free energies of activation for the cis—trans isomerization were determined in a number of cases.

In the present work we describe the synthesis and some chemical and physicochemical properties of a number of cyclic enamino amides, derivatives of 3-(aminomethylene)-2-indolinone, and of some related compounds. It has been reported that derivatives of oxindole react easily with DMF diethyl acetal (Ia) to give the corresponding 3-(dimethylaminomethylene)oxindoles [2]. We have found that both oxindole IIa and N-ethyloxindole IIb react easily at room temperature with the acetal Ia to give 3-(aminomethylene)-2-indolinone (IIIa) and its N-ethyl derivative IIIb in high yields. Similarly, compounds IIa and IIb were condensed with the diethyl acetal Ib, but these reactions surprisingly give rise to other products. Thus, in the case of the unsubstituted oxindole IIa, the expected 3-(α-dimethylaminoethylene)-2-indolinone (IV) was only a minor product, formed along with 3-(α-ethoxyethylidene)-2-indolinone (V). The ethoxyethylidene derivative VI was the only product of the condensation of 1-ethyloxindole IIb with the acetal Ib. To our knowledge, this is the first example of formation of an ethoxymethylene derivative upon treatment of an amide acetal with an active methylene compound [3]. Since the elimination of an ethoxy group from an intermediate of the type A is energetically more favorable than the elimination of a dimethylamino group, the usual outcome of these reactions is the formation of dimethylaminomethylene derivatives.



A

A likely explanation is that the sterically more demanding dimethylamino substituent is eliminated more easily than the ethoxy group from the sterically congested molecule A.

The enamines IIIa, IVa, and the ethoxyethylidene derivative V react easily with amines to give the corresponding secondary enamines VIIa-c. The hydrolysis of the enamine IIIa in hot dilute HCl does not stop at the stage of the corresponding 3-formyl derivative, but gives instead the oxindole IIa after cleavage of the formyl group. A similar reaction has been described earlier [4].

*For Communication 68, see [1].

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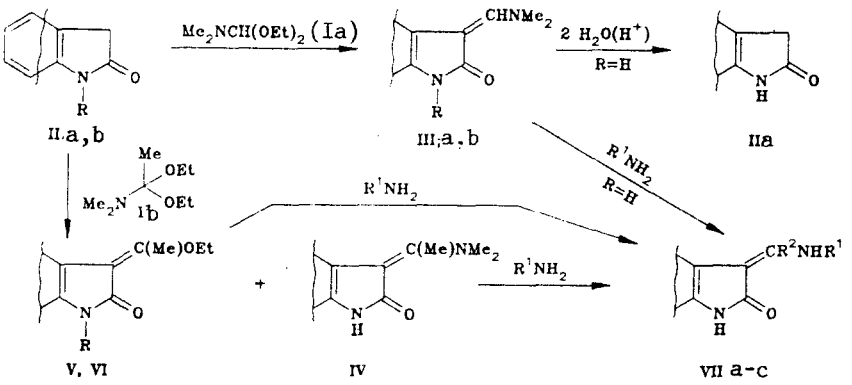
TABLE 1. NMR Spectra of Compounds III-VII

