TABLE I

No.	Compd	Mp,[a] °C	$[\alpha]^{25}D$[b]	Cryst solvent	Formula	Analyses[c]
			N-Bromoacetyl			
1	D-Glucopyranosylamine	187–190	−13.5°	MeOH–Et_2O	$C_8H_{14}N_1O_6Br$	C,H,N
2	D-Galactopyranosylamine	192 dec	+13°	MeOH–Et_2O	$C_8H_{14}N_1O_6Br$	C,H,N
3	L-Fucosylamine	175	+ 2.8°	MeOH–Et_2O	$C_8H_{14}N_1O_5Br$	C,H,N
4	α-Lactosylamine	158	*e*	H_2O–Me_2CO	$C_{14}H_{24}N_1O_{11}Br$	C,H,N
			N-Vinylacetyl			
5	D-Glucopyranosylamine	175	*d*	MeOH–Et_2O	$C_{10}H_{17}N_1O_6$	C,H,N
6	D-Galactopyranosylamine	160	*d*	MeOH–Et_2O	$C_{10}H_{17}N_1O_6$	C,H,N
7	L-Fucopyranosylamine	175	*d*	MeOH–Et_2O	$C_{10}H_{17}N_1O_5$	C,H,N
			N-(4-Acetoxymercuri-3-methoxybutyryl)			
8	D-Glucopyranosylamine	160 dec	− 8°	MeOH–Et_2O	$C_{13}H_{23}N_1O_9Hg$	N[f]
9	D-Galactopyranosylamine	178–180	+12.1°	MeOH	$C_{13}H_{23}N_1O_9Hg$	N[f]
10	L-Fucopyranosylamine	195 dec	+ 3.4°	MeOH	$C_{13}H_{23}N_1O_8Hg$	N[f]

[a] Determined with a Büchi apparatus, and uncorrected. [b] C = 1, H_2O. [c] Rotation very low. [d] Not determined. [e] Analytical values were all within 0.4% of theoretical. [f] Kjeldahl method.

cosylamines were used as starting materials, obviating the need for blocking groups.

Compounds **1–4** and **8–10** (Table I) were tested as irreversible inhibitors of lactose uptake as previously described.[5] Both **1** and **2** were inactive at concentrations of up to 10^{-2} *M*. However both **3** and **4** were inhibitors, **4** showing 100% inactivation of transport at 10^{-3} *M*. This finding demonstrates that a specific inactivation had occurred.[6] On the other hand, compounds **8–10** all gave 100% inactivation at 10^{-4} *M*. This loss of specificity could be due to an extremely rapid mercuration of the essential sulfhydryl by these compounds. Detailed studies of **3** and **4** are in progress.

Experimental Section

Tlc was carried out on silica gel G plates using Me_2CO–MeOH (10:1) as developing solvent; compounds were detected by spraying with concd H_2SO_4 and heating at 120°. The mercurials were examined by paper chromatography using *i*-PrOH–H_2O (4:1) as solvent, and detected with a 0.1% dithizone–$CHCl_3$ spray.

β-D-Glucopyranosylamine, β-D-galactopyranosylamine, and α-lactosylamine were prepared as described.[7] L-Fucopyranosylamine (of unknown anomeric configuration) was prepared as described for the glucoanalog. It was crystallized from H_2O–*i*-PrOH, and had mp 145–150° dec; $[\alpha]^{20}D$ + 3.5° (*c* = 2, H_2O). *Anal.* ($C_6H_{13}N_1O_4$) N.

Bromacetic and vinylacetic anhydrides were prepared by treating the appropriate acid (1 *M* equiv), in dry CCl_4, with DCI (0.5 *M* equiv). Dicyclohexyl urea was filtered off and the CCl_4 removed *in vacuo*.

Acylation.—The glycosylamine (2 mmol) suspended in DMF (2 ml) was treated with the appropriate anhydride (2.5 mmol). After 3 hr at 25°, excess Et_2O was added, and the precipitated *N*-acyl derivative filtered and washed well with Et_2O. Compounds **1–7** were found homogenous by tlc, and were formed in almost quantitative yield.

Mercuration of 5–7.—The *N*-vinylacetylglycosylamine (1 mmol) was refluxed with a solution of $Hg(OAc)_2$ (1.1 mmol) in MeOH (10 ml) for 60 min. After removal of solvent and ACOH *in vacuo*, the residue was crystallized from MeOH. Paper chromatography showed compounds **8–10** to be homogenous, giving single orange spots with dithizone at R_f approximately 0.5. Hg^{2+}, which gives a violet color with dithizone, was not detectable.

(5) J. Yariv, A. J. Kalb, E. Katchalski, R. Goldman, and E. W. Thomas, FEBS Letters, **5**, 173 (1969).

(6) Both *N*-chloroacetyl analogs of **3** and **4** were inactive, showing that the biological activity of **3** and **4** lay in their alkylating capacity.

(7) H. S. Isbell and H. L. Frush, *J. Org. Chem.*, **23**, 1309 (1958); C. A. Lobry de Bruyn and F. H. van Leent, *Rec. Trav. Chim. Pays-Bas*, **14**, 134 (1895); F. Micheel, R. Frier, E. Plate, and A. Hiller, *Ber.*, **85**, 1092 (1952).

