

Bromination of 3-(2-Aminophenyl)sydnone and Related Compounds

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Bromination of 3-(2-aminophenyl)sydnone **2** under a variety of conditions is reported. The products obtained are interrelated by a series of subsequent reactions. One major product is the bromoaryl compound **3**, the first example of bromination on the aryl rather than sydnone ring when the two are in competition. Surprisingly, bromoaminosydnone **9**, prepared from its nitro analogue, was not among the products obtained by direct bromination of **2**.

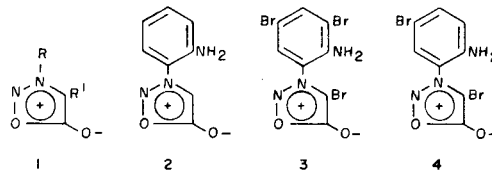
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Sydrones *cf.* **1**, the most widely studied members of the general class of mesoionic compounds [2], are unique, dipolar heteroaromatic species first prepared by Earl and Mackney, in 1935, by the cyclodehydration of *N*-nitrosoglycines [3]. They undergo facile electrophilic aromatic substitution on the sydnone ring and, in this regard, a number of methods (*inter alia* bromine/ethanol/sodium bicarbonate [4], bromine/potassium bromide [5], *N*-bromosuccinimide [5] and bromine/acetic acid/sodium acetate [6]) have been utilized for the preparation of 4-bromo-3-arylsydrones *cf.* **1** (R = Ar, R¹ = Br) from 3-arylsydrones *cf.* **1** (R = Ar, R¹ = H). The selectivity of bromination on the sydnone ring (and not the aryl ring) can be attributed to the activated nature of the sydnone ring [7] and its deactivating effect upon the attached aryl ring (the N-3 position bears a considerable fractional positive charge [8]).

It was of interest, both from mechanistic and synthetic standpoints, to probe the parameters controlling the site of electrophilic attack. We felt that by situating electron-donating groups on the aryl ring we would be able to control whether or not selective or concomitant sydnone/aryl ring substitution occurred. Accordingly, we recently investigated the bromination of a series of dimethylaryl-, methoxymethylaryl- and dimethoxyaryl sydnones [1]. Disappointingly, in no case was selective aryl ring bromination observed but selective sydnone ring bromination could be achieved for every example. However, concomitant aryl and sydnone ring bromination did occur for two of the three dimethoxyaryl sydnones studied and this encouraged us to extend the investigation to include other activated aryl sydnones. The present report deals with our findings regarding the bromination of 3-(2-aminophenyl)sydnone **2** and related compounds.

When the reaction was repeated, using an equimolar quantity of bromine, a mixture containing three major components and a trace amount of **3** was obtained. Using column chromatography one of the products could be cleanly separated, but the other two could not. The former

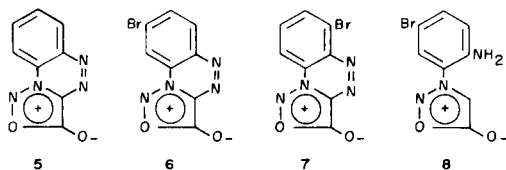
was assigned structure **4** on the basis of microanalysis and spectral data. An ir spectrum of the mixture of two components showed the presence of an amino group as well as typical sydnone C=O and C-H stretches. We suspected that one of the products was the starting material **2** (tlc and hplc evidence) and from the similar R_f of the other compound believed it to be a monobrominated aminophenyl sydnone. Some time ago we showed that **2** reacts with nitrous acid to give the sydnobenzotriazine **5** [10] and this suggested a means to separate and identify the product mixture. Accordingly, the mixture was treated with nitrous acid at 0°. Work-up and column chromatography gave **5** (36%) and a monobromosydnobenzotriazine postulated as **6** (13%) on the basis of microanalysis and spectral data.



Treatment of **2** with excess bromine in ethanol/water/sodium bicarbonate gave the tribromo compound **3**. Surprisingly, apart from in our recent study [1], no other 3-arylsydrones have been similarly brominated on the aryl ring, including the apparently analogous 3-(2- or 4-methoxyphenyl)sydrones (which brominate cleanly on the sydnone ring under these conditions [9]). The structural assignment for **3** was justified *via* microanalysis, the loss of the characteristic C-H stretching frequency (3149 cm⁻¹ in **2**) in the ir spectrum as well as the absence of the sydnone ring proton absorption (δ 6.63 in **2**) in the nmr spectrum. In the latter, the two aryl ring protons appeared as a double doublet ($J_{AB} = 3$ Hz, typical for *meta* coupling). The other possible *meta* dibromo structure (4,6-dibromo, relative to the sydnone ring) was rejected from the unlikelihood that the electron-donating amino group would direct bromines to positions *meta* to itself.