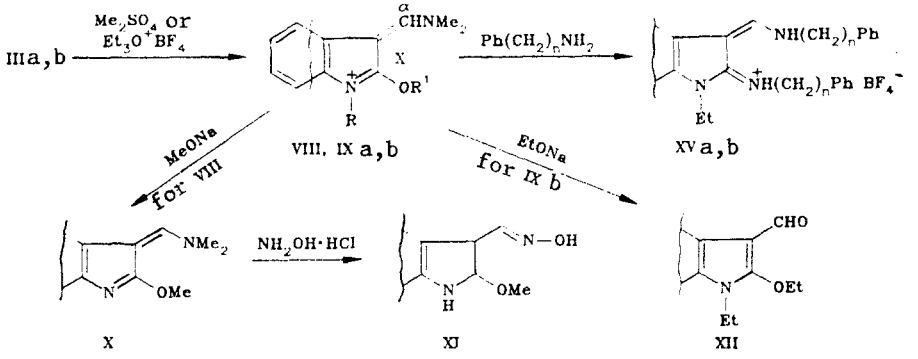
Compound	NMR spectrum (in (DMF-D_6), ppm (J constant, Hz)									Aromatic protons	Isomer contents, %
	α-H or α-CH_3	NH	NH ind. or NR ind.			OCH_3	4-H	β-NMe_2 or β-OC_2H_5	CH_2Ph		
			NH	NCH_2	CH_3						
trans-IIIa	7,59		10,02				7,30	3,36		6,7 . . . 7,1	50
cis-IIIa	7,46		9,90				7,44	3,46			50
trans-IIIb	7,64			3,82 q	1,17 t		7,35	3,37		6,8 . . . 7,1	59
cis-IIIb	7,52			3,83 q	1,17 t		7,49	3,42			41
IV*	2,68		9,86				7,06	3,24		6,7 . . . 7,0	
cis-V	7,79		10,12				7,70	1,47 t 4,40 q		6,7 . . . 7,2	
cis-VI	2,82			3,83 q	1,19 t		7,80	1,48 t 4,42		6,9 . . . 7,3	
trans-VIIa	8,72 d (J=12,4)	10,93 d	10,44				7,65			6,9 . . . 7,2	88
cis-VIIa	7,97 (J=12,6)	9,42					8,00				12
trans-VIIb	8,11 d (J=13,0)	9,21 q	10,14				7,40		4,68 d (J_{NHCH_2}=6,2)	6,9 . . . 7,0	74
cis-VIIb	7,59 (J=14,0)	8,00 q		10,12 s			7,81		4,66 (J_{NHCH_2}=5,7)	6,9 . . . 7,0	26
trans-VIIc	2,53 s	10,97 t		9,88 s			7,42		4,79 d (J_{NHCH_2}=6,1)	6,9 . . . 7,0	
trans-X	7,87			10,30		4,03	7,44	3,42		6,8 . . . 7,0	18
cis-X	7,57					3,99	7,59	3,45			72

*At 20°C compound IV is an averaged structure of two isomers.



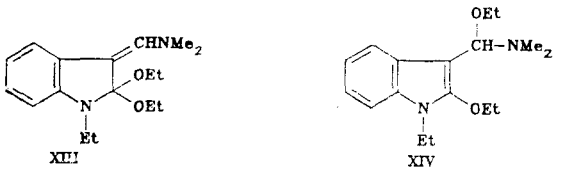
II, III a R=H, b R=Et; V R=H; VI R=Et; VII a R^1=Ph, b,c R^1=$PhCH_2$, a,b R^2=H, b R^2=Me

A considerable negative charge is concentrated at the carbonyl oxygen atom of the tertiary enamino amines IIIa and IIIb. This is due to the combined electron donor effect of both the ring nitrogen and the enamino substituent. Since the O-alkylation of the parent oxindole IIa has been described [5, 6], it was reasonable to assume that the alkylation of IIIa and b would proceed even more easily. Indeed, the O-alkyl derivatives VIII, IXa, and IXb were easily obtained as the corresponding salts upon reaction with dimethyl sulfate or triethyloxonium tetrafluoroborate. These salts are useful synthetic intermediates.



VIII R=H, R^1=Me, X^-=$MeSO_4^-$; IX a R=H, b R=Et; a, b R^1=Et, X^-=BF_4^-; XV a n=1, b n=2

Treatment of the salt VIII with sodium methoxide converted it to the enamino lactim ether X. The lactim ether function of the latter compound turned out to be relatively inert, the reaction of X with hydroxylamine hydrochloride gave rise only to the transamination product, 2-methoxy-3-formylindole oxime (XI). In contrast, the only isolated product from the reaction of the N-substituted tetrafluoroborate IXb with sodium ethoxide was 1-ethyl-2-ethoxy-3-formylindole (XII). It seems likely that in this case the initial attack of the ethoxide anion is not at the 2-position of the indole ring, but at the α-position of the enamine fragment, thus producing 1-ethyl-2-ethoxy-3,3-(dimethylamino, ethoxy)methyl indole (XIV) and not the diethyl acetal of 1-ethyl-3-(dimethylaminomethylene)oxindole (XIII) as the first intermediate.



