TABLE I

Aryloxyurea	Method	M.p., °C.	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N
Phenoxyurea	A	119–120	$C_7H_8N_2O_2$	55.25	5.30	18.41	54.95	5.31	18.57
p-Tolyloxyurea	A	127–128	$C_8H_{10}N_2O_2$	57.82	6.07	16.86	57.62	6.12	16.64
m-Chlorophenoxyurea	A	121–122	$C_7H_7ClN_2O_2$[a]	45.05	3.78	15.02	45.39	4.06	15.40
1-*n*-Butyl-3-phenoxyurea	B	93–94	$C_{11}H_{16}N_2O_2$	63.44	7.74	13.45	63.17	7.93	13.50
1-*n*-Butyl-3-*p*-tolyloxyurea	B	87–88	$C_{12}H_{18}N_2O_2$	64.84	8.16	12.60	65.15	8.29	12.54
1-Allyl-3-phenoxyurea	B	105–106	$C_{10}H_{12}N_2O_2$	62.48	6.29	14.58	62.50	6.42	14.61
1-Phenoxy-3-phenylurea	B	154–155	$C_{13}H_{12}N_2O_2$	68.41	5.30	12.27	68.74	5.35	12.38
1-Cyclohexyl-3-phenoxyurea	B	139–140	$C_{13}H_{18}N_2O_2$	66.64	7.74	11.96	67.04	7.87	12.07
1-(2-Naphthyl)-3-phenoxyurea	B	158	$C_{17}H_{14}N_2O_2$	73.36	5.07	10.07	73.41	5.20	10.16

[a] *Anal.* Calcd.: Cl, 19.00. Found: Cl, 18.93.

Experimental Section[3]

***p*-Tolyloxyamine Hydrochloride.**—The method described Bumgardner and Lilly[4] for phenoxyamine was employed. A mixture of 33.6 g. (0.6 mole) of KOH, 63.8 g. (0.6 mole) of *p*-cresol, 420 ml. of water, and 200 ml. of methylcyclohexane was heated under reflux with stirring, and a solution of 17.0 g. (0.15 mole) of hydroxylamine-O-sulfonic acid in 40 ml. of water was added. After 10 min. the mixture was cooled, the layers were separated, and the aqueous phase was extracted with ether. The combined organic solutions were washed with 1 *N* NaOH and water and were dried ($MgSO_4$). The solution was acidified with ethanolic HCl and the solid which separated was collected. The product consisted of 1.9 g. (8%) of colorless plates, m.p. 96.5° dec.

***m*-Chlorophenoxyamine hydrochloride** colorless plates, m.p. 128–130° dec., was prepared in 2% yield from *m*-chlorophenol and hydroxylamine-O-sulfonic acid by the above method.

Aryloxyureas. Method A.—To a solution of 0.81 g. (0.01 mole) of KCNO in 5 ml. of water was added a solution of 0.01 mole of an aryloxyamine hydrochloride in 20 ml. of water. A solid rapidly separated. The mixture was stirred for 15 min. and filtered. The solid was recrystallized from hexane.

Method B.—A mixture of 0.01 mole of an aryloxyamine hydrochloride and 10 ml. of 1 *N* NaOH was extracted with ether, and the ether solution was dried briefly (K_2CO_3). Then, 0.011 mole of an organic isocyanate was added. After 1 hr. the solution was concentrated on a steam bath to an oil which crystallized upon cooling. The solid was recrystallized from hexane, benzene, or ethanol.

(3) Melting points were determined in a Hershberg apparatus and are uncorrected. Microanalyses were performed by Mr. L. M. Brancone and staff.

(4) C. L. Bumgardner and R. L. Lilly, *Chem. Ind.* (London), 559 (1962).

1-Acyl-1-alkoxy-3-(*p*-tolylsulfonyl)ureas[1]

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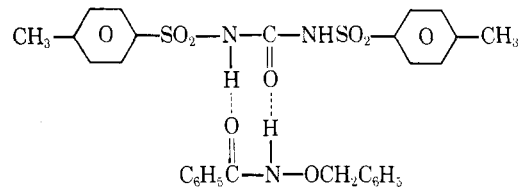
1-Alkyl-3-*p*-tolylsulfonylureas[3] and 1-alkoxy-3-*p*-tolylsulfonylureas[4] have been found to have hypoglycemic activity. On the basis of this, the preparation of 1-acyl-1-alkoxy-3-(*p*-tolylsulfonyl)ureas as possible hypoglycemic agents has been undertaken.

