sample melted at 160.5–161° after recrystallization from acetone–hexane.

Anal. Calcd. for $C_{17}H_{11}O_3$: C, 74.42; H, 8.08. Found: C, 74.37; H, 8.08.

2-Acetyl-1,8-dimethyl-7-methoxy-1,2,3,4,4a,9a-hexahydrofluorene (XXIV).—A solution of methyllithium was prepared from methyl iodide (26 g.) and lithium (2.84 g. in dry ether (100 ml.). The filtered solution of methyllithium was added dropwise to a solution of the acid from the previous experiment (10 g.) in anhydrous 1,2-dimethoxyethane (200 ml.). Stirring was continued for 12 hr. and then the mixture was hydrolyzed by addition of water. The organic solvents were distilled and the product extracted with ether. Evaporation of the ether left a residue (8.84 g.) which immediately crystallized. Recrystallization from methanol afforded the pure ketone which melted at 116.5–120°. From the aqueous alkaline solution there was recovered by acidification about 10% of the starting acid.

Anal. Calcd. for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.62; H, 9.01.

The 2,4-dinitrophenylhydrazone was obtained as an orange, microcrystalline solid after recrystallization from ethyl acetate, m.p. 233–234°.

Anal. Calcd. for $C_{24}H_{28}O_5N_4$: C, 63.70; H, 6.24. Found: C, 63.50; H, 6.29.

1,8-Dimethyl-2-hydroxymethyl-7-methoxy-1,2,3,4,4a,9a-hexahydrofluorene (XXV).—Ester XXIII (19.8 g.) was dissolved in anhydrous ether (50 ml.) and added dropwise to a stirred suspension of lithium aluminum hydride (2.5 g.) in anhydrous ether (200 ml.). The reaction mixture was processed by addition of ethyl acetate and water and then the product extracted with ether. Evaporation of the ether left a viscous liquid (12 g., 70%). A pure sample of this material was prepared *via* the acid phthalate and then by evaporative distillation at 150°/0.04 mm.

Anal. Calcd. for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.19; H, 9.25.

The acid phthalate was prepared by refluxing crude alcohol XXV (34 g.) with a solution of phthalic anhydride (19.5 g.) in anhydrous toluene (200 ml.) for 2 hr. The crude product was taken up in ether and the acid phthalate extracted with 5% sodium carbonate solution; considerable (5.6 g.) nonalcoholic material remained in the ether solution. Acidification of the alkaline solution and crystallization from acetone–hexane yielded 38 g. (71%) of the acid phthalate which melted at 170–170.5° after recrystallization from dilute ethanol.

Anal. Calcd. for $C_{25}H_{22}O_5$: C, 73.51; H, 6.91. Found: C, 73.29; H, 6.95.

1,8-Dimethyl-7-methoxy-2-methylene-1,2,3,4,4a,9a-hexahydrofluorene (XXV).—Alcohol XXV (12 g.) was converted to the methyl xanthate by the procedure of Whitmore and Simpson.[22] The crude xanthate (15.7 g., 97%) was heated under nitrogen at 236–240° for 5 hr. The reaction product was taken up in ether and the solution washed with 10% sodium hydroxide solution, saturated lead acetate, and water. The dried solution was concentrated and chromatographed on alumina. Hexane eluted the desired olefin (3.3 g.) having a strong bond in the infrared spectrum at 11.30 μ. Further elution with benzene eluted a pale yellow solid (3.6 g.) and finally chloroform removed some polymeric material (3.4 g.).

The olefin crystallized when triturated with methanol and after recrystallization from this solvent melted at 83–85°.

Anal. Calcd. for $C_{17}H_{22}O$: C, 84.25; H, 9.15. Found: C, 84.12; H, 9.05.

The pale yellow solid was purified by recrystallization from acetone–methanol and melted at 194–196°, λ_{max}^{EtOH} 220 mμ, 276 mμ.

Anal. Calcd. for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.40; H, 7.72.

A pyrolysis of 93 g. of xanthate at 235–275° yielded only 40.8 g. of this same material, 1,2,8-trimethyl-7-methoxyfluorene (XXVIII).

1,8-Dimethyl-7-methoxy-1,2,3,4,4a,9a-hexahydrofluoren-2-one (XXVII).—A solution of olefin XXVI (1.8 g.) in methylene chloride (100 ml.) was cooled to 0° and ozone introduced until it was no longer absorbed. Zinc dust (2 g.) and acetic acid (10 ml.) were added and the solution warmed to remove the methylene chloride. The solution was filtered and water was added. The product was removed with ether and from the ether extract there was obtained 1.48 g. (81%) of ketone XXVII which melted at 131–132° after recrystallization from methanol.

Anal. Calcd. for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.50; H, 8.32.

(22) F. C. Whitmore and C. T. Simpson, *J. Am. Chem. Soc.*, **55**, 3809 (1933).

Desulfurization with Raney Nickel. II. Sulfonamides[1,2]

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Several representative alkyl halides have been condensed with sodium saccharin and the resulting 1,1,3-trioxo-2-alkylbenzo[*d*]isothiazolines (Ia–f) desulfurized using Raney nickel. Employing common desulfurization methods, the reduction reaction was found to give cyclohexylcarboxamides (*e.g.*, IV) and under very mild conditions, benzamides (Va–e). In comparative alkylation reactions the sodium derivatives of benzenesulfonylbenzamide (IIa), N,N-dibenzenesulfonyloxamide (IIIa) and dibenzenesulfonamide (VIb) were, in general, less satisfactory than sodium saccharin. Reaction between benzenesulfonamide and dimethylformamide in the presence of either benzenesulfonyl chloride, benzoyl chloride, carbobenzoxy chloride, or phosphorus oxychloride was shown to yield N,N-dimethyl-N′-benzenesulfonylformamidine (VII).