A nucleophilic attack at the 2-position of the tetrafluoroborate IXb was observed in its reactions with benzylamine and β-phenylethylamine. These reactions proceeded easily at room temperature and gave rise to the enamino amidines XVa and b, i.e., substitution of the 2-ethoxy group took place concomitantly with the transamination of the enamine function.

Analysis of the NMR spectra of the amines without a substituent at the α-position of the enamine function (IIIa and b, VIIIa and b, and X) showed that at room temperature all groups give two sets of signals (Table 1). As

described previously [7-9], this finding can be explained by the existence of these compounds as two configurational isomers at the enamine C=C double bond. The ratio of the *cis* and *trans* isomers is thereby determined by their relative thermodynamic stabilities. One of the isomers is predominant in the case of compounds VIIa and b (88% for VIIa and 74% for VIIb). This can be explained by the fact that the formation of a stabilizing intramolecular hydrogen bond is only possible in the *trans* isomer.* In agreement with this assignment is the observation of the stronger C_α-NH signal of the more abundant *trans* isomer of compound VIIa at 10.93 ppm, i.e., at a significantly lower field than the corresponding signal of the *cis* isomer (seen at 9.42 ppm). A similar situation is seen with the enamine VIIb. The analysis of the NMR data of other compounds (Table 1) shows similar differences in the chemical shifts of the isomers. Thus, the α-H signals of the *trans* isomers of enamines VIIa and b are shifted downfield in comparison with the same signals of the *cis* isomers ($\Delta\delta_{\alpha-H}$ *trans—cis* is 0.75 ppm for compound VIIa and about 0.40 ppm for VIIb). In contrast, the opposite is tue for the 4-H signals, which resonate at higher fields in the *trans* isomers ($\Delta\delta_{4-H}$ *trans—cis* is —0.35 ppm for VIIa and —0.40 ppm for VIIb). We have applied these findings to the assignment of the configurations of other compounds (IIIa and b). As judged by the relative integral intensities of the high field and low field sets of signals of the α-H and 4-H protons, the tertiary enamines exist either as a mixture of roughly equal amounts of the two isomers (compound IIIb), or one of the isomers predominates only slightly (59% *trans* isomer and 41% *cis* isomer in the case of IIIb). Thus, the steric requirements of the *cis* and *trans* isomers of these compounds are virtually equal.

The assignment of the signals of the dimethylamino group to a certain isomer in the case of compound IIIa (broad singlet at 3.46 ppm and sharp singlet at 3.36 ppm) was carried out in the same way as the assignment of the analogous signals in the spectrum of compound IIIa, where the $N(CH_3)_2$ signal of the less-abundant *cis* isomer was seen as a broad, low-field singlet at 3.42 ppm, as compared to the signal of the *trans* isomer at 3.37 ppm.

The conversion of compounds IIIa and b to the compounds X is associated with increased steric problems for the *trans* isomers in comparison to the *cis* isomers. This gives an opportunity to test the validity of the configurational assignment based on the chemical shifts of the α-H and 4-H signals, as described above. Indeed, applying the above-mentioned criteria, the *cis* isomer of lactim ether X was determined as being the predominant one in solution (72%).

The NMR spectra of the α-aminoethylidene derivatives IV and VIIc differ significantly from those of the aminomethylene derivatives, i.e., the substitution of the α-H atom within the enamine fragment with a methyl group significantly changes the properties of the compounds under study. Thus, at room temperature only one set of signals is seen in the NMR spectra of compounds IV and VIIc. However, whereas the signal of the α-CH_3 group of the secondary enamine VIIc is seen as a sharp singlet at 2.44 ppm, the signal of the same group in the tertiary enamine IV appears significantly broadened at 2.68 ppm. The signal of the Me_2N group at 3.24 ppm is also broadened. These findings are in agreement with a relatively low-barrier *cis—trans* isomerization of compound IV. A similar effect has been reported for other types of enamines on going from the α-unsubstituted to the corresponding α-methylene amines [7, 8]. To determine the energetic requirements of these isomerizations the NMR spectra of compounds IIIa, VIIa, b, IV, and VIIc were recorded at different temperatures. In the case of compounds IIIa and VIIb at 90°C, only a very small broadening of the two sets of signals was seen. Thus, the temperature of coalescence (T_c) is higher than 100°C and the free energy of activation $\Delta G_{C=C}^{\neq}$ is greater than 20 kcal/mole (calculated as described in [8]). For the enamine VIIa, the T_c value of the two sets of signals was found to correspond to energies of activation of 19.3 kcal/mole for the *trans* isomer and 17.9 kcal/mole for the *cis* isomer (see Table 2).

