and ketones; acetone, cyclopentanone cyclohexanone, methyl *n*-propyl ketone, benzaldehyde and 2-ethylhexanal.

The amine bisulfite adducts were characterized. In general they are white crystalline solids, readily crystallized from ethanol or ethanol–ether mixtures. Like the corresponding sodium bisulfite adducts, they are decomposed with acids or alkalies into the amines.

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Amine Bisulfites. II. Their Use as Resolving Agents for Aldehydes and Ketones

BY ROGER ADAMS AND JOHN D. GARBER[1]

The addition products formed from tertiary amine bisulfites and aldehydes or ketones have been described in the first communication.[2] The extension of this study to certain primary amine bisulfites has now been made. The bisulfites of benzylamine, *s*-butylamine, β-phenethylamine, α-phenethylamine, and β-naphthol phenylaminomethane have been allowed to react with acetone, cyclopentanone, cyclohexanone, 3-methylcyclohexanone, benzaldehyde, heptaldehyde, isovaleraldehyde and valeraldehyde. The reactions usually proceeded smoothly and the adducts are white crystalline compounds, readily purified from absolute ethanol or ethanol–water mixtures in the case of the higher molecular weight substances. The melting points range between 100 and 160° as shown in Table I. Although stereoisomers in certain of the adducts are possible one form predominated, for only a single substance was isolated in good yield.

The gradation in properties of the compounds listed in Table I is interesting. It was noticed that if the molecular weight of either the amine or carbonyl compound was increased, the salt-like properties of the bisulfite addition compound became more indefinite, and the solubility in water and ethanol decreased. The stability also was found to vary between wide limits, an observation which made the temperature of recrystallization an important factor. Thus, the *s*-butylamine bisulfite of *n*-valeraldehyde was formed in the usual manner, but the solid, after isolation, immediately began to evolve sulfur dioxide. It could be recrystallized, but by the time the sample was dry enough for analysis it was impure again. On the other hand, the addition compounds of β-naphthol phenylaminomethane bisulfite with most of the carbonyl compounds listed could be boiled in ethanol without appreciable decomposition.

When sulfur dioxide was allowed to bubble through an equimolar mixture of the amine and water, usually with the addition of a little ether or in certain cases of ethanol, a white precipitate was formed. This product, chiefly the amine sulfite, was not isolated, but the introduction of sulfur dioxide was continued until a homogeneous, yellow, viscous liquid was produced. It is postulated that the yellow color of the resulting product is due to a complex, perhaps of the type $(RNH_2)_x:(SO_2)_y$. Such a complex, in the presence of water and a suitable carbonyl compound, reacts to form an amine bisulfite addition compound. The evolution of sulfur dioxide in the latter reaction may be cited as evidence that y is greater than x. Moreover, Bright and Jasper[3] have shown that the 1:1 trimethylamine–sulfur dioxide complex is colorless.

The procedure for forming the adducts with aldehydes and ketones was essentially that previously described.[2] A few isolated experiments were unsuccessful. No reaction product could be isolated from the following combinations: camphor or carbethoxycyclohexanone and *dl*-α-phenethylamine bisulfite; glucose and *dl*-*s*-butylamine bisulfite; benzaldehyde and aniline bisulfite; propiophenone and benzylamine bisulfite (too unstable). In a few instances indicated in the table, no crystalline products formed.

If an optically active amine bisulfite were allowed to react with a racemic aldehyde or ketone, it is apparent that the product would be a mixture of four stereoisomers since a new asymmetric carbon holding the hydroxyl group would be introduced.

$$\underset{dl}{\mathrm{RCHO}} + \underset{d\text{ or }l}{\mathrm{R'NH_3SO_3H}} \longrightarrow \underset{dl\ dl}{\mathrm{RCHOHSO_3}}\underset{d\text{ or }l}{\mathrm{H_3NR'}}$$

Whether or not all four isomers are formed is of minor significance since the success in resolution will depend upon the ease of isolation of a single optically pure product. If this could be accomplished, a relatively simple method of resolving racemic aldehydes and ketones would be available.

