The Preparation of Iminosulfonic Acid Derivatives by Means of Sulfinamides and *N*-Bromosuccinimide

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The preparation of *N*-alkyl and *N*-aryliminosulfonic acid derivatives by the reaction of sulfinamides with bromine or *N*-bromosuccinimide in the presence of amines or sodium *p*-nitrophenolate has been attempted on the assumption that the iminosulfonic acid derivatives might be useful as intermediates in the field of synthetic chemistry.

In this connection, Levchenko and his coworkers[1] have recently reported that *N*-sulfonyl, *N*-ethoxycarbonyl or *N*-acetyl iminosulfonyl chlorides may be prepared by the reaction of arylsulfinyl chlorides with sodium *N*-chlorosulfonamides, sodium ethyl *N*-chlorocarbamate or sodium *N*-chloroacetamide. The amides and esters of iminosulfonic acid are synthesized from the chlorides, and amines and sodium phenolate respectively:[2]

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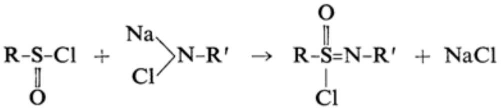
1) E. S. Levchenko, N. Ya. Derkach and A. V. Kirsanov, *Zhur. Obscheĭ. Khim.*, **30**, 1971 (1960); *Chem. Abstr.*, **55**, 7335^{g} (1961); *Zhur. Obscheĭ. Khim.*, **31**, 1971 (1961); *Chem. Abstr.*, **55**, 27175^{g} (1961); E. S. Levchenko, E. S. Kozlov and A. V. Kirsanov, *Zhur. Obscheĭ. Khim.*, **31**, 2381 (1961); *Chem. Abstr.*, **56**, 4653^{h} (1962); *Zhur. Obscheĭ. Khim.*, **32**, 2585 (1962); *Chem. Abstr.*, **58**, 8947^{c} (1963).

2) E. S. Levchenko, N. Ya. Derkach and A. V. Kirsanov, *Zhur. Obscheĭ. Khim.*, **32**, 1208 (1962); *Chem. Abstr.*, **58**, 1388^{g} (1963); E. S. Levchenko, E. S. Kozlov and A. V. Kirsanov, *Zhur. Obscheĭ. Khim.*, **32**, 882 (1962); *Chem. Abstr.*, **58**, 2395^{f} (1963); *Zhur. Obscheĭ. Khim.*, **33**, 565 (1963); *Chem. Abstr.*, **59**, 2701^{f} (1963).



$$\mathrm{R{-}\underset{\underset{O}{\|}}{S}{-}Cl} + \begin{matrix}\mathrm{Na}\\ \mathrm{Cl}\end{matrix}\!>\!\mathrm{N{-}R'} \rightarrow \mathrm{R{-}\overset{\overset{O}{\|}}{\underset{\underset{Cl}{|}}{S}}{=}N{-}R'} + \mathrm{NaCl}$$

R = aryl

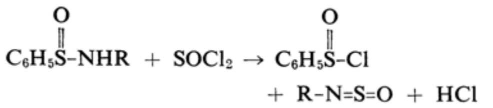
R′ = arylsulfonyl, ethoxycarbonyl or acetyl

However, the method is not applicable to the synthesis of *N*-alkyl or *N*-aryliminosulfonic acid derivatives, because the sodium *N*-chloroalkyl or aryl amides are difficult to handle in the isolated state.

Iminochlorides are generally obtained by the reaction of carboxylic acid amides with phosgene, thionyl chloride or phosphorus pentachloride.3) However, sulfonamides do not give the corresponding iminosulfonyl chlorides4) when treated with the abovementioned chlorinating reagents except in the case of diarylsulfonylimides5) and *N*-dichlorophosphorylarylsulfonamides.4a)

In the present experiment, the preparation of benzene-*N*-phenyliminosulfinyl chloride from benzenesulfinanilide (Ia) and thionyl chloride was attempted first. When a benzene solution of Ia and excess thionyl chloride was refluxed for half an hour, a 87% yield of be benzenesulfinyl chloride and a 88% yield of *N*-sulfinylaniline were obtained instead of the expected iminosulfinyl chloride. *N*-Cyclohexylbenzenesulfinamide (Ib) reacted with thionyl chloride to yield 11% of benzenesulfinyl chloride and 13% of *N*-sulfinylcyclohexylamine, along with a large amount of a dark-colored tarry product.

