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# REACTION OF POTASSIUM SUPEROXIDE WITH 3-NITRO-2-PHENYL-2H-1-BENZOPYRANS AND THEIR DIHYDRO DERIVATIVES

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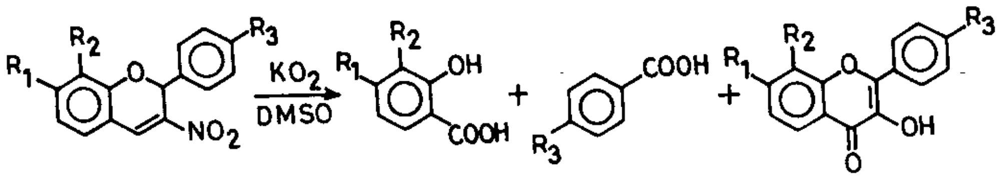
Abstract - 3-Nitro-2-phenyl-2H-1-benzopyrans on treatment with potassium superoxide in dimethyl sulphoxide are degraded mainly to the corresponding salicylic acids and benzoic acids. Formation of flavonols, as a minor product are also observed. The dihydro derivatives of 3-nitro-2-phenyl-2H-1-benzopyrans are converted to the corresponding flavonols by potassium superoxide in benzene containing 18-crown-6 ether.

Intervention of superoxide anion radical in enzymatic oxidation[1-4] has recently been the subject of a number of investigations. $O_2^{\overline{\cdot}}$ , one of the simplest and important anion radical, reacts with various substrates owing to its anionic, radical and redox nature. Although action of superoxides on various substrates has been studied[5-7], their behaviour towards nitro compounds is yet to be properly evaluated. To the best of our knowledge conversion of nitroalkanes to the corresponding carbonyl compounds by the action of electrochemically generated superoxide ion[8] and degradation of β-nitrostyrene[9] to benzoic acid by superoxide in the presence of 18-crown-6-ether are the only two known instances. Apart from this, the factor which prompted us to investigate the action of superoxide on 3-nitro-2-phenyl-2H-1-benzopyrans was the reported superoxide mediated conversion of cyanides to amides in dimethyl sulphoxide medium[10]. It is interesting to note that similar conversion in other solvents could not be achieved. A rationale for such selectivity could be the generation of hydroxy and hydroperoxy anions, species apparently responsible for the conversion, by the interaction of superoxide with dimethyl sulphoxide. Such conversion of cyanide to amide by $H_2O_2$ in basic media is well documented[11]. In our previous study we have observed that hydrogen peroxide in the presence of base converts 3-nitro-2-phenyl-2H-1-benzopyrans to the respective flavonols[12]. Thus keeping these factors in view, both 3-nitro-2-phenyl-2H-1-benzpyrans and their dihydro derivatives were treated with potassium superoxide. Present paper describes our findings.

3-Nitro-2-phenyl-2H-1-benzopyrans (1-6) are chiefly degraded to the corresponding salicylic acids (7-9) and benzoic acid (10-13) on subjection to superoxide treatment in dimethyl sulphoxide (Scheme-1). Besides these degradative products flavonols (14-19) are formed in minor amounts (Scheme-1). Formation of these acids could be rationalized in two ways.



1 $R_1=R_2=R_3=H$
2 $R_1=R_2=H;R_3=OCH_3$
3 $R_1=R_2=H;R_3=Cl$
4 $R_1=OCH_3;R_2=H;$ $R_3=CH_3$
5 $R_1=R_3=H;R_2=OCH_3$
6 $R_1=H;R_2=R_3=OCH_3$

