Experimental

The Resolution of 2-Heptanol.—This was accomplished essentially according to the method of Pickard and Kenyon.[1] The (+)-2-heptanol obtained had the following properties: b.p. 149–150°, $n^{20}D$ 1.4204, $\alpha^{26}D$ +4.12° (l = 0.5 dm., neat), d^{25}_4 0.815 as compared with the following reported[2] values: b.p. 150°, $n^{20}D$ 1.4209, d^{20}_4 0.8185, $[\alpha]^{20}D$ +10.32°.

Optically Active 2-Heptyl Methanesulfonate.—A mixture of 11.5 g. (0.10 mole) of methanesulfonyl chloride and 11.6 g. (0.10 mole) of (+)-2-heptanol was stirred in an ice-bath while 16.8 g. (0.20 mole) of pyridine was added slowly. After three hours, the mixture was worked up as previously described[4] to give 13.5 g. (70%) of (+)-2-heptyl methanesulfonate, b.p. 77–79° (1 mm.), $n^{20}D$ 1.4338, d^{25}_4 1.027, $\alpha^{25}D$ +20.96° (l = 2 dm., neat).

Optically Active 2-Heptyl Hydroperoxide.—A one-phase reaction mixture was prepared from 12.5 g. (0.065 mole) of optically active 2-heptyl methanesulfonate, 32 g. (0.28 mole) of 30% hydrogen peroxide, 100 ml. of methanol, 8 ml. of water and 8.1 g. (0.072 mole) of 50% aqueous potassium hydroxide, which was added with cooling. The mixture was maintained in a water-bath at room temperature for 24 hours and worked up in the manner previously described[4] to give 2.00 g. (24.5%) of optically active 2-heptyl hydroperoxide, b.p. 39–41° at 0.8 mm., $n^{20}D$ 1.4242, d^{20}_4 0.877, $\alpha^{25}D$ −9.96° (l 2 dm., neat), $[\alpha]^{25}D$ −5.66.[8]

The infrared spectrum of this sample was identical to that of the 2-heptyl hydroperoxide previously reported.[4] There was no detectable change in the spectra or the optical rotation after storage for eight months in the dark at 5°. Titration for active oxygen[9] gave the following results. *Anal.* Calcd. for $C_7H_{16}O_2$: O, 12.1. Found: O, 11.45, 11.59, 11.49.

The Reduction of Optically Active 2-Heptyl Hydroperoxide with Lithium Aluminum Hydride.[10]—A suspension of 100 mg. (2.7 moles) of powdered lithium aluminum hydride in 2.5 ml. of ether was cooled while 406 mg. (3.1 moles) of (−)-2-heptyl hydroperoxide was added slowly in 2.5 ml. of ether. Methanol was then added dropwise until the excess lithium aluminum hydride was destroyed, after which 2 ml. of 10% potassium hydroxide was added. The aqueous layer was extracted twice with 1-ml. portions of ether, and the combined ether fractions were dried over sodium sulfate. The ether was evaporated on a steam-bath to leave 231 mg. (84%) of (−)-2-heptanol, $n^{20}D$ 1.4207, $\alpha^{25}D$ −3.70° (l = 0.5 dm., neat). The infrared spectrum of this product was identical to that of 2-heptanol.

The Platinum-catalyzed Reduction of Optically Active 2-Heptyl Hydroperoxide.—A mixture of 415 mg. (3.14 moles) of (−)-2-heptyl hydroperoxide, 15 mg. of platinum oxide and 1.5 ml. of methanol was stirred at 25° in a hydrogen atmosphere for one hour. There was a rapid initial uptake of hydrogen until 50 ml. (64% of the theoretical requirement) was absorbed. The product failed to give a positive test for hydroperoxide. The catalyst was centrifuged from the solution, and the methanol was evaporated to leave 233 mg. (82%) of (−)-2-heptanol, $n^{20}D$ 1.4203, $\alpha^{25}D$ −3.78° (l = 0.5 dm., neat). The infrared spectrum of this sample corresponded with that of 2-heptanol with the exception of a very weak band at 5.85 μ which corresponded to a very strong band of 2-heptanone. That the theoretical amount of hydrogen was not absorbed in this reduction was due to a platinum-catalyzed decomposition of the hydroperoxide[9] as indicated in the following experiment.

