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Novel Dealkylating & Deaminating Reactions of 2-Chlorobenzothiazole, 2-Chlorobenzoxazole, 2-Chloropyridine & Methyl 2-Chloro-5-nitrobenzoate with N-Amino-compounds*†

K. NAGARAJAN, C. L. KULKARNI & R. K. SHAH
CIBA Research Centre, Goregaon East, Bombay 63

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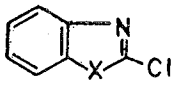
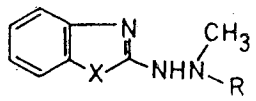
2-Chlorobenzothiazole (I) and N,N-dimethylhydrazine undergo anomalous reaction to yield N-methyl-N-(2-benzthiazolyl)-hydrazine (V) (79%), 2-dimethylaminobenzothiazole (X) (20%) and traces of 2-methylaminobenzothiazole (XI) (1%). With N-aminopiperidine and N-aminomorpholine I forms 2-piperidino-(XIII)- and 2-morpholino-(XIV)-benzothiazoles respectively arising by the deamination of N-aminomorpholine and N-aminopiperidine. 2-Chlorobenzoxazole (II) and N,N-dimethylhydrazine produce preponderantly deaminated derivative XV, some dealkylated product VI and also dimethyl hydrazinobenzoxazole XVI. II also dealkylates N,N-dimethylcyclohexylamine to yield XV and XVII. 2-Chloropyridine and N,N-dimethylhydrazine react under forcing conditions to form 2-dimethylamino-(XVIII)- and 2-methylamino-(XIX)-pyridines. Methyl 2-chloro-5-nitrobenzoate (XXII) demethylates N,N-dimethylhydrazine to form the indazolone XXIII, while benzyl bromide merely quaternizes it. These observations are rationalized and plausible mechanisms suggested.

IN connection with some synthetic work, we attempted to prepare N-(2-benzthiazolyl)-N',N'-dimethylhydrazine (III) by the reaction of 2-chlorobenzothiazole (I) with N,N-dimethylhydrazine in alcohol. A crystalline product, m.p. 137-40°, was readily isolated in about 60% yield. Its analysis and NMR spectrum in $CDCl_3$ [δ 3·37 (*s*, 3H, NCH_3), 4·17 (broad *s*, 2H, washed out by D_2O) and 6·9-7·8 ppm (*m*, 4H)] indicated that the product had one less methyl group than required by formula III, and that it must be one of the monomethyl hydrazines IV or V. The product readily afforded *p*-chlorobenzylidene and 5-nitro-2-furfurylidene derivatives, thus allowing it to be identified as V.

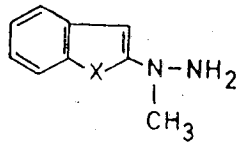
This unexpected result prompted us to study the reaction of 2-chlorobenzothiazole (I) and 2-chlorobenzoxazole (II) with various hydrazines. I and hydrazine are known to produce 2-hydrazinobenzothiazole[1]. Reaction of N-methylhydrazine with I in refluxing alcohol gave V (90%) identical with the one obtained previously. Obviously, the nitrogen carrying the methyl substituent in N-methylhydrazine is more nucleophilic than the other β-Hydroxy-ethylhydrazine likewise gave hydrazine



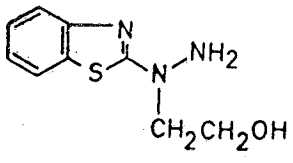
I X = S
II X = O



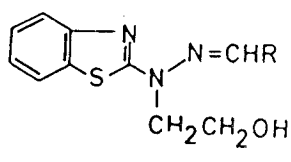
III R = CH_3 X = S
IV R = H X = S
XVI R = CH_3 X = O



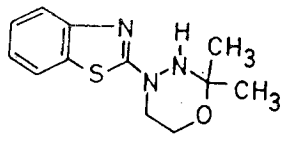
V X = S
VI X = O



VII



VIII



IX

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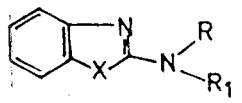
VII, which readily formed acyclic Schiff's bases VIII with aldehydes (NMR CH=N at about δ 8·2 ppm) but the cyclic derivative IX with acetone

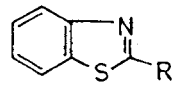
(NMR : $>C<^{CH_2}_{CH_2}$, δ 1·37 ppm).