7 $R_1=R_2=H$
8 $R_1=H;$ $R_2=OCH_3$
9 $R_1=OCH_3,$ $R_2=H$

10 $R_3=H$
11 $R_3=OCH_3$
12 $R_3=Cl$
13 $R_3=CH_3$

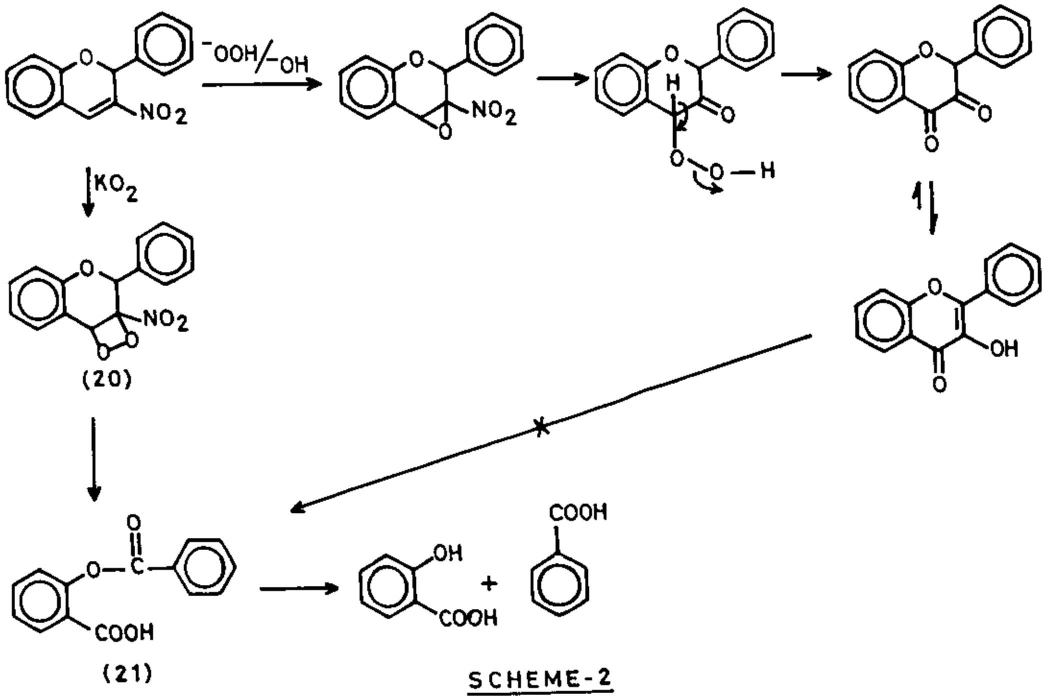
14 $R_1=R_2=R_3=H$
15 $R_1=R_2=H,R_3=OCH_3$
16 $R_1=R_2=H,R_3=Cl$
17 $R_1=OCH_3,R_2=H;$ $R_3=CH_3$
18 $R_1=R_3=H,R_2=OCH_3$
19 $R_1=H,R_2=R_3=OCH_3$

Scheme -1

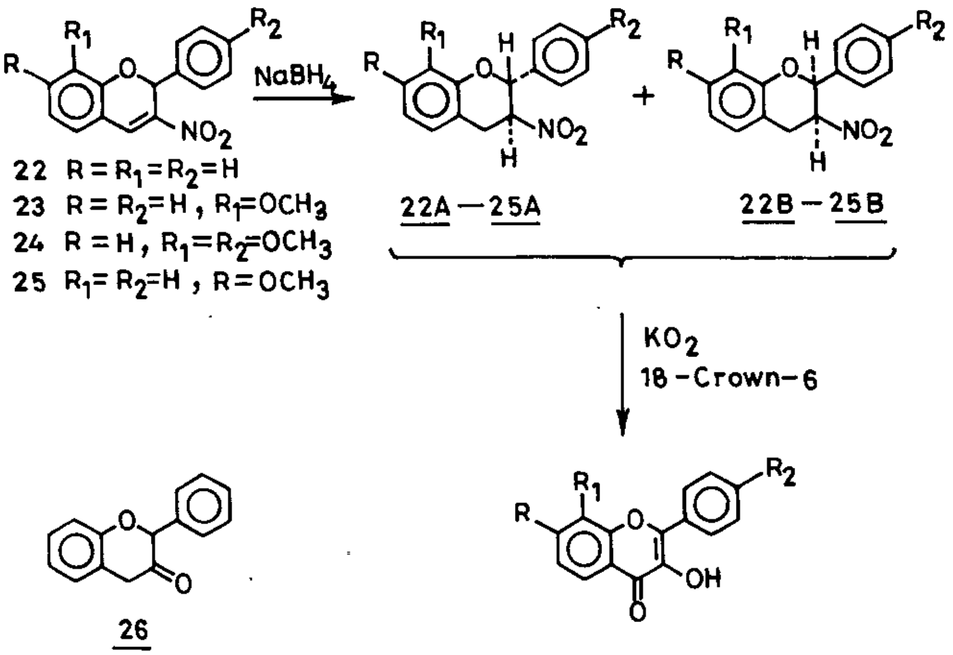
In a possible route nitrobenzopyrans are initially converted to the flavonols which, in turn, are degraded to salicylic acid and benzoic acid via carboxy ester (21).

The other route involves the formation of dioxetane intermediate (20) as proposed by Frimer et al.[9] Since in the present study flavonols are found to be resistant towards degradation under the experimental conditions, this route seems to be untenable. Thus the reaction seems to proceed via dioxetane intermediate even in the absence of 18-crown-6-ether. Most probably the resultant dioxetane transforms to salicylic acid monobenzoate (21) by ring scission followed by oxidation. The resultant ester on hydrolysis gives rise to the acids (Scheme-2). The formation of flavonol can be explained through the hydroperoxide anion, generated from the interaction of potassium superoxide and dimethyl sulphoxide.