Among the various organo-sulfur compounds which have been subjected to desulfurization with Raney nickel, those containing bivalent sulfur are most frequently represented. For example, over three hundred and fifty thioketals[3a] and thiophenes[3b]

(1) A review of desulfurization with Raney nickel by G. R. Pettit and E. E. van Tamelen, "Organic Reactions," Vol. 12, J. Wiley & Sons, Inc., New York, N. Y., 1962, p. 356, may be considered part I of this study.

(2) This investigation was supported in part by National Science Foundation Research Grants G-9585 and G-19500 and by the Upjohn Co., Kalamazoo, Mich.

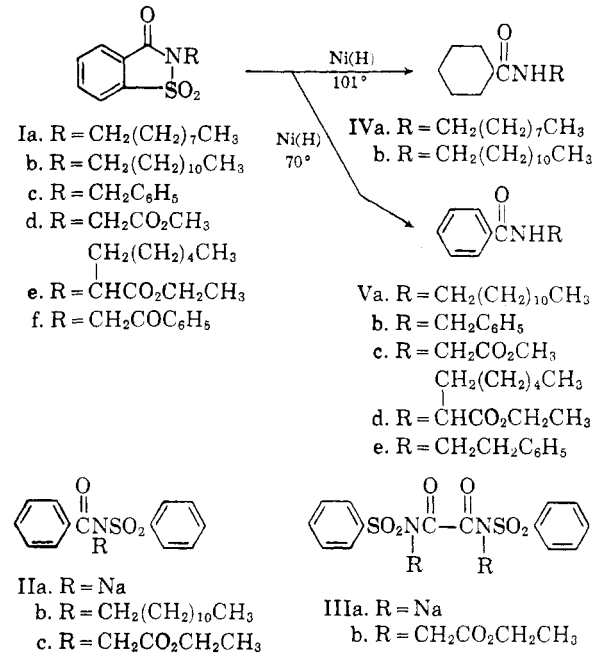
(3) For recent examples refer to (a) P. M. Rao and H. R. Gollberg, *Chem. Ind.* (London), 1317 (1961); H. P. Gervais and A. Rassat, *Bull. soc. chim. France*, 743 (1961); K. Kotera, *Tetrahedron*, **12**, 240 (1961); J. C. Craig, D. M. Temple, and B. Moore, *Australian J. Chem.*, **14**, 84 (1961); L. F. Fieser, C. Yuan, and T. Goto, *J. Am. Chem. Soc.*, **82**, 1996 (1960); and (b) Ya. L. Gol'dfarb and B. P. Fabrichnyi, *Zh. Obshch. Khim.*, **31**, 2057 (1961); Ya. L. Gol'dfarb and S. Z. Taits, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 1698 (1960).

have been desulfurized using Raney nickel. While the reaction has proved valuable and received extensive study in a variety of synthetic and structural problems involving intermediates of these types, desulfurization of, *e.g.*, sulfonamides has remained essentially unexplored.[1,4]

In principle, desulfurization of appropriate sulfonamides would be expected to provide a practical route to certain amides and amines.[5] The present study was primarily concerned with evaluating Raney nickel desulfurization of N-alkylsaccharin derivatives (*cf.*, I) as a method for converting alkyl halides to benzamides. The ready alkylation of sodium saccharin by normally reactive alkyl halides in dimethylformamide solution[6] indicated that the over-all reaction sequence to benzamides might proceed in good yield.

In agreement with our previous experience[6a] a variety of 2-alkylated 1,1,3-trioxobenzo[*d*]isothiazolines (Ia–f) were easily prepared. By contrast, alkylation of sodium benzenesulfonylbenzamide (IIa) or sodium N,N-dibenzenesulfonyloxamide (IIIa) with, for example, ethyl bromoacetate required more vigorous conditions and was generally less satisfactory.[7] Subsequent desulfurization studies were, therefore, limited to the more promising saccharin derivatives.

In earlier work[8] N-benzylsaccharin (Ic) was converted to N-benzylbenzamide in 78% yield employing aged (10 weeks old) W-4 Raney nickel in refluxing (13 hr.) ethanol. Similar treatment of the *n*-nonyl and *n*-dodecyl derivatives (Ia and Ib) using



Ia. R = $CH_2(CH_2)_7CH_3$
b. R = $CH_2(CH_2)_{10}CH_3$
c. R = $CH_2C_6H_5$
d. R = $CH_2CO_2CH_3$
e. R = $CH(CH_2)_4CH_3$ / $CHCO_2CH_2CH_3$
f. R = $CH_2COC_6H_5$

IVa. R = $CH_2(CH_2)_7CH_3$
b. R = $CH_2(CH_2)_{10}CH_3$

Va. R = $CH_2(CH_2)_{10}CH_3$
b. R = $CH_2C_6H_5$
c. R = $CH_2CO_2CH_3$
d. R = $CH(CH_2)_4CH_3$ / $CHCO_2CH_2CH_3$
e. R = $CH_2CH_2C_6H_5$

IIa. R = Na
b. R = $CH_2(CH_2)_{10}CH_3$
c. R = $CH_2CO_2CH_2CH_3$

IIIa. R = Na
b. R = $CH_2CO_2CH_2CH_3$

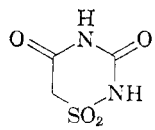
freshly prepared nickel (W-4) in dioxane unexpectedly[9] gave the corresponding cyclohexyl carboxamides (*e.g.*, IVb in 91% yield). Structures for these products were originally proposed on the basis of infrared spectral data and elemental analyses. Comparison with authentic specimens confirmed the course of reduction.