Woodward, Kohman and Harris[4] have enumerated the known resolving reagents for ketones and aldehydes, most of which suffer the disadvantages of difficulty in preparation and of failure to give crystalline derivatives with many carbonyl compounds. They proposed a new reagent *l*-menthyl N-aminocarbamate, which was used by them merely to resolve *dl*-camphor, but which probably will prove to be a much more satisfactory general reagent than any of the others. Sobotka,

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[1] An abstract of a thesis submitted in partial fulfillment of requirements for the degree of Doctor of Philosphy, 1943.

[2] Adams and Lipscomb, THIS JOURNAL, **70**, 519 (1948).

[3] Bright and Jasper, *ibid.*, **65**, 1262 (1943).

[4] Woodward, Kohman and Harris, *ibid.*, **63**, 120 (1941).

et al.,[5] have employed this reagent successfully in the resolution of *dl*-α-ionone.

Of the three optically active amines thus far studied, the two forms of α-phenethylamine were found to be very satisfactory, particularly with respect to the formation and purification of the bisulfites and the adducts with aldehydes and ketones. *l*-Menthylamine and *d*-β-naphthol phenylaminomethane were employed with indifferent success.

When the bisulfite addition compound of *d*-α-phenethylamine and *dl*-3-methylcyclohexanone was crystallized four times from ethanol an optically pure fraction was obtained in 29% yield. This salt was decomposed and the ketone converted to a semicarbazone, $[\alpha]^{20}D$ −21.0°. Adams, Smith and Loewe[6] previously reported a value of −20.7° for the *d*-3-methylcyclohexanone derivative. When the *l*-α-phenethylamine bisulfite addition compound of the *dl*-ketone was treated in a similar manner, the semicarbazone of *l*-3-methylcyclohexanone was isolated.

p-*s*-Butylbenzaldehyde was prepared in yields of 66% from N-methylformanilide and the aryl lithium compound that resulted from the action of lithium on *p*-iodo-*s*-butylbenzene.[7] The bisulfite of *d*-α-phenethylamine formed a well-crystallized product with *p*-*s*-butylbenzaldehyde and a constant melting fraction amounting to 40–48% of the total mixture was isolated. This may indicate that a large portion of the crude reaction product consisted primarily of a single compound. However, decomposition of the salt, gave a *s*-butylbenzaldehyde of such low rotation, $[\alpha]^{33}D$ −0.19°, semicarbazone $[\alpha]^{28}D$ −2.3° that the effectiveness of the resolution is in doubt. The salt may have been a compound composed of two diastereoisomers and only partial resolution was thus realized.

l-Menthylamine bisulfite with *p*-*s*-butylbenzaldehyde yielded a salt which appeared to be pure but, upon decomposition, only optically inactive aldehyde was recovered. This same aldehyde reacted with *d*-β-naphthol phenylaminomethane bisulfite abnormally to form a Schiff base instead of the desired addition compound. The Schiff base is a well-crystallized and easily purified substance with a high optical rotation, $[\alpha]^{30}D$ +240°. This type of Schiff base may offer a convenient intermediate for resolution of certain aldehydes and possibly ketones and is being explored. Sobotka, *et al.*,[5] refer to their attempts (unpublished) to resolve α-phenylpropanol with *d*-β-naphthol phenylaminomethane. The regeneration of the aldehyde in optically active form was unsuccessful because of the conditions of hydrolytic scission. This particular aldehyde is prone to racemization through enolization induced by the reagents used.

An improved synthesis for *dl*-β-methylhydrocinnamaldehyde[8] was developed. β-Bromoisopropylbenzene[9,10] was prepared in 60% yields by the action of allyl bromide on benzene in the presence of sulfuric acid. When the Grignard reagent was formed and allowed to react with N-methylformanilide, there was isolated 35% of the theoretical amount of β-methylhydrocinnamaldehyde. The crude product that resulted from the action of *d*-α-phenethylamine bisulfite on this racemic aldehyde yielded after one recrystallization a fraction $[\alpha]^{32}D$ −20.7°. This fraction was decomposed and the resulting aldehyde was converted to the optically active 2,4-dinitrophenylhydrazone, $[\alpha]^{27}D$ −39.6°. The enantiomorph was obtained by the use of the *l*-amine bisulfite in a similar series of reactions.

