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Studies on Arylhydrazones, Part-XII: Action of Bromine on Ethylhydrogen Mesoxalate Phenylhydrazones

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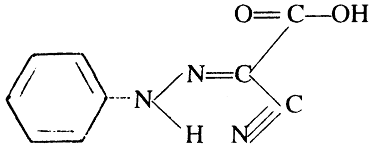
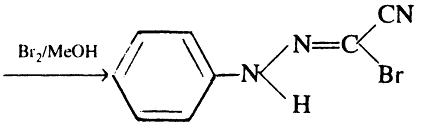
The nature of brominated product is dependent on the amount of bromine and time of reaction in the bromination of ethylhydrogen mesoxalate phenylhydrazones (IV). The products are identified as (Z-) form. Bromination of (IV) further revealed that nuclear bromination first takes place, followed by displacement of COOH group and then again nuclear bromination. It seems that electron withdrawing groups in aromatic nucleus deactivates the ring to such an extent that bromination in the nucleus does not take place even with excess of bromine in the presence of sunlight and on increasing the temperature. On the other hand, electron releasing groups in the aromatic nucleus activate the ring and nuclear bromination occurs with excess of bromine in sunlight.

INTRODUCTION

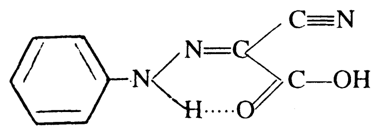
Halogenation of arylhydrazones obtained from the coupling of aryldiazonium salts with ethyl acetoacetate and acetylacetone has been studied by Chattaway and his coworkers[1–3]. Subsequent modifications of the process have also been reported.[4–6] No halogenation has been reported on half esters (IV) except in case of cyanoacetic acid phenylhydrazone[7] (I and II) and it has been observed that E-(I) and Z-(II) forms on bromination in methanol afford only one isomer *i.e.* Z-(III) form of monobrominated product.[7]



E-form (I)



Z-form (III)



Z-form (II)

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Since a number of half esters (IV) were available at hand, it was of great interest to us to study the bromination of half esters (IV) and the results obtained are described in this paper.

EXPERIMENTAL

The bromine solution in acetic acid was prepared by dissolving 6 mL of bromine in 44 mL of glacial acetic acid. Compound (IV, R = H, *o*-NH_2, *p*-NO_2, *o*-OMe and *p*-Me) were prepared by known method.[8]

Preparation of compound (IV, R = *p*-Br)

0.001 Mol of compound (IV, R = H) was dissolved in 10 mL of acetic acid and to it was added bromine solution in acetic acid (0.001 mol). Compound (IV, R = *p*-Br) was slowly separated out as a yellow solid which was recrystallised from acetic acid (yield *ca.* 60%, m.p. 177.78°C).

Preparation of compound (V)

Method (a): 0.001 Mol of compound (IV, R = H) was dissolved in 10 mL of acetic acid and to it was added bromine solution in acetic acid (2 mL) in portion in sunlight. The dark red colour of bromine was discharged and a yellow crystalline solid was separated immediately (yield *ca.* 45%, m.p. 151°C).

Method (b): 0.001 Mol of compound (IV, R= H) was dissolved in 10 mL of acetic acid and then 100 mg of sodium acetate was added to it. The rection mixture was then treated with 0.82 mL of bromine solution in acetic acid drop by drop with shaking. The contents were left overnight when a yellow crystalline compound (V) was obtained (yield *ca.* 60%, m.p. 150–151°C).

Preparation of compound (VII)

250 Mg of compound (IV, R = H) was dissolved in 10 mL of acetic acid and the solution thus obtained was treated with excess of bromine solution in acetic acid (3 mL) in portion till the evolution of gas ceased. A yellow crystalline solid was separated which was filtered and the filtrate was further treated with 2 mL of bromine solution. A colourless crystalline solid was separated which was recrystallised from acetic acid (yield *ca.* 50%, m.p. 122–3°C).

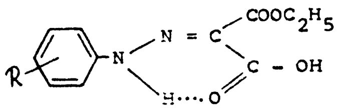
Preparation of compound (VIII)

3 mL of bromine solution in acetic acid was added to a soution of compound (IV, R = *o*-NO_2, *p*-NO_2, *o*-OMe and *p*-Me) (0.001 mol) in acetic acid (10 mL). The contents were left overnight and water was added. A yellow solid was separated out which was recrystallised from acetic acid.