At lower temperatures, a further broadening of the signals of the α-CH_3 and Me_2N groups is observed in the case of enamine IV. At still lower temperatures, these signals split (T_c = —5°C for α-CH_3 and —10°C for Me_2N), and further give rise to two sets of individual signals due to the *cis—trans* isomerization at the enamine C=C double bond. The calculated values for ΔG* are 13.5 kcal/mole for the *trans* isomer and 13.4 kcal/mole for the *cis* isomer.

The signals in the spectrum of compound VIIc do not show any broadening even at temperatures as low as —55°C. Thus, this enamine must exist in solution virtually as one isomer (less than 1% of a second isomer may be present in solution). The low-field location of the α-NH signal at 20°C (10.78 ppm) indicates that this is the *trans* isomer, stabilized by an intramolecular hydrogen bond. The energetic requirements for the isomerization of the compounds studied are summarized in Table 2.

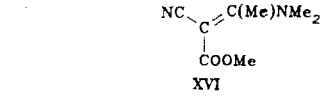
*Throughout this paper we define as *trans* those isomers with a *trans* position of the α-C—H (or α-CH_3) and C=O groups.

TABLE 2. Free Energies of Activation of the $C_3=C_\alpha$ Double Bonds

Compound	T_c, °C	T, °C	Group	Solvent	$\Delta\nu$, Hz	Isomer distribution, %	$\Delta G^{\neq}_{C=C}$, kcal/mole
IIIa	⩾100	20	NH Indole	DMSO-D_6	16	50:50	⩾20
IV	−10	−30	NCH_3	DMF-D	20	55:45	13,5; 13,4
	−5	−30	CH_3	DMF-D	32	55:45	13,5; 13,4
VIIa	90	20	NH Indole	DMF-D_7	60	88:12	19,3; 17,9
VIIb	⩾110	~20	NH Indole	DMF-D_7	38	74:26	>20

As seen from Table 2, there is a significant difference of more than 6.5 kcal/mole between the free energies of activation for the *cis—trans* isomerization of the enamines IIIa and IV. Two factors are most likely to contribute to this difference. First, the steric interactions in enamine IV are greater than in compound IIIa; thus the ground state energy of IV is higher. Second, the positive charge of the transition state is stabilized by the α-methyl group [10].

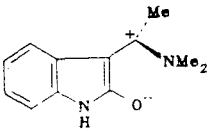
It is interesting to compare the energies of activation for the isomerization of enamine IV and of α-cyano-β-dimethylamino crotonate (XVI) [8].



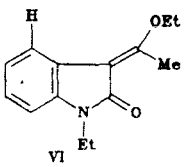
IV XVI

$\Delta G^{\neq}$ = 13,5 and 13,4 kcal/mole $\Delta G^{\neq}$ = 14,9 or 14,8 kcal/mole

Clearly, the overall electron-withdrawing power of the β-substituents in enamine XVI is significantly greater than in enamine IV. One would therefore expect the isomerization barrier of the former compound to be lower than that of the latter. However, exactly the opposite is seen to be the case. If one assumes [8] that the ability for a *cis—trans* isomerization is crucially dependent on the transition state stabilization, then these results are easy to understand. The transition state in the isomerization of enamine IV (where the positive and negative charges are perpendicular) is significantly stabilized by the formation of an aromatic indole ring;* thus the overall free energy of activation of the *cis—trans* isomerization is lower for indole enamines than for acyclic enamines of the type XVI.