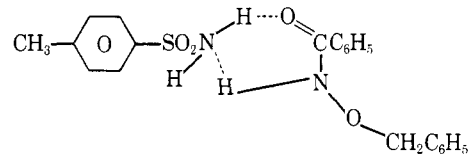
p-Toluenesulfonyl isocyanate, prepared by the method outlined by King,[5] was found to react with N-acetyl-O-*n*-propylhydroxylamine (Ia), N-acetyl-O-allylhydroxylamine (Ib), and N-carbethoxy-O-benzylhydroxylamine (Ic) to give the expected addition compounds. The only chemical property of these adducts that has been observed was their hydrolysis with boiling water to *p*-toluenesulfonamide and the N-acyl-O-alkylhydroxylamine.

RCONHR′

Ia, R = CH_3; R′ = *n*-C_3H_7
b, R = CH_3; R′ = CH_2=$CHCH_2$
c, R = OC_2H_5; R′ = $C_6H_5CH_2$
d, R = C_6H_5; R′ = $C_6H_5CH_2$



II



III

p-Toluenesulfonyl isocyanate failed to give an addition compound with N-benzoyl-O-benzylhydroxylamine (Id) under the same conditions used with the other hydroxylamines. Instead two complexes were isolated. The analysis of one showed it to be a hydrogen-bonded complex II, 1,3-bis-*p*-tolylsulfonylurea with Ia, and the other was a hydrogen-bonded complex III of *p*-toluenesulfonamide with Id. Our interpretation of the infrared spectrum[6] of the former complex led us to suggest structures II. The infrared spectrum of II in Nujol had NH at 3380 and 3220 and CO at 1740 and 1630 cm.$^{-1}$, while 1,3-bis(*p*-tolylsulfonyl)-urea and N-benzoyl-O-benzylhydroxylamine had NH 3295 and CO 1750, and NH 3297 and CO 1647 cm.$^{-1}$, respectively. The lowering of CO and NH absorption frequencies has been found in a number of urea inclusion products.[7,8]

Experimental Section[9]

1-Acetyl-1-propoxy-3-(*p*-tolylsulfonyl)urea.—A solution of 5.7 g. (0.029 mole) of *p*-toluenesulfonyl isocyanate and 3.39 g. (0.029 mole) of N-acetyl-O-*n*-propylhydroxylamine[10] was refluxed for 1 hr. The solvent was evaporated under reduced pressure on a water bath, and the residual oil was crystallized from ether–petroleum ether (b.p. 30–60°) to give white needles. A pure

(1) This investigation was supported by Research Grant E 4173 from the National Institutes of Allergy and Infectious Diseases, Public Health Service. Presented in part at the 19th Annual Northwest Regional Meeting of the American Chemical Society, Spokane, Wash., June 1964.

(2) Taken from the M. S. Thesis of J. D. McCown, University of Idaho, 1964.

(3) F. G. McMahon, Advances in Chemistry Series, No. 45, American Chemical Society, Washington, D. C., 1964, p. 102.

(4) Lucius and Bruning, Belgian Patent 603,268 (April 29, 1960).

(5) C. King, *J. Org. Chem.*, **25**, 352 (1960).

(6) All infrared spectra were run on a Perkin-Elmer 237 Infracord.

(7) A. R. Caniewski, V. Dabrowski, Z. Piasek, and T. Urbanski, *J. Chem. Soc.*, 2340 (1962).

(8) G. B. Barlow and P. J. Corish, *ibid.*, 1706 (1959).

(9) All melting points were determined using capillary tubes, 2 × 90 mm., in an A. H. Thomas melting points apparatus. The microanalyses were by Alfred Bernhardt, Mikroanalytisches Laboratorium, Max-Planck-Institut für Kohlenforschung, Mülheim (Ruhr).

(10) J. H. Cooley, W. D. Bills, and J. R. Throckmorton, *J. Org. Chem.*, **25**, 1734 (1960).

product (5.6 g., 62%) was obtained by recrystallization from CCl_4; infrared (Nujol): NH at 3350, C=O at 1735 m and 1653 s, SO_2 at 1343 and 1170 cm.$^{-1}$.

