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Studies on Single-Electron Transfer Reagents. Part IV[1a-c] Reaction of Nitrogen Heterocycles with Sodium Naphthalenide

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Abstract: *Reactions of several nitrogen heterocycles with sodium naphthalenide in aprotic solvents were investigated. The reactions were quenched with an aqueous buffer. Quinoline reacted by the single-electron transfer pathway to give a 'dimeric' (3), a 'trimeric' product (4) and 4-quinolone. 4-Quinazolinone afforded a single 'dimeric' product (9). Reaction of isoquinoline in monoglyme gave three 'dimeric' products and 4-hydroxy isoquinoline. N-Methyl oxindole gave a 'dimeric' and two 'trimeric' products. The structure of the products were established by spectroscopical techniques including two-dimensional NMR studies.*

INTRODUCTION

Single-electron transfer (SET) reactions of several unsaturated and heterocyclic systems using sodium naphthalenide have been investigated by us. We have found that if the reactions are carried out in aprotic media, dimerisation and disproportionation reactions occur to give novel products. The results for cinnamic acid amides whose dimerisation occur in a diastereoselective manner[1a] have been reported by us. Previous reports of reduction of heterocycles by single-electron transfer reagents were usually carried out in the presence of proton donors[2-7]. The systematic investigation of SET-reagents with heterocycles under aprotic conditions has been undertaken in order to gain insight into the reactivity of anion radicals generated from heterocyclic systems. The present communication reports the reaction of sodium naphthalenide with quinoline, 4-quinazolinone, isoquinoline and N-methyl-oxindole.

RESULTS AND DISCUSSIONS

Quinoline : Reports of reduction studies of quinoline abound in the literature[2,4,5,6]. Both chemical and electrochemical reductions are

reported to give a variety of products, including 2,2' and 3,3'-dimers. Electrochemical reduction[8] was reported to have furnished dimeric and trimeric products which have defied characterisation so far.

During our investigations, quinoline was reacted with sodium naphthalenide in monoglyme at 0°C for 3 h. Quenching the reaction with an aqueous citrate buffer followed by the usual work-up revealed the formation of three products 2, 3 and 4 in addition to a substantial amount of coloured intractable polar compounds.

The dimeric product 3, $C_{18}H_{14}N_2$ (M^+ 258), showed UV and IR characteristics of a substituted quinoline. The mass was uncharacteristic except for peaks at m/z 128 and 127 indicating the presence of a quinolinyl unit in the molecule. The 300 MHz ^{1}H-NMR showed nine aromatic protons (one quinoline ring and one tetrahydroquinoline ring[9a]), an -NH- and four nonaromatic protons. Decoupling experiments showed the presence of the sequence -CH-CH_2-CH- with the methines appearing at low field values of δ 4.41 and δ 4.77, attesting to their benzylic positions. Thus it appeared that the dimer was formed from a disubstituted quinoline with a 2',4'-linked tetrahydroquinoline. The ^{13}C NMR data agreed with the above conclusions. Assignment of all the carbon signals was made from the two-dimensional ^{13}C-^{1}H shift correlation experiments[10], separately optimised for showing 1-bond and long-range (Fig.1) couplings. The appearance of a sharp singlet at δ 8.87 seemed to indicate its attachment to C-2 of the quinoline moiety; this eliminated the two 2,3-linked

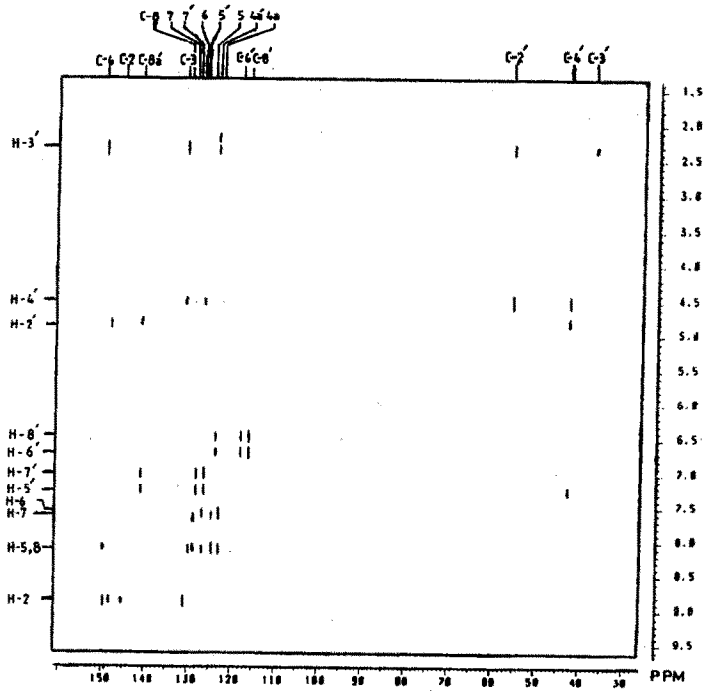


Fig.1 : 300 MHz ^{1}H-/75.5 MHz ^{13}C-NMR heteronuclear shift correlation spectrum of (3) by XHCORR sequence optimised for long-range coupling.

possibilities. The points of attachment of the two moieties could be made from Fig.1. The crucial cross-peaks were those corresponding to $^{3}J_{CH}$ between H-4' to C-3, and H-2' to C-4 which decided in favour of the 4-4', 3-2'-linked structures.

The trimeric product **4**, $C_{27}H_{23}N_3$ (M^+ 389), exhibited UV and IR characteristics of a substituted quinoline. The mass spectrum showed fairly strong peaks at m/z 259 and 130 indicating the presence of a biquinolinyl and a quinolinyl unit respectively in the molecule. The structural features of the molecule were elucidated on the basis of detailed 2D-NMR studies. The 300 MHz ^{1}H NMR showed the presence of fourteen aromatic protons, two exchangeable -NH- and seven non-aromatic protons. Decoupling experiments and the ^{1}H-^{1}H COSY-90° 2D-spectrum (Fig.2) established the interrelationship of the protons and allowed the separation of the three sets of protons attached to the three benzenoid moieties; the most downfield set of aromatic protons corresponded to a quinoline moiety and the two comparatively upfield sets to two tetrahydroquinoline moieties. The ^{1}H-^{1}H-COSY-90°, decoupling experiments and ^{1}H-^{13}C correlation of the non-aromatic moiety showed the presence of the structural unit **5**. Thus it appeared that the trimer was formed from a rigid azabicyclo[3.2.1]octane system with 3,2'- and 4,4'-links between the two tetrahydroquinoline moieties. The third heterocyclic unit was therefore attached to C-2. The points of linkages could be settled unequivocally with the help of ^{1}H-^{13}C long-range optimised XHCORR experiments, a ^{1}H-^{1}H-COSY-long-range experiment and the fully coupled ^{13}C-NMR spectum. Two XHCORR-LR 2D-