Platinum oxide (4.5 mg.) in 0.2 ml. of methanol was reduced in a hydrogen atmosphere over a five-minute period. The platinum suspension was boiled, and the reaction flask was thoroughly flushed with air. Pure 2-heptyl hydroperoxide (200 mg., 1.51 moles) was added in 0.8 ml. of methanol and stirred for 23 hours. At the end of this time, an iodide test for hydroperoxide indicated the presence of only a trace in the reaction mixture. The platinum was removed by centrifugation, and the methanol was boiled off to leave 171 mg. of residue. The infrared spectrum showed absorption maxima at all points corresponding to the spectrum of 2-heptanol. In addition, there was appreciable absorption at 5.85 μ, and there were weak inflections at the other strong absorption points of 2-heptanone. A band at 9.66 μ did not correspond to the spectrum of either 2-heptanol or 2-heptanone. The lithium aluminum hydride reduction method is therefore to be preferred.

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(8) It is interesting to note that the sign of rotation of the 2-heptyl hydroperoxide is the same as that of the alcohol of the corresponding configuration but the magnitude is approximately one half.

(9) C. D. Wagner, R. H. Smith and E. D. Peters, *Anal. Chem.*, **19**, 976 (1947).

(10) The use of lithium aluminum hydride for the reduction of hydroperoxides has been described previously by D. A. Sutton, *Chemistry and Industry*, 272 (1951).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE COLLEGE OF ARTS AND SCIENCES, UNIVERSITY OF LOUISVILLE]

Base-catalyzed Decomposition of Substituted α-(Benzenesulfonamido)-carboxylic Acids and their Acyl Chlorides

BY RICHARD H. WILEY AND RICHARD P. DAVIS[1]

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In a continuation of previous studies the pyridine–acetic anhydride decarboxylation of twelve additional α-(arylsulfonamido)-carboxylic acids has been shown to give 33–97% of carbon dioxide, 18–70% of benzaldehyde, 0–7% of arylsulfonamide and 0–49% of aryl disulfide; the aqueous alkaline decomposition of ten additional α-(arylsulfonamido)-acyl chlorides has been shown to give 37–98% of carbon monoxide, 0–58% of arylsulfonamide and 22–80% of benzaldehyde. The unusual reactions involved have been reinterpreted in terms of a cyclic intermediate I for the pyridine decarboxylation and a displacement reaction at the α-carbon atom (reaction 3) for the alkaline decomposition. Both proposals are consistent with effects produced by introduction of electron donor groups at the α-carbon or in the aryl nucleus and with recognized similar effects.

In preceding papers[2,3] we have described two reactions which take place in the base-catalyzed decomposition of α-(benzene- and *p*-toluenesulfonamido)-phenylacetyl chloride and the related acetic acids. These two reactions are differentiated in that the acyl chlorides decompose when treated with aqueous alkali to give an arylsulfonamide and carbon monoxide (reaction 1) and the acids themselves decompose when heated with pyridine to give an aryl disulfide and carbon dioxide (reaction 2). Aldehydes are obtained from phenylacetic acid (R = C_6H_5) but not from propionic acid (R = CH_3) derivatives.

$$ArSO_2NHCHRCOCl + NaOH \longrightarrow ArSO_2NH_2 + RCHO + CO + NaCl \quad (1)$$

$$ArSO_2NHCHRCO_2H \xrightarrow[Ac_2O]{\text{pyridine}} ArSSAr + RCHO + CO_2 \quad (2)$$

(1) Research Corporation graduate research assistant.

(2) R. H. Wiley and N. R. Smith, THIS JOURNAL, **73**, 4719 (1951).

(3) R. H. Wiley, H. L. Davis, D. E. Gensheimer and N. R. Smith, *ibid.*, **74**, 936 (1952).