The nmr spectrum consisted of a double doublet at δ 8.15 (1H, $J_{AB} = 8$ Hz, $J_{AC} = 2$ Hz) and a multiplet at δ 8.45 (2H), consistent with structure **6** rather than **7**, the other reasonable alternative.

These data suggest that the bromination of **2** to form **8** occurs slowly enough for **8** to compete effectively with **2** for the electrophile. This may be a facet of initial *N*-bromination followed by rearrangement, an approach which might also explain the orientation of the bromination; the position *ortho* to the -NHBr being more sterically hindered than the *para* position.

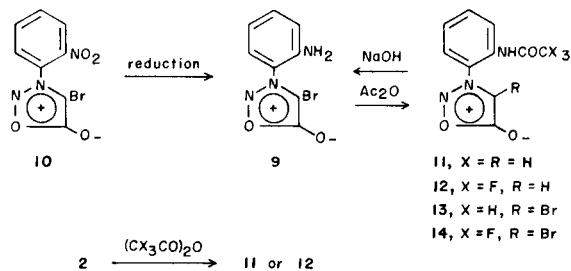


Interestingly, when the bromination of **2** was repeated using one equivalent of bromine in ethanol/acetic acid (in an attempt to "tie-up" the amino function and direct the incoming electrophile to the sydnone ring) the product mixture obtained contained a trace of **3**, **8** (24%), **4** (8%), **2** (12.5%) and small amounts of ring opened materials. Clearly, under weakly basic or acidic conditions, monobromination occurs preferentially on the aryl ring. It is noteworthy that under weakly acidic conditions the amounts of dibromo product **4** and starting material **2** are considerably reduced. This may indicate an interaction of the acid with the sydnone ring, thus increasing its steric volume and decreasing its propensity to react with the electrophile. There is some precedent for this, albeit under considerably more acidic conditions, in that certain 3-arylsydones (eg. 3-(4-tolyl)sydnone) nitrate on the aryl rather than the sydnone ring. In the present case, it is also possible that the position of bromination is affected by an association between the amino function and the sydnone ring; bromination of *meta* and *para* aminophenyl congeners should allow us to test the validity or otherwise of this hypothesis.

From our results we surmise that the reaction of **2** with bromine occurs sequentially to give **8**, **4** or **3**, depending on the amount of bromine provided. To explore this possibility we investigated the bromination of **8** with both one and two equivalents of bromine and the bromination of **4** with one equivalent of bromine. All were transformed cleanly, in good yield, to the appropriate product. Thus, **8** gave **4** with one equivalent and **3** with two equivalents of bromine whereas **3** was formed from **4** with one equivalent of bromine. These results support the premise of a sequential process as well as establishing the interrelationship of the different products.

The isolation of only one monobromo isomer (*i.e.* **8**) (5

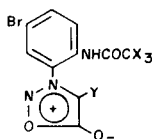
are possible) is intriguing, especially as one might have expected the 4-bromosydnone **9** to be a major product from one or other of these brominations. To the best of our knowledge, this is the first example of selective aryl ring monobromination in the sydnone series. To ascertain that **9** was indeed absent from these brominations we embarked upon its synthesis. Two routes seemed viable, *viz.* selective reduction of 4-bromo-3-(2-nitrophenyl)sydnone **10** [11] or acetyl or trifluoroacetyl protection of the amino function in **2** (to form **11** or **12**, respectively), bromination (to **13** or **14**, respectively) followed by deprotection to yield **9**.