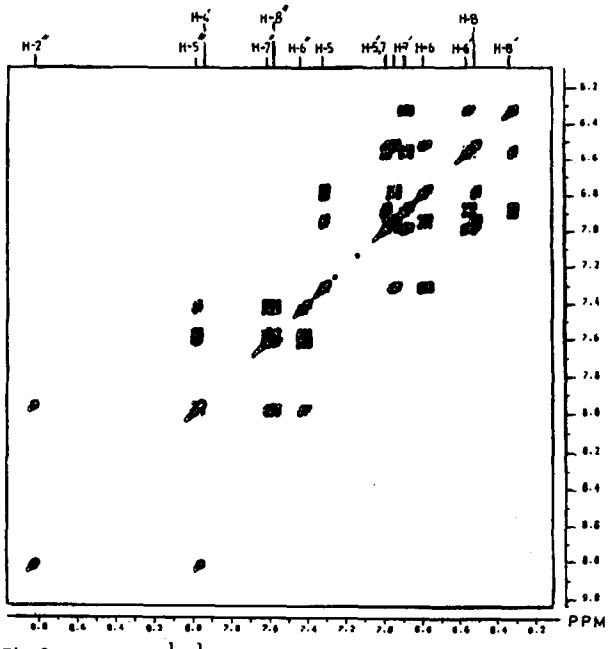
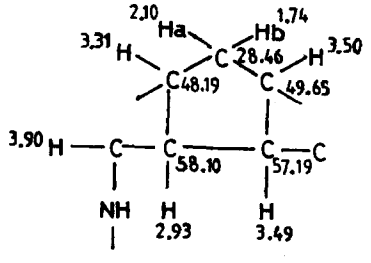


Fig.2 : 300 MHz ^{1}H-^{1}H COSY-90° spectrum of (4) in $CDCl_3$ (Aromatic region).



(5)

spectra were recorded with delay parameters corresponding to the optimisation of cross-peaks corresponding to J_{CH} of ~6.5 Hz (Fig.3) and 9 Hz, the first to emphasise $^{3}J_{CH}$ in aromatic systems while the latter emphasised $^{2}J_{CH}$ in the non-aromatic part. The appearance of downfield doublets at δ 8.82 and δ 7.96, their ^{1}H-^{1}H COSY-90° correlations and small coupling constant (J~2.0 Hz) indicated that these protons were attached to C-2" and C-4" of the quinoline moiety. Thus it appeared that the quinoline ring was attached at C-3", and not at C-4". The positions of attachement (3, 2'- and 4,4'-linked) between the two tetrahydroquinoline moieties in **4** could be ascertained by the observance of cross-peaks corresponding to the following 3-bond couplings in the ^{1}H-^{1}H-COSY-LR spectrum : H-4 (δ 3.49) - H-5 (δ 7.32); H-4' (δ 3.50) - H-5' (δ 6.99); H-2 (δ 3.90) - H-4" (δ 7.96).

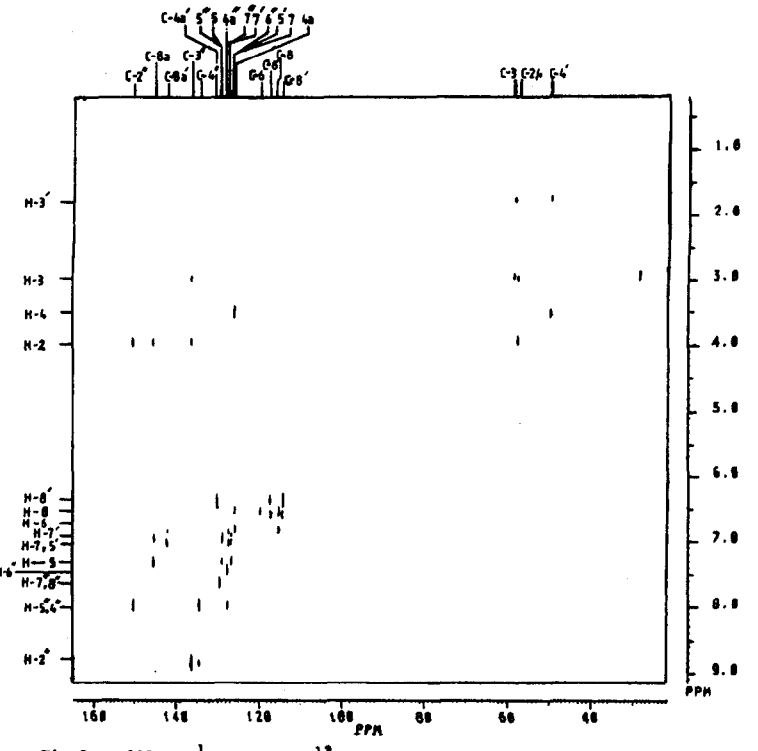
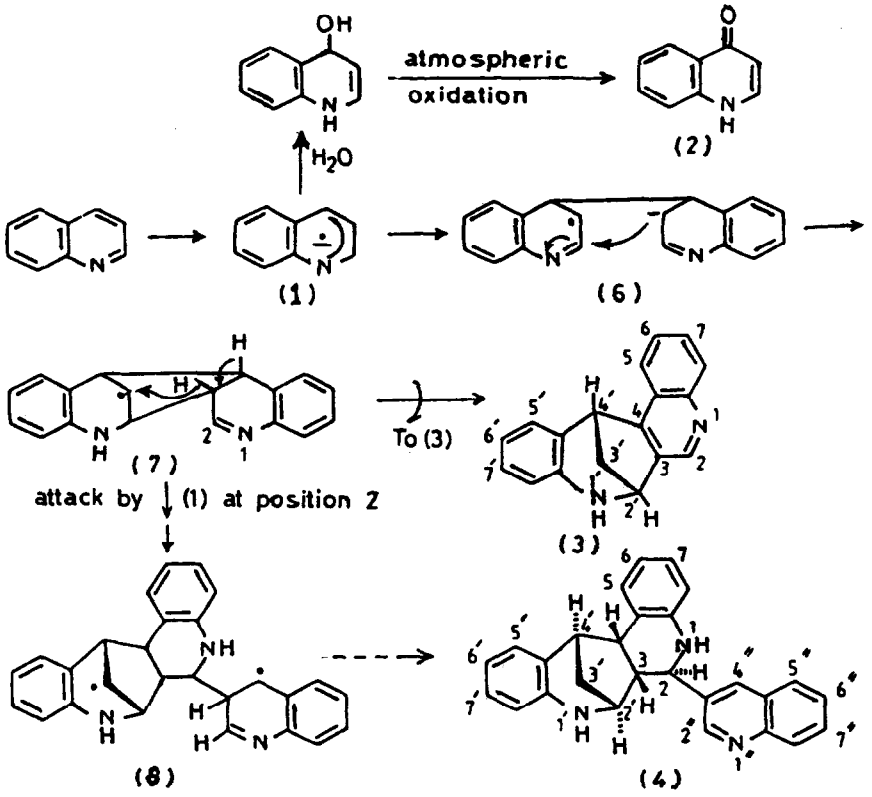


Fig.3 : 300 MHz ^{1}H-/75.5 MHz ^{13}C-Heteronuclear shift correlation spectrum of (4) in $CDCl_3$ using XHCORR sequence optimised for long-range coupling with D_3=0.08 (corresponding to $^{3}J_{CH}$=6.25Hz).