In contrast to the 3-(aminomethylene)oxindoles (compounds III, IV, and VII), only one isomer can be detected in the case of the ethoxymethylene derivatives V and VI. The NMR spectrum of compound VI, recorded at −50°C, does not show any significant broadening of the signals. NOE experiments were carried out to assign the stereochemistry. Thus, high-frequency irradiation of the methyl group of the ethoxy substituent led to ~6% increase in the integral intensity of the 4-H signal, whereas a similar irradiation of the α-methyl group produced no effect on the integral intensity of the 4-H signal. Therefore, the proton in position 4 of the indole ring is proximate to the ethoxy group and the solution configuration of this compound is *cis*.



VI

The NMR spectra of the methyl sulfate and tetrafluoroborate salts VIII, IXa, and IXb (see Experimental) show only one set of signals. However, the α-H and NMe_2 signals of the methyl sulfate VIII are markedly broadened, whereas the α-H signals of the tetrafluoroborates IXa and IXb are sharp, and the signals of the dimethylamino group appear as two sharp singlets of equal intensity. Thus, the *cis—trans* isomerization is easier for the salt VIII than for the tetrafluoroborates IXa and IXb. A possible explanation for this may be the lesser steric demands of the salt VIII, which has a smaller methoxy group as a substituent in position 2, as opposed to an ethoxy group in the case of the salts IXa and b. To quantitatively assess the isomerization of VIII, NMR spectra were recorded at low temperatures. Coalescence of the Me_2N signals was observed at −22°C; for the α-H signal the

*A similar aromatization is known to simplify the electroreduction of indole enamines [11].

TABLE 3. Characterization of Compounds III-XII and XV

Compound	Molecular formula	Solvent	mp, °C	Yield, % (method)
IIIa	$C_{11}H_{12}N_2O$	Acetonitrile, isopropanol	198,5 ... 200	88
IIIb	$C_{13}H_{16}N_2O$	Ethyl acetate	100 ... 102	87
IV	$C_{12}H_{14}N_2O$	Ethyl acetate	204,5 ... 208	23
V	$C_{12}H_{13}NO_2$	Methanol	229 ... 231	49
VI	$C_{14}H_{17}NO_2$	Heptane	94 ... 97	52
VIIa	$C_{15}H_{12}N_2O$	Methanol	266 ... 268	44 (A) 72 (B)
VIIb	$C_{16}H_{14}N_2O$	Isopropanol	196 ... 199	94
VIIc	$C_{17}H_{16}N_2O$	Methanol	238,5 ... 239	76 (A) 90 (B)
VIII	$C_{13}H_{18}N_2O_5S$	Isopropanol	127 ... 129	66
IXa	$C_3H_{17}BF_4N_2O$	Isopropanol Methanol	197 ... 199	53
IXb	$C_{15}H_{21}BF_4N_2O$	Ethanol	127,5 ... 128,5	57
X	$C_{12}H_{14}N_2O$	Hexane	90 ... 92	99
XI	$C_{10}H_{10}N_2O_2$	Ethyl acetate	168 ... 171	71
XII	$C_{17}H_{26}N_2O_2$	Heptane	83 ... 83,5	65
XVa	$C_{25}H_{26}BF_4N_5$	Methanol	214 ... 217	88
XVb	$C_{27}H_{30}BF_4N_5$	Methanol	201 ... 203	76

temperature of coalescence was —48°C. These low temperatures indicate that the isomerization has a low $\Delta G^{\neq}$ value. It should be noted that the dimethylamino group gives rise to two signals at —48°C: a sharp signal at 3.75 ppm and a significantly broadened signal at 3.72 ppm.

EXPERIMENTAL

NMR spectra were recorded on a Varian XL-200, with TMS as the internal standard. Melting points were determined using a Boetius apparatus (GDR). IR spectra were taken in Vaseline oil, using a Perkin—Elmer 457 spectrophotometer; UV spectra were recorded on a Specord M-40.

Data on the compounds prepared are summarized in Table 3. Satisfactory elemental analysis data were obtained.