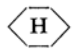
Similarly, the reaction of Ia with phosgene gave a 55% yield of benzenesulfinyl chloride and a 42% yield of phenyl isocyanate.

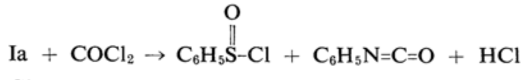


$$\mathrm{C_6H_5\overset{\overset{O}{\|}}{S}{-}NHR} + \mathrm{SOCl_2} \rightarrow \mathrm{C_6H_5\overset{\overset{O}{\|}}{S}{-}Cl} + \mathrm{R{-}N{=}S{=}O} + \mathrm{HCl}$$

(Ia) $R = C_6H_5$

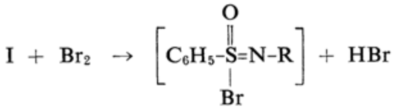
(Ib) R =





$$\mathrm{Ia} + \mathrm{COCl_2} \rightarrow \mathrm{C_6H_5\overset{\overset{O}{\|}}{S}{-}Cl} + \mathrm{C_6H_5N{=}C{=}O} + \mathrm{HCl}$$

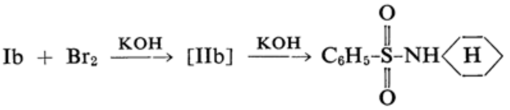
Since the preparation of iminosulfonyl halide or iminosulfinyl halide by a method similar to those used for iminochloride had proved unsuccessful, it was thought advisable to investigate the method of preparing the iminosulfonyl bromide by the oxidation of sulfinamides with bromine, a method shown in the following equation:



$$\mathrm{I} + \mathrm{Br_2} \rightarrow \left[\mathrm{C_6H_5{-}\overset{\overset{O}{\|}}{\underset{\underset{Br}{|}}{S}}{=}N{-}R}\right] + \mathrm{HBr}$$

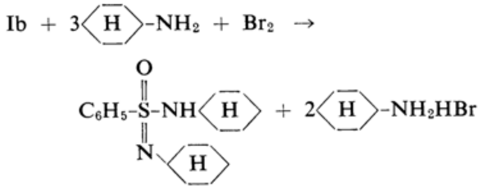
(II)

The expected product, benzene-*N*-cyclohexyliminosulfonyl bromide (IIb), could not be isolated by the addition of bromine to a suspension of Ib in carbon tetrachloride, but cyclohexylamine hydrobromide was obtained in a good yield. It is known that sulfinamides are unstable towards acid;6) therefore, it seemed reasonable to assume that the hydrogen bromide initially produced rapidly react with Ib, thus giving cyclohexylamine hydrobromide. On the other hand, when bromine was added drop-by-drop to a solution of Ib and potassium hydroxide in 50% aqueous ethanol, *N*-cyclohexylbenzenesulfonamide, the oxidized product of Ib, was obtained in a 60% yield. This may be produced by the hydrolysis of the IIb initially formed.



$$\mathrm{Ib} + \mathrm{Br_2} \xrightarrow{\mathrm{KOH}} [\mathrm{IIb}] \xrightarrow{\mathrm{KOH}} \mathrm{C_6H_5{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}{-}NH}\langle\mathrm{H}\rangle$$

It is to be expected that if the above reaction is carried out in the presence of primary or secondary amine instead of potassium hydroxide, IIb will rapidly react with the amine to yield iminosulfonamide. Indeed, when the reaction of Ib with bromine in carbon tetrachloride was attempted at 0°C in the presence of three times as many moles of cyclohexylamine, *N*-cyclohexylbenzene-*N*-cyclohexyliminosulfonamide (III) was obtained in a 32% yield, along with cyclohexylamine hydrobromide. The III was identified by elemental analyses and by means of its infrared spectrum, which has the characteristic bonds of the nitrogen hydrogen bond (3250 $\mathrm{cm^{-1}}$) and of the iminosulfonyl group (1272 $\mathrm{cm^{-1}}$, 1255 $\mathrm{cm^{-1}}$ and 1135 $\mathrm{cm^{-1}}$).7)



$$\mathrm{Ib} + 3\langle\mathrm{H}\rangle\mathrm{{-}NH_2} + \mathrm{Br_2} \rightarrow \mathrm{C_6H_5{-}\overset{\overset{O}{\|}}{\underset{\underset{N\langle H\rangle}{\|}}{S}}{-}NH}\langle\mathrm{H}\rangle + 2\langle\mathrm{H}\rangle\mathrm{{-}NH_2HBr}$$