A more careful study of the desulfurization reaction using N-dodecylsaccharin (Ib) revealed that a 50-min. reaction period at 70° using freshly prepared W-2 Raney nickel would convert this sulfonamide to N-dodecylbenzamide (Va) in 95% yield. Somewhat longer (less than 6 hr.) periods in refluxing ethanol or dioxane using several active and acetone-deactivated[10] Raney nickels led to mixtures of both amides (IVb and Va). When a mixture of W-2 Raney nickel and N-dodecylbenzamide was heated (6 hr.) in refluxing dioxane the cyclohexyl amide (IVb) was formed in 92% yield. Thus, in the case of sulfonamide Ib, hydrogenation of the aromatic ring was not necessarily dependent on an intermediate in the actual desulfurization reaction.

Desulfurization of sulfonamides Ic–e, employing mild (50 min. at *ca.*, 70°) conditions, led to N-benzylbenzamide (Vb), N-benzoylglycine methyl ester[11] (Vc), and N-benzoyl-α-hexylglycine ethyl ester (Vd). However, desulfurization of phenacyl derivative If was accompanied by hydrogenolysis of the benzyl–oxygen bond. The product of this reaction was N-(2-phenylethyl)benzamide (Ve).

A more direct method for alkyl halide → amine transformation, based on hydrogenolysis of an N-

(4) Raney nickel desulfurization of two N-substituted benzylsulfonamides and the three cyclic amides (*i* and two derivatives) reported by G. W. Kenner and M. A. Murray, *J. Chem. Soc.*, S178 (1949), and P. N. Rylander and E. Campaigne, *J. Org. Chem.*, **15**, 249 (1950), appear to represent the only prior examples. A variety of other sulfonamide cleavage reactions have been reviewed by S. Searles and S. Nukina, *Chem. Rev.*, **59**, 1077 (1959). Hydrogenation of an olefinic sulfonamide over Raney nickel has been described by B. Helferich, R. Dhein, K. Geist, H. Jünger, and D. Wiehle, *Ann.*, **646**, 32 (1961).



(5) Furthermore, desulfurization of sulfonamides employing deuterized or tritiated Raney nickel should yield amides with one, and amines bearing two heavy hydrogen atoms specifically bonded to nitrogen. Applications of a similar technique to carbon labeling have been reported by D. K. Fukushima, S. Lieberman, and B. Praetz, *J. Am. Chem. Soc.*, **72**, 5205 (1950); N. P. Buu-Hoï, *Nature*, **180**, 385 (1957); and N. P. Buu-Hoï and N. Dat Xuong, *Compt. rend.*, **247**, 654 (1958).

(6) *Cf.* (a) H. L. Rice and G. R. Pettit, *J. Am. Chem. Soc.*, **76**, 302 (1954) and (b) L. M. Rice, C. H. Grogan, and E. E. Reid, *ibid.*, **75**, 4304 (1953).

(7) Stuart–Briegleb models of the sulfonamides indicated that alkylation of the open-chain amides (II and III) would be less favorable on steric grounds. However, the possibility of decreased basicity and a consequent decrease in nucleophilicity was considered more important.

(8) G. R. Pettit and M. G. Madore; see ref. 1, pp. 401 and 412.

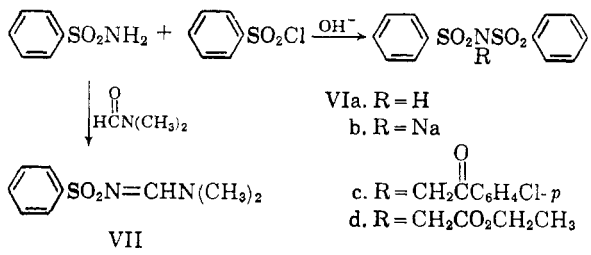
(9) Only several isolated cases of concomitant aromatic system hydrogenation during Raney nickel desulfurization have been observed; consult ref. 1, p. 362.

(10) For example see, H. J. Bestmann and H. Schulz, *Chem. Ber.*, **92**, 530 (1959); and G. B. Spero, A. V. McIntosh, and R. H. Levin, *J. Am. Chem. Soc.*, **70**, 1907 (1948).