The dihydro derivative of 3-nitro-2-phenyl-2H-1-benzopyran was reacted with potassium superoxide in the presence of 18-crown-6-ether in benzene, as the same reaction is sluggish in DMSO, which yielded flavonol. The formation of flavonol could be explained via Nef type conversion of the dihydro derivative to 2-phenyl-2H-1-benzopyran-3(4H)-one (26). Incidentally such Nef type conversion of saturated nitro compounds to the corresponding ketones are known with electrochemically generated superoxides. Further oxidation with superoxide will lead to flavonol[13]. The dihydro derivatives (22AB-25AB) required for the present study are prepared by sodium borohydride reduction of 3-nitro-2-phenyl-2H-1-benzopyrans[14,15] (22-25). During this process dihydro derivatives were obtained as diastereomeric mixture of (22A-25A) and (22B-25B) respectively, which are separated into the pure components by column chromatography (Scheme-3).



SCHEME-2



Scheme – 3

EXPERIMENTAL

Reaction of Potassium Superoxide with 3-Nitro-2-phenyl-2H-1-benzopyrans (1-6)

To a well stirred solution of 3-nitro-2-phenyl-2H-1-benzopyran (1 mmol) in dry dimethyl sulphoxide (15 ml), a powdered potassium superoxide (6 mmol) was added and stirring was continued for additional 8-10 min. The reaction was quenched by pouring the mixture into chilled water. The resultant alkaline solution was acidified with 5% hydrochloric acid and was allowed to stand at room temperature for 1 h. The solution was repeatedly extracted with ethyl acetate and the aqueous layer was discarded.

The organic extract after reducing to 50 ml and cooling was repeatedly extracted with 5% sodium bicarbonate solution. The acid free ethyl acetate extract on concentration and filtration through a silica gel column gave flavonol. The combined bicarbonate extract was freed from the accompanying dimethyl sulfone by shaking the solution with dichloromethane. Mixture of salicylic acid and benzoic acid was obtained from dimethyl sulfone free bicarbonate extract by neutralization with 5% hydrochloric acid and extracting the aqueous layer with ethyl acetate.

The yields of combined acids were varying from 60-70% and the flavonol was obtained in 10-15% yield. The structures of all the acids were confirmed by converting them to the corresponding esters and comparing with authentic samples by GLC. The structures of flavonols were confirmed by comparing their nmr and mass spectral data with those of authentic samples. Spectral data of all these compounds is available in references 15 and 16.

### Reduction of 3-Nitro-2-phenyl-2H-1-benzopyrans (22-25)

To a well stirred solution of 3-nitro-2-phenyl-2H-1-benzopyran (2 mmol) in ethanol (30 ml), sodium borohydride (6 mmol) was added and the stirring continued for further 20 min at ambient temperature. The reaction was quenched by adding 5% hydrochloric acid and the reaction mixture was diluted with water. Extraction with dichloromethane, concentration and chromatography over silica gel (pet. ether-ethyl acetate) yielded initially a trace amount of starting material and then two diastereoisomeric 3-nitro-2-phenyl-3,4-dihydro-2H-1-benzopyrans. The same procedure was used for the reduction of other derivatives. The physical and spectral properties are listed in Tables 1 and 2 respectively.

Table 1

Physical Properties of 3-Nitro-2-phenyl-3,4-dihydro-2H-1-benzopyrans

| Compound | Yield % | mp (lit.[14] m p) °C | Elemental analysis* | | |
|---|---|---|---|---|---|
| | | | C | H | N |
| 22A | 75 | 167-168 (168) | 70.58 | 5.13 | 5.49 |
| | | | 70.23 | 5.36 | 5.30 |
| 22B | 10 | 103-104 (102) | 70.58 | 5.13 | 5.49 |
| | | | 70.36 | 5.23 | 5.46 |
| 23A | 60 | 204-205 | 67.36 | 5.29 | 4.91 |
| | | | 67.28 | 5.35 | 4.80 |
| 23B | 15 | 165-166 | 67.36 | 5.29 | 4.91 |
| | | | 67.12 | 5.08 | 4.72 |
| 24A | 62 | 192-194 | 64.76 | 5.44 | 4.44 |
| | | | 64.51 | 5.32 | 4.38 |

| | | | | | |
|---|---|---|---|---|---|
| <u>24B</u> | 12 | 163-164 | 64.76<br>64.71 | 5.44<br>5.21 | 4.44<br>4.29 |
| <u>25A</u> | 58 | 168-169 | 67.36<br>67.30 | 5.29<br>5.45 | 4.91<br>4.68 |
| <u>25B</u> | 15 | 165 | 67.36<br>67.52 | 5.29<br>5.18 | 4.91<br>4.70 |

*Elemental analysis is given in order calculated and experimented.