It thus appeared that anomalous demethylation occurred only in the reaction of N,N-dimethylhydrazine with I. Hence this was investigated in detail. The total product from one such reaction was carefully chromatographed on a silica gel column. Besides V as the major product, significant amounts of 2-dimethylaminobenzothiazole (X) and traces of 2-methylaminobenzothiazole (XI) were also isolated. The chemical shifts of the N-methyl groups in V, X and XI in their NMR spectra were significantly different from one another and allowed to estimate that the total product (85% yield) from reaction of I with N,N-dimethylhydrazine in alcohol was composed of 79% of V, 20% of X and 1% of XI. I was unreactive towards N-methyl-N-phenylhydrazine and N,N-dimethylcyclohexylamine. It gave only the expected product XII with N-methylpiperazine in 56% yield. On the other hand, N-aminopiperidine was deaminated by I in boiling alcohol. The product XIII obtained in about 70% yield was identical with the one from I and piperidine Likewise, deamination occurred when I and N-aminomorpholine were refluxed together in alcohol. The product obtained in 75% yield was identified as XIV. It was verified that under these conditions neither N-aminomorpholine nor N-aminopiperidine underwent deamination by themselves (VPC analysis). However, it will be of interest to mention that the above two amino compounds underwent deamination on prolonged exposure to light.

It was of interest next to study the behaviour of the more reactive 2-chlorobenzoxazole (II) with N,N-dimethylhydrazine. The reaction was conducted in refluxing alcohol and the total basic product separated by column chromatography on silica gel. The major product was 2-dimethylaminobenzoxazole XV, identical with an authentic sample obtained from II and dimethylamine. The next significant product was a methylhydrazinobenzoxazole, identified as VI, because it was obtained from II and N-methylhydrazine and it readily formed arylidene derivatives A small amount of a third product, m.p. 124-6°, was also detected. From its analysis and NMR spectrum in CCl_4 [$N(CH_3)_2$, *s*, δ 2·78 ppm; 4 aromatic H from 6·8-7·5 ppm, NH, broad singlet at 9·22 ppm washed out by D_2O], this was identified as 2-dimethylhydrazinobenzoxazole (XVI). From NMR analysis of the total product of reaction of II with N,N-dimethylhydrazine, it could be computed that XV, VI and XVI were formed in yields of 77, 16 and 7% respectively.

Unlike I, the chlorobenzoxazole (II) was able to dealkylate tertiary amines, although not very effectively, nor in every case. Thus, when II and N,N-dimethylcyclohexylamine were refluxed together in alcohol for 2 hr, 50% of II was recovered, but 14% of 2-dimethylaminobenzoxazole (XV) and 15% of 2-[(N-cyclohexyl)-N-methylamino]benzoxazole



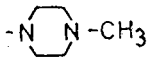


X R = R_1 = CH_3 X = S

XI R = CH_3; R_1 = H X = S

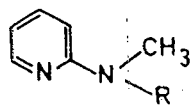
XV R = R_1 = CH_3; X = O

XVII R = CH_3; R_1 = Cyclohexyl; X = O

XII R = 

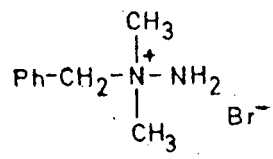
XIII R = 

XIV R = 

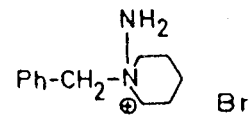


XVIII R = CH_3

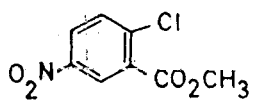
XIX R = H



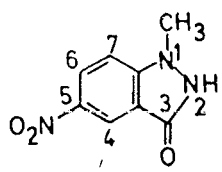
XX



XXI



XXII



XXIII

(XVII) were isolated. The latter was identical with a sample obtained from II and N-methyl cyclohexylamine. Thus statistically N-decyclohexylation was slightly preferred to N-demethylation. N-Benzyl-4-piperidone on the other hand was unaffected by II despite the known facility of N-debenzylation.