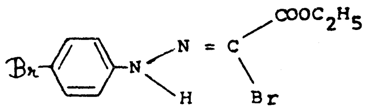
Purity of the product was ascertained by TLC examination.

RESULTS AND DISCUSSION

When ethyl hydrogen mesoxalate phenylhydrazone (IV) (R = H) was dissolved in acetic acid and treated with bromine in acetic acid in sunlight, the colour of bromine was discharged and immediate separation of a yellow crystalline compound took place. The compound proved to be dibrominated product (V).



(IV)

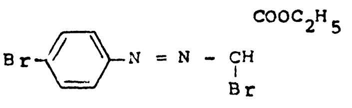


(V)

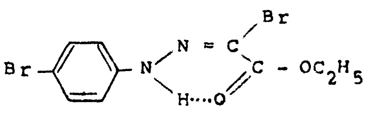
Elemental analysis of yellow crystalline compound corresponds to molecular formula $C_{10}N_2H_{10}O_2Br_2$. In IR spectra,[9] dibromo compound displays a medium band in the region 3240 cm^{-1} which may be assigne to ν(N—H) vibration.[9] A very sharp band at 1705 cm^{-1} occurs due to ν(>C═O) of ester group while a medium band at 1600 cm^{-1} may be assigned to ν(N═C)[9].

The ^1H NMR spectrum of dibromo compound (V) is also consistent with this structural assignment.[10, 11] The appearance of a multiplet between δ 7–7.4 shows the presence of four aromatic protons. A singlet in the region δ 8.3 corresponds to phenyl amino proton of hydrazono group (—NH—N═C<). The signals due to ester methylene and ester methyl protons are observed in the region δ 4.21–4.45 and δ 1.29–1.43 as a quartet and triplet respectively.

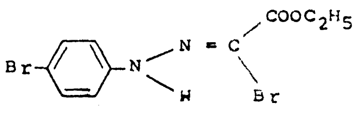
The ^{13}C NMR spectrum[10, 11] of dibromo compound showed resonances at δ 140, 132, 115, 110, 62 and 12. Resonances at δ 62 and δ 12 are assigned to ester methylene and methyl carbon respectively. The remaining four signals could be assigned to aromatic carbons. The imino carbon and ester carbonyl carbon resonances were not observed because they buried with the aromatic carbon. The absence of any signal in the sp^3 region which could be assigned to the methine carbon expected of the azo form (VI) confirms the hydrazono structure (V) for dibromo compound.



(VI)



E - form

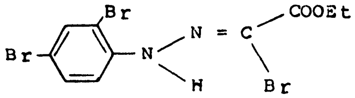


Z - form

(VI)

The dibromo product (V) could exist in two geometrical isomers (E- and Z-). Considering the difference in the environment of methyl and methylene corbons of ester part (as one is the part of chelated ester and the other free ester), we expected two resonances in ^{13}C NMR spectrum for both methyl and methylene carbon. The appearance of only one signal for each carbon suggests that the dibromo product (V) exists in only one isomer. The dibromo product (V) seems to be Z-isomer. In ^{1}H NMR, when intra-molecular H-bonding occurs in such type of compounds, the NH proton suffers a characteristic deshieldinhg[10, 11] and is observed at around δ 13.0. In present case, the NH signal is observed at δ 8.0 which clearly indicates the absence of any type of H-bonding. Similarly in IR spectra, when intra-molecular H-bonding occurs in such type of compounds, the N—H stretching frequency vibration suffers a characteristic red shift[9] and is observed at around 3040 cm^{-1} In present case, the higher shift in N—H (observed at 3240 cm^{-1}) frequency can again be attributed to absence of intramolecular H-bonding. Thuis, on the basis of these evidences, the dibromo product (V) can be deduced to exist in Z-form.

However, on addition of further amount of bromine in acetic acid, the yellow compound dissolved and the solution on standing overnight gave almost colourless needles having melting point 122–3°C. This was characterised as the tribrominated product (VIII) from its IR, ^{1}H NMR, ^{13}C NMR and mass spectral examination.



(VII)

When the reaction was carried out in the presence of sodium acetate the main product was (V) and the mother liquor gave a mixture (V) and (VII). The reaction of half ester (IV, R = *p*-bromo) with excess bromine resulted in (V) as the main product and the mother liquor deposited some tribrominated product (VII).