A quantitative procedure for the determination of sulfur in these addition compounds has been investigated. The "sulfites" and "bisulfites" first reported by Schiff[11] were analyzed for sulfur gravimetrically. He reported that an iodine titration method gave irreproducible results. Since the initial work of Ripper,[12] a great deal has been done on the quantitative determination of aldehydes by means of sodium bisulfite. In a comparison of the modified Ripper method with the excess iodine method, Parkinson and Wagner[13] reported that in general the latter was superior.

Notwithstanding the fact that the reverse reaction of decomposition was involved in the present investigation, the excess iodine method was chosen as a basis for the determination of sulfur. Eventually, a procedure was developed which gave excellent results. The sample was decomposed with aqueous alkali and the solution was poured into water containing a 10% excess of

$$RCHOHSO_3H_3NR' + 2OH^- \longrightarrow RCHO + R'NH_2 + SO_3^= + 2H_2O$$

standard iodine and a slight excess of acid. Backtitration with standard sodium thiosulfate followed immediately. Although several of the addition compounds listed in Table I gave rather poor sulfur analyses, this was undoubtedly due to the difficulty encountered in preparing a pure analytical sample.

Experimental

Amine Bisulfite Addition Compounds.—The following general procedure was adopted for the formation of the amine bisulfite addition compounds listed in Table I. Sulfur dioxide was bubbled through a mixture of amine (0.10 mole) and ether (25 ml.) that contained a slight excess of water (0.11 mole.) The introduction of sulfur dioxide was continued until the initially formed solid was replaced by a homogeneous yellow liquid. This bisulfite solution was poured into an excess (0.20 mole) of the carbonyl compound. Immediately the solution was decolorized, sulfur dioxide was evolved, the reaction mixture became very warm and soon solidified.

It was found more convenient to use ethanol rather than ether in the preparation of the β-naphthol phenyl-

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[5] Sobotka, Block, Cahnmann, Feldbau and Rosen, THIS JOURNAL, **65**, 2061 (1943).

[6] Adams, Smith and Loewe, *ibid.*, **64**, 2087 (1942).

[7] Boedtker, *Bull. soc. chim. France*, [4] **45**, 645 (1929).

[8] v. Braun, Grabowski and Kirchbaum, *Ber.*, **46**, 1266 (1913).

[9] Truffault, *Compt. rend.*, **202**, 1286 (1936).

[10] W. J. Shenk, Jr., private communication.

[11] Schiff, *Ann.*, **140**, 125 (1866).

[12] Ripper, *Monatsh.*, **21**, 1079 (1900).

[13] Parkinson and Wagner, *Ind. Eng. Chem.*, *Anal. Ed.*, **6**, 433 (1934).

TABLE I

AMINE BISULFITE ADDITION COMPOUNDS

Amine	M. p., °C.	Sulfur, %		M. p., °C.	Sulfur, %		M. p., °C.	Sulfur, %		M. p., °C.	Sulfur, %	
		Calcd.	Found		Calcd.	Found		Calcd.	Found		Calcd.	Found
	Acetone			Cyclopentanone			Cyclohexanone			3-Methylcyclohexanone		
Benzyl-	93–94	12.1	13.0	109–110	11.8	11.7	128–128.5	11.0	11.1	127–128	10.6	10.6
dl-α-Phenethyl-	91–93	Unstable		115–116	11.1	11.1	128–129	10.6	10.6	122–125	10.0	10.2
β-Phenethyl-	110–111	12.1	12.3	119–119.5	11.0	11.1	131–132	10.6	10.6	124–126	10.1	10.2
dl-*s*-Butyl-	55–65	Unstable		108–110	13.1	13.4	140–142	12.5	12.6	128–129	11.9	12.0
Heptyl-				110–111	11.4	11.4						
dl-β-Naphthol phenylaminomethane	117–118	8.62	8.23	126–127	7.40	7.71	142–142.5	7.38	7.45	162–164	7.13	7.23
	Benzaldehyde			Heptaldehyde			Isoveraldehyde			*n*-Valeraldehyde		
Benzyl-	119–120	11.0	10.8	104–105	10.3	10.6	105–110	10.6	11.6	107–108	11.1	11.6
dl-α-Phenethyl-	105–106	10.3	10.4	104–106	10.3	10.1	115–116	10.4	11.1	104–106	9.82	11.1
β-Phenethyl-	121–122	10.3	10.4	128–129	10.3	10.1	109–112	10.1	11.1	106–108	10.1	11.1
dl-*s*-Butyl-	110–111	12.1	12.2	91–96	Unstable		118–122	12.0	13.3	Decomposed		
Heptyl-	106–107	10.6	10.4									
dl-β-Naphthol phenylaminomethane	124–139	6.97	7.32	141–142	7.03	7.19	143–144	6.59	7.67	139–140	6.58	7.67

aminomethane bisulfite addition compounds. In all cases the product was collected by filtration and washed with ether before it was recrystallized from either absolute ethanol or an ethanol–water mixture.