3-(Dimethylaminomethylene)oxindole (IIIa). A mixture of 15.0 g (113 mmoles) of oxindole IIa and 19.9 ml of DMF N, N-diethyl acetal in 100 ml of absolute ethanol was stirred at 20°C for 1 h 30 min, then another 6.8 ml of DMF N, N-diethyl acetal was added and stirring continued for another 1 h 30 min. The reaction mixture was subsequently cooled to 5°C, the precipitate filtered off and washed with ethanol to give 17.3 g of compound IIIa. The mother liquor was concentrated to dryness and the residue triturated with ether and 2-propanol, whereupon another 1.3 g of product was obtained. IR spectrum: 3120 (NH), 1680 cm^{-1} (CO). UV spectrum, λ_{max}, nm ($\log \varepsilon$): 210 (4502), 275 (4249), 347 (4159).

1-Ethyl-3-(dimethylaminomethylene)oxindole (IIIb). A mixture of 8.05 g (48.5 mmoles) of oxindole IIb and 8.8 ml of the acetal Ia in 100 ml of absolute ethanol was stirred at 20°C for 3 h, another 3.0 ml portion of the acetal was added, and stirring continued for 1 h. The reaction mixture was then concentrated and the residue triturated with petroleum ether to give 9.08 g of compound IIIb. IR spectrum: 1660 cm^{-1} (CO).

Reaction of Oxindole with N, N-Dimethylacetamide Diethyl Acetal. A mixture of 4.75 g (35.7 mmoles) of oxindole and 6.88 ml of the acetal Ib in 105 ml of absolute ethanol was stirred at 20°C for 1 h, then 1.4 ml of the acetal was added, and stirring continued for 1 h. After cooling, 3.53 g of 3-(α-methoxyethylidene)oxindole (V) was obtained by filtration. IR spectrum: 3140 (NH), 1680 cm^{-1} (CO). UV spectrum, λ_{max}, nm ($\log \varepsilon$): 267 (4463), 298 (4083).

The mother liquor was concentrated, the residue triturated with petroleum ether, then with ether, and filtered to give 1.57 g of 3-(α-dimethylaminoethylidene)oxindole (IV). IR spectrum: 3100-3140 (NH), 1680 cm^{-1} (CO). UV spectrum, λ_{max}, nm ($\log \varepsilon$): 211 (4426), 281 (4194), 366 (4082).

1-Ethyl-3-(α-ethoxyethylidene)oxindole (VI). A mixture of 3.22 g (20 mmoles) of N-ethyloxindole and 3.86 ml of the acetal Ib in 40 ml of absolute ethanol was stirred at 20°C for 3 h. Another 3 ml of the acetal was added and stirring continued for 1 h 30 min. The reaction mixture was concentrated, the residue extracted with ether, the

ether evaporated, and the residue recrystallized from hexane to give 2.4 g of compound VI. IR spectrum: 1680 cm^{-1} (CO).

3-(Phenylaminomethylene)oxindole (VIIa). A. A mixture of 0.6 g (1.9 mmoles) of compound VIII and 0.18 g (0.17 ml, 1.9 mmoles) of aniline in 10 ml of absolute ethanol was stirred at 20°C for 2 h, then refluxed for 1 h 30 min. The mixture was cooled and 0.2 g of compound VIIa was obtained by filtration.

B. A mixture of 0.55 g (2.9 mmoles) of compound IIIa and 0.38 ml (3.9 mmoles) of aniline in 15 ml of absolute ethanol was refluxed for 1 h 30 min. Another 0.17 ml of aniline and 15 ml of ethanol were added and refluxing continued for 2 h. The mixture was then cooled and 0.5 g of compound VIIa was obtained by filtration. IR spectrum: 3140 broad (NH), 1680 cm^{-1} (CO).

3-(Benzylaminomethylene)oxindole (VIIb). A mixture of 0.94 g (5 mmoles) of compound IIIa and 0.64 g (6 mmoles) of benzylamine in 15 ml of absolute ethanol was refluxed for 1 h, cooled, and 1.17 g of compound VIIb obtained by filtration. IR spectrum: 3140 broad (NH), 1680 cm^{-1} (CO). UV spectrum, λ_{max}, nm ($\log \varepsilon$): 209 (4606), 276 (4350), 346 (4197).