(III)

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3) These reactions have been reported by many workers, for example, O. Wallach, *Ann.*, **184**, 1 (1877); J. v. Braun and W. Pinkernelle, *Ber.*, **67**, 1218 (1934).

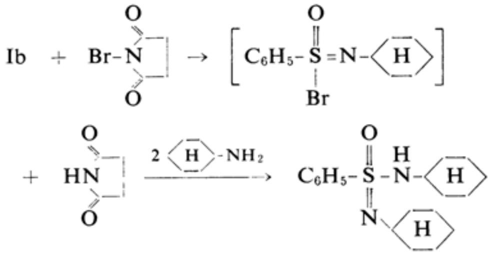
4) a) E. S. Levchenko and A. V. Kirsanov, *Zhur. Obschei. Khim.*, **30**, 1553 (1960); *Chem. Abstr.*, **55**, 3484g (1961). b) J. v. Braun and K. Waissbach, *Ber.*, **63B**, 2836 (1930).

5) E. S. Levchenko, N. Ya. Derkach and A. V. Kirsanov, *Zhur. Obschei. Khim.*, **32**, 1212 (1962); *Chem. Abstr.*, **58**, 4456h (1963).

6) D. Klamann, Chr. Sass and M. Zelenka, *Chem. Ber.*, **92**, 1910 (1959).

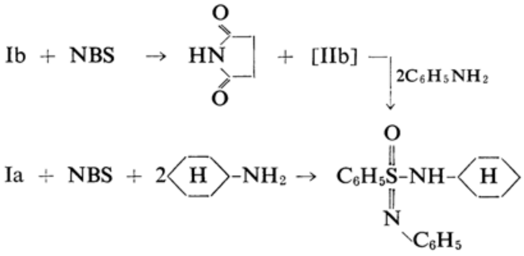
7) E. S. Levchenko, E. S. Kozlov, A. A. Kisilenko and A. V. Kirsanov, *Zhur. Obschei. Khim.*, **33**, 3065 (1963); *Chem. Abstr.*, **60**, 2451h (1964).

When *N*-bromosuccinimide (NBS) was used instead of bromine in the above experiment, III was obtained in a 69% yield, along with succinimide and cyclohexylamine hydrobromide. This reaction is considered to proceed through an initial formation of IIb and succinimide by a reaction of Ib with NBS similar to that of Ib with bromine. The IIb in turn reacts with cyclohexylamine to yield III.



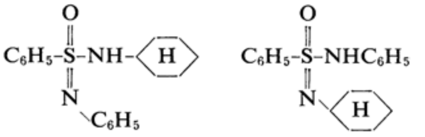
However, the treatment of Ib and NBS in the presence of aniline did not give *N*-cyclohexylbenzene-*N*-phenyliminosulfonamide (IV), presumably because of the facile reaction of NBS with aniline. Instead, IV was obtained in a 73% yield, along with succinimide and aniline hydrobromide, when NBS and Ib were stirred at 0°C for forty minutes in carbon tetrachloride and then two times as many moles of aniline were added to the reaction mixture. On the other hand, the yield of IV decreased to 39% when Ib and NBS were treated for three hours before the addition of aniline. Thus, it seemed reasonable to assume that the intermediate, *N*-cyclohexyliminobenzenesulfonyl bromide (IIb), may be unstable even at 0°C.

On the other hand, IV was also obtained in a 84% yield by the reaction of Ia with NBS in the presence of cyclohexylamine.



(IV)

There may be two tautomeric forms of IVa and IVb for IV. The phenyl group has a greater tendency to attract electrons and IV should, therefore, tend to exist as formula IVa:



(IVa) (IVb)

The results of the reactions of Ia or Ib and NBS in the presence of various amines are summarized in Table I.