The first step in the reaction of quinoline involved SET to give a quinolinide anion radical **1** (Scheme I). The formation of large amount of 4-quinolone **2** during the work-up from **1**, attested to the low reactivity of this species towards further reduction or coupling. However, by prolonging reaction times, appreciable yields of the coupled products could be obtained. **1** coupled with quinoline to give anion radical **6**. Attack of the enamine anion on the imino-double-bond generated **7**, which with appropirate hydrogen transfer led to **3**. **4** was presumably generated by attack at the 3-position of a second quinolinide anion radical on the imino double bond in **7** (Scheme I).



Scheme I

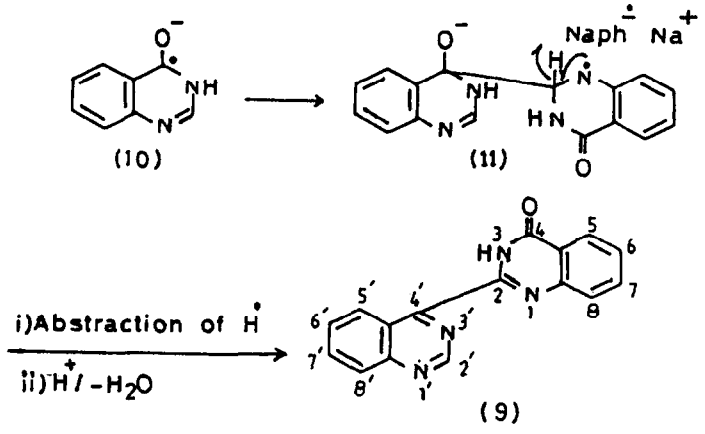
4-Quinazolinone : The reaction of 4-quinazolinone with sodium naphthalenide led to a single product 2-(4'-quinazolinyl)-4-quinazolinone 9, $C_{16}H_{10}N_4O$ (M^+ 274). The UV absorption maxima showed hypsochromic shift similar to 4-quinazolinone. The IR spectrum revealed the presence of an amide carbonyl (1715 cm^{-1}), C=N (1640 cm^{-1}) and -NH/-OH groups (3100-3360 cm^{-1}). Its mass spectrum showed significant peaks corresponding to M^+ (m/z 274), M-1 (m/z 273), M-CHO (m/z 245) and quinazolinyl (m/z 145). The structure was established by detailed NMR studies, which included COSY-45°[11], and 2D-heteronuclear shift correlations by the XHCORR sequence[10], separately optimised for 1-bond and long-range couplings. Homodecoupling and COSY-45° experiments established the presence of a 2-substituted 4-quinazolinone ring system and a quinazoline ring-system, linking was through C-2' or C-4' as only one low-field singlet was present at δ 9.36. The position of attachment could be determined as being at C-4' from the long-range XHCORR spectrum

: the low-field singlet at δ 9.36 did not show $^{3}J_{CH}$ to any protonated carbon. Hence it was situated at C-2', and not at C-4', when a $^{3}J_{CH}$ to the C-5' at δ 10.01 would have been observed.

Single-electron transfer from sodium naphthalenide to a molecule of quinazolinone generated the radical anion 10, which reacted to give the dimeric radical anion 11. Loss of a hydrogen radical, presumably to sodium naphthalenide, and then subsequent dehydration during work-up yielded 9 (Scheme 2). The reaction occurred slowly, presumably due to solubility problems. Prolonging the reaction time from 2 h to 24 h led to an increase in isolated yield from 17% to 62%.

Isoquinoline : Reaction with sodium naphthalenide in monoglyme was carried out at 0°C for 3 h after which the reaction mixture was quenched with the aqueous citrate buffer. Four products 12-15 were separated by chromatographic resolution, and characterised by spectroscopic analysis.

Product 12, $C_{18}H_{12}N_2$ (M^+ 256), m.p. 160°, showed UV and IR spectra similar to those of isoquinoline. Mass and detailed NMR analyses (^{1}H, ^{13}C and 2D established structure 12 for this product. This had been obtained earlier by Li-Xin Dai et al[12] in the reaction of 1-bromo-isoquinoline with zinc-$NiCl_2$-PPh_3.



Scheme 2

Product 14, $C_{18}H_{16}N_2O$ (M^+ 276), m.p. 193° showed IR (KBr) bands at 2300-3000 (br., -NH,-OH) and 1625 (C=N) cm^{-1}. Its 300 MHz ^{1}H NMR spectrum showed nine aromatic protons. The chemical shifts of five of these were comparable to those of 4-hydroxyisoquinoline (13) with the absence of the C-3 singlet at δ 7.94; this indicated that dimerisation

had occurred at the 3-position. The chemical shifts of the four other aromatic protons (δ 7.13-7.24) and the presence of an AB quartet at δ 4.19 and δ 4.02 (J=16.7 Hz, C-1' protons) confirmed the presence of a 1,2,3,4-tetrahydroiosquinoline[9b] moiety. Only one of the C-4'-protons was discernable at δ 4.57 (dd, J=5.8, 5.2 Hz), with the other obscured by overlap with solvent signals.

Product **15**, $C_{18}H_{12}N_2O$ (M^+ 272), m.p. 155°, showed IR (KBr) bands at 2500-3500 cm^{-1} (br, -OH, -NH-), 1620 and 1580 cm^{-1} (α,β-unsaturated amide carbonyl). The dimeric nature of this compound, consisting of an isoquinoline and a 1-isoquinolone unit was indicated by its MS fragmentation pattern, and by its IR and NMR spectra. Structural clarification of the product as **15** followed from detailed NMR studies (Table 1), which included the following 2D-NMR experiments : ^1H-^1H-COSY-45°, XHCORR C-H-correlations separately optimised for 1-bond and long-range (Fig.4) couplings. The presence of the linkage between C-4 of the isoquinoline unit was established by the following observations : (i) absence of H-1 of the isoquinoline unit at δ 9.13; (ii) the signal at δ 8.23 of the isoquinoline unit showed no cross-peaks in the COSY-45° spectrum indicating its attachement to C-3; (iii) cross-peaks were observed in the XHCORR-LR spectrum corresponding to $^3J_{CH}$ between C-4'a to H-6' and H-8', C-8'a to H-5' and H-7'. 4-Hydroxyisoquinoline (**13**), C_9H_7NO (M^+ 145), m.p. 218°, was also obtained as one of the products.