Attempted reduction of **10** with hydrated sodium sulfide [12] or sodium sulfurated borohydride [13] led to complex mixtures of products which were not further pursued. With iron/acetic acid at 90° [14] the only isolable species was the fully reduced product **2**. Clearly none of these methods was viable for the selective reduction required. Recently the use of stannous chloride dihydrate in ethyl acetate (or ethanol) at 60° has been reported as a mild method for nitro group reduction in the presence of a variety of other functional groups [15]. Accordingly, 3-(2-nitrophenyl)sydnone (as a model compound) was reacted with stannous chloride under the standard conditions. After ten minutes, the starting material had been consumed (tlc evidence) and work-up provided the aminosydnone **2** in 44% yield. Reduction of **10** also occurred under the same conditions and, after 20 minutes, **9** was obtained as a stable, yellow crystalline solid in 67% yield. Comparison with the previously obtained bromination mixtures confirmed that, indeed, **9** was not a component thereof. Despite this success, we pursued the alternative synthesis (*viz.* **2** → **9**), mainly as a supplement to the armoury of synthetic methodologies available in these systems. Accordingly, **2** was acetylated and trifluoroacetylated in good yield using acetic- or trifluoroacetic anhydride. Work-up was simple in both cases and product identification (*i.e.* **11** and **12**) was straightforward.

Bromination with one equivalent of bromine proceeded smoothly for both and the 4-bromosydones **13** and **14** were isolated. As a model study, the parent trifluoroacetyl compound **12** was converted to **2** in 60% yield by treatment with aqueous sodium hydroxide (0.1M) for two days at room temperature. In contrast, under the same conditions, the bromo analogue **14** gave a complex mixture

containing only trace amounts of the required bromoaminosydnone **9** (*vide infra*). Presumably, competitive hydrolysis of the sydnone ring occurs. For this reason, hydrolysis of the presumably less labile acetamido group in **13** was not attempted. The bromoacetamido compound **13** was, however, isolated from the reaction of **9** with acetic anhydride, thus establishing their structural relationship. Compound **13** was also utilized in an attempt to unambiguously assign the orientation of the bromine atom on the aryl group of **4**. Unfortunately, **13** proved to be extremely inert to further bromination and we were unable to obtain **15** even under forcing conditions (150°, ethylene glycol, 16 hours). The trifluoromethyl analogue of **15** (*viz.* **16**) was prepared by bromination of the trifluoroacetyl compound **17**, derived from **8**, and by trifluoroacetylation of **4**. Similarly, acetamido compound **18** was readily available from **8**.



15, X = H, Y = Br **16**, X = F, Y = Br **17**, X = F, Y = H **18**, X = H, Y = H

While these data do not unambiguously prove the orientation of the aryl ring bromine atom, they do give further evidence of the close relationship between compounds **4** and **8**. Overall, we have shown that bromination of aryl sydnones can take place selectively on the aryl ring if a suitably activating substituent is situated thereupon; a significant result in terms of synthetic design in the sydnone series. We plan to extend these studies to examine the importance of the position of attachment of the amino group.

EXPERIMENTAL [16]

Attempted Monobromination of 3-(2-Aminophenyl)sydnone. A. Standard Conditions.

To a solution of **2** (1.5 g, 8.47 mmoles) in ethanol (100 ml) was added sodium bicarbonate (0.713 g, 10.36 mmoles) in water (60 ml). Bromine (1.356 g, 8.47 mmoles) in ethanol (50 ml) was added dropwise and stirring continued for 1 hour. The mixture was reduced to one fourth volume, extracted with methylene chloride and the extract dried (drierite). Clouding with petroleum ether gave on standing at 5°, 4-bromo-3-(2-amino-5-bromophenyl)sydnone **4**. Chromatography on silica gel with methylene chloride gave additional dibromo product which was combined with the above to give (0.719 g, 25%) as bright yellow crystals, mp 154-155°; ir: 3455, 3364, 3260 (N-H str), 1745, 1737 (sydnone C=O str) cm^{-1} ; nmr (deuteriochloroform/deuteriodimethylsulfoxide): δ 5.4 (s, 2H), 6.95 (d, 1H, J = 8 Hz), 7.45 (m, 2H).

Anal. Calcd. for $\text{C}_8\text{H}_7\text{Br}_2\text{N}_3\text{O}_2$: C, 28.65; H, 1.49; N, 12.53. Found: C, 28.64; H, 1.48; N, 12.48.

Chromatography failed to resolve two other components of the mixture (0.831 g) which were shown by the following method to be 3-(2-amino-5-bromophenyl)sydnone **8** (0.286 g, 13%), and the starting material **2** (0.545 g, 36%) (estimated yields).

Diazotization of Mixed Components from A.