Analytical Method for the Determination of Sulfur.—The sample (0.3 g.) of amine bisulfite addition compound was weighed into a small erlenmeyer flask and treated with 10 ml. of water. It was immaterial whether complete solution was effected. After 5 ml. of 5% aqueous potassium hydroxide had been added, the flask was stoppered and allowed to stand at room temperature for one hour. It was found that this time could be shortened considerably without affecting the results. The alkaline reaction mixture was poured into an aqueous solution of a 10% excess of standard iodine and just enough 5% sulfuric acid to neutralize the alkali used originally and also the amine formed by the decomposition of the sample. One drop excess of the acid solution was then added, and the iodine titrated with standard sodium thiosulfate. Analyses were carried out in which the sample was heated at 50° with alkali. This modification gave excellent results if the flask was swept out with nitrogen before it was stoppered and heated.

***d*-α-Phenethylamine Bisulfite Addition Compound of *d*-3-Methylcyclohexanone.**—The bisulfite solution was formed in the usual manner from 12 g. of *d*-α-phenethylamine,[14] 2.7 g. of water and 20 ml. of ether. To the viscous, yellow liquid was added 22 g. of *dl*-3-methylcyclohexanone in one portion. Immediately, bubbles of sulfur dioxide were evolved and much heat was produced. Crystallization was induced by scratching and cooling the solution, and after the reaction mixture had solidified ether was added and the paste broken down with a spatula. A yield of 30 g. (96%) of the *d*-α-phenethylamine bisulfite addition compound of *dl*-3-methylcyclohexanone, m.p. 106–113°, resulted. Four recrystallizations of this racemic addition compound from the minimum amount of absolute ethanol at 40° yielded 4.3 g. (29%) of the *d*-α-phenethylamine bisulfite addition compound of *d*-3-methylcyclohexanone, m. p. 126–127°.

Anal. Calcd. for $C_{15}H_{25}O_4NS$: C, 57.11; H, 7.99. Found: C, 57.20; H, 7.24. *Rotation.* 0.1068 g. made up to 5 ml. with water at 26° gave α_D + 0.03°; *l*, 1; $[\alpha]^{26}_D$ + 1.4°.

Semicarbazone of *d*-3-Methylcyclohexanone.[6]—A sample of 0.8 g. of the purified addition compound was decomposed with 10 ml. of 20% hydrochloric acid at 45°. The ketone was extracted with ether, and converted to the semicarbazone in the usual manner. This derivative was recrystallized several times from aqueous ethanol, m.p. 183–183.5°.

Anal. Calcd. for $C_8H_{15}ON_3$: C, 56.78; H, 8.94. Found: C, 57.04, H, 9.09. *Rotation.* 0.0738 g. made up to 5 ml. with ethanol at 20° gave α_D −0.31°; *l*, 1; $[\alpha]^{20}_D$ −21.0°.

***l*-α-Phenethylamine Bisulfite Addition Compound of *l*-3-Methylcyclohexanone.**—Identically the same procedure was used for the formation of the *l*-amine bisulfite and the corresponding addition compound as was used in the case of the *d*-amine. From 12 g. of *l*-α-phenethylamine and 22 g. of *dl*-3-methylcyclohexanone was obtained 29 g. (93%) of the bisulfite addition compound, m. p. 106–113°. The crude material was recrystallized four times from the minimum amount of absolute ethanol at 40°, and 3.9 g. (27%) of the pure bisulfite addition compound of *l*-α-phenethylamine and *l*-3-methylcyclohexanone was removed by filtration, m. p. 126–127°.