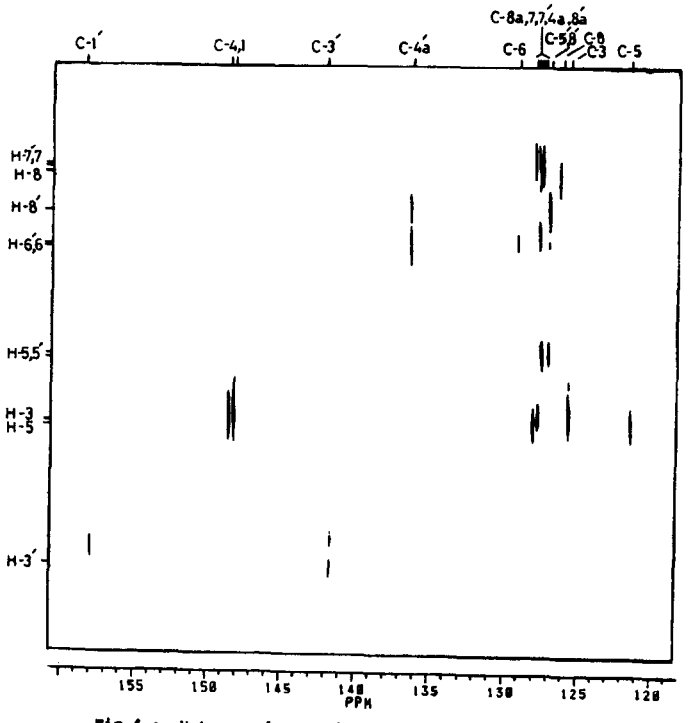


Fig.4 : Heteronuclear shift correlation spectrum of (15)

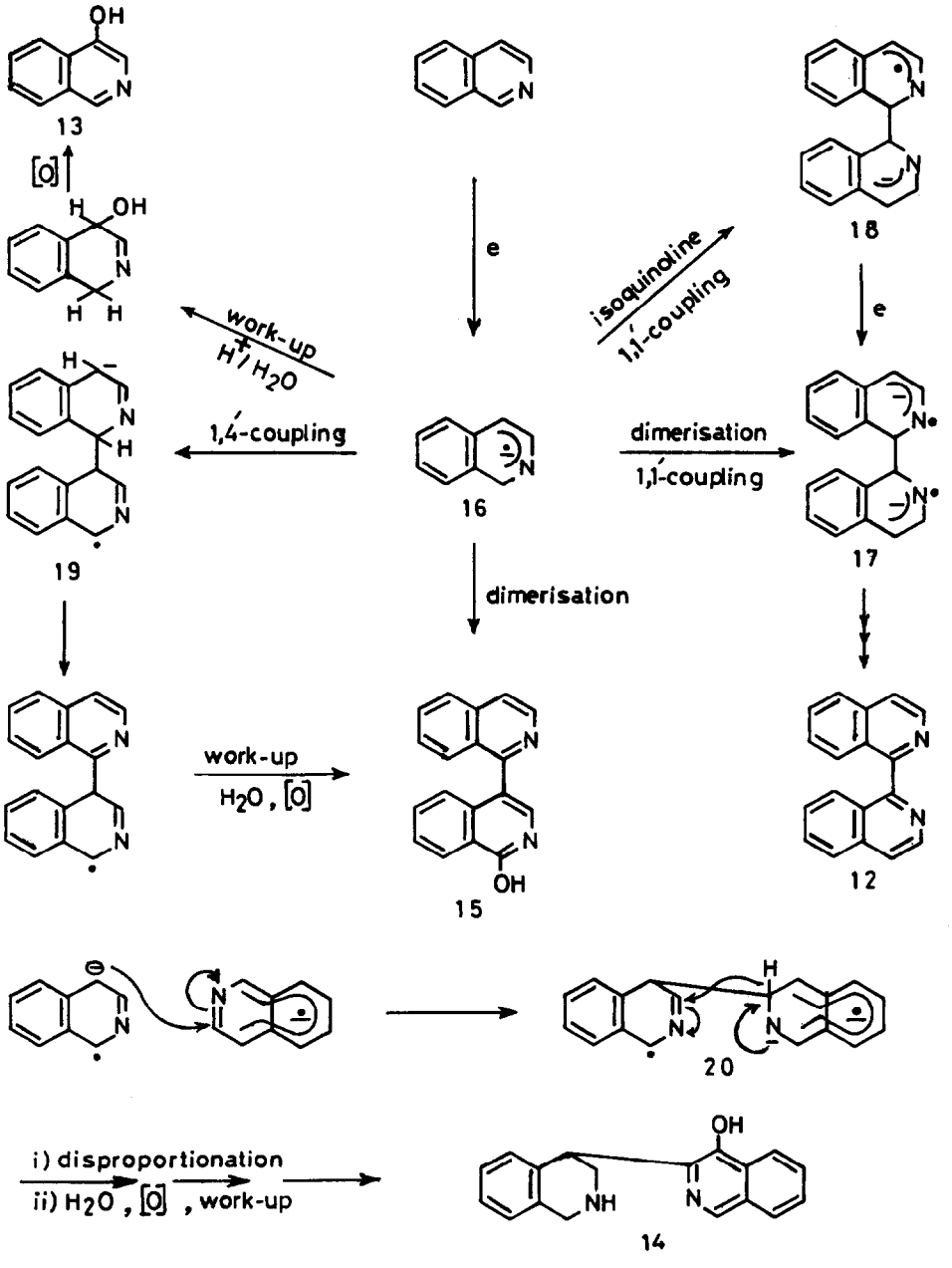
A plausible mechanistic rationale is suggested in Scheme 3.

Table 1 : 300 MHz ^{1}H NMR and 75.5 MHz ^{13}C NMR assignments of (15) in d_6-DMSO

Carbon/ hydrogen	Carbon (δ,ppm)	Hydrogen (δ,ppm)	Multiplicity and coupling constant of proton signal (J,Hz)	Correlation from COSY-45°	Long range correlations of carbon signal with protons ($^{3}J_{CH}$)
1	148.28	-	-	-	H-3 $^{3}J_{CH}$
3	125.63	8.23	s	-	-
4	148.60	-	-	-	H-5 $^{3}J_{CH}$
4a	127.64	-	-	-	H-3 $^{3}J_{CH}$
					H-6 $^{3}J_{CH}$
5	121.38	8.25	d, J=8.5	H-6	-
6	129.09	7.73	t, J=8.3	H-5	H-8 $^{3}J_{CH}$
				H-7	
7	127.70*	7.50	t, J=8.2	H-6	H-5 $^{3}J_{CH}$
				H-8	
8	126.26	7.56	d, J=8.2	H-7	H-6 $^{3}J_{CH}$
				H-6	
8a	127.99	-	-	-	H-5 $^{3}J_{CH}$
					H-7 $^{3}J_{CH}$
1′	157.95	-	-	-	-
3′	141.58	8.63	d, J=5.7	H-4′	-
4′	120.63	7.95	d, J=5.7	H-3′	-
4′a	136.34	-	-	-	H-6′ $^{3}J_{CH}$
					H-8′ $^{3}J_{CH}$
5′	126.98	8.06	d, J=8.2	H-6′	H-7′ $^{3}J_{CH}$
6′	130.42	7.75	t, J=8.2	H-5′	-
				H-7′	
7′	127.55*	7.54	t, J=7.8	H-6′	-
				H-8′	
8′	126.98	7.65	d, J=7.4	H-7′	-
8′a	127.46	-	-	-	H-5′ $^{3}J_{CH}$
					H-7′ $^{3}J_{CH}$

* Values are interchangeable.