TABLE I

α-ARYLSULFONAMIDO ACIDS

Compound	Yield	M.p., °C.	Neut. Equiv. Calcd.	Neut. Equiv. Found	Nitrogen, % Calcd.	Nitrogen, % Found	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
α-Arylsulfonamidopropionic acids										
p-Bromobenzene	70	162	308	307	4.57	4.66	35.06	35.26	3.24	3.35
p-Nitrobenzene	76	175	274	273	10.21	10.24	...	...	...	...
α-Arylsulfonamidophenylacetic acids										
p-Toluene	41	180	305	305	4.59	4.74	59.01	58.76	4.91	4.92
p-Acetamidobenzene	87	229	348	346	8.04	8.07	...	...	...	...
p-Bromobenzene	78	184	370	369	3.78	3.92	45.40	45.67	3.24	3.52
β-Naphthylene	66	165	341	342	4.10	4.13	63.34	63.33	4.39	4.33
p-Nitrobenzene	70	213	336	337	8.33	8.28	...	...	...	...
α-Benzenesulfonamido-*p*-methoxyphenylacetic acid										
	56	166	321	322	4.36	4.53	56.05	56.27	4.71	4.81

We have extended our studies of these reactions to include the decomposition of the eleven additional α-(arylsulfonamido)-carboxylic acids, the related ten acyl chlorides and α-(benzenesulfonamido)-*p*-methoxyphenylacetic acid. The only compounds thus far observed not to react are derivatives of glycine.

The arylsulfonamido acids used in these studies were prepared in 41–87% yields from alanine or α-phenylaminoacetic acid by the improved procedure described in the Experimental section. α-Amino-*p*-methoxyphenylacetic acid was prepared from *p*-methoxybenzaldehyde as previously described[4] and converted to its benzenesulfonamide, a new derivative, by the same procedure. Characterization data for the new compounds are given in Table I. The sulfonamido acids which have been described previously were observed to have neutral equivalents in agreement with theory and melting points in agreement with values given in the literature. The sulfonamido acid chlorides were prepared, as previously described,[3] from the acids by treatment with thionyl chloride. The 2,4-dinitrophenylhydrazones of the aldehydes, the sulfonamides and the disulfides formed in the various reactions were characterized by melting points which were in agreement with values recorded in the literature. The pyridine decarboxylation reactions and the aqueous sodium hydroxide decompositions were run as described in the Experimental section following a procedure similar to that described previously.[2,3] The yields of decomposition products are listed in Tables II and III. Reproducibilities of the yields are indicated by figures for duplicate runs given in these tables. The pyridine–acetic anhydride decarboxylation is more easily controlled and usually gives variations in yields well within ±10%. The hot alkali decomposition is much more susceptible to variations in technique, and different workers in our laboratories have reported variations of ±25% in yields of carbon monoxide from α-ben-

TABLE II

DECARBOXYLATION OF α-ARYLSULFONAMIDO ACIDS

Compound	Yield in mole per cent. CO_2	RCHO	$ArSONH_2$	ArSSAr
α-Arylsulfonamidopropionic acids				
Benzene	58	0	0	40
	65.5			40.2
p-Toluene	57	0	0	44[a]
	40			22.6
β-Naphthalene	57.8	0	0	31.4[b]
p-Bromobenzene	51.6	0	0	49[c]
p-Nitrobenzene	53	0	0	15.6[d]
	46.6			5.9
p-Acetamidobenzene	46.2	0	0	0
	42			
α-Arylsulfonamidophenylacetic acids				
Benzene	81	53	7	5
p-Toluene	97	70	0	0
β-Naphthalene	46	51	28	0
	53	...	3.4	
	78.5	...	6	
p-Bromobenzene	51	58.5	4.3	7.9
p-Nitrobenzene	33	21.5	Trace	4
p-Acetamidobenzene	58	18.3	0	5.9[e]
α-Benzenesulfonamido-*p*-methoxyphenylacetic				
	80	55	0	11.7

[a] M.p. obsd. 45°; reptd. 45°; H. Gilman, L. Smith and H. Parker, THIS JOURNAL, **47**, 859 (1925). [b] M.p. obsd. 139°, reptd. 139°; K. Fries and G. Schurmann, *Ber.*, **47**, 1195 (1914). [c] M.p. obsd. 93.5°, reptd. 93–94°; F. Challenger and A. D. Collins, *J. Chem. Soc.*, **125**, 1379 (1924). [d] M.p. obsd. 181°, reptd. 182°; F. Challenger and A. D. Collins, *ibid.*, **125**, 1379 (1924). [e] M.p. obsd. 182°, reptd. 182°; O. Hinsberg, *Ber.*, **41**, 626 (1908).

