RESULTS AND DISCUSSION

The experimental work carried out would be discussed under headings:

2.1.1 Reaction of p-nitrosophenetole and o-nitrosotoluene with DTB and characterisation of the products.

2.1.2 Probable mechanism of origin of products (2-30).

2.2.1 Reaction of N,N-diphenylnitrosamine and N-methyl-N-phenylnitrosamine with DTB and characterisation of products.

2.2.2 Probable mechanism of origin of products (32-39).

2.1.1 Reaction of p-nitrosophenetole and o-nitrosotoluene with DTB and characterisation of the products

As the reaction of p-nitrosophenetole or o-nitrosotoluene with DTB at room temperature (30°) was very fast, the reactions of these nitrosoarenes with DTB were also carried out keeping the reaction vessels in freezing mixture (temperature 0° or below) with the aim to understand the origin or disappearance.
of various products or intermediates formed during the course of the reaction. Further to create the bio-environment conditions, the reactions were also carried out in solvent system containing CHCl₃-MeOH-buffer (0.067 mM, pH 7.0)¹, the inclusion of CHCl₃-MeOH was necessary keeping in view the limited solubility of nitrosoarenes or DTB in aqueous buffer.

Reaction of p-nitrosophenetole 1 with DTB

In case of p-nitrosophenetole, the formation of hydroxylamine 52a and azoxybenzene 3 was detected immediately on paper/TLC, and the concentration of hydroxylamine was maximum between 2-6 hours (Table-1) and then started decreasing at 8 hours, and at about 16 hours it was found to be absent in the reaction mixture, while the concentration of azoxybenzene was found to increase till nitrosophenetole was present in the reaction mixture. The presence of hydroxamic acid 7 and its O-acetyl ester 8, was detected within 10 minutes of start of the reaction. For the detection of 8, the TLC plate after heating when sprayed with FeCl₃ solution or diazotized sulfanilic acid, gave brownish-violet or reddish-brown color respectively (ester probably gets hydrolysed or rearranged on heating). The concentration of hydroxamic acid 7 or its ester 8 was found to increase up to 16 hours of the start of the reaction and at about 24 hours the ester was found to be in traces. Though at the end of 24 hours the reaction was stopped and processed for the
The sign + (or ++, +++ and so on) against each product indicate its concentration at various time intervals and not with respect to other products.

*Spot on TLC gave positive response to ferric chloride solution as well as diazotised sulfanilic acid.

TABLE-1
p-Nitrosophenetole 1 + DTB (0°)

<table>
<thead>
<tr>
<th>Products</th>
<th>5 min</th>
<th>10 min</th>
<th>20 min</th>
<th>30 min</th>
<th>45 min</th>
<th>2 hrs</th>
<th>4 hrs</th>
<th>6 hrs</th>
<th>8 hrs</th>
<th>12 hrs</th>
<th>16 hrs</th>
<th>24 hrs</th>
<th>$R_f$(Solvent system)</th>
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<tr>
<td>52a</td>
<td>+</td>
<td>+</td>
<td>++</td>
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<td>+++</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>0.18(K)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>0.39(C)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
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<td>+++</td>
<td>++++</td>
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<td>++++</td>
<td>0.27(C)</td>
</tr>
<tr>
<td>6</td>
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<td>+</td>
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<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>0.53(K)</td>
</tr>
</tbody>
</table>
isolation of products, but a small portion of it when kept for a longer time, it was found that at around 48 hours, even hydroxamic acid could not be detected on TLC. The amidophenol 6 or its acetyl ester 10, were first detected on paper/TLC at 2 and 4 hours or the start of the reaction respectively and then their concentration increased with time, while the concentration of the hydroxamic acid/its ester decreased, indicating the rearrangement of hydroxamic acid or its ester to corresponding amidophenol or its ester. It was further observed that the small portion of the reaction mixture which was kept for longer time, indicated the absence of amidophenol 6 at about 66 hours and only its ester 10 was present in good concentration in the reaction mixture, indicating further acetylation of 6 to 10. The presence of azobenzene 2 could only be detected at about 6 hours, while in buffer system it was first detected at 45 minutes of the start of the reaction. It is interesting to observe that in solvent CHCl₃, the presence of free amine (p-phenetidine) could not be detected on TLC during the entire course of the reaction, while from the reaction mixture carried out in buffer, its formation was first detected at 10 minutes and which increased up to 6 hours and at the end of 16 hours its presence could not be detected. Further, the reaction which was carried out in buffer, indicated the appearance of products 14 and 17 (Ehrlich positive) at 7 and 8 hours respectively. Due to the complex nature of the reaction mixtures, the presence of
The sign + (or ++, +++ and so on) against each product indicate its concentration at various time intervals and not with respect to other products.

*Spot on TLC gave positive response to ferric chloride solution as well as diazotised sulfanilic acid.

<table>
<thead>
<tr>
<th>Products</th>
<th>5 min</th>
<th>10 min</th>
<th>20 min</th>
<th>30 min</th>
<th>45 min</th>
<th>2 hrs</th>
<th>4 hrs</th>
<th>6 hrs</th>
<th>8 hrs</th>
<th>12 hrs</th>
<th>16 hrs</th>
<th>24 hrs</th>
<th>R_f (Solvent system)</th>
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<tr>
<td>52b</td>
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<td>++++</td>
<td>++++</td>
<td>++++</td>
<td>++++</td>
<td>++++</td>
<td>+++</td>
<td>0.13(G)</td>
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<tr>
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<td>-</td>
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<td>+</td>
<td>++</td>
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<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>0.18(G)</td>
</tr>
</tbody>
</table>

The sign + (or ++, +++ and so on) against each product indicate its concentration at various time intervals and not with respect to other products.
<table>
<thead>
<tr>
<th>Product</th>
<th>$R_C$</th>
<th>$R_{30}$</th>
<th>$R_{30B}$</th>
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<tbody>
<tr>
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<td>0.20</td>
<td>5.46</td>
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<tr>
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<td>36.07</td>
<td>35.01</td>
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<tr>
<td>5</td>
<td>0.15</td>
<td>0.18</td>
<td>0.26</td>
</tr>
<tr>
<td>6</td>
<td>8.12</td>
<td>7.97</td>
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</tr>
<tr>
<td>9</td>
<td>2.07</td>
<td>1.91</td>
<td>4.96</td>
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<td>5.20</td>
<td>6.20</td>
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<td>0.08</td>
<td>0.15</td>
<td>0.16</td>
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<td>0.27</td>
<td>0.23</td>
<td>0.30</td>
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<td>-</td>
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<td>-</td>
<td>0.60</td>
</tr>
<tr>
<td>17</td>
<td>-</td>
<td>-</td>
<td>2.29</td>
</tr>
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</table>

$R_C$ : Reaction at 0°; Solvent chloroform  
$R_{30}$ : Reaction at 30°; Solvent chloroform  
$R_{30B}$ : Reaction at 30°; Solvent chloroform-methanol-phosphate buffer (pH 7.0, 0.067M)
other products 6, 7, 9, 11, 13, 15 and 16 could not be detected. The reaction carried out in buffer gave additional products 14, 16 and 17 (diphenylamine derivatives), N-acetylhydrazobenzene 15, and larger quantities of azobenzene 2 and phenacetin 9 (Table-3).

Reaction of \(\sigma\)-nitrosotoluene 18 with DTB

In a reaction of \(\sigma\)-nitrosotoluene with DTB, the presence of azoxybenzene 20, hydroxamic acid 24 and its acetyl ester 21, and hydroxylamine 52b were all detected immediately within 5-10 minutes of the start of the reaction (Table-2). In contrast to \(\pi\)-nitrosophenetole in solvent chloroform, the formation of amine (\(\sigma\)-toluidine) at 0\(^\circ\) was first detected at about 20 minutes, its concentration increased between 2-12 hours, and at the end of 24 hours (reaction time) it was found to be absent. The formation of amine in buffer was noted to be in larger quantities, but at the end of reaction (24 hours) it was found to be absent. The concentration of hydroxamic acid 24 and its ester 21 increased with the reaction time, but at 16 hours the concentration of 24 started falling and in one of the experiments where the reaction mixture was allowed to stand for about 50 hours, 24 was found to be all converted to 21. The presence of amidophenol 28 was first detected at about 8 hours and at the end of the reaction (24 hours) there was only slight
### TABLE-4

Reaction of o-Nitrosotoluene 15.0 g (0.123M) with DTB 30.0 g (0.123M)