Scheme 3


13
[O]
work-up
H⁺/H₂O
e
isoquinoline
1,1-coupling
18
e
1,4-coupling
dimerisation
1,1-coupling
16
17
19
dimerisation
work-up
H₂O, [O]
15
12
20
i) disproportionation
ii) H₂O, [O], work-up
14

Isoquinoline accepts an electron from sodium naphthalenide to give the anion radical **16**. The isoquinoline anion radical, in the absence of proton donors in the reaction medium, underwent a variety of reactions to yield dimeric species. In **16**, the positions of anion and radical activity are the sites 1 and 4. Dimerisation could occur either to give a 1,1'-linkage (product **12**) or a 1,4'-linkage (product **15**). **16** behaving as an aza-allyl anion, could function as a nucleophile to attack the 2,3-imino bond in a second anion radical species **16** to generate **20**, which by a reaction-sequence involving disproportionation and oxidation during work-up, yields **14**. If the reaction was quenched after 15 minutes, 4-hydroxyisoquinoline was the overwhelmingly major product. In view of its stability, the isoquinoline anion-radical can be used as a SET-reagent. Compared to sodium naphthalenide, the extra electron is accomodated in a lower-lying LUMO, so that electron transfer is expected to be comparatively more facile from the isoquinolinide anion-radical.

N-Methyloxindole : N-Methyloxindole (**21**) was reacted with sodium naphthalenide in monoglyme at 0°C for 3 h, after which the reaction was quenched with an aqeuous citrate buffer to give three products - **22**, **23** and **24**.

Product **22**, $C_{18}H_{14}N_2O_2$ (M^+290), m.p. 270° showed absorption maxima at 391, 360, 270nm (log ε : 4.02, 3.93, 4.25). Its IR spectrum (KBr) showed characteristic bands at 1680 cm^{-1} (carbonyl) and 1610 cm^{-1} (olefinic double bond). The 300 MHz ^1H NMR spectrum was similar to that of N-methyloxindole except for two features : (i) the C_3-methylene protons were lacking, and (ii) the C_4-proton was markedly deshielded. This indicated that dimerisation had occurred at the 3-positions with the formation of double bond between two moieties. The NMR spectra (^1H and ^{13}C) which showed half the number of signals, and mass spectral fragmentations supported the structural formulation **22**.

Products **23** and **24**, $C_{27}H_{23}N_3O_3$, exhibited almost identical UV and IR absorption spectra, similar to those of N-methyloxindole. Their 300 MHz ^1H NMR spectra showed the presence of twelve aromatic protons, two methine singlets along with three singlets for three N-methyl groups. The complicated nature of the ^1H-spectra in the aromatic region was analysed by extensive decoupling experiments as well as by ^1H-^1H-COSY separately optimised for one-bond and long-range couplings. The chemical shifts of the aromatic protons were similar to those of N-methyloxindole except those of the protons assigned to C-4, C-4' and C-4". The positions of many of the signals were different for **23** and **24**, the most marked difference being for C-4,

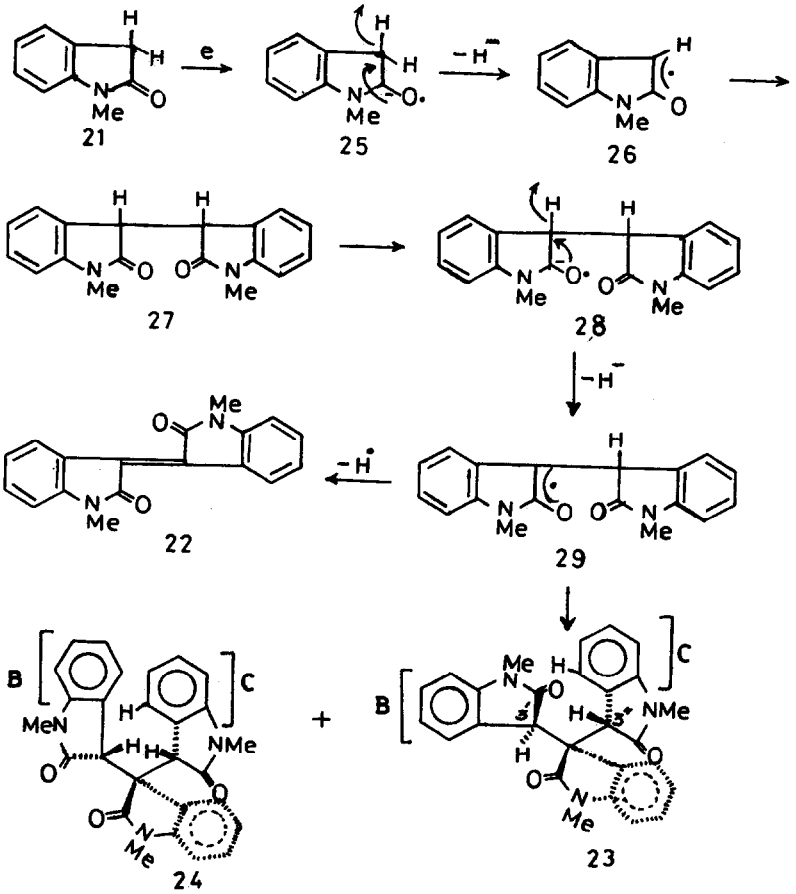
C-4' and C-4" protons and the non-aromatic methines. The assignments are collected in Table 2. MS and detailed NMR analyses of **23** and **24** indicated that N-methyloxindole had trimerized at C-3 in the heterocyclic ring. Since their spectra revealed the presence of similar structural features, **23** and **24** differed in their stereochemisty. A compound of the general formula X-Y-X where X and Y are chiral centres is capable of existing in four stereoisomers - two optically active forms bearing an enantiomeric relationship, and two optically inactive diastereoisomers by internal compensation. An inspection of molecular models showed that **23** and **24** were capable of existing in many conformations of which the least - hindered ones are those shown (Scheme 4). The isomer in which C-3' and C-3" are of opposite chirality (R_rS and S_sR) are capable of existing in two conformers where the positions of rings (B) and (C) are exactly interchanged. In this isomer (**24**), the ^{13}C and ^{1}H-chemical shifts of all the ring carbons and protons would exactly interchange in the two conformers. A similar situation is not possible for the other isomer (**23**), where C-3' and C-3" are of similar chirality (R*R*). **24**, m.p. 250°, was identified as the isomer where C-3' and C-3" had opposite chiralities (R_rS and S_sR) from 300 MHz ^{1}H-NMR studies. The key to the problem was found when ^{1}H-^{1}H decoupling experiments were being performed to determine the coupling patterns for the aromatic protons in **24**. Irradiation of the proton at δ 5.33 (H-4") led to the saturation of the signal at δ 7.89 (H-4') - changes in coupling pattern were observed in the protons at δ 7.07 (H-5') and δ 6.46 (H-5"). Similar interrelationships were observed during decoupling studies for the following pairs of protons: i) δ 7.07 (H-5') and δ 6.46 (H-5") and ii) δ7.35 (H-6') and δ 7.12 (H-6"). The rotational barrier between the conformers was fairly low, and hence during recording of the NMR experiment a change-over of one conformer to the other could occur. A construction of molecular models, showed that this change-over is possible with ring systems (B) and (C) sliding part each other with low non-bonded interactions only where centres C-3' and C-3" had opposite chiralities. In the three-dimensional representation of both **23** and **24** (Scheme 4), it has been observed that the H-4" falls in the shielding zone of C=O (2') in case of **23**; it is in the shielding zone of aromatic ring of N-methyloxindole (ring B) in case of **24**. Hence H-4" appears at extraordinarily high-field values for a benzenoid proton. When the ^{1}H NMR spectrum of **24** was recorded at different temperatures (24°, 34°, 44°) only those protons (the aromatic protons and N-methyls of ring-systems B and C) affected by the change in conformation gradually broadened. This situation did not exist for **23** where irradiation of the