(4) F. Tiemann and K. Köhler, *Ber.*, **14**, 1976 (1881).

TABLE III

DECOMPOSITION OF α-ARYLSULFONAMIDOACYL CHLORIDES

Compound	Yield in mole per cent. CO	RCHO	$ArSO_2NH_2$	Parent Acid[a]
α-Arylsulfonamidopropionyl chlorides				
Benzene	58	0	0	21
p-Toluene	55	0	41	16
β-Naphthalene	30	0	5	30
p-Bromobenzene	37	0	6.7	27
p-Nitrobenzene	27	0	0	0
p-Acetamidobenzene[b]	..	...	...	..
α-Arylsulfonamidophenylacetyl chlorides				
Benzene	48	65	54	0
	98	22	49	0
p-Toluene	80	80	46.5	14
β-Naphthalene	59	25.3	58	34
p-Bromobenzene	53	52	31	16
p-Nitrobenzene	58	36	33	40
p-Acetamidobenzene[b]	..	...	...	..

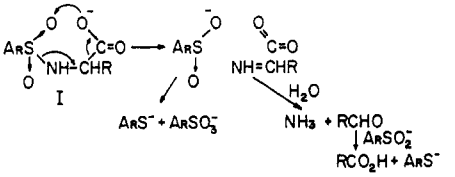
[a] $ArSO_2NHCHRCO_2H$ formed by hydrolysis of the chloride. [b] Decomposed too rapidly to control.

zenesulfonamidophenylacetyl chloride. It is believed that the values given in Tables II and III fall within these limits.

The pyridine–acetic anhydride decarboxylation of the series of α-(arylsulfonamido)-propionic acids described in Table II gives 40–65% yields of carbon dioxide and 22–49% yields of disulfide with the exceptions of the acetamidobenzene and *p*-nitrobenzene derivatives. The products from the former were possibly lost through hydrolysis during attempted isolation and from the latter by oxidation–reduction reactions involving the nitro group. With none of these propionic acid derivatives have we recovered any acetaldehyde or sulfonamide. This is probably partly due to the fact that acetaldehyde and the amide are consumed in the reduction leading to the disulfide, which is actually obtained in highest yields from propionic types. The α-(arylsulfonamidophenyl)-acetic acids decarboxylate to give 33–97% yields of carbon dioxide. These yields are generally higher than the yields obtained from the corresponding propionic derivatives. Benzaldehyde is recovered in 18–70% yields. This probably is not due solely to its ease of isolation as compared to acetaldehyde but may be due to a less rapid consumption in the formation of the disulfide. The introduction of the electron donor *p*-methoxy group in the benzene nucleus does not materially alter the decarboxylation. The 80% yield of carbon dioxide and 55% yield of *p*-methoxybenzaldehyde are within the limits established for the series and only the increased yield, 11.7%, of disulfide appears distinctive. This yield of disulfide from the aryl acid is much lower than that obtained from propionic derivatives.