3-(α-Benzylaminoethylidene)oxindole (VIIc). A. A mixture of 1.01 g (5 mmoles) of compound IV and 0.74 g (0.75 ml, 6.9 mmoles) of benzylamine in 25 ml of absolute ethanol was refluxed for 1 h 40 min. The mixture was cooled and 1.0 g of compound VIIc obtained by filtration. IR spectrum: 3100, 3140 (NH), 1650 cm^{-1} (CO). UV spectrum, λ_{max}, nm ($\log \varepsilon$): 210 (4478), 275 (4349), 343 (4261).

B. Compound VIIc was obtained from compound V and benzylamine as described in **A**.

Hydrolysis of 3-(Dimethylaminomethylene)oxindole. A solution of 0.85 g of compound IIIa in 25 ml of 0.01 N HCl was refluxed for 2 h 30 min. The mixture was filtered, the filtrate cooled to 5°C for 24 h, and 0.25 g of oxindole IIa filtered off. The filtrate was concentrated and the residue recrystallized from heptane to give another 0.16 g of compound IIa.

2-Methoxy-3-(N, N-dimethylaminomethylene)indolenium Methyl Sulfate (VIII). A mixture of 2.75 g (14.6 mmoles) of compound IIIa and 1.43 ml of dimethyl sulfate in 40 ml of dichloroethane was refluxed for 1 h 40 min. Another 0.3 ml portion of dimethyl sulfate was then added and refluxing continued for 2 h. The solvent was evaporated, the residue triturated first with petroleum ether, then with 2-propanol, cooled, and filtered to give 3.03 g of compound VIII. IR spectrum: 3400 broad (NH), 1660 cm^{-1}. NMR spectrum (DMF-D_7): 8.59 (1H, br.s, α-H), 7.80 (1H, s, 4-H), 4.37 (3H, s, OCH_3), 3.74 (6H, br.s, NMe_2), 3.56 ppm (3H, s, $MeSO_4^-$).

2-Ethoxy-3-(N, N-dimethylaminomethylene)indoleninium Tetrafluoroborate (IXa). A mixture of 1.31 g (6.3 mmoles) of triethyloxonium tetrafluoroborate and 1 g (5.3 mmoles) of compound IIIa in 25 ml of chloroform was stirred first for 3 h at 20°C, then for 1 h 30 min at 45-50°C. The precipitated product was filtered off and washed with 10 ml of 2-propanol. Yield 0.85 g of IXa. IR spectrum: 3260 (NH), 1660 cm^{-1}. NMR spectrum (DMF-D_7): 13.22 (1H, br.s, NH), 8.66 (1H, s, α-H), 7.80 (1H, s, 4-H), 4.70 (2H, q, OCH_2), 3.75 (3H, s, NCH_3), 3.74 (3H, s, NCH_3), 1.55 ppm (3H, t, OCH_2CH_3).

1-Ethyl-2-ethoxy-3-(N, N-dimethylaminomethylene)indoleninium Tetrafluoroborate (IXb). A mixture of 2.16 g (10 mmoles) of compound IIIb and 2.28 g (12 mmoles) of triethyloxonium tetrafluoroborate in 20 ml of dichloroethane was stirred at 50°C for 2 h, another 0.5 g of triethyloxonium tetrafluoroborate was added and the mixture refluxed for 2 h 30 min. The solvent was evaporated and the residue triturated sequentially with heptane, ether, and 2-propanol to give 1.9 g of the product IXb. IR spectrum: 1660 cm^{-1}. NMR spectrum (in $CDCl_3$): 8.60 (1H, s, α-H), 7.60 (1H, s, 4-H), 4.54 (2H, q, OCH_2CH_3), 4.16 (2H, q, NCH_2CH_3), 3.76 (3H, s, NCH_3), 3.63 (3H, s, NCH_3), 1.53 (3H, t, OCH_2CH_3), 1.42 ppm (3H, t, NCH_2CH_3).