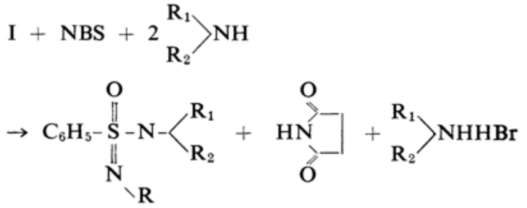
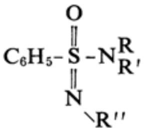
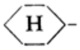
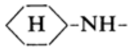
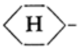
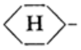
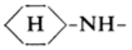


TABLE I. PREPARATION OF BENZENEIMINOSULFONAMIDES



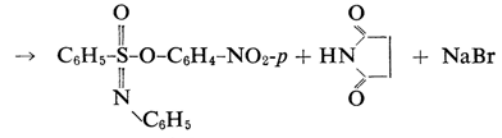
$C_6H_5-\underset{\underset{\displaystyle N\diagdown R''}{\|}}{\overset{\overset{\displaystyle O}{\|}}{S}}-N\genfrac{}{}{0pt}{}{R}{R'}$

$\genfrac{}{}{0pt}{}{R}{R'}\rangle N-$	R''	Yield %	M. p. °C	Formula	C, % Found	C, % Calcd.	H, % Found	H, % Calcd.	N, % Found.	N, % Calcd.
n-$C_6H_{13}NH-$		53	52—54[a, b]	$C_{18}H_{30}N_2OS$	66.66	67.05	9.61	9.38	8.93	8.68
		69	100—101[b]	$C_{18}H_{28}N_2OS$	67.39	67.47	8.81	8.81	8.50	8.74
		55	75—76[b]	$C_{17}H_{26}N_2OS$	66.71	66.64	8.75	8.55	9.21	9.44
n-C_4H_9NH-	C_6H_5	81	52—53[b]	$C_{16}H_{20}N_2OS$	66.71	66.64	7.22	6.99	9.87	9.72
n-$C_6H_{13}NH-$	C_6H_5	94	49—50[b]	$C_{18}H_{24}N_2OS$	68.32	68.33	7.83	7.65	9.14	8.85
	C_6H_5	84	149—150[c]	$C_{18}H_{22}N_2OS$	68.63	68.77	7.16	7.05	8.92	8.91
	C_6H_5	95	115—116[d]	$C_{17}H_{20}N_2OS$	67.88	67.98	6.53	6.71	9.54	9.33
	C_6H_5	95	107—108[d]	$C_{16}H_{18}N_2O_2S$	63.78	63.56	6.22	6.00	9.34	9.27

a) B. p. 168—172°C/0.13 mmHg. b) Recrystallized from petroleum ether. c) Recrystallized from alcohol. d) Recrystallized from ligroin.

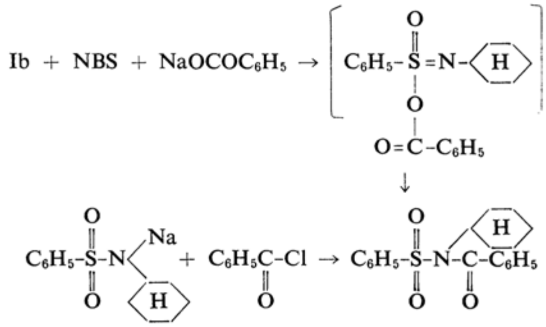
Next, the preparation of the *p*-nitrophenyl ester of iminosulfonic acid by the reaction of Ia with NBS and sodium *p*-nitrophenolate was attempted. When the suspension of Ia, NBS and sodium *n*-nitrophenolate in carbon tetrachloride was stirred at 0°C for about 10 hr., *p*-nitrophenyl benzene-*N*-phenyliminosulfonate (V) was obtained in a 48% yield. The infrared spectrum of V contains characteristic bands assignable to a nitro group (1349 cm^{-1}) and a iminosulfonyl group (1250 cm^{-1} and 1190 cm^{-1})[7].