Anal. Calcd. for $C_{15}H_{25}O_4NS$: C, 57.11; H, 7.99. Found: C, 57.16; H, 8.02. *Rotation.* 0.2137 g. made up to 5 ml. with water at 28° gave α_D −0.06°; *l*, 1; $[\alpha]^{28}_D$ −1.4°.

Semicarbazone of *l*-3-Methylcyclohexanone.—This compound was prepared from 0.8 g. of the *l*-amine bisulfite addition compound of the *l*-ketone in the same manner as its stereoisomer. After the product had been recrystallized several times from aqueous ethanol the semicarbazone of *l*-3-methylcyclohexanone was pure, m. p. 183–183.5°.

Rotation. 0.0840 g. made up to 5 ml. with ethanol at 20° gave α_D + 0.35°; *l*, 1; $[\alpha]^{20}_D$ +20.8°.

***p*-Iodo-*s*-butylbenzene.**[7]—A mixture of 160 g. of *s*-butylbenzene, 127 g. of iodine, 39 g. of iodic acid, 50 ml. of water and 350 ml. of glacial acetic acid was allowed to reflux in a 1-l. flask (ground glass connections) equipped with a water-cooled condenser. Heating was continued for several hours and then the solution was decanted from the excess iodine into an equal volume of water. The lower layer was separated and boiled with an equal volume of methanolic potassium hydroxide for thirty minutes. The lower layer was separated, washed with water, dried over anhydrous magnesium sulfate, filtered and distilled *in vacuo*. A total of 84 g. (53%) of *s*-butylbenzene was recovered from the fore-run, and 81 g. (55%, based on *s*-butylbenzene actually consumed) of *p*-iodo-*s*-butylbenzene was obtained, b. p. 115–118° (12 mm.); n^{30}_D 1.5642.

***p*-*s*-Butylbenzaldehyde.**—The technique of Adams and Carlin[15] for the preparation of aldehydes from aryl lithium

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[14] Ingersoll, Org. Syntheses Coll. Vol. II, p. 506.

[15] Adams and Carlin, THIS JOURNAL, **65**, 360 (1943).

compounds and N-methylformanilide[16] was used. A 500-ml. three-necked round-bottomed flask was provided with a mercury-sealed Hershberg wire stirrer, a reflux condenser, a nitrogen inlet tube and an outlet tube fitted with a stopcock. The stirrer and condenser mounts were each equipped with ground glass joints, and the top of the reflux condenser was made so that a special ground glass joint dropping funnel could be inserted. A rapid stream of dry, oxygen-free nitrogen was passed through the flask, which contained 25 ml. of anhydrous ether; and, simultaneously, 2.78 g. of lithium was cut into small pieces and allowed to fall through the central neck. The rate of flow of nitrogen was reduced to one bubble (through a 6″ column of sulfuric acid) per second, the stirrer started and a solution of 46 g. of *p*-iodo-*s*-butylbenzene in 60 ml. of anhydrous ether was added at such a rate that refluxing was maintained throughout the addition.

The solution was stirred for one hour, and then a mixture of 26 g. of N-methylformanilide with an equal volume of ether was added dropwise. Enough heat was generated to cause the solvent to reflux. The solution was stirred overnight and then poured into a mixture of 200 ml. of water, 11 ml. of concentrated sulfuric acid and 100 g. of ice. The ether layer was separated and the aqueous layer was extracted three times with 100-ml. portions of ether. The combined ether extract was dried over anhydrous sodium sulfate, filtered and the solvent removed. The fraction that boiled at 116–118° (15 mm.) was *p*-*s*-butylbenzaldehyde, $n^{25}\mathrm{D}$ 1.5240; yield 19.8 g. (66%).

***d*-α-Phenethylamine Bisulfite Addition Compound of *l*-*p*-*s*-Butylbenzaldehyde.**—Sulfur dioxide was passed into a mixture of 25.4 g. of *d*-α-phenethylamine, 4.0 g. of water and 75 ml. of ether. The amine bisulfite solution was poured into 44 g. of slightly yellow *dl*-*p*-*s*-butylbenzaldehyde. After the reaction mixture had solidified, 300 ml. of ether was added, the flask stoppered and the mixture allowed to stand overnight in the ice-box. The addition compound was collected on a filter and washed with ether until white. The yield was 71 g. (92%) of crude product, m. p. 90–95°. A solution of 20 g. of the above addition product in 350 ml. of chloroform at 45° was allowed to stand at room temperature but no crystals appeared. After addition of 200 ml. of dry ether, the solution was placed in an ice-box overnight. It thus yielded 4 g. of white crystals, m. p. 103–104°. Further recrystallization from either chloroform or ethanol failed to yield a fraction of higher melting point.