<table>
<thead>
<tr>
<th>Product</th>
<th>( R_C )</th>
<th>( R_{30} )</th>
<th>( R_{30B} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>2.51</td>
<td>1.57</td>
<td>5.60</td>
</tr>
<tr>
<td>20</td>
<td>23.26</td>
<td>18.73</td>
<td>25.50</td>
</tr>
<tr>
<td>21</td>
<td>29.15</td>
<td>12.97</td>
<td>9.85</td>
</tr>
<tr>
<td>22</td>
<td>0.19</td>
<td>-</td>
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</tr>
<tr>
<td>23</td>
<td>0.54</td>
<td>0.37</td>
<td>0.97</td>
</tr>
<tr>
<td>24</td>
<td>7.23</td>
<td>22.52</td>
<td>10.72</td>
</tr>
<tr>
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<td>0.07</td>
</tr>
<tr>
<td>27</td>
<td>0.08</td>
<td>0.06</td>
<td>0.25</td>
</tr>
<tr>
<td>28</td>
<td>0.42</td>
<td>3.01</td>
<td>2.33</td>
</tr>
<tr>
<td>29</td>
<td>0.66</td>
<td>0.55</td>
<td>1.25</td>
</tr>
<tr>
<td>30</td>
<td>0.05</td>
<td>0.03</td>
<td>0.05</td>
</tr>
</tbody>
</table>

- \( R_C \): Reaction at 0°; Solvent chloroform
- \( R_{30} \): Reaction at 30°; Solvent chloroform
- \( R_{30B} \): Reaction at 30°; Solvent chloroform-methanol-phosphate buffer (pH 7.0, 0.067M)
increase in its concentration, indicating the possibility of very slow rearrangement of hydroxamic acid 24 in contrast to 7. The product pattern in a reaction of o-nitrosotoluene with DTB in organic solvent CHCl$_3$ or buffer remained the same, but products like azobenzene 19, acetanilide 25, N-acetyl-hydrazo 23 and diphenylamine derivatives (27 and 29) were isolated in higher quantities from a reaction carried out in buffer system (Table-4).

Reaction of p-nitrosophenetole and o-nitrosotoluene with DTB at 0°, 30° or in chloroform-methanol-buffer (0.06 mM, pH 7.0) yielded a mixture of products which were isolated by the combined procedure of column chromatography, PTLC and fractional crystallization. The products with their quantities are given in Scheme-1 in their sequence of elution from column.

Characterization of products

Compound 2 was an orange yellow crystalline product. Its IR (cm$^{-1}$) indicated bands characteristic for C-O-C (1250, 1042) and p-disubstituted phenyl (848); PMR($\delta$) displayed signals at 7.86 (d, 4H, J=8 Hz, aromatic, adjacent to azo group), 6.95 (d, 4H, J=8 Hz, aromatic, adjacent to ethoxy group) and other 10 aliphatic H appeared as quartet at 4.12 (J=7 Hz, 2 x CH$_3$CH$_2$O) and triplet at 1.45 (J=7 Hz, 2 x CH$_3$CH$_2$O); MS indicated M$^+$ at
m/z 270 (found and calculated) and other characteristic peaks at m/z 241 (M⁺-CH₂CH₃), 149 (M⁺-C₆H₄OCH₂CH₃) and 121 (C₆H₄OCH₂CH₃)⁺. Its mixed mp with an authentic sample² remained undepressed (prepared by the reported procedure)³.

Compound 3 was obtained as bright yellow crystalline product. Its IR (cm⁻¹) was characteristic for -N=N=O (1299) and C-O-C (1250 and 1042); PMR (δ) indicated 8 aromatic H with one doublet at 8.35 (4H, J=9 Hz, adjacent to azoxy, another doublet at 6.95 (4H, J=9 Hz, adjacent to ethoxy), of the 10 aliphatic H, a quartet and a triplet characteristic for two ethoxy groups; MS gave molecular ion at 286 (found and calculated) and other important peaks at m/z 270 (M⁺-O), 257 (M⁺-CH₂CH₃), 241 (M⁺-CH₃CH₂O) and 149 (H₃CH₂COC₆H₄NN)⁺. Its identity was further confirmed from its mp⁴ and through its synthesis³.

Compound 4 was obtained as a yellow crystalline product. It was assigned the molecular formula C₁₀H₁₁N⁰₄ from its elemental analysis and MS. MS gave molecular ion at m/z 209 (found and calculated) and other characteristic peaks at m/z 194 (M⁺-CH₃), 180 (M⁺-CH₂CH₃) and 167 (M⁺-ketene). Its IR (cm⁻¹) gave bands characteristics for N-H (3279), C=O (1720), amide I (1664) and amide II (1524); PMR (δ) displayed two singlets, one at 7.65 (H-3) and another at 6.0 (H-6), a broad band at 8.3 (NH), a singlet at 2.3 (3H, N-COCH₃) and signals for one ethoxy group. The identity of the product 4 was further
confirmed from its mp and synthesis from 6.

Product 5 was obtained as white shining crystalline solid. Its IR (cm⁻¹) was characteristic for O-COCH₃ (1724, 1220 and 1042); PMR (δ) exhibited signals at 7.3 (s, 4H, aromatic) and 2.35 (s, 6H, 2 x O-COCH₃); MS indicated M⁺ at m/z 194 (found and calculated) and other characteristic peaks at m/z 152 (M⁺-ketene) and 110 (M⁺-twice loss of ketene). Its structure was further established from its mixed mp with an authentic sample (prepared by acetylation of β-hydroquinone).

Product 6 was obtained as shining colorless crystals. It gave orange-red color with diazotized sulfanilic acid and its UV maxima at 215, 248 and 287 nm showed a bathochromic shift to 230, 258 and 305 nm respectively in alkali showing the presence of phenolic hydroxyl group. IR (cm⁻¹) was characteristic for CH (3450), NH (3333), amide I (1650) and amide II (1538); PMR (δ) displayed 3 aromatic H, H-3 at 6.39 and H-6 (d, J=6 Hz), 2.2 (s, 3H, N-COCHO) and one ethoxy group having the usual pattern; MS gave molecular ion at m/z 195 (found and calculated) and other characteristic peaks at m/z 177 (M⁺-H₂O) and 153 (M⁺-ketene). Further its mp tallied with that reported in the literature.

Product 7 was separated from product 6 through PTLC as a brown solid residue which gave violet color with ferric chloride solution (Hydroxamic acid). Its IR (cm⁻¹) indicated
bands characteristic for NH (3110), N-COCH$_3$ (1615); PMR (δ) gave signals at 7.45 (d, 2H, J=9 Hz, aromatic) and another doublet at 6.9 (2H, J=9 Hz, aromatic protons adjacent to ethoxy), 2.2 (s, 3H, N-COCH$_3$) and one ethoxy group with usual pattern; MS gave molecular ion m/z 195 (found and calculated) and other characteristic peaks at m/z 179 (M$^+$-O) and 153 (M$^+$-ketene). Its mp tallied with that reported in the literature$^8$.

Product 9 was obtained as white shining leaflets. Its IR (cm$^{-1}$) was characteristic for NH (3226), amide I (1667), amide II (1563); PMR (δ) exhibited signals at 7.45 (d, 2H, J=9 Hz, H-2 and H-6, aromatic), 6.95 (d, 2H, J=9 Hz, aromatic, adjacent to ethoxy), 2.2 (s, 3H, N-COCH$_3$), 1.8 (s, NH) and usual pattern of ethoxy protons; MS gave M$^+$ at m/z (found and calculated) and other characteristic peaks at m/z 150 (M$^+$-CH$_2$CH$_3$), 137 (M$^+$-ketene) and 108 (137-CH$_2$CH$_3$). Its mixed mp with an authentic sample$^9$ remained undepressed.

Product 10 was obtained as white shining feathery crystals and gave orange color with freshly diazotized sulfanilic acid. Its IR (cm$^{-1}$) gave bands characteristic for N-H (3226), ester stretchings (1730 and 1220), amide I (1675) and amide II (1515); PMR (δ) displayed 3 aromatic H which gave one doublet at 7.85 (1H, J=9 Hz, H-3), 6.7-6.9 (m, 2H, H-4 and H-6), 2.35 (s, 3H, O-COCH$_3$), 2.15 (s, 3H, N-COCH$_3$) and one ethoxy protons with
usual pattern; MS indicated molecular ion at m/z 237 and other important peak at m/z 195 (M⁺-ketene), 153 (M⁺-twice ketene) and 124 (153-CH₂CH₃). The correlation of product 10 to 6 was established as 10 on alkaline hydrolysis gave 6 and which on treatment with DTB gave 10. Its mp tallied with the authentic sample.