(11) An interesting review of synthetic methods leading to glycine and derivatives has been prepared by J. P. Greenstein and M. Winitz, "Chemistry of the Amino Acids," Vol. 3, J. Wiley & Sons, Inc., New York, N. Y., 1961, p. 1961.

alkylated dibenzenesulfonamide (VI),[12] was next considered. An attempt to improve the original preparation[13] of dibenzenesulfonamide (VIa) by condensing benzenesulfonamide with benzenesulfonyl chloride in hot dimethylformamide gave instead a new substance, N,N-dimethyl-N′-benzenesulfonylformamidine (VII). The structure assigned formamidine VII was consistent with its elemental composition, infrared spectrum,[14] and production of benzenesulfonamide, formic acid, and dimethylamine during acid hydrolysis[15] with 10% hydrochloric acid. Repeating the reaction between benzenesulfonamide and dimethylformamide using either benzoyl chloride or carbobenzoxy chloride in place of benzenesulfonyl chloride again led to formamidine VII, although in lower yields. Substituting phosphorus oxychloride for the acid halides gave similar results.[16,17]

Eventual synthesis of dibenzenesulfonamide from benzenesulfonyl chloride and aqueous ammonia[18] provided a satisfactory route to sodium salt VIb. Alkylation of sodium dibenzenesulfonamide by *p*-chlorophenacyl bromide (*i.e.*, VIb → VIc) was easily accomplished in hot dimethylformamide. However, a similar reaction employing ethyl bromoacetate required addition of sodium iodide and gave only fair yields of glycine derivative VId. Attempts to condense amide VIb with, *e.g.*, dodecyl bromide, ethyl α-bromopropionate, or ethyl α-bromobutyrate were unsuccessful.[19] By this time, the inefficient nature of sodium dibenzenesulfonamide as starting material for a general preparative route to amines was established and further work in this area was discontinued.



The present study suggests that Raney nickel desulfurization of 1,1,3-trioxobenzo[*d*]isothiazolines to amide derivatives may occasionally be a useful alternative to the well known Gabriel[20] phthalimide procedure.

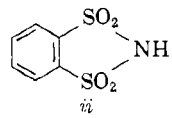
Experimental[21]

Methyl α-(2-1,1,3-Trioxobenzo-[*d*]-isothiazoline) Acetate (Id).[22]—Methyl chloroacetate (25 g., 0.23 mole) was added to a mixture of sodium saccharin (60 g., 0.25 mole) and dimethylformamide (200 ml.). Before pouring the hot reaction mixture into water, stirring and heating at reflux were continued 1 hr. The crystalline product (Id, 49 g., 84%) which separated on cooling recrystallized from methanol–water as colorless crystals, m.p. 121–123°, ν_{max}^{KBr} 1765, 1740, and 1220 cm.$^{-1}$.

Anal. Calcd. for $C_{10}H_9NO_5S$: C, 47.15; H, 3.56; N, 5.49; S, 12.57. Found: C, 47.24; H, 3.64; N, 5.31; S, 12.35.

Ethyl α-Hexyl-α-(2-1,1,3-trioxo-benzo[*d*]isothiazoline) Acetate (Ie).—The preceding experiment was repeated employing ethyl α-bromocaprylate (2.5 g., 0.01 mole).[23] Cooling an aqueous (500 ml.) solution of the reaction mixture led to 2.9 g. (83%), m.p. 59–64°, of crystalline product. One recrystallization from ethanol gave colorless plates (2.4

(12) Selection of dibenzenesulfonamide resided with its potential availability in quantity from benzenesulfonyl chloride. On theoretical grounds, an amide such as *ii* appeared more amenable to alkylation (*cf.*, footnote 7) and subsequent desulfurization. However, the difficulties inherent in preparing reasonable quantities of a cyclic aliphatic or aromatic desulfonamide made this choice somewhat impractical for preliminary work: see, for example; V. Petrow, O. Stephenson, and A. M. Wild, *J. Pharm. Pharmacol.*, **12**, 705 (1960); and W. R. H. Hurtley and S. Smiles, *J. Chem. Soc.*, 1821 (1926).



ii

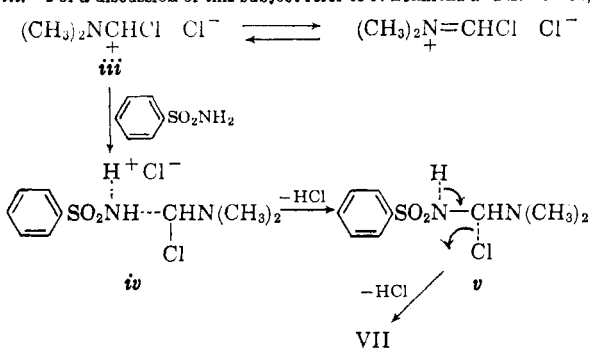
(13) Farbwerke vorm. Meister Lucius and Brüning, German Patent, 125390; *Chem. Zentr.*, II, 1185 (1901).

(14) An infrared spectral study of benzenesulfonylformamidines has recently been described by G. Tosolini, *Chem. Ber.*, **94**, 2731 (1961).

(15) A mechanistic study of N,N,-diarylformamidine hydrolysis in acid solution has been presented by R. H. De Wolfe, *J. Am. Chem. Soc.*, **82**, 1585 (1960).

(16) This experiment lent additional support to the formamidine structure, since reaction between *p*-toluenesulfonamide, dimethylformamide, and phosphorus oxychloride has been reported to yield N,N-dimethyl-N′-*p*-methylbenzenesulfonylformamidine: C. King, *J. Org. Chem.*, **25**, 352 (1960); *cf.*, also ref. 14.