Table 2

Spectral Properties of 3-Nitro-2-phenyl-3,4-dihydro-2H-1-benzopyrans

| Compound | ir (nujol)$_{max}$ cm$^{-1}$ | $^1$H-nmr (CDCl$_3$), δ (ppm) |
|---|---|---|
| <u>23A</u> | 1380, 1560(NO$_2$) | 3.27 (1H, dd, $J_{gem}$ = 16 Hz, $J_{vic}$ = 5 Hz, C$_4$-H), 3.63 (1H, dd, $J_{gem}$ = 16 Hz, $J_{vic}$ = 5 Hz, C$_4$-H), 3.9 (3H, s, OMe), 4.88-5.18 (1H, m, C$_3$-H), 5.6 (1H, d, J = 7 Hz, C$_2$-H), 6.7-7.07 (3H, m, Ar-H), 7.43 (5H, m, Ar-H). |
| <u>23B</u> | 1380, 1560(NO$_2$) | 3.4 (2H, d, J = 4 Hz, C$_4$-H), 3.92 (3H, s, OMe), 5.17-5.32 (1H, m, C$_3$-H), 5.6 (1H, d, J = 3 Hz, C$_2$-H), 6.74-7.06 (3H, m, Ar-H), 7.4 (5H, s, Ar-H). |
| <u>24A</u> | 1380, 1555(NO$_2$) | 3.28 (1H, dd, $J_{gem}$ = 17 Hz, $J_{vic}$ = 6 Hz, C$_4$-H), 3.64 (1H, dd, $J_{gem}$ = 17 Hz, $J_{vic}$ = 6 Hz, C$_4$-H), 3.82 (3H, s, OMe), 3.88 (3H, s, OMe), 4.92-5.14 (1H, m, C$_3$-H), 5.46 (1H, d, J = 7 Hz, C$_2$-H), 6.7-7.04 (5H, m, Ar-H), 7.3-7.4 (2H, m, Ar-H). |
| <u>24B</u> | 1380, 1555(NO$_2$) | 3.37 (2H, d, J = 6 Hz, C$_4$-H), 3.84 (3H, s, OMe), 3.92 (3H, s, OMe), 5.12-5.26 (1H, m, C$_3$-H), 5.58 (1H, d, J = 4 Hz, C$_2$-H), 6.74-6.98 (5H, m, Ar-H), 7.2-7.3 (2H, m, Ar-H). |
| <u>25A</u> | 1390, 1565(NO$_2$) | 3.25 (1H, dd, $J_{gem}$ = 17 Hz, $J_{vic}$ = 6 Hz, C$_4$-H), 3.69 (1H, dd, $J_{gem}$ = 17 Hz, $J_{vic}$ = 6 Hz, C$_4$-H), 3.8 (3H, s, OMe), 4.94-5.16 (1H, m, C$_3$-H), 5.4 (1H, d, J = 7 Hz, C$_2$-H), 6.66-6.98 (3H, m, Ar-H), 7.42 (5H, s, Ar-H). |
| <u>25B</u> | 1390, 1565(NO$_2$) | 3.4 (2H, d, J = 5 Hz, C$_4$-H), 3.82 (3H, s, OMe), 5.14-5.28 (1H, m, C$_3$-H), 5.4 (1H, d, J = 3 Hz, C$_2$-H), 6.7-7.02 (3H, m, Ar-H), 7.42 (5H, s, Ar-H). |

### Reaction of 3-Nitro-2-phenyl-3,4-dihydro-2H-1-benzopyrans ( 22AB-25AB ) with Potassium Superoxide

To a well stirred solution of 3-nitro-2-phenyl-3,4-dihydro-2H-1-benzopyran (0.5 mmol) and 18-crown-6-ether (0.12 mmol) in dry benzene (15 ml) potassium superoxide (2 mmol) was added and the stirring continued for an additional 5 min. The reaction was quenched by pouring the mixture into chilled water. Extraction of the aqueous layer with ethyl acetate, concentration and chromatography over silica gel (pet. ether-ethyl acetate) yielded the starting material and flavonol (25-30%) simultaneously. Similarly other reaction of the series were carried out. The structures of the compounds obtained from this reaction were confirmed by comparison of their nmr and mass spectral data[15,16] with those of authentic samples.

### Reaction of Potassium Superoxide with Flavonol

To a well stirred solution of flavonol (0.2 mmol) in dry dimethyl sulphoxide (5 ml), potassium superoxide (1 mmol) was added and the stirring was continued at ambient temperature. Monitoring the reaction by tlc showed the presence of starting material unchanged even after 4 h. The reaction was quenched by pouring the mixture into chilled water. Neutralization of the alkaline solution extraction with ethyl acetate and concentration gave the flavonol.

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