Ia + NBS + $NaOC_6H_4NO_2$-*p*



(V)

When the reaction of Ib, NBS and sodium benzoate was carried out, colorless needles were obtained in a high yield, along with succinimide and sodium bromide. These needles were identified as *N*-benzoyl-*N*-cyclohexylbenzenesulfonamide (VI) by elementary analyses and by a comparison of them with an authentic sample prepared by the reaction of sodium *N*-cyclohexylbenzenesulfonamide with benzoyl chloride. This finding suggests that an initially-formed IIb reacted with sodium benzoate to give the intermediate, iminosulfonic benzoic anhydride, which in turn rearranged to yield VI.[8]



(VI)

Experimental

Benzenesulfinanilide (Ia) and *N*-Cyclohexylbenzenesulfinamide (Ib).—These compounds were prepared, according to the method of Klaman et al.,[6] from phenylmagnesium bromide and the corresponding *N*-sulfinylamine.

The Reaction of Ia with Thionyl Chloride.—To a suspension of Ia (2.17 g., 0.01 mol.) in anhydrous benzene, excess thionyl chloride (3.0 g., 0.025 mol.) was added, the mixture was then refluxed for half an hour. After the solvent and the excess thionyl chloride had been removed, benzenesulfinyl chloride (1.42 g., 88%; b. p. 90—93°C/4 mmHg) and *N*-sulfinylaniline (1.20 g., 87%; b. p. 96—98°C/18 mmHg) were obtained.

When Ib (2.23 g., 0.01 mol.) was used in place of Ia in the above experiment, benzenesulfinyl chloride (0.17 g., 11%) and *N*-sulfinylcyclohexylamine (0.19 g., 13%; b. p. 55°C/4 mmHg) were obtained, along with a large amount of a tarry product.

The Reaction of Ia with Phosgene.—To a suspension of Ia (2.17 g., 0.01 mol.) in anhydrous benzene, 30% phosgene in toluene (3.3 g., 0.01 mol.) was added drop-by-drop under cooling; the mixture was then refluxed for half an hour. A 55% yield of benzenesulfinyl chloride (0.88 g.) and a 42% yield of phenyl isocyanate (0.50 g.) were obtained by fractional distillation.

***N*-Cyclohexylbenzenesulfonamide.**—To a solution of Ib (2.23 g., 0.01 mol.) and potassium hydroxide (1.34 g., 0.034 mol.) in 50% aqueous ethanol, bromine (1.60 g., 0.01 mol.) was added drop-by-drop under cooling. The mixture was evaporated to dryness under reduced pressure, and the residue was extracted with hot ligroin to give colorless needles (1.43 g. (60%); m. p. 89—90°C (undepressed by admixture with an authentic sample)).

***N*-Cyclohexylbenzene-*N*-cyclohexyliminosulfonamide (III).**—a) To a mixture of Ib (2.23 g., 0.01 mol.) and cyclohexylamine (3.07 g., 0.031 mol.) in 30 ml. of carbon tetrachloride, bromine (1.60 g., 0.01 mol.) was added drop-by-drop under cooling; cyclohexylamine hydrobromide and succinimide were thus precipitated. The filtrate was evaporated, and the dark-colored residue was chromatographed on alumina. III was eluted with ether and recrystallized from petroleum ether (1.02 g. (32%); m. p. 100—101°C).

Found: C, 67.39; H, 8.81; N, 8.50; S, 10.18. Calcd. for $C_{18}H_{28}N_2OS$: C, 67.47; H, 8.81; N, 8.74; S, 9.99%.

b) A mixture of cyclohexylamine (3.07 g., 0.031 mol.), Ib (2.23 g., 0.01 mol.) and *N*-bromosuccinimide (NBS) (1.78 g., 0.01 mol.) in carbon tetrachloride was stirred for 3 hr. at 0°C and then for an additional 3 hrs. at room temperature. III was obtained from the filtrate in a 69% yield (2.20 g.; m. p. 100—101°C). Similarly, when *N*-bromophthalimide was used instead of NBS in the above experiment, III was obtained in a 50% yield.

***N*-Cyclohexylbenzene-*N*-phenyliminosulfonamide (IV).**—a) A mixture of Ia (2.17 g., 0.01 mol.) and NBS (1.78 g., 0.01 mol.) in carbon tetrachloride (30 ml.) was stirred for 40 min. at 0°C; then aniline (2.05 g., 0.022 mol.) was added, and the mixture was stirred for 3 more hr. The precipitate was collected and washed with water and weighed; 1.20 g., m. p. 140—143°C. The filtrate, after the solvent had been removed, gave an additional IV (1.10 g.); total yield, 2.30 g. (73%). The IV was recrystallized from ethanol (m. p. 149—150°C).