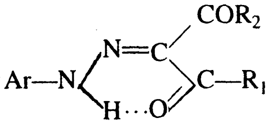
The colourless needles (m.p. 122–3°C), on the basis of elemental analysis and molecular weight determination (M^+ 429) correspond to molecular formula $C_{10}N_2O_2H_9Br_3$. In IR spectrum, the N—H stretching vibration was observed at 3280 cm^{-1} as a medium band.[9] The two strong bands in the region 1722 cm^{-1} and 1587 cm^{-1} are assignable to ν(>C=O) and ν(N=C) frequency vibrations respectively.[9] Thus it may be concluded that the tribromo product (VII) exists in Z-form.

The ^{13}C NMR spectrum of the tribromo compound showed resonances at δ 159, 138, 134, 117, 114, 112, 108, 63 and 13.0. Out of the five low intensity peaks at δ 159, 138, 114, 112 and 108, the one at δ 159 is obviously assignable to the ester carbonyl. Considering the nature of the substituents the resonances at δ 139 and δ 114 can safely be assigned to ipso carbons.[10, 11]

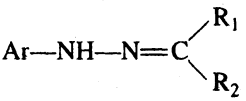
We have assigned the resonance at δ 108 of low intensity to imino carbon (—N=C<). That it is a quatenary carbon resonance and not of the other ring carbons, is shown by SFORD (single frequency off resonance decoupling where upon this signal appeared as a singlet) confirming the hydrazone structure (VII) for this compound.[10, 11]

Our assignment of the resonance at δ 108 to the imino carbon atom may not appear very much convincing in the light of previous reports for such carbons in phenylhydrazones of simple aldehydes and ketones in which case the resonance for imino carbon has been observed in the region (δ 145–149) but is well explained considering the difference in the nature of the groups attached to this carbon and the consequence thereof, on the geometry and electronic charge distribution in the molecule. In simple hydrazones the imino carbon atom carries alkyl groups (+ I effect) whereas in the present case the electron withdrawing carbethoxy group and Br (–I effect) are linked to it.

On the basis of X-ray analysis of a series of hydrazones of both types, those which contain a terminal carbonyl group (set A) and those which don't, contain an alkoxy group (set B), Vickery *et al.*[12] have concluded that the ring $—NH—N{=}C<$ fragment of all the hydrazones is almost planar and also that $—N{=}C—$ bond length in set B is less than bond length of $N{=}C$ in set A *i.e.* $N{=}C$ bond length is smaller in the case of phenylhydrazones of simple aldehydes and ketones.



(Set A)



$$Ar—NH—N{=}C\begin{matrix}R_1\\R_2\end{matrix}$$

(Set B)

(where R_1, R_2 = Alkyl or H).

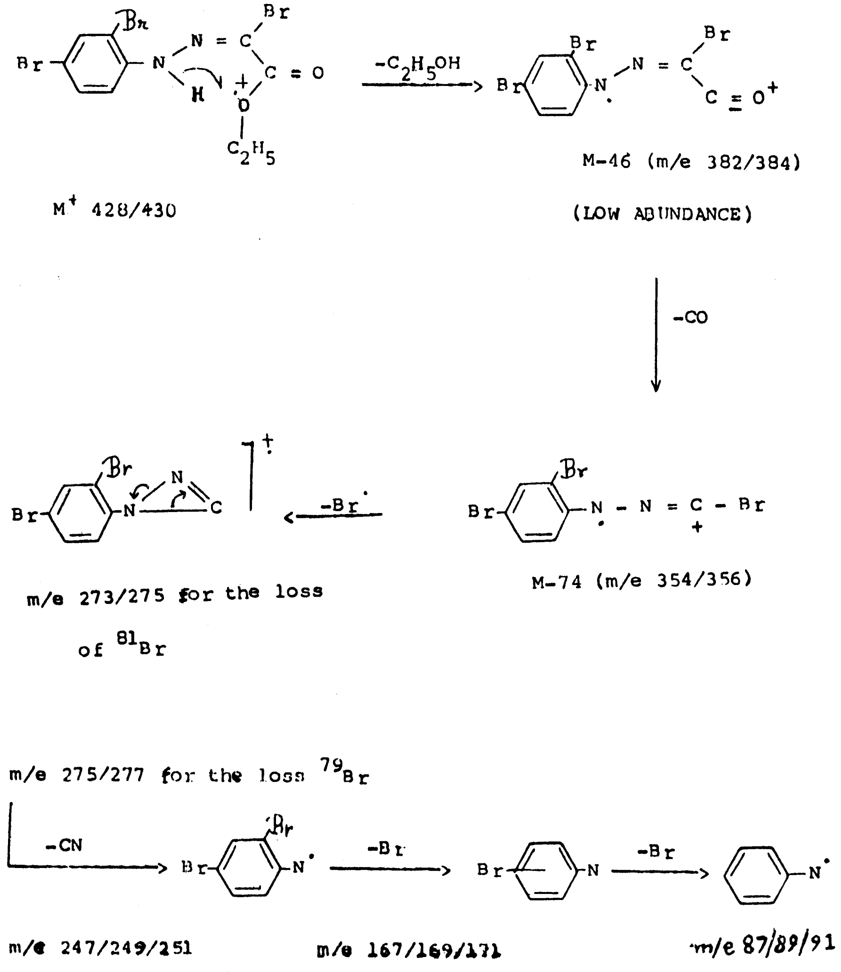
In the light of the generally accepted concept that the shorter the bond, the greater the extent of delocalisation[10, 11] and hence deshielding the imino carbon of set A (with terminal carbonyl groups, as in the present case) will be expected to be shielded compared to set B, with no carbonyl groups. This is what we are observing here.