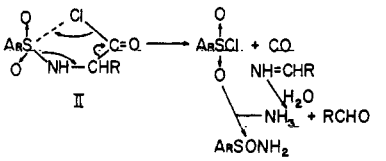
The hot alkaline decomposition of the α-(arylsulfonamido)-acyl chlorides to carbon monoxide, aldehydes and sulfonamide ($ArSONH_2$) is a highly unusual reaction and, for this reason, the confirmatory data presented here for ten additional compounds are of more than usual significance. The α-(arylsulfonamido)-propionyl chlorides gave 37–58% of carbon monoxide and up to 41% of the substituted benzenesulfonamide. As with the pyridine–acetic anhydride reaction, no acetaldehyde has been obtained from the propionic derivatives. The α-(arylsulfonamido)-phenylacetyl chlorides give 48–98% of carbon monoxide, 31–58% of the substituted benzenesulfonamide and 22–80% of benzaldehyde. These yields do not include any allowance for recovered acid formed by simple hydrolysis of the acid chloride. If this allowance is made the yields of carbon monoxide for the benzene, *p*-toluene, β-naphthalene and *p*-nitrobenzene derivatives are 98, 94, 93 and 98%, respectively, which indicates that the reaction is practically quantitative. The unusual rapidity with which the *p*-acetamidobenzene derivatives react is noteworthy. With each reactant, propionic and phenylacetic acid derivatives, the reaction was too rapid to control. The gas was evolved so rapidly that it could not be contained in the system we were using.

In the preceding paper in this series, a mechanism was proposed for coördinating the two reactions—loss of carbon dioxide and loss of carbon monoxide—in terms of carbanion intermediates. The difficulty in accepting a carbanion mechanism for these reactions is that the carbanion intermediates one may write usually require removal by base of a proton which appears less acidic, and thus less likely to react with the base, than some other proton such as that on the amide nitrogen or that of the carboxylic acid, or require removal of a proton from a carbon in preference to hydrolysis of an acid chloride. These difficulties can be avoided for the pyridine decarboxylation by postulating a cyclic, concerted process involving the carboxylate ion as in (I) and the following reactions.



I

The decomposition of the acid chlorides cannot be easily explained by a cyclic process. A concerted process such as II fails to indicate the significant role of the base catalyst. Another possi-



II

bility for this reaction involves a displacement at the α-carbon atom in which the hydroxyl ion displaces a $(:COCl)^-$ anion. The latter is a formyl chloride fragment and would logically dissociate to carbon monoxide and the chloride ion. The other fragment obviously can form the aldehyde and sulfonamide by reversal of a typical carbonyl addition reaction. The displacement probably

$$ArSO_2NHCHR{:}COCl \longrightarrow$$

$$+$$

$$(:OH)^- \qquad ArSO_2NHCHR + (:COCl)^- \quad (3)$$

$$\downarrow \qquad\quad OH$$

$$ArSO_2NH_2 + RCHO$$

takes place with the acyl chloride, but not the free acid, because the increased electron attracting characteristics of the chlorine atom result in an increased electron deficiency at the α-carbon atom and an increased ease of dissociation of the $(:COCl)^-$ fragment. This is consistent with previously recognized effects such as those which make halogenation at the α-carbon atom easier with the acyl halide than with the free acid.

What information is available about the influence of substituents on these reactions is consistent with the electronic requirements operating in the cyclic intermediate (I) and the displacement reaction (3). Thus, glycine derivatives, in which by comparison no electron donor group is present on the α-carbon, fail to undergo the reactions which take place readily with the assistance of an electron donor methyl or phenyl group substituted on the α-carbon. Also, the introduction of the

electron-donor, *p*-acetamido group in the aryl nucleus results in a significant acceleration of the reaction. Apparently, the presence of the electron-attracting nitro group is not nearly so significant a factor since the characteristics of the reaction, so far as noted in this study, are not markedly altered by its presence. Although this suggests that factors in addition to that of electron release are important, a similar anomaly may be noted in the failure of the electron-attracting characteristics of the nitro group to produce the predicted effect in mixed benzoin reactions where *p*-nitrobenzaldehyde, which should have an increased acceptor capacity, actually is inexplicably unreactive.

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Experimental

Preparation of Arylsulfonamido Acids.—The procedure used in preparing the compounds listed in Table II is given in detail for the preparation of α-(*p*-bromobenzenesulfonamido)-propionic acid. Certain modifications of this procedure followed with other compounds are indicated in the comments following the detailed preparation.