(17) Reaction between dimethylformamide and certain acid chlorides or phosphorus oxychloride is believed to yield dissociated halide *iii*. For a discussion of this subject refer to J. Žemlička and Z. Arnold,



Collection Czech. Chem. Commun., **26**, 2852 (1961); Z. Arnold, *ibid.*, **26**, 1113 (1961); and a review by H. Eilingsfeld, M. Seefelder, and H. Weidinger, *Angew. Chem.*, **72**, 836 (1960). Formation of N,N-dimethyl-N′-benzenesulfonylformamidine might then proceed *via* intermediates such as ion-pair *iv* and transition state *v*.

(18) *Cf.*, F. Runge, H. J. Engelbrecht, and G. Preusser, *Chem. Ber.*, **86**, 1571 (1953).

(19) The decreased reactivity of sodium dibenzenesulfonamide in these alkylation reactions as compared to sodium benzenesulfonylbenzamide was attributed primarily to decreased basicity (*cf.*, footnote 7) of the anion. In addition, apparent refractiveness of the longer-chain α-bromo esters may have been due in part to instability of the corresponding N,N-disulfonyl derivatives: see, B. Helferich and H. Grunert, *Ann.*, **545**, 178 (1940).

(20) S. Gabriel, *Ber.*, **20**, 2224 (1887). A recent application of this reaction sequence has been reported by V. I. Shvets, L. V. Volkova, and N. A. Preobrazhenskii, *Zh. Obshch. Khim.*, **31**, 2184 (1961).

(21) All solvent extracts were dried over magnesium sulfate or sodium sulfate before concentration. Melting points are uncorrected and were observed using open Kimble glass capillaries in a silicone oil bath. Infrared data and microanalyses were provided, respectively, by Dr. R. A. Hill of this laboratory and Dr. A. Bernhardt, Max-Planck Institute, Mülheim, Germany.

(22) Preparation of this substance was carried out by M. G. Madore. For the ethyl ester derivative of Id consult O. J. Magidson and S. W. Gorbatschow, *Ber.*, **56**, 1810 (1923).

(23) K. Auwers and R. Bernhardi, *ibid.*, **24**, 2209 (1891).

g.) melting at 64–66°. Following four recrystallizations from ethanol an analytical specimen melted at 66–67°; ν_{max}^{Nujol} 1740, 1725, and 1240 cm.$^{-1}$.

Anal. Calcd. for $C_{17}H_{23}NO_5S$: C, 57.77; H, 6.56; N, 3.96; S, 9.07. Found: C, 57.75; H, 6.40; N, 4.18; S, 8.93.

Sodium N-Benzenesulfonylbenzamide (IIa).—Preparation of N-benzenesulfonylbenzamide was carried out essentially as reported by Thompson.[24] The following general procedure was employed for preparation of sodium derivatives. An equivalent weight of sodium methoxide in dry methanol or ethanol was added to a concentrated solution of the amide in ethanol. The mixture was cooled and the sodium salt which separated was collected, washed with benzene, and dried at room temperature.

N-Dodecyl-N-benzenesulfonylbenzamide (IIb).—A mixture of *n*-dodecyl bromide (1.8 g., 0.007 mole), sodium iodide (0.5 g., 0.0033 mole), sodium N-benzenesulfonylbenzamide (4.0 g., 0.014 mole), and dimethylformamide (15 ml.) was heated at reflux for 2 hr. Solvent was removed *in vacuo* and 5% aqueous sodium hydroxide (200 ml.) added to the residue. After cooling, with stirring, the oily phase crystallized; weight 2.1 g. Several recrystallizations from isopropyl alcohol gave pure colorless microcrystals melting at 51–52°, ν_{max}^{KBr} 1685 cm.$^{-1}$.

Anal. Calcd. for $C_{25}H_{35}NO_3S$: C, 69.88; H, 8.21; N, 3.26; S, 7.46. Found: C, 69.76; H, 7.99; N, 3.48; S, 7.43.

N-Benzoyl-N-benzenesulfonylglycine Ethyl Ester (IIc).—The preceding experiment was repeated using ethyl bromoacetate (1.2 g., 0.007 mole). Before dilution with water the mixture was heated at 135° for 1 hr. A chloroform solution of the product was successively washed with water, aqueous sodium bisulfite, and water, and concentrated (steam bath) to dryness. The residue recrystallized from ethanol–petroleum ether as colorless needles, m.p. 109–114°, and weighed 1.32 g. (54%). Five recrystallizations from ethanol raised the melting point to 117–118°, ν_{max}^{KBr} 1740, 1695, 1250, and 1210 cm.$^{-1}$.

Anal. Calcd. for $C_{17}H_{17}NO_5S$: C, 58.77; H, 4.93; N, 4.03; S, 9.23. Found: C, 58.71; H, 4.90; N, 4.13; S, 8.91.

N,N′-Bis(carbethoxymethyl)-N,N′-dibenzenesulfonyloxamide (IIIb).—A mixture of ethyl bromoacetate (1.7 g., 0.01 mole), sodium iodide (0.1 g.), sodium N,N-dibenzenesulfonyloxamide (IIIa, 2.0 g., 0.005 mole)[25] and dimethylformamide (8 ml.) was heated at 130° for 2 hr. The dark brown reaction mixture was poured into 5% aqueous sodium hydroxide and crude product (1.0 g., 36%) was isolated as described above (*cf.*, IIc). Several recrystallizations from ethanol (Norit-A) yielded a pure specimen as colorless needles; weight 0.85 g., m.p. 119–120.5°, $\nu_{max}^{CHCl_3}$ 1760, 1740, and 1690 cm.$^{-1}$.