As an extension of this study, the behaviour of 2-chloropyridine towards N,N-dimethylhydrazine was studied. There was no reaction under reflux alone or in alcohol, but when the mixture was heated at 150° in a sealed tube for 24 hr, reaction occurred. Careful chromatography of the basic product afforded 2-dimethylaminopyridine (XVIII, 35%) and 2-methylaminopyridine (XIX, 9%) Benzyl bromide only attacked the tertiary nitrogen in N,N-dimethylhydrazine and N-aminopiperidine in refluxing alcohol to form quaternary salts XX and XXI. A similar reaction occurred with N,N-dimethylcyclohexylamine. On the other hand, methyl 2-chloro-5-nitrobenzoate (XXII), with a very reactive chlorine atom (unpublished data), underwent reaction with N,N-dimethylhydrazine to give the indazolone XXIII as the only isolable product in 23% yield. The product was identical with the one obtained from XXII and N-methylhydrazine.

With these data on hand, it was possible to speculate on the mechanism of the reactions of I and II with N,N-dimethylhydrazine. It is likely that the action of this hydrazine on I (Chart 1) is initiated by the formation of the quaternary salt XXIV, either by direct displacement of the halogen by the more nucleophilic tertiary nitrogen, or by its addition to the C=N in I followed by rearomatization and expulsion of Cl^-. Cl^- may now attack a methyl group (path 1) to give V, in a manner analogous to the dealkylations by cyanogen bromide[2] or chloroformic esters[3]. The deaminated product X is likely to arise from XXIV by attack of Cl^- on NH_2 (path 2). A radical mechanism is not excluded but considered unlikely. The origin of XI in this experiment is not clear. It may be formed from V by reduction by the hydrazine. But neither V nor VI was obviously affected by N,N-dimethylhydrazine in refluxing alcohol. The extremely negligible yield of XI, however, does not warrant detailed speculation.

Quaternary salts similar to XXIV may be formed in the reaction of N-aminopiperidine or N-aminomorpholine. In these cases, it is conceivable that CH_2 groups attached to the positive nitrogen are less accessible to Cl^- than the NH_2 group. This would result in deamination and formation of products XIII and XIV. Quaternary salts XX and XXI from benzyl bromide do not undergo deamination or dealkylation presumably because the $-\overset{|}{\underset{|}{N_+}}-C$ and $-\overset{|}{\underset{|}{N_+}}-N$ bonds in them are not as weakened as in XXIV, where additional weakening results from withdrawal of electrons by C=N and S. On the other hand, in a similar complex of N,N-dimethylhydrazine with XXII, the *para*-NO_2 and *ortho*-C=O groups will facilitate the cleavage of a $N-CH_3$ bond by Cl^-. 2-Chloropyridine is less reactive than 2-chlorobenzothiazole. Hence, it apparently does not quaternize N,N-dimethylhydrazine in refluxing alcohol. Under forcing conditions, this is achieved and followed by demethylation to XVIII, which may be further transformed to XIX.

2-Chlorobenzoxazole (II) can be expected to be more reactive than 2-chlorobenzothiazole (I) because of greater inductive withdrawal of electrons by oxygen compared to sulphur. It may be thus possible for it to quaternize N,N-dimethylcyclohexylamine, unlike I (Chart 2). Attack of methyl or cyclohexyl group by Cl^- would lead to the observed products XV and XVII. It is also conceivable that II, being more active than I, would be less discriminating towards the two N atoms in N,N-dimethylhydrazine. Thus, both salts XXV and XXVI, may be formed, the former predominating in keeping with the greater nucleophilicity of the more substituted N. The expected rapid proton loss from XXVI would afford XVI. Attack by Cl^- on CH_3 (path 1) and on NH_2 (path 2) in XXV would lead to products VI and XV respectively (Chart 2).

It was stated earlier that N,N-dimethylhydrazine reacted with I to give demethylated (V) and deaminated (X) products in a ratio of about 4:1. Under identical conditions, II gave the demethylated (VI) and deaminated (XV) products in a ratio of about 1:5. This could be rationalized, if it is assumed that in the quaternary salts XXIV and XXV, a certain amount of hydrogen bonding occurs as shown. If sulphur is able to participate more effectively in this bonding than oxygen, the NH_2 nitrogen in XXIV will be less positive than it is in XXV. This would result in greater attack on