Anal. Calcd. for $C_{13}H_{18}N_2O_5S$: C, 49.68; H, 5.73; N, 8.92; S, 10.19. Found: C, 49.75; H, 5.71; N, 8.86; S, 10.24.

1-Acetyl-1-allyloxy-3-(*p*-tolylsulfonyl)urea was prepared similarly, m.p. 155.5–156.5°, in 29% yield.

Anal. Calcd. for $C_{21}H_{22}N_2S_2O_5$: C, 56.50; H, 4.93; N, 6.28; S, 14.35. Found: C, 56.00; H, 4.97; N, 6.43; S, 14.81.

This product decomposed to give *p*-toluenesulfonamide upon chromatography on alumina.

2-Benzyloxy-4-(*p*-tolylsulfonyl)allophonate.—A solution of 3.2 g. (0.016 mole) of N-carbethoxy-O-benzyloxyhydroxylamine[11] and 3.2 g. (0.016 mole) of *p*-toluenesulfonyl isocyanate in dry benzene was refluxed for 3 hr. The solvent was removed and 3.8 g. (60%), m.p. 97.5–99°, was obtained by recrystallization from CCl_4.

Anal. Calcd. for $C_{18}H_{20}N_2O_6S$: C, 55.10; H, 5.10; N, 7.14; S, 8.16. Found: C, 55.06; H, 5.14; N, 7.26; S, 8.25.

***p*-Toluenesulfonyl Isocyanate with N-Benzoyl-O-benzylhydroxylamine. Formation of Complexes. 1,3-Bis(*p*-tolylsulfonyl)urea with N-(Benzyloxy)benzamide (II) and N-(Benzyloxy)benzamide with *p*-Toluenesulfonamide (III).**—A solution of 4.9 g. (0.025 mole) of *p*-toluenesulfonyl isocyanate and 2.8 g. (0.0123 mole) of N-benzoyl-O-benzylhydroxylamine in 25 ml. of benzene was refluxed for 2 hr. The solvent was evaporated, and the residue was recrystallized from acetone–petroleum ether and a product (II) (5.0 g., 67%) was isolated, m.p. 129–130°.

Anal. Calcd. for $C_{29}H_{29}N_3O_7S_2$: C, 58.59; H, 4.71; N, 7.07; S, 10.77. Found: C, 58.71; H, 4.79; N, 7.08; S, 10.73.

From the mother liquor (acetone–petroleum ether) was obtained 1.8 g. (33%) of a second solid (III), m.p. 92–94°. The infrared spectrum of III in chloroform showed NH at 3420, 3400, 3355, and 3230–3275 (broad) and CO at 1675 cm.$^{-1}$. The n.m.r. spectrum of III in $CDCl_3$ showed CH_3 δ 2.40, CH_2 5.02, ArH 7.21–7.87, 5 peaks 14H.

Anal. Calcd. for $C_{21}H_{22}N_2O_4S$: C, 53.32; H, 5.53; N, 7.04; O, 16.08. Found: C, 53.27; H, 5.50; N, 7.04; O, 16.28.

II was readily converted to III, ethyl *p*-toluenesulfonylcarbamate, *p*-toluenesulfonamide, and N-benzoyl-O-benzylhydroxylamine when recrystallization from ethanol was attempted. III was readily decomposed to *p*-toluenesulfonamide and N-benzoyl-O-benzylhydroxylamine by boiling with water, and III could be formed by refluxing equimolar quantities of *p*-toluenesulfonamide and N-benzoyl-O-benzylhydroxylamine in ethanol.

(11) L. W. Jones and E. E. Fleck, *J. Am. Chem. Soc.*, **50**, 2023 (1928).

Monothiophenyl Malonate

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Monothiophenyl malonate is a useful intermediate in the synthesis of malonyl coenzyme A, but although two methods of its preparation have been reported[1,2] the product has in each case been an oil. By a modification of the method of Trams and Brady[1] we have isolated the product as an analytically pure crystalline solid.