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[8] A similar rearrangement is observed in the case of the carboxylic imidic anhydride produced by the reaction of sodium carboxylate with imidoyl chloride; it yields diacylamides. O. Mumm, H. Hesse and H. Volquartz, *Ber.*, **48**, 388 (1915); F. Cramer and K. Baer, ibid., **93**, 1231 (1960).

Found: C, 68.63; H, 7.16; N, 8.92. Calcd. for $C_{18}H_{22}N_2OS$: C, 68.77; H, 7.05; N, 8.91%.

When a mixture of Ib and NBS in carbon tetrachloride was stirred for 3 hr. at 0°C before the addition of aniline as in the above experiment, the yield dropped to 1.22 g. (39%).

b) Similarly, when a mixture of Ib (2.17 g., 0.01 mol.), NBS (1.78 g., 0.01 mol.) and cyclohexylamine (3.07 g., 0.031 mol.) was stirred for 2 hr. at 0°C and then for an additional 3 hr. at room temperature, IV was obtained in a 84% yield (2.65 g.).

The other iminosulfonamides were prepared by the reaction of Ia or Ib, NBS and 2 mol. of the corresponding amines. The results are listed in Table I.

***p*-Nitrophenyl Benzene-*N*-phenyliminosulfonate (V).**—A mixture of Ia (2.23 g., 0.01 mol.), NBS (1.78 g., 0.01 mol.) and sodium *p*-nitrophenolate (1.78 g., 0.011 mol.) in 30 ml. of carbon tetrachloride was stirred for 10 hr. at 0°C. The filtrate, after the solvent had been removed, gave a dark-colored syrup. When a small portion of ethanol was added to the syrup, pale yellow V was crystallized out (1.70 g., 48%; m. p. 70—72°C). When it was recrystallized from ethanol, its m. p. was 72—73°C.

Found: C, 60.75; H, 3.91; N, 8.07. Calcd. for $C_{18}H_{14}N_2O_4S$: C, 61.01; H, 3.98; N, 7.91%.

***N*-Benzoyl-*N*-cyclohexylbenzenesulfonamide (VI).**—A mixture of Ib (2.23 g., 0.01 mol.), NBS (1.78 g., 0.01 mol.), and sodium benzoate (1.44 g., 0.01 mol.) in 30 ml. of carbon tetrachloride was stirred for 3 hrs. at 0°C and then for an additional 3 hr. at room temperature. The precipitate was collected and washed with water to give VI (2.44 g. (71%), m. p. 140—142°C). When it was then recrystallized from ethanol, its m. p. was 143—144°C. The infrared spectrum (KBr) showed strong absorptions at 1650 cm^{-1} (C=O of amide linkage) and at 1330 cm^{-1} and 1160 cm^{-1} (SO_2 linkage).

Found: C, 66.18; H, 6.13; N, 3.82; S, 9.40. Calcd. for $C_{19}H_{21}NO_3S$: C, 66.46; H, 6.16; N, 4.08; S, 9.32%.

When the same reaction was carried out in tetrahydrofuran, methylene chloride or ether, the yield of VI decreased to 58%, 17% or 5% respectively.

This compound VI can also be prepared by the reaction of sodium *N*-cyclohexylbenzenesulfonamide with benzoyl chloride.

Summary

It has been found that *N*-substituted benzenesulfinamides (I) react with thionyl chloride to give benzenesulfinyl chloride and the corresponding *N*-sulfinylamines, and that they are oxidized by treatment with bromine in an alkaline solution to give *N*-substituted sulfonamides.

When these benzenesulfinamides are treated with bromine or *N*-bromosuccinimide (NBS) in the presence of various primary or secondary amines, the corresponding benzeneiminosulfonamides are obtained in high yields. Similarly, the reaction of I, NBS and sodium *p*-nitrophenolate or sodium benzoate yields *p*-nitrophenyl benzeneiminosulfonate or *N*-benzoylbenzensulfonamide. These reactions are considered to proceed through the benzeneiminosulfonyl bromides formed by the oxidation of sulfinamides with bromine or NBS.

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