QUANTITATIVE DECARBOXYLATIONS OF ELECTRONEGATIVELY SUBSTITUTED BENZOIC ACIDS VIA THE SCHMIDT REACTION

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Reaction mechanism studies involving isotopic carbon frequently require the isolation, for isotopic analysis, of a particular carbon atom in a molecule. If the atom of interest is bonded to an aromatic ring, a common approach to its isolation involves an oxidation to the substituted aromatic carboxylic acid followed by decarboxylation to furnish carbon dioxide for mass spectrometric analysis or radio assay. While it is always desirable that this degradation to carbon dioxide be accomplished in high overall yield, for isotope effect studies it is essential. The most frequently employed methods for the decarboxylation step include the Schmidt reaction, the Hunsdiecker silver salt degradation, and the copper chromite – quinoline reaction. The relative merits of these methods have been discussed recently (1) and a thorough review of the Schmidt reaction has appeared (2). The major deficiency of the Schmidt reaction for this purpose was shown to be the poor yields obtained with aromatic acids bearing electronegative substituents (1), the presence of which so lowers the yield of carbon dioxide that the method is of little use for isotope effect studies. To our knowledge, however, most of the previous results have been obtained using *concentrated* sulphuric acid, either as the reaction medium or as a catalyst in a heterogeneous reaction mixture. While Newman and Gildenhorn (3) have reported the use of 100% sulphuric acid for the decarboxylation of 2,6-dimethyl substituted benzoic and terephthalic acids and Briggs, de Ath, and Ellis (4) noted the adverse effects of water on yields from this reaction, no studies of the Schmidt reaction on *m*- and *p*-substituted benzoic acids in anhydrous sulphuric acid appear in the literature. We have found that the yield of carbon dioxide from these acids is dramatically increased, if "100% sulphuric acid"* is used as the reaction medium.

Virtually quantitative yields of carbon dioxide, together with high yields of the appropriately substituted aniline, have been obtained for a series of meta- and para-substituted benzoic acids bearing a variety of electron-withdrawing groups. Typical data are listed in Table I in which the results for benzoic and *p*-anisic acids are included for comparison. The yields noted for the various anilines represent *lower* limits for the method, since these data represent the quantity of material actually isolated after recrystallization either as the aniline or as a derivative. The yields of carbon dioxide were obtained by precipitation as barium carbonate in the usual way (5). It is clear from these results that sulphonation is not an important side reaction for those acids having electron-withdrawing substituents although the presence of electron-releasing groups may lead to significant quantities of sulphonated products, as indicated by the reduced yields of the aniline from *p*-anisic and benzoic acids. No attempt was made to isolate sulphonated products from these reactions.

The reaction conditions (2 h at 40 °C) were chosen for convenience and to allow comparison with previous results using concentrated sulphuric acid (1, 6). These conditions are not particularly drastic and the reaction proceeds smoothly at even lower temperatures. Furthermore, Deno and his co-workers (7) have demonstrated that much more reactive species can be treated with, and recovered from, sulphuric acid solutions

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**Prepared by the addition of the calculated amount of 95%* H_2SO_4 *to 20% oleum.*

TABLE I

Modified Schmidt reaction on benzoic acids

	Sulphuric acid concentration				
	96%	100%		20% oleum	
	% yield:				
Substituent	Barium carbonate	Barium carbonate	Aniline	Barium carbonate	Aniline
None	90.5	96.5	67*	—	—
4-OCH_3	91.8	96.5	0*	—	—
4-F	71.7	99.5	92	—	—
4-Cl	51.3	98.0	99	—	—
4-Br	50.3	97.5	96	—	—
4-CN	7.6	100.0	73†	—	—
4-CF_3	—	97.4	41‡	—	—
4-NO_2	8.1	99.0	99	—	—
3-NO_2	6.1	98.3	100	—	—
3,5-di-NO_2	—	3.2	—	97.6	82

*Sulphonation would be expected.
†As *p*-aminobenzamide.
‡As N-acetyl derivative.

without serious decomposition. While it would appear that the Schmidt reaction is complete in a shorter period of time, no quantitative kinetic data have been obtained to date. Each experiment was allowed to continue for 2 h to ensure that all of the evolved carbon dioxide was collected in the gas absorption trap.