Anal. Calcd. for $C_{22}H_{24}N_2O_{10}S_2$: C, 48.87; H, 4.45; N, 5.18; S, 11.87. Found: C, 49.02; H, 4.53; N, 5.08; S, 11.59.

Raney Nickel Desulfurization of 1,1,3-Trioxo-2-nonylbenzo[*d*]isothiazoline (Ia).—A mixture of W-4 Raney nickel (8 ml., 30 days old),[26] N-nonylsaccharin (Ia, 1.0 g.),[6b] and dioxane (40 ml.) was heated at reflux 15 hr. The solid phase was collected on Celite and washed with dioxane. Concentrating the combined filtrate to dryness provided a waxy solid (0.75 g.). One recrystallization from methanol–water gave 0.60 g. (73%) of colorless needles melting at 59–61°. Several recrystallizations from the same solvent yielded a pure sample of N-nonylcyclohexylcarboxamide (IVa); m.p. 61–62°, ν_{max}^{KBr} 3250, 2900, and 1640 cm.$^{-1}$.

Anal. Calcd. for $C_{16}H_{31}NO$: C, 75.82; H, 12.33; N, 5.53. Found: C, 76.07; H, 12.17; N, 5.58.

The product was identical[27a] with an authentic sample, m.p. 62°, prepared from nonylamine and the acid chloride derivative of cyclohexanecarboxylic acid.

N-Dodecylcyclohexylcarboxamide (IVb) A. By Raney Nickel Desulfurization of 1,1,3-Trioxo-2-dodecyl-benzo[*d*]-isothiazoline (Ib).—A solution of N-dodecylsaccharin (Ib, 2.54 g.)[6a] in dioxane (50 ml.) containing suspended W-2 Raney nickel (14 ml., 30 days old)[28] was heated at reflux for 6 hr. The nickel residue was collected and washed with dioxane. Removal of solvent from the filtrate led to 1.89 g. (91%) of amide (IVb) melting at 73–74°. The colorless crystals weighed 0.78 g. (84%), m.p. 74–75°, following recrystallization from methanol–water. An analytical sample recrystallized from the same solvent as colorless needles, m.p. 75–76°.

Anal. Calcd. for $C_{19}H_{37}NO$: C, 77.22; H, 12.62; N, 4.94. Found: C, 77.22; H, 12.15; N, 4.87.

Products reflecting various stages of reduction (as evidenced by infrared spectral studies) were obtained when similar experiments were performed using shorter reaction periods and either ethanol or acetone as solvent.

B. By Raney Nickel Reduction of N-Dodecylbenzamide (Va).—A mixture of W-2 Raney nickel (15 ml., 10 days old),[28] N-dodecylbenzamide (2.0 g., prepared as noted below) and dioxane (150 ml.) was heated at reflux 6 hr. The product (1.91 g., 92%), m.p. 74–75°, was recovered as illustrated in procedure A. Recrystallization from methanol–water afforded 1.85 g. of colorless needles (IVb) melting at 74.5–75.5°.

C. By Acylation of *n*-Dodecylamine.—The amide (IVb) obtained from cyclohexanecarboxylic acid chloride and *n*-dodecylamine melted at 75–76° following recrystallization from methanol–water. Comparison[27a] with the products obtained in procedures A and B established their mutual identity.

N-Dodecylbenzamide (Va).—In a typical experiment, W-2 Raney nickel (4 ml., 5 days old)[28] was added to a solution of N-dodecylsaccharin (Ib, 0.5 g.) in ethanol (50 ml.). Following a 50-min. period at 70° (with stirring) the mixture was filtered and insoluble by-products were washed with ethanol. Concentrating, *in vacuo*, the filtrate gave a residue (0.39 g., 95%), m.p. 67° with sintering from 50°, which recrystallized from methanol–water as colorless crystals, m.p. 67–69°. The product (Va) was identical[27a] with an authentic sample[29] (m.p. 67–69°) of N-dodecylbenzamide.

Raney Nickel Desulfurization of 1,1,3-Trioxo-2-benzylbenzo[d]isothiazoline (Ic).—To a solution of N-benzylsaccharin (Ic, 2.0 g.)[6a] in dioxane (100 ml.) was added 14 ml. of Raney nickel (W-2, 12 days old).[28] The mixture was stirred and heated at 70 ± 4° for 50 min. After collecting and washing nickel by-products, the filtrate was concentrated (*in vacuo*) to dryness. Following recrystallization from chloroform–petroleum ether, the colorless residue (1.2 g., m.p. 63–96°) melted at 104.5–107° and weighed 0.87 g. (57%). Comparison[27a] with an authentic specimen (m.p. 106–107°) of N-benzylbenzamide (Vb)[30] established identity of the product.

Raney Nickel Desulfurization of Methyl α-(2-1,1,3-Trioxobenzo[d]-isothiazoline) Acetate (Id).—Desulfurization of isothiazoline Id (1.0 g.) was accomplished as described in the preceding experiment. The crude product (0.55 g.) melted at 72–78°. Recrystallization from benzene–petroleum ether gave methyl hippurate (0.45 g., 60%) as colorless needles, m.p. 80–81.5° (lit.,[31] m.p. 80.5°). The ester (Vc)

(24) Q. E. Thompson, *J. Am. Chem. Soc.*, **73**, 5841 (1951).