Table 2 : ^{1}H NMR (300 MHz) and ^{13}C NMR (75.5 MHz) of **23** and **24** in $CDCl_3$ at 25°C

Carbon/ Hydrogen	COMPOUND 23			COMPOUND 24		
	^{1}H NMR chemical shift (δ, ppm)	^{13}C NMR chemical shift (δ, ppm)	Multiplicity and coupling constant (J, Hz) - ^{1}H NMR	^{1}H NMR chemical shift (δ, ppm)	^{13}C NMR chemical shift (δ, ppm)	Multiplicity and coupling constant (J,Hz) - ^{1}H NMR
1($N-CH_3$)	3.16	26.13	3H, s	2.74	25.96	3H, s
2	-	175.57	-	-	173.81	-
3	-	55.28	-	-	54.44	-
3a	-	127.42	-	-	127.03	-
4	7.32	123.46	1H,dd,J=7.5,0.9	6.65	122.59	1H, d, J=7.8
5	6.92	122.68	1H,td,J=7.5,1.0	7.22	121.48	1H, td, J=7.8,1.2
6	7.12	129.33	1H,td,J=7.7,1.2	6.73	128.69	1H,td,J=7.5,0.9
7	6.45	108.07	1H,d,J=7.7	6.15	108.04	1H,dd,J=7.4,0.9
7a	-	144.81	-	-	144.75	-
1'(NCH_3)	3.25/2.76	26.96/25.68	3H, S	3.27	26.33	3H, S
2'	-	174.91	-	-	174.80	-
3'	5.60	44.36	1H, S	5.03	48.09	1H, S
3'a	-	124.82	-	-	125.58	-
4'	6.86	123.82	1H,d,J=7.5	7.89	127.03	1H,d,J=7.5
5'	6.71	121.97	1H,td,J=7.3,1.0	7.07	122.48	1H,br t,J=7.6
6'	7.00	128.10	1H,td,J=7.7,1.0	7.35	129.48	1H,br t,J=7.7
7'	6.52	107.63	1H,d,J=7.7	6.72	108.40	1H,d,J=7.6
7'a	-	144.17	-	-	145.41	-
1"($N-CH_3$)	2.76/3.25	25.68/26.29	3H, S	2.82	26.00	3H, S
2"	-	174.64	-	-	174.34	-
3"	5.15	44.36	1H, S	4.11	46.71	1H, S
3"a	-	124.68	-	-	123.90	-
4"	5.45	123.52	1H,d,J=7.5	5.33	123.51	1H,d,J=7.5
5"	6.43	121.31	1H,td,J=7.8,0.9	6.46	121.92	1H,br t,J=7.6
6"	7.06	128.35	1H,td,J=7.8,1.0	7.12	128.83	1H,br t,J=7.5
7"	6.70	107.91	1H,d,J=7.7	6.73	108.15	1H,br.d,J=7.6
7"a	-	144.17	-	-	145.15	-

Note : Proton-proton coupling information was obtained from 2D-COSY and decoupling experiments.

Scheme 4



individual aromatic signals caused saturation of the particular signals only. Moreover, the ^{1}H NMR spectrum of 23 did not change in appearance when recorded at three diferent temperatures (24°, 34°, 44°) unlike 24.

N-Methyloxindole 21 accepts an electron from sodium naphthalenide to give the anion radical 25. This anion radical forms the oxaallyl radical 26 by loss of hydride. This can dimerise to give 27, which accepts an electron to form another radical anion 28, which is transformed to 29 by the loss of hydride ion. 29 can attack the oxaallyl radical 26 to form the diastereoisomeric mixture of 23 and 24. Alternatively 29 can loss a hydrogen radical to give dimer 22 (Scheme 4).

EXPERIMENTAL

Mps were determined on an electrically heated Kofler Block apparatus and are uncorrected. UV spectra were measured on a Varian 634S spectrophotometer in 95% aldehyde-free ethanol and IR spectra on a Perkin-Elmer Model 782 spectrophotometer. 300 MHz ^{1}H NMR spectra and 75.5 MHz ^{13}C NMR spectra as well as 2D NMR (^{1}H-^{1}H-COSY and Heteronuclear Shift Correlation) were recorded with a Bruker AM-300L superconducting magnet NMR spectrometer using a 5mm ^{1}H-^{13}C-dual probe operating with the Bruker DISR861 or DISR871 software. Chemical shifts are quoted in ppm relative to tetramethylsilane (TMS) (internal reference) for solutions in deuteriochloroform as stated. Mass spectra were obtained with a Jeol JMS D-300 mass spectrophotomer. Elemental analyses were carried out by the microanalytical laboratory, Department of Chemistry, Calcutta University.

Neutral alumina (Glaxo) was used for column chromatography and analytical TLC was performed using Merck silica gel G. Organic extracts were dried over anhydrous Na_2SO_4. 4-Quinazolinone was prepared by a standard procedure[13]. Analytical samples were routinely dried over P_2O_5 *in vacuo*. Monoglyme was dried over sodium.

General method for preparation of Sodium Napthalenide [14] : A slight excess of sodium (~1.2 molar proportion) was added to a solution of naphthalene in anhydrous monoglyme under dry nitrogen at 5-10°. The reaction mixture was stirred for 2 h at this temperature. The resulting solution of the reagent was dark green in colour. The reagent keeps for about a day under nitrogen but deteriorates thereafter.