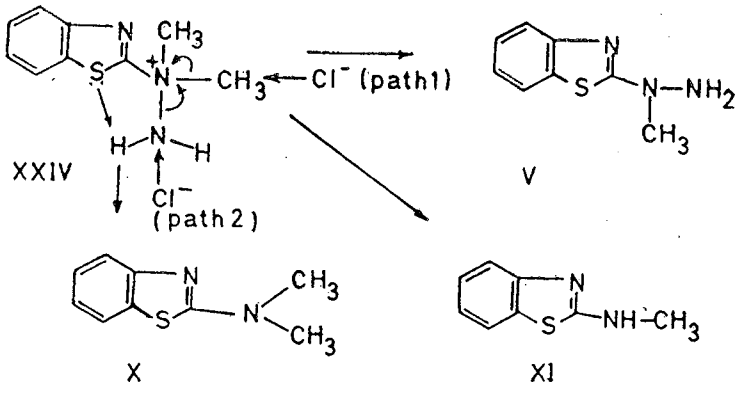


Chart 1 — Mechanism of reaction of 2-chlorobenzothiazole (I) with N,N-dimethylhydrazine

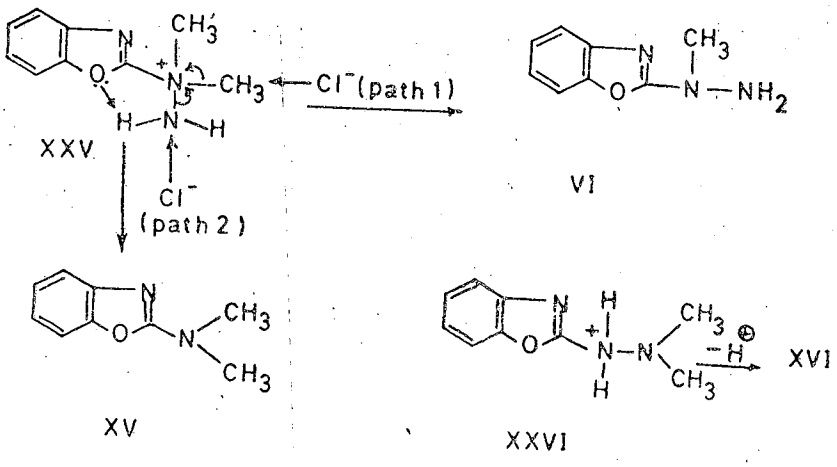


Chart 2 — Mechanism of reaction of 2-chlorobenzoxazole (II) with N,N-dimethylhydrazine

TABLE 1 — RELATIVE YIELDS OF V, X AND XI FROM 2-CHLOROBENZOTHIAZOLE AND N,N-DIMETHYLHYDRAZINE

Expt No.	Solvent	Me_2NNH_2 moles	Total yield %	Approx. % yield of V	X	XI
1	Ethanol	3	85	79	20	1
2	do	3	85	77	19	4
3	$CHCl_3$	3	88	57	42	1
4	Benzene	3	83	62	37	1
5	Ether	3	85	81	18	1
6	do	1	20	69	30	1
7	do	3	5	83	16	1
8	do	1	5	57	32	11

Sl No. 1 at reflux temp. Sl Nos 2-8 at 25°. Duration of reaction 1 hr for Sl No. 1, 7 and 8 and 20 hr for the rest.

TABLE 2 — RELATIVE YIELDS OF VI, XV AND XVI FROM 2-CHLOROBENZOXAZOLE AND N,N-DIMETHYLHYDRAZINE

Expt No.	Solvent	Me_2NNH_2 moles	Total yield %	Approx. % yield of VI	XV	XVI
1	Ethanol	3	70	14	78	8
2	do	3	75	16	78	6
3	$CHCl_3$	3	95	9	82	9
4	Benzene	3	95	15	63	22
5	Ether	3	87	24	49	27
6	do	1	50	22	58	20
7	do	3	62	26	46	28
8	do	1	50	27	54	19

Sl No. 1 at reflux and the rest at 25°. Duration of reaction 1 hr for 1, 7 and 8, and 20 hr for the rest.

this nitrogen in XXV (path 2 — deamination) than in XXIV.

A number of experiments were then performed in which I and II were separately allowed to react with rigorously purified N,N-dimethylhydrazine in alcohol, benzene, chloroform or ether. Number of molar equivalents of hydrazine, temperature were systematically varied.