Anal. Calcd. for $C_{19}H_{27}O_4NS$: S, 8.79. Found: S, 8.68. *Rotation.* 0.3911 g. made up to 25 ml. with ethanol at 27° gave α_D + 0.11°; *l*, 2; $[\alpha]^{27}\mathrm{D}$ + 3.52°.

***l*-*p*-*s*-Butylbenzaldehyde.**—A sample of 10 g. of the addition compound from *d*-α-phenethylamine bisulfite and *l*-*p*-*s*-butylbenzaldehyde, m. p. 103–104°, was decomposed with 75 ml. of 5% hydrochloric acid, and the aldehyde extracted with ether. The combined ether extract was dried over anhydrous magnesium sulfate, filtered and distilled under diminished pressure. The yield of *l*-*p*-*s*-butylbenzaldehyde, b. p. 115–116° (13 mm.), $n^{25}\mathrm{D}$ 1.5247, was 2.6 g. (59%).

Anal. Calcd. for $C_{11}H_{14}O$: C, 81.44; H, 8.69. Found: C, 81.16; H, 8.94. *Rotation.* 2.1345 g. made up to 6.63 ml. with ethanol at 33° gave α_D −0.06°; *l*, 1; $[\alpha]^{33}\mathrm{D}$ −0.19°.

Semicarbazone of *l*-*p*-*s*-Butylbenzaldehyde.—A small sample of addition compound, m. p. 103–104°, was decomposed with 15% sulfuric acid. The aldehyde was recovered by an ether extraction and converted to the semicarbazone. Two recrystallizations from ethanol yielded a white product, m. p. 206–207°.

Anal. (racemic modification) Calcd. for $C_{12}H_{17}ON_3$: C, 65.73; H, 7.81. Found: C, 65.63; H, 7.91. *Rotation.* 0.0765 g. made up to 10 ml. with ethanol at 28° gave α_D −0.01°; *l*, 1; $[\alpha]^{28}\mathrm{D}$ −1.3°.

Reaction of *d*-β-Naphthol Phenylaminomethane Bisulfite and *dl*-*p*-*s*-Butylbenzaldehyde.—In a 125-ml. erlenmeyer flask which contained 15 ml. of a 50% mixture of ethanol and ether and 3.0 g. of water, 5 g. of *d*-β-naphthol phenylaminomethane, $[\alpha]^{28}\mathrm{D}$ + 45.8°, was added. Sulfur dioxide was introduced until the solid dissolved and the solution had a characteristic yellow color. To this bisulfite solution was added 5 g. of *dl*-*p*-*s*-butylbenzaldehyde. There was no evidence of reaction after the mixture had stood in the ice-box for a week, but when the flask was kept at room temperature for two days, beautiful acicular crystals appeared, m. p. 164–165°, which may be recrystallized from ethanol. Since this product did not decolorize iodine, it was assumed that it was not a bisulfite addition compound.

Rotation. 0.1069 g. made up to 10 ml. with chloroform at 30° gave α_D + 2.56°; *l*, 1, $[\alpha]^{30}\mathrm{D}$ +240°.

Since it was thought the product might be a Schiff base it was synthesized by a direct method. To a solution of 0.2 g. of *d*-β-naphthol phenylaminomethane in 15 ml. of ethanol was added a few drops of *dl*-*p*-*s*-butylbenzaldehyde and one drop of 10% aqueous sodium hydroxide. The precipitate, which formed immediately, was recrystallized several times from ethanol, m. p. 166–166.5°. The mixture of this product and the one obtained above showed no depression when melted.

Anal. Calcd. for $C_{28}H_{27}ON$: C, 85.46; H, 6.92. Found: C, 85.31; H, 7.09.