Clearly the use of "100% sulphuric acid" in the Schmidt reaction affords sufficiently high yields of carbon dioxide for isotope work, but it is also interesting that the substituted aniline is formed in high yield. It appears, therefore, that this slight modification of the standard method may offer a straightforward route to certain substituted anilines which may be difficult and (or) tedious to prepare by other methods. All except one of those substituents in the present series are unaffected by the reagents. The lone exception, the cyano group, is hydrolyzed readily to the amido grouping in sulphuric acid producing a good yield of *p*-aminobenzamide. Our survey included 3,5-dinitrobenzoic acid to examine the effect of two strongly electron-withdrawing substituents on the yield of the reaction products. While reaction in "100% sulphuric acid" was negligible, the use of 20% oleum afforded a quantitative yield of carbon dioxide and an 82% yield of 3,5-dinitroaniline.

EXPERIMENTAL

The general procedure was similar to that described previously (6). An absorption train was set up, following the method of Phares (8), and to a cold (0°) solution of 1–2 mmole of the benzoic acid in 5 ml of sulphuric acid of the appropriate concentration was added sodium azide (15% excess over a 1:1 mole ratio, NaN_3:RCOOH). After connection to the absorption traps, the temperature of the reaction mixture was maintained at 40 ± 1° for 2 h while the evolved carbon dioxide was swept into 0.2 *M* carbonate free sodium hydroxide by a slow stream of purified nitrogen. The carbon dioxide was precipitated as barium carbonate in the usual way (5). Great care was taken in all operations to avoid contamination with extraneous carbon dioxide and suitable blanks were run at regular intervals to check the operations. To isolate the aniline, the reaction mixture was poured into cold water, sufficient alkali was added to make the solution definitely basic, and the product removed by ether extraction. Removal of the ether was followed by recrystallization of the residue in the case of the solid anilines; otherwise a suitable solid derivative was prepared and recrystallized. In the case of *p*-aminobenzamide (from *p*-cyanobenzoic acid), the reaction mixture was poured onto 15 g of ice and, with external cooling, was neutralized with concentrated NH_4OH (just basic to litmus); the insoluble amide was filtered off and recrystallized from EtOH/H_2O.

All of the starting materials, except *p*-trifluoromethylbenzoic acid which was kindly supplied by Prof.

A. N. Bourns, are commercially available and the purity of each was checked by a melting point determination. The compounds were purified by recrystallization before use if the melting point indicated the presence of impurities.

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LA RÉACTION DU SULFURE DE BORE AVEC LES ALCOOLS

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Moissan (1) rapporte que le sulfure de bore réagit avec certaines molécules organiques sans toutefois préciser le mode d'action du sulfure ou la nature des produits ainsi obtenus. Au cours d'une étude systématique de l'interaction de B_2S_3 avec différents types de composés organiques (2) la réaction de ce sulfure avec les alcools a été étudiée.

On a constaté que les alcools, tant aliphatiques qu'aromatiques, conduisent aux esters orthoboriques correspondants, avec de bons rendements, la réaction s'accompagnant d'un dégagement de H_2S.

$$6ROH + B_2S_3 \rightarrow 2(RO)_3B + 3H_2S,$$

où $R = CH_3, C_2H_5, n\text{-}C_3H_7, n\text{-}C_6H_{13}, n\text{-}C_7H_{15}, C_6H_5, \alpha\text{-}C_{10}H_7$.

Cependant, certains phénols nitrés demeurent complètement inertes vis-à-vis le sulfure. Cette absence de réaction ne peut se justifier par une inhibition simple due au groupe nitro car le phénol donne une réaction avec B_2S_3 même en présence d'une quantité équimoléculaire de nitrobenzène. Cette réaction demeure à l'étude afin d'en préciser, si possible, le mécanisme.

PARTIE EXPÉRIMENTALE

Réaction du sulfure de bore avec les alcools

A une suspension de 12 g (0.10 mole) de sulfure de bore, préparé selon le mode usuel (2), dans le benzène anhydre, on ajoute 61 g (0.60 mole) d'hexanol normal redistillé. L'addition s'accompagne d'un échauffement prononcé et d'un fort dégagement de H_2S, ce gaz étant capté sous forme de sulfure de plomb. On isole ainsi 0.26 mole de gaz sulfhydrique. Après un reflux de 3 h, la masse réactionnelle est filtrée. Le résidu

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