An aliquot of the mixed components (0.270 g) from the previous reactions was diazotized by suspending the solid in a mixture of water (10 ml) and concentrated hydrochloric acid (3.85 ml) at 0°. A solution of sodium nitrite (1.95 g, 28.3 mmoles) in water (4 ml) was added dropwise and stirring continued for 1 hour at 0°. The mixture was neutralized with sodium bicarbonate and extracted with methylene chloride. The organic phase was dried (drierite), reduced in volume, and columned on silica gel in methylene chloride to give 8-bromosydn[4,3-c]benzo-1,2,4-triazine **6** (0.075 g, 0.28 mmole), mp 145-146° dec; ir: 3079 (aromatic C-H str), 1785, 1757 (sydnone C=O str) cm^{-1} ; nmr (deuteriochloroform/deuteriodimethylsulfoxide): δ 8.15 (dd, 1H, $J_{AB} = 8$ Hz, $J_{AC} = 2$ Hz), 8.45 (m, 2H).

Anal. Calcd. for $\text{C}_8\text{H}_5\text{BrN}_4\text{O}_2$: C, 35.95; H, 1.12; N, 20.97. Found: C, 36.32; H, 1.13; N, 20.62.

Further elution gave sydn[4,3-c]benzo-1,2,4-triazine **5** (146 mg, 0.776 mmole) identical (ir, tlc, mp) to an authentic sample.

Attempted Monobromination of 3-(2-Aminophenyl)sydnone. B. Acidic Conditions.

To a stirred solution of **2** (1.0 g, 5.65 mmoles) in ethanol (40 ml) and acetic acid (4.5 ml) was added bromine (0.0904 g, 5.65 mmoles) in ethanol (15 ml) dropwise. After 5 minutes the mixture was poured into water (100 ml), neutralized with sodium bicarbonate and extracted with methylene chloride. Evaporation *in vacuo* followed by repeated chromatography on silica gel using methylene chloride as eluant gave, first, 4-bromo-3-(2-amino-5-bromophenyl)sydnone **4** (0.152 g, 8%) followed by 3-(2-amino-5-bromophenyl)sydnone **8** (0.342 g, 24%), mp 173-174°; ir: 3451, 3353, 3254 (N-H str), 3120, 3140 (sydnone C-H str), 3105 (aromatic C-H str), 1750 (sydnone C=O str) cm^{-1} ; nmr (deuteriodimethylsulfoxide): δ 5.95 (s, 2H), 6.85 (d, 1H, J = 8 Hz), 7.40 (m, 3H).

Anal. Calcd. for $\text{C}_8\text{H}_6\text{BrN}_3\text{O}_2$: C, 37.52; H, 2.36; N, 16.41. Found: C, 37.37; H, 2.42; N, 16.23.

Further elution gave unreacted **2** (0.125 g, 13%).

4-Bromo-3-(2-aminophenyl)sydnone. 4.

To a solution of **8** (0.10 g, 0.39 mmole) in ethanol (3 ml) was added a solution of sodium bicarbonate (0.036 g, 0.43 mmole) in water (3 ml). Bromine (0.065 g, 0.41 mmole) in ethanol (3 ml) was added dropwise with stirring. After 75 minutes the mixture was poured into water (50 ml) and extracted with methylene chloride. The organic phase was dried (drierite) and evaporated to dryness *in vacuo*. Crystallization of the residue from methylene chloride/petroleum ether gave **4** (0.109 g, 83%) identical (tlc, ir, mp) to an authentic sample.

4-Bromo-3-(2-amino-3,5-dibromophenyl)sydnone 3. a) By Bromination of 3-(2-Aminophenyl)sydnone 2.

To a solution of **2** (0.55 g, 3.11 mmoles) in ethanol (35 ml) was added sodium bicarbonate (2.0 g, 24 mmoles) in water (25 ml). Bromine (2.5 g, 15.6 mmoles) in ethanol (25 ml) was added dropwise and stirring continued for 24 hours. The mixture was filtered, poured into water (15 ml) and reduced to dryness *in vacuo* at 35°. Several crystallizations from methylene chloride/petroleum ether gave insoluble inorganic powder which was removed by filtration. Final crystallization from methylene chloride/petroleum ether at 5° afforded **3** (0.728 g, 56%) as brown-red crystals, mp 149-150° dec; ir: 3458, 3332, 3240, 3205 (N-H str), 3078 (aromatic C-H str), 1750 (sydnone C=O str) cm^{-1} ; nmr (deuteriochloroform/deuteriodimethylsulfoxide 10:1): 5.67 (s, 2H), 7.37 (d, 1H, J = 3 Hz), 7.77 (d, 1H, J = 3 Hz).