***l*-Menthylamine Bisulfite Addition Compound of *dl*-*p*-*s*-Butylbenzaldehyde.**—Sulfur dioxide was passed into a mixture of 14.3 g. of *l*-menthylamine (Eastman Kodak Co.), 3.0 g. of water and 25 ml. of ether. When the formation of the amine bisulfite was complete, 18 g. of *dl*-*p*-*s*-butylbenzaldehyde was added. Although there was very little heat effect, the reaction mixture soon solidified. The product was collected on a filter and washed thoroughly with absolute ether, m. p. 109–114°. The yield was 11.6 g. (32%).

Rotation. 0.2220 g. made up to 25 ml. with ethanol at 27° gave α_D −0.21°; *l*, 2; $[\alpha]^{27}\mathrm{D}$ −11.6°.

A solution of 11 g. of the crude product from the *d*-amine bisulfite and the *dl*-aldehyde in 50 ml. of absolute ethanol at 50° was allowed to stand at room temperature. When this solution was filtered, 7 g. of addition compound, m. p. 112–115°, was obtained. This fraction was dissolved in the minimum amount of ethanol at 45° and the resulting solution again allowed to stand at room temperature. A crop that weighed 1.02 g. was isolated, m. p. 117–118°. The semicarbazone of the aldehyde obtained by decomposition of this fraction was optically inactive.

Anal. Calcd. for $C_{21}H_{37}O_4NS$: S, 8.02. Found: S, 7.80. *Rotation.* 0.1375 g. made up to 10 ml. with ethanol gave α_D −0.16; *l*, 1; $[\alpha]^{33}\mathrm{D}$ −11.6°.

β-Bromoisopropylbenzene.[9,10]—A 1-l., three-necked flask was fitted with a mercury-sealed Hershberg wire stirrer, a water-cooled condenser and a dropping funnel. Into the flask was introduced 420 ml. of benzene (dried over anhydrous calcium chloride) and 81.5 ml. of concentrated sulfuric acid. The stirrer was started and the temperature maintained at 40 ± 2° throughout the addition of 175 g. (1.45 moles) of allyl bromide. Vigorous stirring was continued for five hours and then the reaction mixture was allowed to stand overnight. The benzene layer was separated, washed consecutively with 30 ml. of concentrated sulfuric acid, 50 ml. of water which was saturated with sodium sulfate, 50 ml. of 10% aqueous sodium hydroxide and finally with 50 ml. of water. The benzene layer was placed in a 1-l. round-bottomed flask arranged for steam distillation. When no more oil appeared in the condensate, the layers were separated and the water layer extracted with 100 ml. of benzene. The combined organic extract was dried over anhydrous magnesium sulfate, filtered and the solvent removed. The yield of β-bromoisopropylbenzene was 166 g. (58%); b. p. 109–111° (16 mm.); $n^{25}\mathrm{D}$ 1.5462.

β-Methylhydrocinnamaldehyde.[8]—The Grignard reagent was formed from 6.0 g. of magnesium, 51 g. of β-bromoisopropylbenzene and 100 ml. of dry ether. After this solution was heated under reflux for one hour, 35 g. of

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(16) Fieser and Jones, *Org. Syntheses*, **20**, 66 (1940).

N-methylformanilide in an equal volume of ether was added. A vigorous reaction ensued, and when the addition was complete the solution was heated under reflux for two hours. The Grignard reaction mixture was decomposed with 100 ml. of 5 *N* sulfuric acid. When all of the solid had dissolved, the ether layer was separated and shaken for thirty minutes with an equal volume of saturated sodium bisulfite. The sodium bisulfite addition compound was collected on a filter and washed with ether. Upon decomposition of the salt with aqueous sodium bicarbonate, a yield of 13 g. (35%) of *dl*-β-methylhydrocinnamaldehyde, b. p. 92–93° (14 mm.), n^{30}_D 1.5106, was obtained.

Anal. Calcd. for $C_{10}H_{12}O$: C, 81.04; H, 8.16. Found: C, 80.08; H, 8.56.

The 2,4-dinitrophenylhydrazone of *dl*-β-methylhydrocinnamaldehyde was prepared in the usual manner. The crude product was dissolved in ether and extracted with three portions of 1:1 hydrochloric acid. The ether layer was separated, the solvent removed and the residue recrystallized several times from ethanol; yellow crystals, m. p. 123–123.5°.