Compound 11 was obtained as dark red crystals. It was assigned the molecular formula C₁₈H₂₀N₂O₄ on the basis of its elemental analysis and MS. Its MS gave M⁺ at m/z 328 (found and calculated) and other characteristic peaks at m/z 313 (M⁺-CH₂), 299 (M⁺-CH₂CH₃), 286 (M⁺-ketene) and 257 (286-CH₂CH₃); IR (cm⁻¹) indicated bands characteristic for N-H (3226), quinone C=O (1695), amide I (1639) and amide II (1515); PMR ($) exhibited signals at 8.2 (br, NH), 8.0 (s, quinoid, possibly H-3), 7.0 (s, 4H, aromatic), 6.0 (s, quinoid, possibly H-6), 2.2 (s, 3H, N-COCH₃) and signals characteristic for two ethoxy groups, 4.15 (m, 4H, 2 x OCH₂CH₃) and 1.25-1.60 (m, 6H, 2 x OCH₂CH₃)
Its identity was further confirmed from its mp and through its synthesis by refluxing 4 and p-phenetidine in solvent benzene. Compound 13 was obtained as yellow crystalline product and gave reddish-orange colour with Dragendorff's reagent. Its solution in various solvents gave intense green fluorescence. It was assigned the molecular formula $C_{18}H_{15}N_3O$ from its elemental analysis and MS. MS gave molecular ion at m/z 289 (found and calculated) and other characteristic peaks at m/z 260 ($M^+-CH_2-CH_3$), 244 ($M^+-OCH_2-CH_3$) and 121 ($C_6H_4OCH_2-CH_3^+$). Its IR (cm$^{-1}$) gave bands characteristic for C=C (1580, 1493 and 1468), C-N (1345) and C-O-C (1206); PMR ($\delta$) displayed signals at 8.87 (s, 2H, H-4 and H-6, pyridine), 8.0 (d, 2H, J=6Hz, H-2 and H-8, pyridine), 7.7 (d, 2H, J=6Hz, H-1 and H-9, pyridine), 7.1-7.4 (m, 4H, benzene), one ethoxy group gave its usual PMR signal. Its identity was further confirmed through its unambiguous synthesis by treating 1 and 12 with triphenylphosphine at 0-2° in dilute solution.

Compound 14 was obtained as shining cream colored feathery crystalline product. It gave yellow color with Ehrlich reagent and green color with ferric chloride solution which soon turned red thus indicating the presence of diphenylamine moiety. It was assigned the molecular formula $C_{16}H_{19}NO_2$ on the basis of its elemental analysis and mass spectrum. Its MS gave $M^+$ at m/z 257.
(found and calculated) and other characteristic peaks at \( m/z \) 228 \((M^+ - \text{CH}_2\text{CH}_3)\) and 200 \((228-\text{CO})\); IR \((\text{cm}^{-1})\) indicated characteristic for N-H \((3333)\) and C-O-C \((1250 \text{ and } 1053)\); PMR \((\delta)\) exhibited multiplet at 6.9-7.15 for 8H aromatic, a broad peak for \( \Phi_2\text{NH} \) at 5.35 and displayed signals for two ethoxy groups. Its mp tallied with that reported in the literature\(^{12}\).

Compound 15 was obtained as white crystals which gave yellow color on standing with Ehrlich reagent and red color on standing with ferric chloride solution. It was assigned molecular formula \( \text{C}_{18}\text{H}_{22}\text{N}_2\text{O}_3 \) from its elemental analysis and MS. MS indicated molecular ion \( m/z \) 314 \((\text{found and calculated})\) and other characteristic peaks at \( m/z \) 272 \((M^+ - \text{ketene})\), 178 \((M^+ - \text{NHC}_6\text{H}_4\text{OC}_2\text{H}_5)\) and 136 \((\text{NHC}_6\text{H}_4\text{OC}_2\text{H}_5)^+ \). Its IR \((\text{cm}^{-1})\) gave bands characteristic for N-H \((3195)\), amide I \((1656)\), amide II \((1515)\) and C-O-C \((1250 \text{ and } 1047)\); PMR \((\delta)\) displayed signals at 7.35 \((d, 2H, J=9 \text{ Hz, aromatic, adjacent to N-\text{COCH}_3})\), 6.8-7.0 \((m, 6H, \text{ aromatic})\), 2.2 \((\text{br, } 3H, \text{ N-\text{COCH}_3})\), 1.65 \((\text{br, NH})\) and gave usual signals characteristic for two ethoxy groups.

Compound 16 obtained as colorless crystalline product, gave yellow color with Ehrlich reagent and greenish blue color with ferric chloride solution thus, indicating the presence of diphenylamine moiety. It was assigned molecular formula
C_{18}H_{22}N_{2}O_{3} on the basis of elemental analysis and MS. Its MS indicated molecular ion m/z 314 (found and calculated) and other characteristic peaks at m/z 296 (M^+-H_2O), 272 (M^+-ketene) and 243 (272-CH_2CH_3); IR (cm\(^{-1}\)) gave bands characteristic for N-H (3125), amide I (1639, amide II (1515) and C-O-C (1242 and 1047); PMR (\(\delta\)) displayed 7H aromatic, at 7.4-7.7 (m, 2H adjacent to N-COCH_3), 6.7-7.1 (m, 5H), broad peaks at 6.0 and 1.8 for \(\varphi_2\)NH and NH-COCH_3 respectively, 2.15 (s, 3H, N-COCH_3) and two ethoxy protons gave signals as usual.

Compound 17 was obtained as silky light brown crystalline product. It gave yellow color with Ehrlich reagent which changed to red and with ferric chloride solution it gave reddish-brown color which on standing initially changed to violet and then finally to brownish-violet indicating the presence of diphenylamine moiety. It was assigned the molecular formula C_{16}H_{18}N_{2}O_{2} from its elemental analysis and MS. Its MS gave molecular ion m/z 270 (found and calculated) and other characteristic peaks at m/z 271 (M^+1), 241 (M^+-CH_2CH_3) and 199 (241-ketene); IR (cm\(^{-1}\)) indicated bands characteristic for N-H (3125), amide I (1639), amide II (1505) and C-O-C (1239 and 1042); PMR (\(\delta\)) exhibited signals at 7.5 (d, 2H, J=9 Hz, aromatic, adjacent to N-COCH_3), 6.9-7.3 (m, 6H, aromatic), 5.4-5.6 (br, \(\varphi_2\)NH), 2.18 (s, 3H, N-COCH_3), 1.68 (br, NH-COCH_3) and one ethoxy gave signals as usual.
Compound 19 was obtained as a red crystalline product. Its PMR ($) displayed characteristic signals at 7.75 (d, 2H, J=7 Hz, aromatic H-6 and H-6'), 7.3-7.5 (m, 6H, aromatic) and 2.7 (s, 6H, 2 x CH₃). MS gave molecular ion m/z 210 (found and calculated) and other characteristic peaks at m/z 119 (M⁺⁻C₆H₄CH₃) and 91 (C₆H₄CH₃)⁺. Further its mixed mp with the authentic sample⁹b remained undepressed (authentic sample was prepared from g-nitrotoluene by the reported procedure)³.

Product 20 obtained as long yellow needles, exhibited its PMR ($) signals characteristic for 8 aromatic H at 8.1-8.3 (m, H-6), 7.7-7.8 (m, H-6'), 7.3-7.5 (m, 6H) and 6 aliphatic H at 2.5 (s, 3H, -CH₃), 2.3 (s, 3H, -CH₃). MS gave molecular ion m/z 226 (found and calculated) and other characteristic peaks at m/z 208 (M⁺⁻O) and 105 (C₆H₄CH₃N)⁺. Its mixed mp with the authentic sample⁹b remained undepressed.

Compound 21 obtained as whitish cream colored crystalline product was assigned molecular formula C₁₁H₁₃N₄O₃ on the basis of its elemental analysis and MS. Its MS gave M⁺ at m/z 207 (found and calculated) and other characteristic peaks at m/z 208 (M⁺⁺1), 165 (M⁺⁻ketene), 148 (208-acetic acid), 123 (M⁺⁻twice loss of ketene). IR (cm⁻¹) had characteristic bands for N-OCOCH₃ (1773, 1174) and N-COCH₃ (1653). Its PMR ($) indicated 4 aromatic H as multiplet at 7.5-7.8, other characteristic
signals at 2.55 (s, 3H, N-OCOCH$_3$), 2.3 (s, 3H, N-COCH$_3$) and 2.2 (s, 3H, CH$_3$). Its structure was further confirmed as on hydrolysis with dilute ammonia it gave known product 24.

Compound 22 was isolated as a white fluffy crystalline product. Its IR (cm$^{-1}$) gave bands characteristic for N-H (3225), amide I (1655), amide II (1587) and C-O (1320). PMR ($) displayed signals at 7.65 (s, 6H, aromatic), 9.5 (br, 2 x NH), 2.35 (s, 6H, 2 x N-COCH$_3$) and 2.15 (s, 6H, 2 x CH$_3$). MS indicated M$^+$ at m/z 296 (found and calculated) and other characteristic peaks at m/z 297 (M$^+$+1), 254 (M$^+$-ketene) and 212 (M$^+$-twice loss of ketene). Its identity was further confirmed through its synthesis from o-tolidine$^{13}$.