The results obtained so far (Tables 1 and 2) do not permit rigorous conclusions about the mechanisms operating in these reactions. Obviously, more detailed and much kinetic work is necessary. However, the data in Tables 1 and 2 do indicate that very high yields of dealkylated and deaminated products are obtainable from reaction of N,N-dimethylhydrazine and 2-chlorobenzothiazole (I) or 2-chlorobenzoxazole (II) under mild conditions. In this respect, these reactions are reminiscent of the dealkylations by cyanogen bromide[2] and chloroformic esters[3] and it can be predicted that the latter reagents will also cause facile dealkylations and deaminations of N,N-disubstituted hydrazines. Similar behaviour can be expected for other chloroazoles.

Experimental Procedure

NMR spectra were determined on a Varian A-60 instrument; chemical shifts (δ) are quoted in ppm downfield from TMS internal standard.

Reaction of 2-chlorobenzothiazole (I) *with N,N-dimethylhydrazine* — To N,N-dimethylhydrazine (4·8 g) in ethanol (20 ml) was added I (4·1 g). After being left overnight at room temperature, the solution was diluted with water and extracted with ether. The dried ether extract on evaporation gave an oil (3·2 g) which rapidly crystallized. Recrystallization from ethanol gave pure V (2·1 g), m.p. 137-40°; NMR in $CDCl_3$: 3·37 (NCH_3) (Found: C, 54·00; H, 5·04; N, 23·05; S, 17·89. $C_8H_9N_3S$ requires C, 53·62; H, 5·06; N, 23·45; S, 17·86%). The residue after evaporating the mother liquor was chromatographed over silica gel (70 g, 0·05-0·2 mm particle size, E. Merck) and the column developed with benzene-chloroform (1:1·5). Fractions of 50 ml were collected. Fractions 11-22 were combined and evaporated. The residue was recrystallized from aq. MeOH to give X (0·3 g), m.p. 88-90°; NMR in $CDCl_3$: 3·08 ($-\underset{\displaystyle CH_3}{\overset{\displaystyle |}{N}}-CH_3$), 6·8-7·8 (4 aromatic H) (Found: C, 60·92; H, 5·89; N, 15·23. $C_9H_{10}N_2S$ requires C, 60·66; H, 5·66; N, 15·72%), identical with an authentic sample[4]. Fractions 28-34 were combined and evaporated and the residue (0·60 g) treated with 2*N* HCl, when a crystalline salt precipitated out. Recrystallization from ethanol gave V.HCl (0·25 g), m.p. and m.m.p. 232-4°. The mother liquor was basified and extracted with ether. The ether layer was evaporated and the crystalline residue recrystallized from CCl_4 to give XI (0·1 g), m.p. 132-4°; NMR in $CDCl_3$: 3·01 (*s*, NCH_3), 5·95 (broad *s*, NH, washed out by D_2O) and 6·8-7·8 ppm

(*m*, 4 aromatic H), identical with an authentic sample[4].

For a comparative study of effect of solvent, temperature, duration and molar proportions of hydrazine used, the total basic product from each reaction was isolated and its NMR spectrum in $CDCl_3$ run. Relative percentages of V, X and XI were estimated by measuring the integrated intensities of the methyl peaks, allowance being given for V and XI having one $N-CH_3$ group each against two for X. The validity of this was checked in the NMR spectrum of an artificial mixture of V (50 mg), X (11 mg) and XI (3 mg) in $CDCl_3$. The ratio of integrated intensities of the respective methyl signals at 3·37, 3·12 and 3·03 ppm was in agreement with the one expected on the basis of milliequivalents of solutes. The results of the comparative study are presented in Table 1.

Reaction of I *with N-methylhydrazine* — I (4·8 g) was added to the hydrazine (4·1 g) in ethanol (10 ml) and the mixture refluxed for 2 hr, diluted with water and the product crystallized from ether to give V (3·4 g), m.p. 136-8°, undepressed by admixture with the preparation from the previous experiment. V yielded a *p*-chlorobenzylidene derivative with *p*-chlorobenzaldehyde in refluxing ethanol, m.p. 147-8° (from $CHCl_3$-hexane) (Found: C, 59·96; H, 4·08; N, 14·11. $C_{15}H_{12}ClN_3S$ requires C, 59·71; H, 4·01; N, 13·93%) and with 5-nitrofurfural, a 5-nitro-2-furfurylidene derivative, m.p. 257-9° (from THF-alcohol) (Found: C, 51·67; H, 3·43; N, 18·03. $C_{13}H_{10}N_4O_3S$ requires C, 51·66; H, 3·34; N, 18·54%).