Anal. Calcd. for $C_{16}H_{16}O_4N_4$: C, 58.53; H, 4.91. Found: C, 58.35; H, 5.09.

_d_-α-Phenethylamine Bisulfite Addition Compound of _l_-β-Methylhydrocinnamaldehyde.—The amine bisulfite was formed by the action of sulfur dioxide on 4.5 g. of *d*-α-phenethylamine, 1.0 g. of water and 15 ml. of ether. When bisulfite formation was complete, 6.0 g. of crude *dl*-β-methylhydrocinnamaldehyde was added in one portion. The solid addition product was isolated by filtration and washed with ether, m. p. 95–115°; yield 7.0 g. (54%).

All of the crude bisulfite addition compound of the *d*-amine and the *dl*-aldehyde was dissolved in 30 ml. of 95% ethanol at 45°. When the solution was allowed to stand at room temperature, 1.78 g. of glistening, white crystals were isolated, m. p. 131.5–132°.

Anal. Calcd. for $C_{18}H_{25}O_4NS$: S, 9.12. Found: S, 9.20. *Rotation.* 0.0870 g. made up to 5 ml. with ethanol at 32° gave α_D −0.36; *l*, 1; $[\alpha]^{32}_D$ −20.7°.

2,4-Dinitrophenylhydrazone of _l_-β-Methylhydrocinnamaldehyde.—Approximately 0.5 g. of the first fraction of the *d*-amine bisulfite addition compound of *l*-β-methylhydrocinnamaldehyde was decomposed and converted to the 2,4-dinitrophenylhydrazone, which was purified in the same manner as the corresponding derivative of the *dl*-aldehyde. A yellow crystalline product was isolated, m. p. 97–97.5°.

Rotation. 0.0681 g. made up to 10 ml. with chloroform at 27° gave α_D −0.27°; *l*, 1; $[\alpha]^{27}_D$ −39.6°.

_l_-α-Phenethylamine Bisulfite Addition Compound of _d_-β-Methylhydrocinnamaldehyde.—Sulfur dioxide was passed into 4.8 g. of *l*-α-phenethylamine, 1.0 g. of water and 10 ml. of ether. To the resulting solution 5.0 g. of pure *dl*-β-methylhydrocinnamaldehyde, b. p. 93–94° (16 mm.), was introduced. The reaction mixture solidified when allowed to stand in the ice-box for a few hours and the product was filtered, m. p. 88–115°; yield, 7.2 g. When a mixture of 6 g. of the bisulfite addition compound of the *l*-amine and the *dl*-aldehyde in 20 ml. of absolute ethanol and 0.25 ml. of water at 45° was allowed to stand at room temperature, 1.03 g. of acicular crystals were formed, m. p. 130–131°.

Anal. Calcd. for $C_{18}H_{25}O_4NS$: S, 9.12. Found: S, 9.05. *Rotation.* 0.1411 g. made up to 10 ml. with ethanol at 32° gave α_D + 0.30; *l*, 1; $[\alpha]^{32}_D$ +21.3°.

Summary

1. Several primary amines were converted to their bisulfites and these were added to various aldehydes and ketones. The adducts were usually white crystalline products, melting in the range 100–160°, and readily purified from ethanol or ethanol–water mixtures.

2. The optically active forms of α-phenethylamine were converted to their bisulfites and when they reacted with *dl*-3-methylcyclohexanone or *dl*-β-methylhydrocinnamaldehyde yielded products from which pure salts were isolated. Upon decomposition, the optically active aldehyde or ketone resulted. Only partial resolution of *dl*-*p*-*s*-butylbenzaldehyde was affected in the same manner.

3. *d*-β-Naphthol phenylaminomethane and *l*-menthylamine bisulfites did not give satisfactory results in the resolution of the three aldehydes and ketones used.

4. *p*-*s*-Butylbenzaldehyde was prepared from the aryl lithium compound, resulting from the action of lithium on *p*-iodo-*s*-butylbenzene, and N-methylformanilide. A new synthesis of β-methylhydrocinnamaldehyde from the Grignard of β-bromoisopropylbenzene and N-methylformanilide appears to be an improvement over those previously used.

5. A satisfactory quantitative method for determination of sulfur in the adducts of amine bisulfites and aldehydes or ketones is described.

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