Resonances at δ 63 are assigned to the ester methylene carbon and those at δ 13 to the ester methyl carbon in analogy with the literature value.[10, 11]

The ^{1}H NMR spectrum of compound (VII) is also consistent with the structural assignment.[10, 11] Thus a low field N—H resonance at δ 10.93 (1H, S), ester methylene and methyl signals at δ 5.18-5.8 (2H, q) and δ 1.56–1.67 (3H, t) and multiplets in the region δ 9-9.3 (hidden coupling δ 7.5-6.43) (3H, m) are the characteristics of aromatic protons.

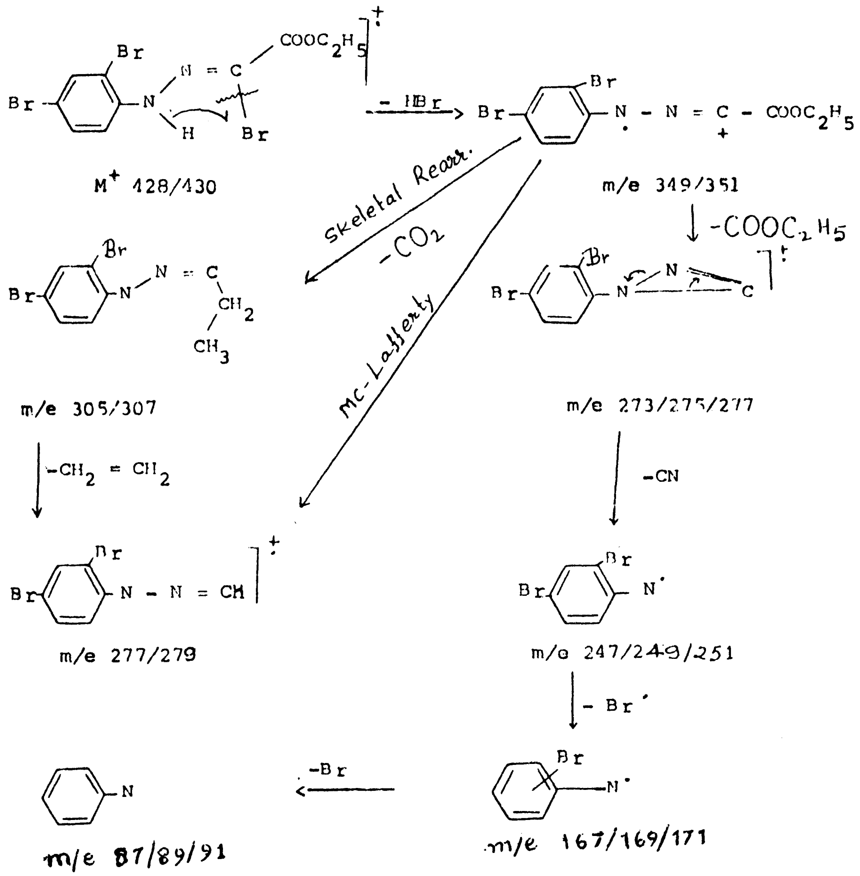
The mass spectrum of the compound (VII) shows excellent evidence[13] for three bromine atoms with peaks at 426, 428, 430 and 432 in the required intensity 1 : 3 : 3 : 1. The molecular ion M^+ at 430 was the base peak. The molecular ions 428 and 430 are found to have the highest intensity (R.I. 991 at 1000 and Σ % 23.16 and 23.37 respectively) amongst all the ions. The greater intensity of M^+ observed in this case must therefore depend upon its stability *i.e.*, the rate of its decomposition into daughter ions. Since bromine is essentially an electron withdrawing group, it is expected to impede the process of fragmentation by cleavage of N—N bond. The large size of bromine atom as well as the increased C—Br distance, however, reduce considerably the mesomeric effect of bromine and hence its decomposition into daughter ions. Thus, reactions governed by higher appearance potential largely determine the intensity of M^+ in this case.