Experimental Section[3]

To a mixture of 4.17 g. (40 mmoles) of malonic acid and 30 ml. of dimethylformamide was added at 0–5°, 2.2 g. (20 mmoles) of benzenethiol[4] all at once; a dark blue solution resulted. A solution of 9.1 g. (44 mmoles) of dicyclohexylcarbodiimide in 50 ml. of dimethylformamide was placed in an addition funnel and added dropwise to the magnetically stirred solution at 0–5°. Addition was completed in 30–45 min. The mixture was then stirred for 2–3 hr. at 0–5°. During the addition and subsequent stirring the color changed from blue to yellow. The mixture was added to 600 ml. of ice water, stirred for several minutes, and collected on a sintered-glass funnel. The yellow solid, which consisted mainly of dicyclohexylurea, was washed with 150 ml. of ice water and 200 ml. of ether. The two phases of the filtrate were separated and the aqueous phase was extracted with 200 ml. of ether. The ethereal extracts were combined and washed with 100 ml. of 0.01 *M* HCl and 200 ml. of ice water. This solution was then dried ($MgSO_4$, Darco) for 0.5 hr. The solvent was removed by a rotary evaporator at room temperature and reduced pressure. The residual golden brown oil was dissolved in 10 ml. of toluene and diluted with 40 ml. of petroleum ether (b.p. 30–60°). The nearly colorless crystals which separated were collected and recrystallized from the same solvent. The yield was 0.5–0.7 g. (13–18%), m.p. 72–73°, ultraviolet absorption $\epsilon_{237}^{CH_3CN}$ 4200. A 10% $CHCl_3$ solution in a 0.1-mm. NaCl cell absorbed strongly in the infrared at 1740 cm.$^{-1}$.

Anal. Calcd. for $C_9H_8O_2S$: C, 55.09; H, 4.11; S, 16.34. Found: C, 55.07; H, 4.09; S, 16.44.

(1) E. G. Trams and R. O. Brady, *J. Am. Chem. Soc.*, **82**, 2972 (1960).

(2) R. Bressler and S. J. Wakil, *J. Biol. Chem.*, **236**, 1643 (1961).

(3) The melting point was determined in a capillary by means of a calibrated, electrically heated block. Ultraviolet and infrared spectra were measured, respectively, by Beckman DU and Perkin-Elmer 137-B spectrophotometers. Elemental analyses were carried out by Clark Microanalytical Laboratory, Urbana, Ill.

(4) Benzenethiol frequently causes severe dermatitis. Rubber gloves should be worn and all operations should be conducted in an efficient hood.

The Reaction of Chloramine with Mercaptopyridine and Mercaptopyrimidine Derivatives

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The reaction of chloramine with heterocyclic mercaptans has, in every instance that was investigated, resulted exclusively in the sulfenamido derivative. The resulting compounds are of considerable interest because of the known biological and agricultural application of the closely related aminopyridine analogs[1,2] and the extremely potent germicidal action of 2-mercaptopyridine N-oxide.[3]

Experimental Section

All the melting points were taken in capillary tubes and were corrected (ASTM specification thermometers). The molecular weights were obtained by use of a Mecrolab Osmometer, Model 302. Sucrose and benzil were employed as standards.

2-Sulfenamidopyridine.—An aqueous solution of chloramine was prepared by the slow addition of 90 ml. of iced 1.84 *M* NaOCl solution to 278 ml. of 1.84 *M* NH_3 solution previously cooled to −5°. To the resulting chloramine solution, an aqueous solution of the sodium salt of 2-mercaptopyridine was added slowly taking care that the temperature did not exceed 5°. The sodium salt was prepared by dissolving 16.5 g. (0.15 mole) of 2-mercaptopyridine in 75 ml. of 2 *M* NaOH solution. The product precipitated immediately on addition of the sodium salt to the chloramine solution. The crude product was filtered, dried under vacuum to remove excess water, and recrystallized from a petroleum ether–isopropyl alcohol mixture. This resulted in 10.5 g. (55% yield) of a white crystalline product, m.p. 79–80°.

The other compounds were made with appropriate modifications of the general method described above. The results are listed in Table I.

(1) H. E. Thompson, C. P. Swanson, and A. G. Norman, *Botan. Gaz.*, **107**, 476 (1946).

(2) F. Leonard, F. A. Barkley, E. V. Brown, F. E. Anderson, and D. M. Green, *Antibiot. Chemotherapy*, **6**, 261 (1956).

(3) W. A. Lott and E. Shaw, *J. Am. Chem. Soc.*, **71**, 71 (1949).