Product 23, obtained as cubical crystals gave yellow color with Ehrlich reagent and brownish-violet (changing to reddish-violet with ferric chloride solution. Its IR (cm$^{-1}$) gave characteristic bands for N-H (3355), amide I (1667). PMR ($) gave signals at 7.2-7.75 (m, 6H aromatic and NH proton buried underneath), 2.4 (s, 3H, N-COCH$_3$), 2.3 (s, 3H, 1 x CH$_3$ ortho to N-COCH$_3$) and 2.2 (s, 3H, 1 x CH$_3$). MS gave molecular ion m/z 254 (found and calculated) and other important peaks at m/z 212 (M$^+$-ketene) and 106 ($\text{H}_3\text{C}-\text{C}_6\text{H}_4\text{NH}$)$^+$. Its structure was further confirmed through its synthesis from o-hydrazotoluene.
Compound 24 was obtained as light brown crystals which gave violet color with ferric chloride solution (hydroxamic acid). Its IR (cm⁻¹) was characteristic for O-H, broad band (3226-2654), C=O (1626) and N-O (980). PMR (δ) displayed signals at 7.45 (m, 4H, aromatic), 2.4 (s, 3H, N-COCH₃) and 1.95 (s, 3H, CH₃). MS indicated M⁺ at m/z 165 (found and calculated) and other characteristic peaks at m/z 149 (M⁺-O) and 123 (M⁺-ketene). Further, its mixed mp with authentic sample¹⁴ remained undepressed (hydroxamic acid derivative was prepared from the corresponding hydroxylamine)¹⁴.

Product 25, obtained as shining colorless needles, indicated bands in IR (cm⁻¹) characteristic for N-H (3333), amide I (1665) and amide II (1577). PMR (δ) gave signals at 7.8-8.0 (m, 1H, aromatic, H-6), 7.2-7.5 (m, 3H, aromatic), 2.3 (s, 3H, N-COCH₃) and 2.2 (br, 3H of CH₃ and NH buried under it). MS gave molecular ion at m/z 149 (found and calculated) and other important peaks at m/z 107 (M⁺-ketene) and 106 (M⁺-CH₂CO). Finally its identity was confirmed from its mp and through its synthesis from o-toluidine⁹c.

Compound 26 was obtained as light brown crystals giving yellow color with Ehrlich reagent and bright-red color with Dragendorff's reagent. It was assigned molecular formula C₁₄H₁₆N₂ from its elemental analysis and MS. Its MS indicated
M⁺ at m/z 212 (found and calculated) and other characteristic peaks at m/z 197 (M⁺-CH₃), 133 (M⁺-C₅H₅N), 117 (C₆H₄ NCCH₃)⁺ and 106 (C₆H₄ NHCH₂)⁺ or (C₅H₄ NCHCH₃)⁺. IR (cm⁻¹) indicated band characteristic for N-H (3226). PMR (δ) displayed signals at 8.6-8.8 (m, H-6 of pyridine and NH), 6.7-7.5 (m, 3H of pyridine and 3H of benzene), 6.2-6.6 (m, H-6 of benzene), 4.6 (q, 1H of methine, J=9 Hz), 2.3 (s, 3H, CH₃ attached to benzene), 1.6 (d, 3H, CH₃ attached to methine). Its structure was further confirmed through its synthesis starting from 2-acetylpyridine and 2-toluidine.

Compounds 27 and 29 both gave light yellow color with Ehrlich reagent (changing to yellowish-green on keeping) and dirty brown color with ferric chloride solution indicating the presence of diphenylamine moiety. Molecular formula of both products was assigned C₁₅H₁₆N₂O from their elemental analysis and MS. MS of both 27 and 29 gave molecular ion at m/z 254 (found and calculated) and other characteristic fragments at m/z 212 (M⁺-ketene) and 106 (C₆H₄ CH₂ NH)⁺. PMR (δ) of 27 gave signals for 7 aromatic H at 6.6-7.6 while the 7 aromatic H of 29 gave characteristic signals at 7.6 (d, J=8 Hz, adjacent to NHCOCH₃), 7.2-7.4 (m, 2H) and 6.75-6.85 (m, 4H). NH proton of diphenylamine moiety in 27 was buried under aromatic protons at 6.6-7.6 while in 29 corresponding proton appeared at 5.35 as a broad signal. Of the 9 aliphatic H, 3 protons of N-COCH₃ in
both 27 and 29 appeared at 2.3 and 6 protons of two methyl appeared at 2.2 of compound 27 and 2.25 in compound 29. Further the mp of 29 tallied with that reported in the literature. Compound 28, obtained as white crystalline product, gave orange-red color with diazotized sulfanilic acid and its UV maxima at 277.5 nm showed a bathochromic shift to 296 nm in alkali showing presence of phenolic hydroxyl group. It was assigned molecular formula C₉H₁₅NO₂ from its elemental analysis and MS. MS gave M⁺ at m/z 165 (found and calculated) and other characteristic peaks at m/z 123 (M⁺-ketene) and 122 (M⁺-CH₃CO). IR (cm⁻¹) was characteristic for N-H, O-H (broad band, 3333-2778), amide I (1613) and amide II (1563). PMR (δ) displayed 3 aromatic H and NH of NHCOCH₃ at 6.9-7.3 as multiplet, 8.35 (s, OH), 2.36 (s, 3H, N-COCH₃), and 2.3 (s, 3H, CH₃). The possible formation of another rearranged product 4-hydroxy-2-methylphenylacetamide is ruled out as the product has its reported mp 130°, while mp of product 28 was found to be 169-170°.

Product 30, obtained as light brown fluffy residue gave yellow color with Ehrlich reagent and orange color with diazotized sulfanilic acid indicating both amino and phenolic OH functions. In UV, the maxima at 256 nm showed a bathochromic shift to 286 nm in alkali, further confirmed the presence of
phenolic OH. The compound being in small quantity the analyses other than UV and MS could not be carried out. On the basis of our experience with the products isolated and identified from the reaction mixture of o-nitrosotoluene and DTB, UV and MS, a tentative structure is proposed for the product 30. The product gave $M^+$ at $m/z$ 270 (found and calculated) and other characteristic peaks at $m/z$ 228 ($M^+$-ketene), 227 ($M^+-CH_3CO$) and 164 ($M^+-C_6H_4NHCH_3$). The other possibility of the structure 30A can be ruled out, as this compound on treatment with alkali is expected to give 30B, which is expected to have same intense color with absorption in a visible range.
2.1.2 Probable mechanism of origin of products

Takeuchi et al. first time treated nitrosobenzene with DTB in solvent chloroform at room temperature and reported the isolation of a lone product azoxybenzene 44 in 85% yield and origin of which was considered from the interaction of nitrosobenzene 41 and reactive intermediate O-acetylphenylhydroxylamine 42 (Scheme-2).

\[
\begin{align*}
\text{41} & \quad \text{O} \\
\text{40} & \\
\text{12} & \quad + \quad 2 \cdot \text{42} \\
\text{42} & \quad + \quad \text{41} \\
\text{43} & \quad \stackrel{\text{CH}_3\text{COOH}}{\longrightarrow} \\
\text{44} & \\
\end{align*}
\]

SCHEME 2
Juneja et al\textsuperscript{18} repeated the above reaction and besides azoxybenzene 44 in 60\% yield, also isolated azobenzene, \textsubscript{N}-phenylacetohydroxamic acid and its O-acetyl ester, acetonilide and 4-acetamidodiphenylamine and the origin of these products was explained through the involvement of reactive intermediate 42.

In an attempt to explain the possible mechanism of hydrogen transfer from coenzyme NADH to substrate, Pandit et al\textsuperscript{19} used Hantzsch ester 45 as NADH model and unsaturated acyl chloride 46 and acyl anhydride as substrate. Based on kinetic studies, they proposed that the hydride transfer to terminal carbon of double bond of acid chloride proceeds via an intermolecular process, to result in an ion pair 47, which after proton donation by the pyridinium salt to the anionic moiety, gives reduced acid chloride 48 (Scheme-3).
As DTB is also a dihydropyridine derivative, with acyl carrier group, could be considered as NAD(P)H and acetyl-CoA model. Analogously, using nitrosoarenes as substrate, it could be invoked that DTB through hydride transfer may first generate ion pair 50 and which after acetyl cation donation by highly reactive N-acetylpiperidinium ion results in N-acetoxyarylamine (Scheme-4).
As the presence of hydroxylamine 52 was detected on TLC just after the start of the reaction, it could be either that the hydroxylamine anion 51 leaches out of the solvent cage to result in 52 or the intermediate 42, might hydrolyse after spotting on TLC plate. Except from the product pattern, we could not prove the conclusive existence of the reactive intermediate 42, in the reaction mixture. O-Acylhydroxylamines have been reported\textsuperscript{20} to react with KI to liberate iodine. Unfortunately, we found that not only the reaction mixture liberated iodine but the control containing only DTB solution also liberated iodine. Hydroxylamines under certain conditions on treatment with acetylating agents have been found\textsuperscript{21} to give O-acylhydroxylamines, but in the present reaction conditions, the conversion of 52 to 42 can be ruled out on the basis as 52 did not react with DTB at 0° or below. Rather, the hydrolysis of 42 to 52 could be favoured as the reaction proceeds, as it was found that the reaction mixture which was almost neutral at its beginning started becoming acidic with the time. The tables 1 and 2 also indicate that the hydroxylamine concentration was at its maximum between 2-8 hours, this time has usually been observed as the peak time for the formation of 42 and also of all related products.