Reaction of Quinoline with Sodium Naphthalenide : Quinoline (1.7g, 0.013 mol) was added at 0°C to a solution of sodium naphthalenide (from 2.73g, 0.021 mol of naphthalene) in anhydrous monoglyme under dry nitrogen. The reaction was complete in 3 h as evidenced on the reaction mixture turning a brownish colour. The reaction mixture was poured into 150 mL water, and then acidified with an aqueous buffer solution of citric acid - sodium citrate (pH ~ 4.5). The resulting mixture was extracted with $CHCl_3$ (3 x 50 mL). The $CHCl_3$ extract was washed successively with aqueous $NaHCO_3$ solution and water, dried (Na_2SO_4) and evaporated under reduced pressure to leave a brown gum which was purified by chromatography over neutral alumina. Chromatography separated the three products : dimer 3, (400 mg,

23.4%), mp 167° and trimer 4, (300 mg, 17.4%), mp 172°, from the benzene eluates, and 4-quinolone 2, (240 mg, 12.4%), mp 198°, from the benzene-EtOAc (4:1) eluates. *Dimer* 3, (Found C, 83.4; H 5.3; N 10.6 $C_{18}H_{14}N_2$ requires C, 83.6; H, 5.4; N, 10.8%); UV (EtOH) 367, 317, 282, 255, 226nm (logϵ : 3.29, 3.40, 3.60, 3.81, 4.45); IR (KBr) 3380, 3220, 1600 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ : 2.26 (1H, d, J 10.7 Hz, 3'-H_b), 2.44 (1H, td, J 10.6, 4.2 Hz, 3'-H_a), 4.32 (1H, s, -NH-), 4.41 (1H, d, J 4.0 Hz, 4'-H), 4.77 (1H, d, J 3.7 Hz, 2'-H), 6.36 (1H, d, J 7.9 Hz, 8'-H), 6.88 (1H, td, J 7.7, J 1.4 Hz, 7'-H), 6.58 (1H, td, J 7.5, 0.9 Hz, 6'-H), 7.13 (1H, dd, J 7.4, 1.2 Hz, 5'-H), ~7.48 (1H, dd, J 7.5, 1.2 Hz, 6-H), 7.56 (1H, dd, J 7.5, 1.4 Hz, 7-H), ~7.98 (1H, dd, J 1.2 Hz, 8-H), 8.00 (1H, br.d, J~8.2 Hz, 5-H), and 8.87 (1H, s, 2-H) ppm; ^1H-^1H-COSY experiments showed inter-correlation between two separate sets of protons - 5-H, 6-H, 7-H, 8-H, and 5'-H, 6'-H, 7'-H, 8'-H; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ : 145.05 (2-C), 130.98 (3-C), 149.63 (4-C), 122.95 (4a-C), 124.40 (5-C), 126.73 (6-C), 128.68 (7-C), 129.88 (8-C), 148.27 (8a-C), 55.72 (2'-C), 36.85 (3'-C), 42.66 (4'-C), 123.96 (4a'-C), 126.36 (5'-C), 118.07 (6'-C), 128.19 (7'-C), 116.03 (8'-C), 140.88 (8a'-C) ppm; m/z 258 (100%), 257 (93.3%), 231 (5.7%), 230 (8.1%), 202 (4.7%), 129 (M^{++} 7.1%), 128 (9.5%) and 127 (11.9%); *Trimer* 4, (Found C, 83.0; H, 5.7; N, 10.5 $C_{27}H_{23}N_3$ requires C, 83.3; H, 5.9; N, 10.8%), UV (EtOH) 360, 304, 229, 217nm (log ϵ : 2.77, 3.83, 4.59, 4.61); IR (KBr) 3397, 3292, 1600, 1500, 1490cm^{-1}; m/z 389 (11.1%), 260 (5%), 259 (19.4%), 257 (6.2%), 168 (4.9%), 132 (2.9%), 131 (25.6%), 130 (100%), 129 (5.2%), 128 (5.8%), 103 (4.6%) and 102 (2.6%). ^1H NMR (300 MHz, $CDCl_3$) δ: 2.10 (1H, dt, J 11.5, 4.4 Hz, 3'-H_a), 1.74 (1H,d, J 11.5 Hz, 3'-H_b), 2.93 (1H,t, J 8.6 Hz, 3-H), 3.31 (1H,d, J 3.3 Hz, 2'-H), ~3.49 (1H,d, J 8.5 Hz, 4-H), ~3.50 (1H,d, J 4.4 Hz, 4'-H), 3.90 (1H,d, J 8.6 Hz, H-2), 3.99 (2H,s, 1,1'-NH), 6.32 (1H,d, J 7.6 Hz, H-8'), 6.52 (1H,d, J 7.7 Hz, H-8), 6.56 (1H,t, J 7.6 Hz, H-6'), 6.79 (1H,t, J 7.7 Hz, H-6), 6.88 (1H,td, J 7.6 Hz, 1.4 Hz, H-7'), 6.95 (1H,t, J 7.7 Hz, H-7), 6.99 (1H,dd, J 7.4, 1.4 Hz, H-5'), 7.32 (1H,d, J 7.6 Hz, H-5), 7.42 (1H,t, J 7.5 Hz, H-6'), 7.57 (1H,d, J 7.2 Hz, H-8"), 7.96 (1H,d, J 1.9 Hz, H-4"), 7.98 (1H,dd, J 6.9, 1.5 Hz, H-5"), 8.82 (1H,d, J 1.9 Hz, H-2") ppm; ^1H-^1H COSY experiments showed inter-correlation between three separate sets of protons - 5-H, 6-H, 7-H, 8-H; 5'-H, 6'-H, 7'-H, 8'-H and 5"-H, 6"-H, 7"-H, 8"-H; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ : 57.32 (2-C), 58.17 (3-C), 57.19 (4-C), 125.94 (4a-C), 128.86 (5-C), 119.65 (6-C), 126.63 (7-C), 115.27 (8-C), 145.40 (8a-C),

48.19 (2'-C), 28.46 (3'-C), 49.65 (4'-C), 130.13 (4'a-C), 126.81 (5'-C), 117.29 (6'-C), 127.37 (7'-C), 114.21 (8'-C), 142.31 (8'a-C), 150.45 (2"-C), 136.29 (3"-C), 134.15 (4"-C), 128.18 (4"a-C), 129.06 (5"-C), 126.81 (6"-C), 127.65 (7"-C), 129.34 (8"-C), 147.73 (8"a-C), 147.73 (8"a-C) ppm.