(25) The amide was prepared as described by R. Adams and W. Reifschneider, *ibid.*, **78**, 3825 (1956), and converted to its sodium derivative (see IIa).

(26) A. A. Pavlic and H. Adkins, *ibid.*, **68**, 1471 (1946).

(27) Established by mixture melting point determination and infrared spectral comparison in (a) potassium bromide or (b) tetrahydrofuran.

(28) H. R. Billica and H. Adkins, "Organic Syntheses," Coll. Vol. 3, J. Wiley & Sons, Inc., New York, N. Y., 1955, p. 176.

(29) R. Sasin, W. A. Butte, Jr., A. L. Borror, and G. S. Sasin, *J. Am. Oil Chemists Soc.*, **34**, 358 (1957); *Chem. Abstr.*, **51**, 16346 (1957).

(30) C. Blacher, *Ber.*, **28**, 434 (1895).

(31) H. Rinderknecht and C. Niemann, *J. Am. Chem. Soc.*, **70**, 2605 (1948).

was identical[27a] with a sample prepared by methylation of N-benzoylglycine with diazomethane.

Raney Nickel Desulfurization of Ethyl α-Hexyl-α-(2,1,1,3-trioxobenzo[*d*]isothiazoline) Acetate (Ie).—Isothiazoline Ie (1.0 g.) was desulfurized using W-2 Raney nickel (7 ml., 5 weeks old)[28] essentially (1-hr. reaction period) as described above (*cf.*, Ic). An infrared spectrum of the colorless oily product (0.75 g.) was consistent with an ethyl N-benzoyl-α-hexylglycine (Vd) structure. A pure sample was prepared by evaporative distillation (bath temperature 120–130°) *in vacuo* (0.03 mm.).

Anal. Calcd. for $C_{17}H_{25}NO_3$: C, 70.07; H, 8.65; N, 4.81. Found: C, 69.85; H, 8.65; N, 4.93.

Raney Nickel Desulfurization of 1,1,3-Trioxo-2-phenacylbenzo[*d*]isothiazoline (If).—Raney nickel (W-2, 5 ml., 1 day old)[28] desulfurization of N-phenacylsaccharin (If, 0.6 g.)[32] was accomplished as illustrated using N-benzylsaccharin (Ic). Three recrystallizations of the crude product (0.32 g.) from methanol–water gave a pure specimen of N-(2-phenylethyl)benzamide (Ve), m.p. 116–118°. This substance was identical[27a] with an authentic sample (m.p. 117–118°).[33]

N,N-Dimethyl-N′-benzenesulfonylformamidine (VII). Procedure A.—Dimethylformamide (40 ml.) was added to an intimate mixture of benzenesulfonyl chloride (26 g.) and sodium benzenesulfonamide (7.5 g.). The resulting exothermic reaction raised the temperature to 50°. Heating was continued at reflux for 20 min. The bright yellow mixture was cooled, diluted with water, and extracted with chloroform. Removal of solvent from the combined solvent extract gave a residue which crystallized from ethanol as colorless rods, m.p. 128–131°, weighing 7.0 g. (77%). Several recrystallizations from chloroform–petroleum ether raised the melting point to 131.5–132.5°; ν_{max}^{KBr} 1625, 1350, 1155, 1095, 915, and 860 cm.$^{-1}$.

Anal. Calcd. for $C_9H_{12}N_2O_2S$ (212); C, 50.92; H, 5.70; N, 13.20; S, 15.11. Found: C, 51.24; H, 5.59; N, 13.20; S, 14.91; mol. wt. (Rast), 238 and 241.

Substituting benzenesulfonyl chloride with either benzoyl chloride (6.0 g.) or carbobenzoxy chloride (7.5 g.) led to, respectively, 23 and 29% yields of formamidine VII.

Procedure B.—A mixture of benzenesulfonamide (1.0 g., 0.0064 mole), benzenesulfonyl chloride (1.12 g., 0.0064 mole), and dimethylformamide (0.93 g., 0.013 mole) was heated (steam bath) for 30 min. The viscous liquid was cooled, diluted with 5% aqueous sodium hydroxide, and extracted with chloroform. After washing the extract with water and concentrating, it was diluted with petroleum ether and cooled. The colorless crystalline product (VII) weighed 0.51 g. (37%) and melted at 131–132.5°.

Procedure C.—Phosphorus oxychloride (6 ml.) was added to a solution of dimethylformamide (4.5 g., 0.05 mole) and benzenesulfonamide (7.5 g., 0.05 mole) in toluene (10 ml.). After the ensuing vigorous reaction subsided 15 ml. of toluene was added to the two-phase (liquid) mixture and heating was continued at reflux for 6 hr. Following removal of solvent *in vacuo*, the yellow residue was triturated with 5% aqueous sodium hydroxide (10 ml.) and the insoluble product was collected. Recrystallizing the formamidine (VII) from ethanol gave 3.9 g. (37%), m.p. 129–131°, of colorless crystals.

Samples of formamidine VII prepared using procedures A–C were shown to be identical by mixture melting point comparison.