Action of I *on β-hydroxyethylhydrazine* — I (4·8 g) was added to the hydrazine (11·4 g) with cooling. Ethanol (20 ml) was then added and the mixture heated under reflux for 1·5 hr. Upon concentration and dilution with water, a crystalline product was obtained which recrystallized from aq. ethanol to give VII (5·8 g), m.p. 153-4° (Found: C, 51·74; H, 5·60; N, 20·39. $C_9H_{11}N_3OS$ requires C, 51·67; H, 5·30; N, 20·09%), forming a maleate, m.p. 138-40° (from ethanol-ether) (Found: C, 47·54; H, 4·67; N, 13·20. $C_{13}H_{15}N_3O_5S$ requires C, 48·00; H, 4·65; N, 12·92%). Aldehyde derivatives VIII from VII were made in refluxing ethanol in the presence of a few drops of conc. HCl during 1 hr and are listed in Table 3.

When VII (4·5 g) and acetone (5 ml) were refluxed together for 3 hr in ethanol (25 ml) containing conc. HCl (5 drops), product IX (4·9 g), m.p. 99-104°, was obtained and was crystallized from ether-hexane; m.p. 103-7° (Found: C, 58·13; H, 6·04; N, 17·08. $C_{12}H_{15}N_3OS$ requires C, 57·82; H, 6·07; N, 16·86%).

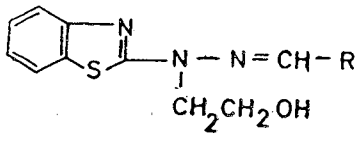
Reaction of I *with N-methylpiperazine* — I (5 g) and N-methylpiperazine (9 g) in ethanol (20 ml) were heated under reflux for 2 hr and the solution diluted with water. The precipitate was recrystallized from ether-hexane to give XII (5·9 g), m.p. 92-93° (Found: C, 61·85; H, 6·56; N, 17·94. $C_{12}H_{15}N_3S$ requires C, 61·78; H, 6·48; N, 18·02%).

Reaction of I *with N-aminopiperidine* — N-Aminopiperidine (1·5 g) and I (0·85 g) in ethanol (5 ml) were heated under reflux for 2 hr. Dilution with water and extraction with ether gave an oil (1·4 g), which was chromatographed on a column of silica gel (30 g) in benzene-chloroform (1 : 2). The first two 25 ml fractions were evaporated to give unreacted I (0·3 g). Fractions 3-10 were combined and crystallized from hexane to give XIII (0·7 g), m.p. 93-95° (Found: C, 65·99; H, 6·54; N, 12·65. $C_{12}H_{14}N_2S$ requires C, 66·03; H, 6·47; N, 12·84%), identical with the product (2·2 g) from reaction of I (1·7 g) and piperidine (1·7 g).

Reaction of I *with N-aminomorpholine* — I (1·7 g) and N-aminomorpholine (2·04 g) heated together in ethanol (10 ml) for 2 hr gave crude XIV (1·65 g), m.p. 119-21°. Recrystallization from ethanol gave pure XIV, m.p. 123-5° (Found: C, 60·30; H, 5·73; N, 12·40. $C_{11}H_{12}N_2OS$ requires C, 59·99; H, 5·49; N, 12·72%), identical with the product (1·1 g), obtained from I (0·85 g) and morpholine (1·3 g).

Reaction of 2-chlorobenzoxazole (II) *with N,N-dimethylhydrazine* —II (9 g) was added to the hydrazine (10·8 g) when an exothermic reaction took place. Ethanol (50 ml) was added and the mixture heated under reflux for 1 hr. The solution was diluted with water and extracted with ether. The dried ether extract was evaporated to give a partially