Significant peaks at (M-46) and (M-74) are also observed in this case. These arise by effective charge localisation at alkyl oxygen followed by H-scrambling from N—H and subsequent α-cleavage (Scheme-1).

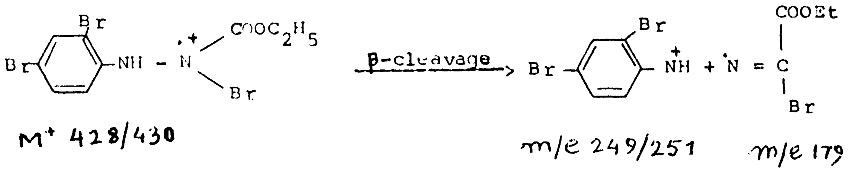


Scheme-1

Alternatively the peaks at m/e 273/275/277 may also form according to scheme-2.

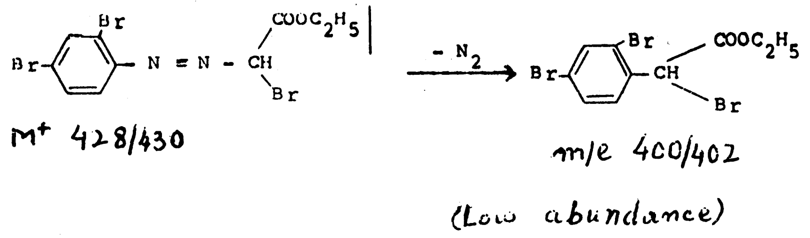


Scheme-2



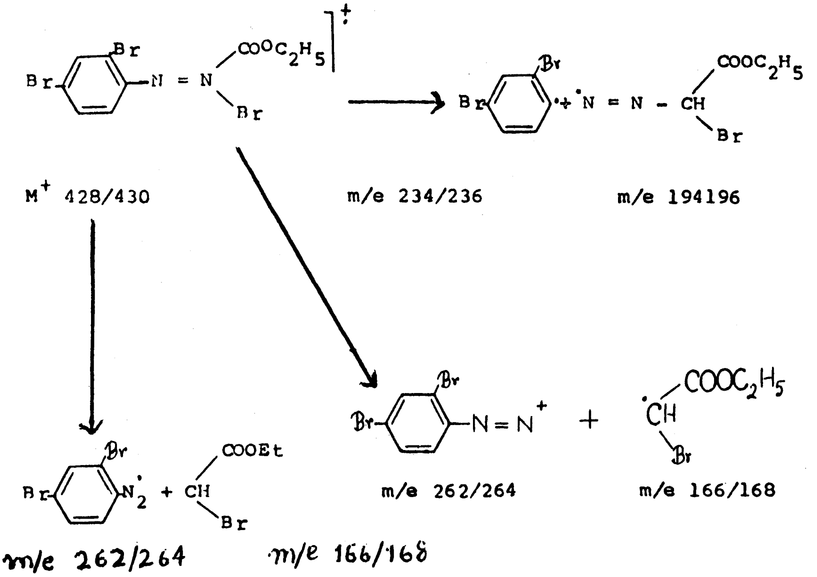
Fragmentation of hydrazone group depends upon effective charge localisation at the imino nitrogen atom.

Tribromo product (VII) shows $(M-28)^+$ peak of very small intensity probably due to loss of neutral nitrogen (Scheme-3) which is a common feature of this class of azo compounds.[14] The ion $(M-28)^+$ may also form by loss of neutral $CH_2{=}CH_2$ fragmentation of ester function.



Scheme-3

Tribromo compound also gives the ions by cleavage of C—N bond on either side of the azo linkage —N=N— (Scheme-4).