Hydrolysis of N,N-dimethyl-N′-benzenesulfonylformamidine (VII).—A mixture of the formamidine VII (2.0 g.) and 10% hydrochloric acid (20 ml.) was heated at reflux for 2 hr. The product (1.34 g., 90%), m.p. 150–152°, which crystallized on cooling, was identical[27b] with an authentic sample of benzenesulfonamide.[34]

(32) H. Eckenroth and K. Klein, *Ber.*, **29**, 329 (1896).

(33) A. Bischler and B. Napieralski, *ibid.*, **26**, 1903 (1893).

(34) C. Schotten and W. Schlömann, *Ber.*, **24**, 3687 (1891); and ref. 24.

The filtrate was subjected to steam distillation and the distillate was adjusted to pH 8–9 with 10% aqueous sodium hydroxide. After concentrating the distillate to *ca.* 5 ml., *p*-bromophenacyl bromide (2.6 g.) in ethanol (10 ml.) was added and the solution was heated (steam bath) 1 hr. The crystalline product which separated on cooling weighed 2.0 g. and melted at 102–107°. A 0.3-g. portion of the crude solid was chromatographed on Merck acid-washed alumina. A fraction (0.03 g.) eluted with petroleum ether–benzene melted at 139–140° (lit.,[35] m.p. 140°) and was identical[27a] with a pure sample of *p*-bromophenacyl formate.[35]

The aqueous solution containing no steam volatile material was made basic (sodium hydroxide) and treated with *p*-toluenesulfonyl chloride (2.0 g.). Collecting the insoluble product led to 1.6 g. (89%) of N,N-dimethyl-*p*-toluenesulfonamide, m.p. 79–81° (lit.,[36] m.p. 78–79° and 80–81°).

Sodium Dibenzenesulfonamide (VIb).—A solution of benzenesulfonyl chloride (77 g., 0.44 mole) in acetone (80 ml.) was added slowly to a stirred solution of ammonium chloride (10.8 g., 0.2 mole) in water (280 ml.). Rapid stirring was continued at ice-bath temperature while the pH was maintained at *ca.* 8 with 10 *N* sodium hydroxide. Cooling was discontinued when the reaction appeared nearly complete. Addition of base was continued at room temperature until the pH (*ca.* 8) remained constant. After removing approximately one half of the solvent, the mixture was acidified with excess concentrated hydrochloric acid. The sulfonamide (VIa) which precipitated weighed 54 g. (83%) and melted at 152–154°.

Occasionally, the crude product contained a greater quantity of impurity. In this event the amide was dissolved in 5% aqueous sodium hydroxide and acidified to *ca.* pH 6 with hydrochloric acid. Precipitate was removed and the filtrate was further acidified until the disulfonamide separated. Five recrystallizations from benzene provided a pure specimen as colorless needles, m.p. 157.5–158.5° (lit.,[37] m.p. 157–158°).

Anal. Calcd. for $C_{12}H_{11}NO_4S_2$: C, 48.48; H, 3.73; N, 4.72; S, 21.56. Found: C, 48.59; H, 4.05; N, 4.79; S, 21.19.

The sodium derivative was prepared as in the case of sodium N-benzenesulfonylbenzamide (IIa).

N-(*p*-Chlorophenacyl)dibenzenesulfonamide (VIc).—A mixture of sodium dibenzenesulfonamide (2.0 g., 0.006 mole), *p*-chlorophenacyl bromide (0.8 g., 0.0035 mole), and dimethylformamide (5 ml.) was heated on the steam bath for 3 hr. The crude product was isolated as illustrated for glycine derivative IIc and recrystallized from ethanol; yield, 0.99 g. (65%), m.p. 174–176°. An analytical sample recrystallized from ethanol as colorless needles melting at 175.5–176.5°, ν_{max}^{Nujol} 1715 cm.$^{-1}$.

Anal. Calcd. for $C_{20}H_{16}ClNO_5S_2$: C, 53.38; H, 3.59; Cl, 7.88; S, 14.25. Found: C, 53.49; H, 3.43; Cl, 7.73; S, 14.11.

N,N-Dibenzenesulfonylglycine Ethyl Ester (VId).—Heating (1-hr. reflux) a mixture composed of sodium dibenzenesulfonamide (6.9 g.), sodium iodide (0.8 g.), ethyl bromoacetate (4.2 g.), and dimethylformamide (25 ml.), and isolation of crude product as described for N-dodecyl-N-benzenesulfonylbenzamide (IIb) gave at an solid (4.1 g., 51%) melting at 70–73°. Several recrystallizations from ethanol afforded pure colorless needles; m.p. 76–77°, ν_{max}^{Nujol} 1770 and 1215 cm.$^{-1}$.

Anal. Calcd. for $C_{16}H_{17}NO_6S_2$: C, 50.12; H, 4.47; N, 3.65; S, 16.73. Found: C, 49.93; H, 4.51; N, 3.52; S, 16.52.

(35) C. D. Hurd and R. E. Christ, *J. Am. Chem. Soc.*, **57**, 2007 (1935).

(36) S. Clarke, J. Kenyon, and H. Phillips, *J. Chem. Soc.*, 1225 (1930); and H. O. Chaplin and L. Hunter, *ibid.*, 1114 (1937).

(37) After this experiment was completed a similar study reported by N. N. Dykhanov, *Zh. Obshch. Khim.*, **29**, 3602 (1959), came to our attention. *Cf.*, also, ref. 13.