TABLE 3 — ALDEHYDE DERIVATIVES OF THE REACTION PRODUCT FROM I AND β-HYDROXYETHYLHYDRAZINE



R	Recrystallized from	m.p. °C	Yield %	Mol. formula	Found (%)			Calc. (%)		
					C	H	N	C	H	N
Ph—CH=CH-	$CHCl_3$-EtOH	209-10	85	$C_{18}H_{17}N_3OS$	66·79	5·43	12·86	66·86	5·30	13·00
p-Methoxyphenyl	$CHCl_3$	184-5	60	$C_{17}H_{17}N_3O_2S$	62·28	5·10	13·00	62·37	5·24	12·84
p-Chlorophenyl	$CHCl_3$-hexane	195-6	75	$C_{16}H_{14}ClN_3OS$	58·03	4·33	12·59	57·92	4·25	12·67
Phenyl	$CHCl_3$-hexane	193-4	86	$C_{16}H_{15}N_3OS$	64·94	5·32	—	64·63	5·09	14·14
2-Furyl	$CHCl_3$-EtOH	167-9	54	$C_{14}H_{13}N_3O_2S$	58·47	4·75	14·40	58·53	4·56	14·63
2-Thienyl	$CHCl_3$-EtOH	182-3	70	$C_{14}H_{13}N_3OS_2$	55·68	4·25	13·89	55·44	4·32	13·86

crystalline solid (9 g), which was recrystallized several times from ether to give VI (0·7 g), m.p. 129-32° (see below). The mother liquors were combined and evaporated and the residue chromatographed over a column of silica gel (80 g) in benzene-chloroform (1:1). The column was developed with the same mixture and 25 ml fractions collected.

Fractions 4-15 on evaporation gave 2-dimethylaminobenzoxazole (XV) (3·5 g), m.p. 89-91° (from aq. MeOH); NMR in $CDCl_3$: 3·08 (*s*, $N-CH_3$) and

6·7-7·4 (*m*, 4 aromatic H), identical with the product (10·5 g) from II (12·2 g) and dimethylamine (10·8 g) in ethanol (30 ml) (Found: C, 66·79; H, 6·27; N, 17·54. $C_9H_{10}N_2O$ requires C, 66·65; H, 6·22; N, 17·27%).

Fractions 31-52 on evaporation gave XVI, which was recrystallized from ether-hexane; 0·7 g, m.p. 124-6°; NMR in CCl_4: 2·78 (*s*, $N-CH_3$), 6·8-7·5 (*m*, 4

aromatic H) and 9·22 (broad *s*, NH) (Found: C, 61·01; H, 6·35. $C_9H_{11}N_3O$ requires C, 61·00; H, 6·26%).

Further elution of the column with $CHCl_3$ and $CHCl_3$ containing 1% MeOH gave VI (1 g; total 1·7 g), m.p. 129-32° (from aq. MeOH); NMR in CCl_4: 3·25 (*s*, NCH_3), 4·42 (broad *s*, NH_2, disappears with D_2O) and 6·8-7·7 (*m*, 4 aromatic H) (Found: C, 59·20; H, 5·62; N, 25·34. $C_8H_9N_3O$ requires C, 58·88; H, 5·56; N, 25·75%).

Results of a comparative study of the relative proportions of XV, XVI and VI formed in the reaction between II and N,N-dimethylhydrazine under various conditions are presented in Table 2. The analysis was done by measuring the integrated intensities of the methyl peaks due to the three products in the NMR spectrum of the total basic product from each reaction. The intensities were adjusted for the fact that VI had one methyl group while XV and XVI had two each.

Action of II *on N-methylhydrazine* — II (4·62 g) and the hydrazine (3 g) heated together in ethanol (15 ml) for 1 hr gave VI (2 g), m.p. 128-31°, identical with the previous preparation. VI afforded a *p*-chlorobenzylidene derivative, m.p. 169-71° (from $CHCl_3$-hexane) (Found: C, 63·16; H, 4·35; N, 14·40. $C_{15}H_{12}ClN_3O$ requires C, 63·05; H, 4·24; N, 14·71%) and a 5-nitro-2-furfurylidene derivative, m.p. 215-18° (from THF-ethanol) (Found: C, 54·71; H, 3·66; N, 19·22. $C_{13}H_{10}N_4O_4$ requires C, 54·55; H, 3·52; N, 19·58%).