Takeuchi et al\textsuperscript{6} treated nitrosobenzene with DTB, and isolated azoxybenzene in 85% yield and proposed path a (Scheme-5).
We have found that in a reaction of nitrosoarenes with DTB, the presence of hydroxylamine has always been detected right from the start of the reaction, and which in presence of nitrosoarenes (path b) could also contribute to the formation of azoxy compounds. In separate experiments, both N-hydroxyphenetidine and N-hydroxytoluidine reacted with corresponding nitrosobenzenes in CHCl$_3$ at 0$^\circ$C to result in immediate formation of respective azoxy compounds (3, 20). As indicated in tables, azoxy (3, 20) is still the major product isolated from the reaction mixtures. Though the formation of azoxy through path c is well documented in literature$^{22-24}$,
in the present reaction conditions path a and (Scheme-5) make the major contribution as at any time the concentration of reactive nitrenes in the reaction could be considered to be very small.

The origin of hydroxamic acids (7, 24) and esters (8, 21), amidophenols (6, 28) and ester 10 could be seen through the

\[
\text{H}_3\text{CO}N\text{O}\text{COCH}_3
\]

\[
\text{H}_3\text{CO}N\text{COCH}_3
\]

\[
\text{NHCOCH}_3
\]

\[
\text{NHCOCH}_3
\]

\[
\text{H}_3\text{C}N\text{COCH} = \text{CH}_3
\]

\[
\text{H}_3\text{C}N\text{COCH} = \text{CH}_3
\]

\[
\text{H}_3\text{C}N\text{COCH} = \text{CH}_3
\]

\[
\text{H}_3\text{C}N\text{COCH} = \text{CH}_3
\]

SCHEME 6 a
SCHEME 6b

SCHEME 6c
schemes 6a-6d. In a reaction of p-nitrosophenetole or o-nitrosotoluene with DTE, the formation of hydroxamic acids and their esters was detected almost immediately after the start of the
reaction. \(\text{N-Acetoxyarylamine 42, seems to rearrange fast to the more thermodynamically stable hydroxamic acid}^{21,25}\) or because of its strong basic nature\(^{28}\) accept acetyl cation to form O-acetylhydroxamic acid. But in case of \(p\)-nitroso-phenetole, due to the presence of \(p\)-ethoxy group, the hydroxamic acid and its acetyl derivative seem to undergo facile intramolecular rearrangement to corresponding amido-phenol and acetyl ester. The presence of electron-donating groups at \text{para} position has been reported to favour such rearrangements\(^8,27\).

In separate experiments of \(p\)-nitroso-phenetole or \(o\)-nitrosotoluene with DTB, it was found that in case of \(p\)-nitroso-phenetole at the end of 60 hours, only O-acetyl ester of amidophenol 10 was detected while in case of

\[
\begin{align*}
\text{COCH}_3 \\
\text{H}_3\text{C}_2\text{O} \\
\text{N} \\
\text{O} \\
\text{C} \\
\text{H}_3 \\
\text{NAc} \\
\text{OAc}
\end{align*}
\]

\(o\)-nitrosotoluene at 50 hours only O-acetyl ester of hydroxamic
acid 21 was detected, indicating that even after 24 hours of the reaction time (the time when the presence of nitrosoarene was not detected on TLC), the reaction mixture has powerful acetylating species probably 40A or 40B. It was also interesting to observe that the reaction mixture at the end of 24 hours when washed with distilled water and organic layer allowed to stand for drying over anhydrous Na₂SO₄ had still active acetylating species as the hydroxamic acid/amidophenol detected in sufficient concentration in organic layer just after washing got converted to their corresponding esters on standing at room temperature or even in refrigerator. As seen through schemes 6b and 6c, DTB failed to acetylate hydroxamic acid/amidophenol/hydroxylamine in solvent CHCl₃ at 0°, however, at room temperature, very slow acetylation property was observed indicating that in the reaction mixture it is not DTB as such which acts as acetylating agent, rather it seems acetylpyridinium ions 40A/40B formed from DTB after loss of possible hydride ions. In separate experiments, the powerful acetylating agent, N-acetyl-N-benzylimidazolinium bromide converted amidophenol/hydroxamic acid/hydroxylamine fast to corresponding esters in CHCl₃ even at 0°. As the presence of hydroxylamine was detected in the reaction mixture right from its start, scheme 6c could also be considered to contribute to the origin of hydroxamic acid or its acetyl derivative. The presence of free reactive acetylating species 40A, 40B
in the reaction mixture support the proposed leakage of hydroxylamine anion from ion pair 50 (Scheme-4). Recently, it has been shown that \(-N=O\) function in nitrosoarenes has also nucleophilic character and could react with glyoxylic acid (scheme-6d) to give hydroxamic acid, N-hydroxyformanilide\(^{29}\).

Having the same analogy, it could be invoked that nitroso function in the reaction mixture in presence of potent acetyl donor, (40A or 40B) could attack the electrophilic acetyl cation and then end in hydroxamic acid. However, there is no evidence

\[
\begin{align*}
\text{H} & \quad 53-\text{s} \\
\text{H}^+ & \quad 55 \\
\end{align*}
\]

\[X = \text{o} - \text{CH}_3; \quad X = \text{p} - \text{OC}_2\text{H}_5; \quad X = \text{o} - \text{CH}_3
\]

SCHEME 7
to support this proposed pathway.

Scheme 7, describes the possible generation of reactive electrophilic species, nitrenium ion 54 or amine radical 55 through the process of heterolytic (path a) or homolytic (path c) cleavage, or nitrenes 53 through α-elimination (path b). N-Acetoxyarylamines have been considered the ultimate reactive metabolite of carcinogenic arylamines and amides, generated in situ mainly by the cytosolic enzyme systems N-hydroxylamine: acetyl-CoA O-acetyl transferase and N-arylhydroxamic acid N,O-acyltransferase (AHAT).
cleave heterolytically to generate nitrenium ion and which get covalently bound to tissue nucleophile and thus be responsible for the process of mutagenesis and initiation of cancer. Juneja et al.\(^{36-38}\) in their attempts to synthesize \(\text{N-acetoxyarylamine}\) have also reported the generation of such reactive species.

The electron withdrawing groups in the ring stabilise \(\text{N-acetoxyarylamine}\), and \(\text{N-}(2,4\text{-dinitrophenyl})\text{hydroxylamine}\) could be conveniently converted to \(\text{N-acetoxyarylamine}\)\(^{39}\). However,
there is no report in literature on getting a pure sample of N-acetoxyarylamine having no substituents or having electron donating group. The N-acetoxy-$\beta$-phenetidine 42a generated in the reaction mixture from $\beta$-nitrosophenetole having electron donating $\beta$-ethoxy group is expected to be highly unstable and reactive.

The isolation of products 13 from the reaction mixture of $\beta$-nitrosophenetole and 26 from the reaction mixture of $\alpha$-nitrosotoluene gives conclusive evidence of the involvement of nitrenes (path b, Scheme-7) in these reaction mixtures and evidence of which would be discussed in the mechanism of origin of these products. It has been reported$^{40}$ that arylnitrenes having electron-donating substituents particularly at para-position when generated in dilute acetic acid get converted to nitrenium ions, lends support to the proposed pathway d (Scheme-7). In the reaction of nitrosoarenes with DTB, a simultaneous loss of acetic acid has been considered in the origin of azoxybenzene (Scheme-2) and in its support we also found that the reaction mixture which was initially neutral got acidic as the reaction proceeds and under such conditions it is quite logical to assume that arylnitrenes if generated in the reaction are likely to be partially converted to nitrenium ions (path d, Scheme-7). At the moment there is no evidence with us to show the generation of amine radicals (path c, Scheme-7).
Product 5 has been isolated from the reaction of p-nitroso-phenetole with DTB in solvent CHCl₃ (0.15-0.18%) and in buffer.
SCHEME-10 ORIGIN OF PRODUCTS 4 AND 11.