Anal. Calcd. for $\text{C}_8\text{H}_4\text{Br}_3\text{N}_3\text{O}_2$: C, 23.19; H, 0.97; N, 10.14. Found: C, 23.54; H, 0.95; N, 9.89.

b) By Bromination of 3-(2-Amino-3,5-bromophenyl)sydnone 8.

To a solution of **8** (0.10 g, 0.39 mmole) in ethanol (2 ml) was added a solution of sodium bicarbonate (0.072 g, 0.86 mmole) in water (2 ml). Bromine (0.131 g, 0.82 mmole) in ethanol (3 ml) was added dropwise with stirring. After 1 hour the mixture was poured into water (30 ml) and extracted with methylene chloride. The organic phase was dried (drierite), reduced to a thick oil and crystallized from methylene chloride/petroleum

ether to give **3** (0.109 g, 67%) identical (tlc, ir, mp) to an authentic sample.

c) By Bromination of 4-Bromo-3-(2-amino-5-bromophenyl)sydnone **4**.

To a solution of **4** (0.10 g, 0.3 mmole) in ethanol (2 ml) was added solution of sodium bicarbonate (0.026 g, 0.31 mmole) in water (2 ml). Bromine (0.05 g, 0.315 mmole) in ethanol (3 ml) was added dropwise and stirring continued for 30 minutes. The mixture was poured into water (30 ml) and filtered. The filtrate was extracted with methylene chloride and the organic phase dried (drierite) and reduced *in vacuo*. Crystallization from methylene chloride/petroleum ether gave **3** (0.60 g, 48%) identical (tlc, ir, mp) to an authentic sample.

Reduction of 3-(2-Nitrophenyl)sydnone.

3-(2-Nitrophenyl)sydnone (8.14 g, 39.3 mmoles) was dissolved in ethyl acetate (80 ml) and stannous chloride dihydrate (44.36 g, 196.6 mmoles) was added. The mixture was stirred for 35 minutes at 70°, cooled, poured into water (200 ml), neutralized with sodium bicarbonate and filtered. The filtrate was extracted with methylene chloride and the remaining residue digested in hot methylene chloride and refiltered. Combination of the organic phases followed by drying (drierite) and reduction *in vacuo* gave a yellow-orange solid which was crystallized from methylene chloride/petroleum ether to yield 3-(2-aminophenyl)sydnone **2** (3.06 g, 44%) identical (tlc, ir, mp) to an authentic sample.

4-Bromo-3-(2-aminophenyl)sydnone **9**.

4-Bromo-3-(2-nitrophenyl)sydnone **10** was treated as above to give **9** (3.68 g, 67%), mp 130-132°; ir: 3465, 3360, 3226 (N-H str), 1771, 1750 (sydnone C=O str) cm^{-1} ; nmr (deuteriochloroform): δ 5.1 (s, 2H), 6.8 (m, 4H).

Anal. Calcd. for $\text{C}_8\text{H}_6\text{BrN}_3\text{O}_2$: C, 37.50; H, 2.36; N, 16.41. Found: C, 37.35; H, 2.29; N, 16.14.

3-(2-Acetamidophenyl)sydnone **11**.

3-(2-Aminophenyl)sydnone **2** (0.5 g, 2.82 mmoles) was dissolved in acetic anhydride (10 ml) and stirred for 20 hours. Evaporation on standing overnight gave a light yellow oil which was crystallized from methylene chloride/petroleum ether to give **11** (0.42 g, 68%), mp 176-178°; ir: 3310, 3290 (N-H str), 3130 (sydnone C-H str) 1740 (sydnone C=O str) cm^{-1} ; nmr (deuteriochloroform): δ 2.0 (s, 3H), 6.83 (s, 1H), 7.65 (m, 4H), 9.65 (s, 1H).

Anal. Calcd. for $\text{C}_{10}\text{H}_9\text{N}_3\text{O}_3$: C, 54.79; H, 4.11; N, 19.18. Found: C, 54.90; H, 4.17; N, 18.89.

3-(2-Trifluoroacetamidophenyl)sydnone **12**.