Action of II *on N,N-dimethylcyclohexylamine* — A mixture of II (4·6 g) and N,N-dimethylcyclohexylamine (3·8 g) in ethanol (25 ml) was heated under reflux for 2 hr. A crystalline material separated which was filtered. This was identical with the HCl salt of the amine used. The filtrate was concentrated, diluted with water and extracted into ether. The ether layer was stripped of basic product with 2*N* HCl and then evaporated to give unreacted II (2·4 g). The basic product (2 g) recovered from the acid extracts was chromatographed over a column of silica gel (30 g) in benzene. The column was developed with the same solvent.

Fractions 3-12 gave XVII as an oil (1 g), b.p. 155-65°/0·5 mm; NMR in CCl_4: 0·8-2·2 (broad *m*,

10H), 2·95 (*s*, NCH_3), 4·1 (broad *s*, $-N-C-$) and

6·7-7·5 (*m*, 4 aromatic H), forming a HCl salt, m.p. 176-8° (from ethanol-ether) (Found: C, 63·34; H, 7·46; N, 10·64. $C_{14}H_{19}ClN_2O$ requires C, 63·03; H, 7·18; N, 10·50%), identical with the HCl salt of XVII prepared from II and N-methylcyclohexylamine.

Fractions 15-30 gave XV (0·7 g), m.p. 90-92°, identical with an authentic sample.

Action of 2-chloropyridine on N,N-dimethylhydrazine — 2-Chloropyridine (5·6 g) and the hydrazine (9 g) were heated together in a sealed tube at 150° overnight. The product was extracted with ether and distilled at 45-55°/1 mm to give an oil (4·4 g). This was chromatographed over a column of silica gel (40 g), the column being developed with benzene and 25 ml fractions collected. Fractions 2-13 gave 1·95 g oil, which was distilled at 70°/8 mm to give XVIII; NMR in $CDCl_3$: 3·03 (*s*, $N-CH_3$),

(*m*, H at C-3, C-5), 7·37 (*m*, C-4 H) and 8·17 (*m*, C-6 H). Fractions 18-31 gave XIX (0·5 g), b.p. 85°/8 mm; NMR in $CDCl_3$: 2·87 (*s*, $N-CH_3$), 4·78 (broad *s*, NH, washed out by D_2O), 6·37 (*m*, C-3 H), 6·58 (*m*, C-5 H), 7·4 (*m*, C-4 H) and 8·1 (*m*, C-6 H).

Action of methyl 2-chloro-5-nitrobenzoate (XXII) *on N,N-dimethylhydrazine** — XXII (10·8 g) and the hydrazine (6 g) were heated together at 100° for 4 hr. The mixture was poured into water and the residue crystallized from acetone-methanol to give indazolone XXIII (2·2 g), m.p. 285-6°; NMR in DMSO-d_6: 3·87 (*s*, N-CH_3), 6·1 (broad *s*, NH), 7·4 (*d*, $J = 10$ Hz, C-7 H), 8·1 (*q*, $J = 10$, 2 Hz, C-6 H) and 8·63 (*d*, $J = 2$ Hz, C-4 H) (Found: C, 49·69; H, 3·86; N, 22·05. $C_8H_7N_3O_3$ requires C, 49·74; H, 3·65; N, 21·76%), identical with the product (7·9 g) from the reaction of XXII (10·8 g) and methylhydrazine (4·6 g).

Action of benzyl bromide on N,N-dimethylhydrazine — Benzyl bromide (3·2 g) and the hydrazine (3·6 g) in ethanol (20 ml) were heated under reflux for 6 hr. The solution was concentrated and treated with ether. The product was crystallized from ethanol-ether to give XX (3·4 g), m.p. 145-7°; NMR in $CDCl_3$+DMSO-d_6: 3·52 (*s*, $N-CH_3$), 5·12

(*s*, Ph-CH_2—), 6·2 (broad *s*, NH_2) and 7·25-8·0 (*m*, 5 aromatic H). (Found: C, 47·07; H, 6·77; N, 12·03. $C_9H_{15}BrN_2$ requires C, 46·76; H, 6·54; N, 12·12%).

Action of benzyl bromide on N-aminopiperidine — The halide (7·8 g) and the hydrazine (5 g) were heated together in ethanol (100 ml) under reflux overnight. The solution was concentrated to a small volume and treated with ether. The gummy precipitate became crystalline slowly and was recrystallized from ethanol-ether to give XXI (3·7 g),

*Experiment performed by Dr P. Madhavan Pillai.