54-s oxidation by 53-t or 54-t or on column

54-s + 6 OH oxidation by 53-t or 54-t or on column

54-s oxidation by 53-t or 54-t or on column

SCHEME-10 ORIGIN OF PRODUCTS 4 AND 11.
system (0.26%). The mechanism of its origin could be considered through scheme-9. The ultimate toxigenic metabolite of phenacetin has been identified to be N-acetyl-$p$-benzoquinoneimine 61, and which itself has been considered\(^4\) to arise from N-hydroxy 7 or N-acyloxy 8 metabolites of phenacetin. It has been found\(^4\) that 61 at low pH may decompose further to 59. DTB has been found to convert 59 to phenylene-1,4-diol diacetate 5.\(^6\) Though 7 and 8 as such have not been isolated from the reaction of $p$-nitrosophenetole with DTB, their presence was shown through color reactions and TLC studies.

Products 4 and 11 have been isolated from the reaction of $p$-nitrosophenetole with DTB in both CHCl$_3$ or buffer system.
SCHEME 11 ORIGIN OF PRODUCT 13
The origin of these products could be invoked through scheme-10.  
54 generated initially in singlet state in the reaction mixture could undergo intermolecular insertion reaction at the reactive C-5 of 6 to give 62, and which seems to be further oxidised either by the triplet 54-t or 53-t on column in the process of elution to end in 11. The product 4 seems to arise from 11 after hydrolysis. Product 6 on oxidation with m-perchlorobenzoic acid gave 4 and which on further treatment with phenetidine in solvent CHCl₃ could be converted to 11, though in very low yields. These reactions establish conclusively the correlation of 4 and 11.

The origin of fluorescent compound 13 through the interaction of 54-t in its triplet state and 12, is probably the unique(Scheme-11) example of its type yet unreported in the literature. In this case, the triplet nitrene 54-t undergoes C-H insertion reactions,

![Diagram](image)

probably stepwise across two rings in 12. There are well
documented examples in literature where carbazole ring systems have been synthesized through the generation of \( \text{o-substituted nitrenes in biphenyl system. In these examples, the nitrene generated is suitably substituted to undergo intramolecular reaction with little change in entropy of activation, but in the origin of 13, 12 and 54 have to be forced closer to have negative entropy, and this may explain its isolation in low yield, 0.23 to maximum 0.30%. The involvement of nitrene (possibly triplet) in the origin of 13 was unequivocally established as 13 could be synthesized in 2.21% yield, by treating a mixture of \( \text{p-nitrosophenetole (50 mg, 0.33 mM and bipyridine (1.20 g, 7.7 mM)} \) with \( \text{(PPh)}_3 \) in solvent chloroform (250 ml) under \( \text{N}_2 \) at 0°. Nitrosoarenes on treatment with triphenylphosphine are well documented to generate nitrene. In the halogenated solvent chloroform, the initially generated singlet nitrene may undergo spin inversion to drop to its stable triplet state as the heavy atom solvents have been documented to induce such inversions. While designing experiments to synthesize 13, we took care that, (i) nitrene generated should be in low concentration to avoid dimerisation or interaction with nitrosoarene (using less quantities of nitrosophenetole, 0.33 mM and more volume of chloroform, 250 ml), (ii) the available nucleophile bipyridine should be in much larger concentration (1.20 g, 7.7 mM), (iii) the reaction should be done at 0° and under \( \text{N}_2 \) atmosphere (to slow down the reaction}
rate, avoid interaction of \( \text{O}_2 \) with triplet nitrene), (iv) the solvent used should be halogenated (to induce spin inversion). Under all other conditions as given in table 6, product 13 could only be isolated in traces. The inclusion of free-radical scavanger dihydroquinone in the above reaction failed to produce 13, lending further support to the involvement of triplet nitrene. Replacement of solvent chloroform by benzene also failed to give product 13.

The formation of product 26 from the reaction of o-nitroso-

\[
\begin{align*}
\text{Product 53-5} & \quad \text{Product 69} \\
\text{Product 72} & \quad \text{Product 73} \\
\text{Product 74} & \quad \text{Product 73 (DTB)} \\
\text{Product 26} & \quad \text{Product 73 (H}_2/\text{PtO}_2) \\
\end{align*}
\]

SCHEME 12
toluene with DTB is another interesting example of involvement of reactive intermediate nitrene 53, possibly generated from N-acetoxyarylamine (42, Scheme-7). o-Nitrosotoluene\(^ {16,45a}\) and o-nitrotoluene\(^ {22,46}\) on treatment with triethyl phosphate have been reported to give N-o-tolyl-2-acetimidylpyridine 73, and which on further hydrogenation with \(\text{H}_2\) in presence of PtO\(_2\) has been converted to 26\(^ {16}\) (Scheme-12). The mechanism (Scheme-12) proposed for the origin of 26 has been adopted after the proposed

\[
\begin{align*}
\text{ArNO} \quad \text{(EtO)}_3\text{P} &\quad \text{ArN} \quad \text{ArNO}_2 \quad \text{(EtO)}_3\text{P} \\
\text{ArN} \quad \text{CH}_3 &\quad \text{ArN} \quad \text{CH}_3 \\
\text{ArN} \quad \text{O} \quad \text{P(OEt)}_3 &\quad \text{ArN} \quad \text{O} \quad \text{P(OEt)}_3 \\
\text{N} \quad \text{CH}_3 &\quad \text{N} \quad \text{CH}_3 \\
\text{C} = \text{N} \quad \text{Ar} + \text{(EtO)}_3\text{PO} &\quad \text{C} = \text{N} \quad \text{Ar} + \text{(EtO)}_3\text{PO}
\end{align*}
\]

SCHEME 13

mechanism for the formation of product 73 (Scheme-13)\(^ {46}\). In contrast to attack of 74 on reactive intermediate 70 (Scheme-13), in the present reaction mixture the basic reactive intermediate
N-acetoxyarylamine 42, appears to attack 70 and then result in product 26 after reduction (Scheme-12).

In a reaction of p-nitrosophenetole with DTB in solvent system CHCl₃-MeOH-buffer (pH 7.0), additional four products 14, 15, 16 and 17 were isolated and characterised, however, the product pattern in a reaction of o-nitrosotoluene with DTB in solvent chloroform (at 0° or 30°) or CHCl₃-MeOH-buffer almost remained the same. The formation of products 14, 15, 16, 17, 22, 23, 27, 29 and 30 could also be considered through the involvement of reactive intermediates, nitrenium ion, nitrene or amine radical originated from N-acetoxyarylamine 42 (Scheme-7). It was further interesting to observe that these products could only be isolated from the reaction mixtures showing the presence of sufficient free amine (p-phenetidine/o-toluidine), and in a reaction of p-nitrosophenetole with DTB in CHCl₃ (at 0° or 30°) where the presence of free amine could not be detected on TLC, we failed to isolate the products 14-17.

Intermolecular attack of an aromatic nucleus by electrophilic ethoxycarbonyl, sulfonyl and cyanonitrenes to result in N-substituted azepines or anilines through the intermediate involvement of benzaziridine is well documented. Benzaziridine has also been considered as the likely intermediate in the intermolecular substitution of activated substrates by aryl nitrenes. For the origin of product 13,
SCHEME-14 ORIGIN OF PRODUCTS 14, 16 AND 17.
we have unambiguously shown the involvement of nitrenes. We further propose that the formation of products 14, 16 and 17 could also be considered through the involvement of nitrenes (Scheme-14). The benzaziridine intermediates 76 or 77, through loss of ammonia (path a) or ethoxy group (path b) as such or probably further facilitated by hydride ion may result in products 14 or 17 respectively. The intermediate 77 (path c) after hydride assisted opening of benzaziridine ring or as such through 77A, seem to give product 16 through intermediate 79.

The products 14, 16 and 17 were only isolated from the reaction of p-nitrosoaniline with DTB in a polar solvent system CHCl₃-MeOH-buffer. N-Acetoxyarylamine 42 generated in the polar solvent may undergo favourable heterolytic cleavage to generate nitrenium ions, and the involvement of these ions for the origin of products 14, 16 and 17 could be seen through schemes 16 and 17. The intermediate 80 (Scheme-16) could rearrange⁵³,⁵⁴ to either 16 through 79 or 82 through 81, however, product 82 could not be isolated. It was interesting to observe that 14 could also be isolated from a reaction of N-hydroxy-p-phenetidine with DTB under N₂ in solvent CHCl₃. In this reaction mixture, the presence of free p-phenetidine was also noted on TLC. The isolation of this product from this reaction mixture favours more its possible origin through Scheme-14 (path a). N-Hydroxyarylamines are well known to generate free
nitrenes\textsuperscript{55,56}. The origin of products 27 and 29 could also be considered through the involvement of nitrenium ions (Scheme-18). In a reaction of o-nitrosotoluene with DTB, the presence of free amine was detected on TLC in all the three reaction conditions. The formation of product 30 (Scheme-18), could possibly be through the involvement of nitrene rather than nitrenium ion. The involvement of nitrenium ion in presence of amidophenol 28 is more likely to end in anilino derivatives ortho- or para- to -OH of amidophenol or phenoxy derivatives. As the limited structural evidences available
support structure 30, the involvement of nitrenium ions in its origin may be ruled out.