α-(*p*-Bromobenzenesulfonamido)-propionic Acid.—To a solution of 3.0 g. (0.045 mole) of potassium hydroxide in 25 ml. of water was added 2.0 g. (0.0225 mole) of alanine. This solution was chilled and stirred while a solution of 5.72 g. (0.0225 mole) of *p*-bromobenzenesulfonyl chloride in 25 ml. of benzene was added. After stirring vigorously for four hours and standing 15 hours, 15 ml. of water was added to dissolve the potassium salt. The aqueous layer was separated and concentrated under vacuum to 20 ml. Acidification precipitated 4.8 g., 70% of the theoretical amount, of crude α-(*p*-bromobenzenesulfonamido)-propionic acid. Recrystallization from water gave white crystals, m.p. 162°.

Both of the *p*-bromobenzenesulfonamido derivatives were prepared by this procedure. The use of ether or acetone as a solvent for the chloride was less convenient. The other substituted sulfonamides were prepared by adding the sulfonyl chloride as such, using no solvent, directly to the reaction mixture in a procedure otherwise identical with that described from the bromo derivative. The acetamido derivative was precipitated by acidification of the reaction mixture immediately after the four-hour reaction period and without concentration by evaporation to prevent loss by hydrolysis.

The yields, melting points and analytical data for the new compounds are listed in Table I.

Decarboxylation of the α-Arylsulfonamidopropionic and Phenylacetic Acids.—A 1.21–4.00 g. (0.005–0.013 mole) sample of the acid was weighed into a 25-ml. distilling flask. To this was added a 6 molar excess (2.8–7.4 ml.) of acetic anhydride (95%) and a 5 molar excess (2.0–5.4 ml.) of pyridine. The side arm of the flask was attached to a gas buret. The neck of the flask was closed with a cold finger extending about 4 cm. below the side arm. The reactants were heated slowly to gentle reflux and held at this temperature until gas evolution ceased. The collected gas was passed through 5% sodium hydroxide solution and the decrease in volume taken as the volume of carbon dioxide evolved. The residual, insoluble gas contained no carbon monoxide, as evidenced by its insolubility in cuprous chloride solution in the one sample thus tested. The reaction mixture was poured onto a mixture of 3.0 ml. of concd. sulfuric acid and ice. The resulting mixture was extracted with ether. The ether extracts were washed with water and 5% aqueous sodium bicarbonate and divided into two portions. Part A was evaporated to remove the ether and the residue taken up in alcohol and combined with an alcoholic solution of 2,4-dinitrophenylhydrazine. The precipitated phenylhydrazone was collected, dried and weighed to give the percentage yield of aldehyde. Part B was extracted with 5–10% aqueous sodium hydroxide. The remaining ether solution was evaporated to remove the ether. The residue was either extracted with petroleum ether to obtain the disulfide, which was then recrystallized from alcohol, or was steam distilled to remove the aldehyde and then treated with petroleum ether to isolate the disulfide. The sodium hydroxide extract was acidified and ether extracted to obtain the sulfonamide. Several minor variations of the procedures for isolation of the disulfide from the gummy residue were used. The data are summarized in Table II.

Decarboxylation of the α-(Arylsulfonamido)-propionyl and Phenylacetyl Chlorides.—One gram of the α-arylsulfonamido acid was refluxed with 3–5 ml. of purified thionyl chloride. The excess thionyl chloride and gaseous reaction products were removed by heating under vacuum. The acid chlorides thus prepared have been shown in some instances to be substantially pure by conversion in high yield (50–70%) to their amides and are not amenable to purification by usual techniques. For these decarboxylation studies the chlorides were prepared in a 25-ml. distilling flask in which the decarboxylation was to be run. The side arm of the flask was attached to the gas buret and 15 ml. of boiling 5% aqueous sodium hydroxide was added to the flask, preheated to 90°, through a separatory funnel. That volume of the collected gas soluble in cuprous chloride was taken as the yield of carbon monoxide. The reaction mixture was cooled and extracted with ether. The ether extracts were evaporated and the residue treated with 2,4-dinitrophenylhydrazine in ethanol to precipitate the 2,4-dinitrophenylhydrazone of the aldehyde. The ether-extracted reaction residue was acidified to precipitate the arylsulfonamide, which was separated, and concentrated to precipitate the α-arylsulfonamido acid. The data are summarized in Table III.

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