Reaction of 4-Quinazolinone with Sodium Naphthalenide : 4-Quinazolinone (1.46 g, 0.01 mol) was added at 0°C to a solution of sodium naphthalenide (from 2.04 g, 0.016 mol of naphthalene) in anhydrous monoglyme under dry nitrogen. The reaction mixture was stirred for 2 h at room temperature. It was worked up as described earlier for quinoline. The crude mixture was subjected to column chromatography over neutral alumina. Naphthalene was eluted by petroleum ether, dihydronaphthalene by petroleum ether-benzene (3:1), while the benzene-EtOAc (1:1) eluate afforded a small amount of product **9** (90 mg, 17.0%), as a crystalline solid, mp 244-45°, (found C, 69.8; H, 3.6; N, 20.1 $C_{16}H_{10}O$ requires C, 70.1; H, 3.7; N, 20.4%); UV (Dioxan)352, 340, 244 nm (log ϵ : 3.99, 3.99, 4.16); IR (KBr) 3100-3360, 1715, 1640, 1620, 1580 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ : 7.56 (1H, td, J 7.6, 1.0 Hz, 6-H), ~7.78 (1H, td, J 8.0, 1.3 Hz, 6'-H), 7.81 (1H, td, J 8.0, 1.5 Hz, 7-H), 7.94 (1H, br d, J 8.4 Hz, 8-H), 7.96 (1H, td, J 8.4, 1.4 Hz, 7'-H), 8.09 (1H, br d, J 8.5 Hz, 8'-H), 8.34 (1H, dd, J 7.9, 1.4 Hz, 5-H), 9.36 (1H, s, 2'-H) and 10.01 (1H, br dd, J 8.1, 1.0 Hz, 5'-H); ^1H-^1H COSY experiments showed inter-correlations between two separate sets of protons 5-H, 6-H, 7-H, 8-H and 5'-H, 6'-H, 7'-H, 8'-H. This was confirmed by decoupling experiments which allowed determination of the relative orientation of these protons in the two rings. ^{13}C NMR (75.5 MHz, $CDCl_3$) δ : 122.78 (4a'-C), 122.92 (4a-C), 126.82 (5-C), 128.12 (5'-C), 128.62 (6-C), 128.83 (8-C), 129.16 (8'-C), 129.45 (6'-C), 134.50 (7'-C), 134.70 (7-C), 148.44 (8a-C), 148.95 (8a'-C), 152.61 (4'-C), 153.02 (2'-C), 153.29 (2-C), 160.97 (4-C); m/z 274 (M^+,100%), 273 (45.9%, M-1), 245 (13.0%, M-CHO), 219 (3.3%, M-CHO-CN), 145 (2.6%, M-$C_8H_5N_2$), 129 (6.6%), 119 (16.3%), 102 (12.4%) and 91 (8.4%). Increase in the reaction time to 24 h caused the isolated yield of **9** to increase to 0.33 g (62%).

Reaction of Isoquinoline with Sodium Naphthalenide : Isoquinoline (1.7 g, 0.013 mol) was added at 0°C to a solution of sodium naphthalenide (from 2.73 g, 0.021 mol of naphthalene) in anhydrous monoglyme under dry nitrogen. After 3 h the reaction mixture was worked up similarly to the above and chromatographed over neutral alumina. Chromatography yielded

four different products : 12 (440 mg, 26.3%); mp 160°, from benzene eluates; (Found C, 83.9; H 4.5; N 10.4 $C_{18}H_{12}N_2$ requires C, 84.3; H, 4.7; N, 10.6%); IR (KBr) 1620, 1580, 1560, 1490, 1370, 1322, 870, 840, 800, 750 cm^{-1}; m/z 256 (42%, M^+), 255 (100%, M-1), 228 (3.4%, M-1-HCN), 128 (11.5%), and 127 (7.0%); 13 (240 mg, 12.3%) mp 218°, from benzene-EtOAc (4:1) eluates; m/z 145; 14 (250 mg, 13.8%), mp 193°, from benzene-EtOAC (9:1) eluates; (Found : C, 78.0; H, 5.6; N, 9.8 $C_{18}H_{16}N_2O$ requires C, 78.2; H, 5.8; N, 10.1%), IR (KBr), 3000-2300 (br), 1625, 1560, 1540, 850, 753, 741, 738 cm^{-1} ; ^1H NMR (300 MHz, d_6-DMSO) δ : 8.72 (1H, s, 1-H), 8.11 (1H, d, J 8.8 Hz, 5-H), 7.68 (1H, t, J, 8.1 Hz, 6-H), 7.59 (1H, t, 8.1 Hz, 7-H), 7.99 (1H, d, J 8.2 Hz, 8-H), 4.02 and 4.19 (2H, AB quartet, J 16.7 Hz, 1'-H), 4.57 (1H, dd, J 5.8, 5.2 Hz, 4'-H), 7.24 (1H, d, J 5.4, 5'-H), 7.13-7.18 (3H, m, 6', 7', 8'-H); 15 (360 mg, 20%) mp 155°, from EtOAc eluates; (Found C, 79.1, H, 4.1; N, 10.1 $C_{18}H_{12}N_2O$ requires 79.4; H, 4.4; N 10.3%) IR (KBr) 3500-2500, 1620, 1580, 1510, 1330, 1310, 760, 745 cm^{-1}; m/z 272 (52%, M^+), 271 (100%, M-1), 243 (7.9%, M-HCO), 242 (14.5%, M-1-CHO), 216 (11.8%, M-HCO-HCN), 189, 112 and 108.

Reaction of N-Methyloxindole with Sodium Naphthalenide : N-Methyloxindole (0.33 g, 2.2x 10^{-3} mol) was added at 0°C to a solution of sodium naphthalenide (from 2.04g, 0.016 mol of naphthalene) in anhydrous monoglyme under dry nitrogen. After 3h the reaction mixture was worked up as described earlier and subjected to column chromatography over neutral alumina. Chromatography yielded three different products : 22 (60 mg, 18.7%) mp 270°, from the petroleum ether-benzene (1:3) eluates, (Found C, 74.1; H, 4.6; N, 9.3 $C_{18}H_{14}N_2O_2$ requires C, 74.5; H, 4.5; N 9.6%), IR (KBr) 1680, 1610 cm^{-1}; m/z 290 (100%, M^+); ^1H NMR (300 MHz, $CDCl_3$) δ : 3.21 (3H, s, 1,1'-NCH_3), 9.13 (2H, d, J=7.9 Hz, 4,4'-H), 6.99 (2H, td, J=7.8, 0.9 Hz, 5,5'-H), 7.28 (2H, td, J=7.6, 0.9 Hz, 6,6'-H), 6.71 (2H, d, J=7.7 Hz, 7,7'-H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ : 26.07 (1,1'-NCH_3), 167.96 (2,2'-C), 145.12 (3,3'-C), 121.55 (3a, 3'a-C), 122.35 (5,5'-C), 129.81 (6,6'-C), 107.59 (7,7'-C), 145.12 (7a,7'a-C) ppm; 23 (90 mg, 27.5%), mp 250°, from benzene-EtOAc (4:1) eluates, (Found C, 73.9; H, 5.1, N, 9.3 $C_{27}H_{23}J_3O_3$ requires C, 74.1; H, 5.3; N, 9.6%), IR (KBr) 1710-1680, 1600 cm^{-1}; m/z 291 (100%, M-C_9H_8NO), 262 (13.0% M-C_9H_8NO-HCO), 247 (32.0%, M-C_9H_8NO-HCHO-CH_3), 234 (17.2%), 233 (17.7%), 232 (14.3%), 219 (24.8%), 218 (12.1%); 24 (140 mg, 42.8%), mp 250° from benzene-EtOAc (4:1) eluates [Found C, 73.8; H, 5.1; N, 9.4 $C_{27}H_{23}N_3O_3$ requires C, 74.1; H, 5.3; N, 9.6%); IR (KBr) 1720-1690, 1600 cm^{-1}; m/z 291 (100%, M-C_9H_8NO), 248 (3.5%, M-C_9H_8NO-CO), 247 (9.2%, M-C_9H_8NO-HCHO-CH_3), 234 (5.1%), 233 (3.1%), 232 (4.7%), 219 (5.2%).

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