2-Methoxy-3-(N, N-dimethylaminomethylene)indolenine (X). To a solution of sodium methoxide, prepared from 0.13 g of Na and 15 ml of methanol, was added portionwise 1.57 g (5 mmoles) of compound VIII at a temperature of 8-10°C. The mixture was then stirred at 20°C for 3 h and subsequently refluxed for 15 min. The solvent was evaporated, 50 ml of dichloroethane was added to the residue, and the insoluble sodium methyl sulfate filtered off. The dichloroethane was then removed and the residue triturated with petroleum ether to give 1 g of compound X. IR spectrum: 1640 cm^{-1} (C=N).

2-Methoxy-3-formylindole Oxime (XI). A mixture of 0.75 g (3.7 mmoles) of compound X, and 0.28 g (4.0 mmoles) of hydroxylamine hydrochloride in 10 ml of absolute ethanol was stirred at 20°C for 4 days. The mixture was then filtered, the filtrate concentrated, and the residue triturated first with petroleum ether, then with water to give 0.5 g of compound XI. IR spectrum: 3260 broad (OH, NH), 1620 cm^{-1} (C=N). NMR spectrum (DMF-D_7): 11.62 (1H, br. s, OH), 10.36 (1H, s, NH), 8.33 (1H, s, α-H), 7.86 (1H, m, 4-H), 4.13 ppm (3H, s, OCH_3).

1-Ethyl-2-ethoxy-3-formylindole (XII). To a solution of sodium ethoxide, prepared from 0.75 g of Na and 30 ml of absolute ethanol, was added, at 5°C, 3.32 g (10 mmoles) of the tetrafluoroborate IXb. The mixture was stirred at 10-15°C for 1 h and the precipitate filtered off. The filtrate was concentrated and the residue triturated with hexane to give 1.47 g of compound XII. IR spectrum: 1630 cm^{-1} (CO). NMR spectrum ($CDCl_3$): 10.19 (1H, s, CHO), 4.62 (2H, q, OCH_2CH_3), 4.01 (2H, q, NCH_2CH_3), 1.54 (3H, t, OCH_2CH_3), 1.38 ppm (3H, t, NCH_2CH_3).

1-Ethyl-3-(benzylaminomethylene)-2-benzylimmonium Tetrafluoroborate (XVa). To a solution of 1.0 g (3 mmoles) of compound IXb in 20 ml of absolute ethanol was added dropwise 1.07 g (1.1 ml, 10 mmoles) of benzylamine at 20°C. The mixture was stirred at 20°C for 3 h, concentrated, and the residue triturated with petroleum ether and ethyl acetate to give 0.5 g of compound XVa. A second crop (0.7 g) of product was obtained from the ethyl acetate mother liquor. IR spectrum: 3470 (NH), 1630 cm^{-1}. NMR spectrum (DMF-D_7): 8.56 (1H, s, α-H), 4.92 (1H, s, CH_2), 4.72 (1H, s, CH_2), 4.33 (2H, q, CH_2CH_3), 1.38 ppm (3H, t, CH_2CH_3).

1-Ethyl-3-(β-phenylethylaminomethylene)-2-(β-phenylethyl)immonium Tetrafluoroborate (XVb). A mixture of 1.0 g (3 mmoles) of compound IXb and 1.21 g (10 mmoles) of β-phenylethylamine in 20 ml of absolute ethanol was stirred at 20°C for 4 h. The mixture was cooled and 0.3 g of the precipitated product XVb was obtained by filtration. From the filtrate, another 0.8 g of XVb was recovered by concentration and trituration of the residue with 2-propanol. IR spectrum: 3480 (NH), 1640 cm^{-1}. NMR spectrum (DMF-D_7): 9.17 (1H, s, NH^+), 8.16 (1H, s, NH), 8.05 (2H, m, 4-H and α-H), 4.16 (2H, q, CH_2CH_3), 4.01 (2H, t, CH_2NH^+), 3.81 (2H, q, CH_2NH), 3.09 [4H, m, 2(CH_2Ph)], 1.17 ppm (3H, t, CH_2CH_3).

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