To 3-(2-aminophenyl)sydnone **2** (0.30 g, 1.69 mmoles) in methylene chloride (20 ml) was added trifluoroacetic anhydride (0.39 g, 1.865 mmoles) dropwise with stirring. After 45 minutes, the mixture was washed with water, dried (drierite) and reduced to a yellow oil *in vacuo*. Crystallization from methylene chloride/petroleum ether gave **12** (0.28 g, 60%) as white crystals, mp 178-180°; ir: 3250, 3200 (N-H str), 3150 (sydnone C-H str), 1740 (sydnone C=O str) cm^{-1} ; nmr (deuteriochloroform): δ 7.14 (s, 1H), 7.75 (s, 4H), 11.25 (s, 0.5H).

Anal. Calcd. for $\text{C}_{10}\text{H}_5\text{F}_3\text{N}_3\text{O}_3$: C, 43.96; H, 2.20; N, 15.38. Found: C, 44.27; H, 2.20; N, 15.31.

4-Bromo-3-(2-acetamidophenyl)sydnone **13**. a) By Bromination of 3-(2-Acetamidophenyl)sydnone **11**.

To **11** (0.15 g, 0.69 mmole) in ethanol (3 ml) was added a solution of sodium bicarbonate (0.11 g, 1.37 mmoles) in water (4.5 ml). With stirring, bromine (0.114 g, 0.713 mmole) in ethanol (3 ml) was added dropwise and after 30 minutes the mixture was extracted with methylene chloride. The extract was dried (drierite) and evaporated to a thick oil which was triturated with diethyl ether to afford **13** (200 mg, 98%), mp 140-141° dec; ir: 3300 (N-H str), 1740 (sydnone C=O str) cm^{-1} ; nmr (deuteriochloroform): δ 2.0 (s, 3H), 7.6 (m, 4H), 9.65 (s, 1H).

Anal. Calcd. for $\text{C}_{10}\text{H}_8\text{BrN}_3\text{O}_3$: C, 40.27; H, 2.68; N, 14.10. Found: C, 40.13; H, 2.81; N, 13.77.

b) By Acylation of 4-Bromo-3-(2-aminophenyl)sydnone **9**.

4-Bromo-3-(2-aminophenyl)sydnone **9** (0.08 g, 0.313 mmole) was dissolved in acetic anhydride (10 ml) and the mixture stirred for 18 hours. Evaporation on standing gave white crystals which were recrystallized from methylene chloride/petroleum ether to give **13** (0.032 g, 34%) identical (ir, tlc) to an authentic sample.

4-Bromo-3-(2-trifluoroacetamidophenyl)sydnone **14**.

To a solution of **12** (0.20 g, 0.733 mmole) in ethanol (5 ml) was added a solution of sodium bicarbonate (0.068 g, 0.80 mmole) in water (3 ml). Bromine (0.123 g, 0.77 mmole) in ethanol (3 ml) was added dropwise with stirring. After 30 minutes the mixture was poured into water (30 ml), neutralized with sodium bicarbonate, extracted with methylene chloride, the extract dried (drierite) and reduced *in vacuo*. Crystallization from methylene chloride/petroleum ether gave **14** (0.205 g, 79%), mp 147-148°; ir: 3233, 3177, 3131, (N-H str), 3039 (aromatic C-H str), 1725 (sydnone C=O str) cm^{-1} ; nmr (deuteriochloroform/deuteriodimethylsulfoxide): δ 7.7 (m, 4H), 11.0 (s, 0.5H).

Anal. Calcd. for $\text{C}_{10}\text{H}_5\text{BrF}_3\text{N}_3\text{O}_3$: C, 34.09; H, 1.42; N, 11.93. Found: C, 33.87; H, 1.60; N, 11.70.

Deprotection of 3-(2-Trifluoroacetamidophenyl)sydnone **12**.

3-(2-Trifluoroacetamidophenyl)sydnone **12** (0.060 g, 0.24 mmole) was dissolved in aqueous sodium hydroxide (3 ml, 0.16M) and ethanol (1.5 ml) and the mixture was warmed to 40° for 5 minutes. Stirring was continued for 60 hours at room temperature whereupon the mixture was saturated with sodium chloride and extracted with methylene chloride. The dried organic extract gave on standing, 3-(2-aminophenyl)sydnone **2** (0.025 g, 68%) as yellow needles identical (tlc, ir, mp) to an authentic sample.