In the reaction of \( p \)-nitrosophenetole or \( o \)-nitrosotoluene with DTB in solvent system CHCl\(_3\)-MeOH-buffer, the products azo-, 2, 19, N-acetylhydrazo-, 15, 23 and anilides, 9 and 25 have been isolated in higher concentration than when the reaction was
carried out in solvent CHCl₃ (Tables 3 and 4). It was noted that usually the free amine concentration (monitored through TLC at various time intervals) in the reaction mixture carried out in buffer system was higher than in solvent chloroform. In a reaction of p-nitrosophenetole with DTB in CHCl₃, where we could not detect free amine on TLC, N-acetyl-hydrazo compound 15 was not formed, however, phenacetin 9, the precursor of which could only be p-phenetidine was isolated though in lesser yields than in buffer system, indicating that whatever the small amount of free amine is formed in solvent CHCl₃ gets fast converted to 9. The free amines on treatment with DTB in CHCl₃ could be easily converted to their respective anilides. The formation of products 9 and 25 could be seen through Scheme-19. Nitrenium ion in its singlet state by hydride abstraction (path a) or nitrenium ion \(^{57,58}\) and nitrene \(^{59,60}\) in their triplet state (favoured in CHCl₃)\(^{61,62}\) by stepwise hydrogen abstraction (path b) probably from the DTB or solvent system get converted to 9 or 25 through amine intermediate. The formation of products 9, 25 and N-acetylhydrazo- 15 and 23 in higher concentration in polar solvent system, CHCl₃-MeOH-buffer appears to involve more nitrenium ions, which seem to arise due to favoured heterolytic cleavage of N-acetoxyarylamine 42. N-Acetoxyarylamines which have been considered to be soft acids\(^{26}\) could react with soft base, hydride probably through SN\(^2\) mechanism to also result in free amine (path c). However, even
if this pathway operates its contribution should be small, as it should be rather more favoured in CHCl₃ than in more polar solvent buffer system.

Scheme 20 could be considered to explain the possible origin of N-acetylhydrazo- compounds 15 and 23. Path a may be
more prominent in a polar solvent system. Though in synthetic reaction, azo compounds have been considered as precursors of hydrazo but DTB failed to reduce azo 2 or 19 to respective hydrazo compounds. The synthetically prepared hydrazo compounds could be conveniently converted to N-acetyl derivative by DTB at room temperature in solvent CHCl₃. In the thermolysis of phenylazide in decalin, hydrazobenzene, including benzidine, azobenzene and aniline have been isolated. Amine radicals, arising from triplet nitrene by hydrogen abstraction from the solvent have been considered precursors for the formation of hydrazobenzene⁴⁵ᵇ, lends support to path b. N-Acetoxyarylamine possibly through its homolytic cleavage could also generate amine radicals. However, we have no evidence to support this proposed pathway. In certain N-O, cleavage to generate amine radicals has been reported⁶³.

Scheme-21, explains the possible origin of azo products 2 and 19. Reaction in polar solvent systems having higher concentration of amines in the reaction mixture gave higher concentration of 2 and 19. p-Phenetidine and o-toluidine with their corresponding nitrosobenzenes in solvent chloroform gave respective azo compounds (path a). In the reaction mixture there is little possibility of dimerisation of reactive intermediate nitrene to contribute to azo compounds (path b). However, hydrazobenzene formed in the reaction mixture (Scheme-20) could be dehydrogenated by their respective triplet nitrene/nitrenium
ion to corresponding azo compounds (path c). In one of our

\[
\begin{align*}
2 \quad x &= p-O\text{C}_2\text{H}_5 \\
19 \quad x &= o - \text{CH}_3
\end{align*}
\]

\[
O\text{NH}_2 + O-N=O \xrightarrow{a} O-N=N-O \xleftarrow{b} 2 O-N.
\]

\[
c \quad 53-t \text{ or } 54-t
\]

\[
O-NH-NH-O
\]

\[
O-N=N-O \xrightarrow{\text{DTB, cold or reflux}} O-N=N-O
\]

\[
0 \quad 3, 20 \quad 2, 19
\]

**Scheme 21**

reactions of ethyl-\(p\)-nitrosobenzoate with DTB, we could isolate hydrazo derivative and azo compound in much higher concentration than even azoxy derivative. In these studies we found that mixture of ethyl-\(p\)-aminobenzoate and ethyl-\(p\)-nitrosobenzoate under the reaction conditions failed to give corresponding azo derivative indicating the possibility of path c. In the synthesis of azo compounds from reduction of nitro or nitroso-
benzenes, azoxy compounds have been considered as precursors
of azo compounds. But we have found that azoxy compounds on treatment with DTB in CHCl₃/buffer system at room temperature or reflux remained unreacted, thus ruling out its possible origin from azoxy compounds in the reaction mixture.

2.2.1 Reaction of N,N-diphenylnitrosamine and N-methyl-N-phenylnitrosamine with DTB and characterisation of products

The reaction mixture yielded a mixture of products which were isolated by combined procedure of column chromatography and preparative thin layer chromatography. The products isolated with their quantities are enlisted in Scheme-22 in their sequence of elution.

Compound 32 was obtained as white crystalline product. Its IR (cm⁻¹) gave bands characteristic for N-H (3226) and C-N (1316); PMR (δ) displayed signals at 6.70-7.25 (m, 10H, aromatic) and 5.40-5.55 (br, NH); MS indicated molecular ion at m/z 169 (found and calculated) and another characteristic peak at m/z 77 (C₆H₅)⁺; further its mp corresponded with the reported literature value.

Compound 33 was obtained as greenish sticky product and was assigned molecular formula C₂₆H₂₃N₃O on the basis of its elemental analysis and MS. Its MS gave molecular ion at
\[
\text{H}_3\text{C}_6\xrightarrow{\text{R}} \text{N} \xrightarrow{\text{N}} \text{N} \xrightarrow{\text{=}} \text{O} + \text{H}_3\text{C} \xrightarrow{\text{C}} \text{N} \xrightarrow{\text{O}} \text{C} \xrightarrow{\text{C}} \text{CH}_3
\]

31 \( R = \text{C}_6\text{H}_5 \)

36 \( R = \text{CH}_3 \)

32 \( R = \text{C}_6\text{H}_5 \)

37 \( R = \text{CH}_3 \)

34

35 \( R = \text{C}_6\text{H}_5 \)

38 \( R = \text{CH}_3 \)

Oily product

39

SCHEME 22
m/z 393 (found and calculated) and other characteristic peaks at m/z 351 (M⁺-ketene), 183 [(C₆H₅)₂NNH]⁺ and 168 [(C₆H₅)₂N]⁺; IR (cm⁻¹) indicated band characteristic for N-COCH₃ (1677); PMR (δ) exhibited signals at 7.1-7.3 (m, 12H, aromatic), 6.9-7.0 (m, 8H, aromatic) and 2.2 (s, 3H, N-COCH₃).

Compound 34, obtained as pale-yellow oily product was assigned the molecular formula C₄H₇NCU from its elemental analysis and MS. The compound on hydrolysis with dilute ammonia gave positive test for hydroxamic acid (violet color with aqueous FeCl₃), indicating the product as probably the O-acetyl ester of acetohydroxamic acid. This is further confirmed as its IR was characteristic for N-OCOCH₃ (1790) and N-COCH₃ (1724). Its MS indicated M⁺ at m/z 117 (found and calculated) and other characteristic peaks at m/z 75 (M⁺-ketene) and 74 (M⁺-acetyl); PMR (δ) displayed signals at 7.2-7.4 (br, NH), 2.36 (s, 3H, N-OCOCH₃), 2.30 (s, 3H, N-COCH₃). Its identity was finally confirmed by comparison with an authentic sample prepared from hydroxylamine hydrochloride and acetic anhydride in presence of pyridine.

Compound 35 was obtained as white crystalline product. Its IR (cm⁻¹) gave band characteristic for N-COCH₃ (1667); PMR (δ) exhibited signals at 7.2-7.5 (m, 10H, aromatic) and 2.1 (s, 3H, N-COCH₃); MS gave molecular ion at m/z 211 (found and calculated) and other characteristic peaks at m/z 169(M⁺-ketene).
and 77 (C₆H₅)⁺. Its identity was confirmed by comparison with an authentic sample prepared by refluxing diphenylamine with a mixture of acetic anhydride and pyridine.