Scheme-4

Although the intensities of these ions are quite low, the fragmentation mode (Schemes-3 and 4) shows that the tribromo compound may exist in the azo form. It has been found that substituted benzaldehyde phenylhydrazones undergo thermal rearrangement to the azo form[15] and then suffer fragmentation to give ions at m/e 105 for Ph N_2^+ and 91 for Ph CH_2^+ by cleavage of C—N bond on either side of the azo linkage —N=N—. This rearrangement is a low energy process and can occur at much lower energy. In the present case, the tribromo derivative may undergo similar thermal rearrangement (since the intensities of ions are quite low) to some extent and produce fragments characteristic of azo compounds.

Bromination of half ester (IV, R = H) further revealed that with one mole of bromine, nuclear bromination takes place (as shown below).

$$\text{IV (R = H)} \xrightarrow{\text{1 mole Br}_2} \text{IV (R} = p\text{-bromo)}$$

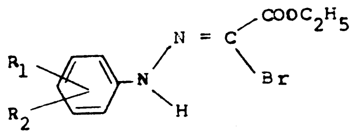
The identity of *p*-bromo half ester IV (R = *p*-bromo), having m.p. 177–8°C, was established by comparing it with an authentic sample of ethyl hydrogen mesooxalate-*p*-bromophenylhydrazones (IV, R = *p*-bromo) prepared[8] by the action of perchloric-formic acid on diethyl mesoxalate-*p*-bromophenylhydrazone. The m.p. of the mixture of these two *p*-bromo compounds does not depress.

With two moles of Br_2 or treatment of *p*-bromo half ester (IV, R = *p*-Br) with one mole of bromine gives the dibromo derivative (V).

$$\text{IV (R} = p\text{-Br)} \xrightarrow[\text{Br}_2]{\text{1 mole of}} \text{(V)} \xleftarrow[\text{Br}_2]{\text{2 mole of}} \text{IV (R = H)}$$

Finally, with excess of bromine, tribrominated product (VII) is formed. Thus, it may be concluded that nuclear bromination first takes place followed by displacement of —COOH group and then again nuclear bromination.

Ethyl hydrogen mesoxalate *p*-nitrophenylhydrazone (IV, R = *p*-NO_2) however resisted bromination in acetic acid, since the half ester crystallised readily even from hot solution but in warm acetic anhydride undergoes bromination and the compound was found to be α-bromo glyoxalate *p*-nitrophenylhydrazone (VIII, R_1 = *p*-NO_2, R_2 = H).



(VIII)

Similarly the corresponding *o*-nitro half ester (IV, R = *o*-nitro) also resisted bromination in nucleus and afforded ethyl α-bromo glyoxalate-*o*-nitrophenylhydrazone (VIII, R_1 = *o*-nitro, R_2 = H).

Thus it seems that electron withdrawing groups in aromatic nucleus deactivated the ring to such an extent that bromination in the nucleus did not take place even with excess of bromine in the presence of sunlight and on increasing the temperature. On the other hand, electron releasing groups in the aromatic nucleus activated the ring and nuclear bromination was observed with excess of bromine in sunlight *e.g.* *o*-OMe derivative of half ester (IV, R = *o*-OMe) gave ethyl α-bromo-2-*o*-methoxy-4-bromophenylhydrazone (VIII, R_1 = *o*-OMe, R_2 = *p*-Br) and *p*-methyl derivative (IV, R = *p*-Me) likewise gave (VIII, R_1 = *o*-Br, R_2 = *p*-Me).

TABLE-1
PHYSICAL CONSTANTS AND ANYALYTICAL DATA OF COMPOUND (VIII)

S. No.	Name of compound (Colour)	m.p. (°C)	% analysis Found (Calcd.)			
			N	C	H	Br
1.	$R_1 = p\text{-}NO_2, R_2 = H$ (Pale yellow)	202	13.57 (13.29)	37.02 (37.97)	3.93 (3.16)	26.01 (25.31)
2.	$R_1 = o\text{-}NO_2, R_2 = H$ (Yellow)	136	14.05 (13.29)	38.83 (37.97)	2.81 (3.16)	24.73 (25.31)
3.	$R_1 = o\text{-}OMe, R_2 = p\text{-}Br$ (Pale yellow)	125	7.85 (7.36)	35.35 (34.73)	3.87 (3.15)	42.79 (42.10)
4.	$R_1 = o\text{-}Br, R_2 = p\text{-}Me$ (Pale yellow)	130	8.61 (7.69)	37.73 (36.26)	2.73 (3.29)	43.13 (43.95)

The identity of the compound (VIII) was established on the basis of elemental analysis (Table-1) and IR spectral studies which gives only one band at around 1710 cm^{-1} for carbonyl group.

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