Attempted Deprotection of 4-Bromo-3-(2-trifluoroacetamidophenyl)sydnone **14**. i) With Potassium Carbonate.

To **14** (0.10 g, 0.284 mmole) in methanol (5 ml) was added a solution of potassium bicarbonate (0.04 g, 0.284 mmole) in water (2 ml). After stirring for 5 hours, tlc showed only starting material to be present.

ii) With Sodium Hydroxide.

To **14** (0.050 g, 0.142 mmole) in ethanol (2 ml) was added an aqueous solution of sodium hydroxide (3 ml, 0.16M). The mixture was stirred for 15 hours after which time, starting material and traces of three other components were observed by tlc. After 85 hours the mixture was extracted with methylene chloride and tlc of the organic phase showed starting material, three components of much lower R_f , and a trace of material matching an authentic sample of **9**.

Attempted Bromination of 4-Bromo-3-(2-acetamidophenyl)sydnone **13**.

Bromination of **13** was attempted in ethanol, using 1.1 equivalents of bromine and 1.2 equivalents of sodium bicarbonate, at temperatures ranging from ambient to 92° in a pressure vessel. In all cases, only starting material was recovered. The addition of iron filings did not change the outcome of the reaction. Attempted bromination in ethylene glycol monomethyl ether at 100° for 17 hours in a pressure vessel also gave only starting material. With ethylene glycol, at 150° for 16 hours, a complex mixture, all components of which had a lower R_f value than either the starting material or an authentic sample of **15** was obtained.

3-(2-Trifluoroacetamido-5-bromophenyl)sydnone **17**.

To 3-(2-amino-5-bromophenyl)sydnone **8** (0.10 g, 0.39 mmole) in methylene chloride (5 ml) was added trifluoroacetic anhydride (0.103 g, 0.494 mmole) dropwise. The mixture was stirred for 1 hour, evaporated to an oil *in vacuo* and crystallized from methylene chloride/petroleum ether to give **17** (0.13 g, 93%), mp 102-103°; ir: 3423 (N-H str), 3156 (sydnone C-H str), 3121, 3029 (aromatic C-H str), 1728, 1720 (C=O str) cm^{-1} ; nmr (deuteriochloroform): δ 6.75 (s, 1H), 7.75 (m, 3H), 11.0 (s, 0.5H).

Anal. Calcd. for $\text{C}_{10}\text{H}_5\text{BrF}_3\text{N}_3\text{O}_3$: C, 34.09; H, 1.42; N, 11.93. Found: C, 33.78; H, 1.68; N, 11.65.

4-Bromo-3-(2-trifluoroacetamido-5-bromophenyl)sydnone **16**. a) By Trifluoroacetylation of 4-Bromo-3-(2-amino-5-bromophenyl)sydnone **4**.

To **4** (0.10 g, 0.298 mmole) in methylene chloride (5 ml) was added trifluoroacetic anhydride (0.069 g, 0.329 mmole) dropwise. The mixture was stirred for 10 minutes, washed with water, dried (drierite) and evaporated to an oil *in vacuo*. Crystallization from methylene chloride/petroleum ether gave **16** (0.088 g, 68%), mp 149-150°; ir: 3437, 3226 (N-H str), 3050 (aromatic C-H str), 1743 (sydnone C=O str), 1725 (trifluoroacetamido C=O str) cm^{-1} ; nmr (deuteriochloroform): δ 7.7 (m, 3H), 11.2 (s, 1H).

Anal. Calcd. for $\text{C}_{10}\text{H}_6\text{Br}_2\text{F}_3\text{N}_3\text{O}_3$: C, 27.84; H, 0.93; N, 9.74. Found: C, 28.11; H, 1.10; N, 9.82.

b) By Bromination of 3-(2-Trifluoroacetamido-5-bromophenyl)sydnone **17**.

To a solution of **17** (0.08 g, 0.227 mmole) in ethanol (4 ml) was added a solution of sodium bicarbonate (0.021 g, 0.25 mmole) in water (3 ml). Bromine (0.038 g, 0.122 mmole) in ethanol (3 ml) was added dropwise with stirring. After 1 hour the reaction mixture was poured into water (25 ml), extracted with methylene chloride, the extract dried (drierite) and evaporated to an oil *in vacuo*. Crystallization from methylene chloride/petroleum ether gave **16** (0.064 g, 65%) identical (ir, tlc, mp) to an authentic sample.

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