Compound 38 was obtained as white leaflets. Its IR (cm⁻¹) gave band characteristic for N-COCH₃ (1667); PMR (δ) displayed signals at 7.5-7.8 (m, 5H, aromatic), 3.45 (s, 3H, N-CH₃) and 2.0 (s, 3H, N-COCH₃); MS gave M⁺ at m/z 149 (found and calculated) and other characteristic peak at m/z 107 (M⁺-ketene). Its mp tallied with that reported in the literature.

Product 39 was highly unstable and could not be identified as it decomposed while trying to purify by PTLC.

2.2.2 Probable mechanism of origin of products

DTB loses hydride ion with concomitant loss of acetyl cation thus simulating the reduction and acetylation properties of NAD(P)H and acetyl-CoA respectively. We have earlier found that nitrosoarenes on treatment with DTB even at 0° gave different products which have been considered to originate from the reactive intermediate N-acetoxyarylamine. But in the present studies, N-nitroso derivatives failed to react with DTB at room temperature and this low reactivity may be due to the following resonance forms:

\[
\begin{align*}
\text{H}_5\text{C}_6\text{N} & \quad \text{N} = \text{O} \\
\text{H}_5\text{C}_6 & \quad \text{N} = \text{N} - \text{O}
\end{align*}
\]
N,N-Diphenylnitrosamine and N-methyl-N-phenylnitrosamine on refluxing with DTB for 6-7 hours in chloroform under nitrogen atmosphere gave products given in Scheme-22.

TLC studies were carried out at different time intervals to know the sequence of formation/disappearing of products during the course of the reaction. Diphenylamine 32 was first detected within half an hour of the start of the reaction and its concentration gradually decreased till the completion of the reaction (disappearance of N,N-diphenylnitrosamine on TLC).

\[
\begin{align*}
\text{H}_5\text{C}_6 - N - N &= O & \xrightarrow{\text{DTB}} & \text{H}_5\text{C}_6 - N - H \\
31 & & 32
\end{align*}
\]

LiAlH\textsubscript{4} has been shown to reduce N,N-diphenylnitrosamine 31 to diphenylhydrazine 86. But in the reaction of N,N-diphenyl-

\[
\begin{align*}
\text{H}_5\text{C}_6 - N - N &= O & \xrightarrow{\text{LiAlH}_4\text{ in ether}} & \text{H}_5\text{C}_6 - N - \text{NH}_2 \\
31 & & 86
\end{align*}
\]

nitrosamine with DTB, the formation of either diphenylhydrazine or its acetylated product could not be detected. Similarly,
catalytic reduction of $N,N$-diphenyl nitrosamine has been reported in the presence of (i) Raney nickel or platinum, (ii) finally divided palladium on CaCO$_3$ or BaSO$_4$ to give diphenylamine, ammonia$^{64,65}$, diphenylamine and nitrogen respectively. We find that under these catalytic reductions, the nitrogen in $N-N=0$ group is being lost as ammonia in (i) and as nitrogen in (ii). In our reaction conditions, during the formation of diphenylamine, we failed to detect the evolution of ammonia as such or after heating the aqueous extract of reaction mixture with sodium hydroxide.

In the catalytic reduction of $N,N$-diphenyl nitrosamine in presence of Pd on CaCO$_3$/BaSO$_4$, the involvement of tetraphenyltetrazane 87 has been proposed$^{66}$. Though the liberation of $N_2$ has not been monitored, but in the absence of ammonia gas, it could be presumed that in the origin of diphenylamine from the reaction
of nitrosamine with DTB, the reaction follows the path as proposed in the catalytic reduction with Pd on CaCO₃/BaSO₄₆⁴,⁶⁵.

A copious evolution of brown fumes of NO₂ was observed an hour after the start of the reaction. It was detected with the help of ferrous sulfate and starch iodide papers which turned black and blue respectively. Other products as N-acetyldiphenylamine and O-acetylacetohydroxamic acid were detected with the help of TLC. It is very interesting to note that N-acetyldiphenylamine 35 and O-acetylacetohydroxamic acid 34 formed simultaneously with the liberation of nitrogen dioxide (brown fumes). Diphenylamine 32 on refluxing with DTB in CHCl₃, failed to give N-acetyl derivative 35, while N-methylaniline

\[
\begin{align*}
\text{H}_5\text{C}_6 & \quad \text{N} \quad \text{H} \quad \text{DTB} \quad \text{H}_5\text{C}_6 \\
\text{H}_5\text{C}_6 & \quad \text{N} \quad \text{H} \quad \text{DTB} \quad \text{H}_5\text{C}_6
\end{align*}
\]

under similar conditions was converted to its N-acetyl derivative.
SCHEME 23 ORIGIN OF N-ACETYL DERIVATIVE (35, 38), O-ACETYLACETOHYDROXAMIC ACID (34) AND NO₂.
From the reaction mixture of diphenylnitrosamine, both free amine and N-acetyl derivatives were isolated in 22.8% and 7.3% but from the reaction of N-methyl-N-phenyl nitrosamine, free amine could be detected only in traces, and N-acetyl derivative 38 was the major product.

Scheme-23 could be considered to explain the almost simultaneous origin of N-acetyl derivatives of amine (35 and 38), O-acetylacetohydroxamic acid 34 and NO₂, within 2-3 hours of the start of the reaction. Denitrosation of nitrosamine to result in amine and NO₂ has been reported to be catalyzed by HCl, and in such denitrosation the initial protonation of nitrosamine and acceptance of the leaving nitrosonium ion by chloride ion have been considered to be the essential steps (path d). The carbonyl group has also been considered to play a significant role in denitrosation reactions. Having the same analogy, the denitrosation of nitrosamines in the reaction mixture could be considered to be catalyzed by the acetyl cation (instead of H⁺) and the leaving nitrosonium be accepted by the available nucleophiles in the reaction mixture as hydride or acetate (liberated as in Scheme-25, path b and d or from acetic acid and bipyridine). The HNO₈, through path b, could be considered to convert to 34 (O-acetylacetohydroxamic acid) directly by the acceptance of one hydride and two acetyl cations or through an intermediate 89, by stepwise acceptance of acetyl cation. The intermediate 89, even if formed seems to be fast
SCHEME 24 ORIGIN OF N-ACETYL DERIVATIVE (35,38) AND O-ACETYLACETOHYDROXAMIC ACID (34).

SCHEME 25 ORIGIN OF 1,1,3,3-TETRAPHENYL-2-ACETYLTRIAZANE (33).
converted to 34, and behaves like almost direct conversion of 88 to 34, as O-acylhydroxylamines have been found to change to thermodynamically more stable product hydroxamic acid 90, and which was not detected during the entire course of the reaction. NO₂ could arise either from decomposition of HNO₂ (path c) or from acetylnitrite (path e).

The origin of products 34, 35 and 38 could also be seen through Scheme-25. The intermediate formation of N-acetyl 91 and N-acetoxy-N-acetylhydrazine 92 is based on our observation of reaction of arylnitroso compounds with DTB. The hydride and acetylation assisted cleavage of N-N bond in hydrazo 92 could result in formation of 34, 35 and 38. The failure to isolate 92 from the reaction mixture is expected to be due to its very high instability and reactivity. In the reaction of p-nitroso-phenetole with DTB, we also failed to isolate the reactive N-acetoxy-N-acetylarylamine, rather only the ortho rearranged product could be isolated.

The formation of 1,1,3,3-tetraphenyl-2-acetyltriazane 33 could be considered through Scheme-25. The highly reactive intermediate 91 and 92, could easily lose acetate ion to give 93 and 94 respectively. 93 could be further acetylated to intermediate 94, and which through path c, could react with the available diphenylamine to result in product 33. In the reaction of N-methyl-N-phenyl nitrosamine with DTB, the product
corresponding to 33, was not isolated. For the formation of 33, from 94 (Scheme-25, path c), the presence of free amine is essential, but in the reaction of N-methyl-N-phenylnitrosamine with DTB, the free N-methylaniline detected any moment during the course of the reaction, was found to be either absent or only in traces.

In the metabolic studies of N-nitroso compounds, attention has mostly been devoted to the side chain rather than -N-N=O function. But in the present investigations of reaction of N-nitroso compounds with DTB, an ideal model for NAD(P)H and acetyl-CoA, it is interesting to find that N-nitroso compounds under reducing conditions in presence of acetyl cation could lead to cleavage of -N-N=O to convert N=O group to CH₃CO-NH-OCOCH₃, a hydroxylamine derivative. Hydroxylamine as such has been reported to be a potent mutagen. The O-acetylacetohydroxamic acid has been found to be a good acetylation agent; aniline on shaking for a few minutes with 34 was converted to acetanilide and 34 was converted to hydroxamic acid.

The biological implications of this powerful acetylation agent when generated in situ have yet to be assessed.