Acknowledgment.—I thank Drs. J. Yariv and A. J. Kalb for testing the compounds and for discussions, also Mrs. S. Rogozinsky and Mr. R. Heller for microanalyses. This work was supported in part by a European Molecular Biology Organization fellowship.

1-Substituted 3-[(5-Nitrofurfurylidene)amino]-2-imidazolidinones

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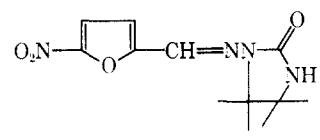
Received October 29, 1969

The activity of nifuradene[1] (**1**) led to an investigation of its use as a urinary tract antibacterial agent.[2] An intensive synthetic program was initiated to produce a series of compounds which were substituted on the imino nitrogen of **1**. This paper describes the synthesis and antibacterial activity of these compounds.



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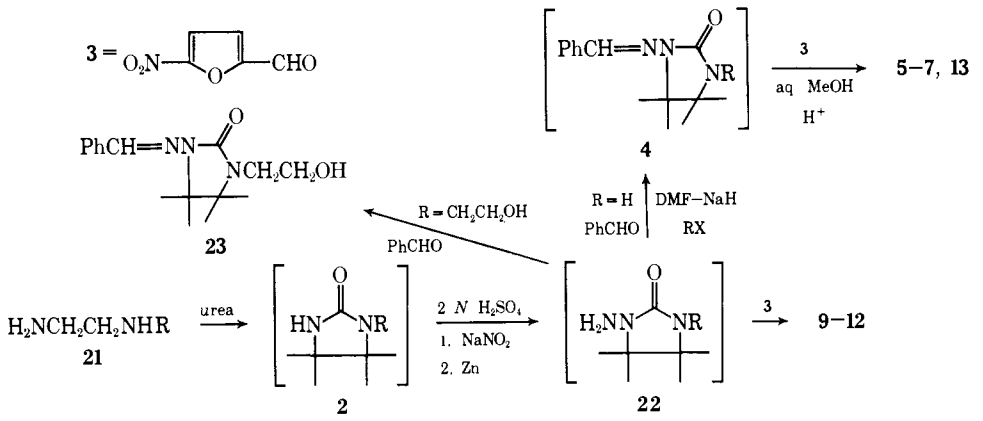
Chemistry.—Several pathways were utilized in the preparation of the compounds. The first route started with an appropriately N-substituted ethylenediamine (**21**) which was heated with urea to form a 1-substituted 2-imidazolidinone (**2**) (see Scheme I). These ethyleneureas were nitrosated and then reduced with Zn dust in 2 *N* H_2SO_4. Condensation of the resulting 3-amino-1-substituted-2-imidazolidinones (**22**) with 5-nitro-2-furaldehyde (**3**) yielded **9–12**. The second route in-

(1) Renafur E, 1-[(5-nitrofurfurylidene)amino]-2-imidazolidinone.

(2) J. R. O'Connor, H. E. Rossell, J. G. Michels, P. V. Newland, and W. F. Carey, IIIrd International Congress of Chemotherapy, July 22–27, 1963, Stuttgart, Germany, Paper C-52.

SCHEME I



volved the alkylation of **4** (R = H). Thus, when the nitrosation and reduction were carried out on **2** (R = H), the resulting 1-amino-2-imidazolidinone (**22**, R = H) was condensed with PhCHO to give **4** (R = H). The alkylation of **4** (R = H) was effected in DMF using NaH and the appropriate halide. The crude **4** was hydrolyzed with aqueous methanolic HCl in the presence of **3** to produce **5–7** and **13**.

When **22** (R = CH_2CH_2OH) was condensed with PhCHO, the resultant benzylideneamino-2-imidazolidinone **23** became the starting material for two reaction sequences. The first involved the chlorination of **23** to give 1-benzylideneamino-3-(2-chloroethyl)-2-imidazolidinone (**24**). Amination of **24** with morpholine followed by acid hydrolysis in the presence of **3** yielded the 2-morpholinoethyl hydrochloride **19**. In the second sequence, the treatment of **23** with TsCl in pyridine gave 1-benzylidineamino-3-(2-*p*-toluenesulfonyloxyethyl)-2-imidazolidinone (**25**). When **25** was refluxed in an EtOH solution of EtONa followed by acid hydrolysis in the presence of **3**, the 2-ethoxyethyl compound **14** was obtained. The iodo derivative **16** was prepared by heating **25** in a DMF solution of NaI with subsequent acid hydrolysis and concurrent condensation with **3**.

The chlorination of **9** with $SOCl_2$ yielded **15**. In a similar manner **10** and **11** were chlorinated to give **17** and **18**, respectively. The two remaining compounds, **8** and **20**, were prepared from **1** by different routes. When **1** was heated in 5% aqueous HCHO, the hydroxymethyl compound **8** was obtained whereas nitrosation in AcOH gave **20**.

Biologic Activity.—Compounds were tested for *in vitro* antibacterial activity by procedures described previously for the determination of minimal inhibitory concentration (MIC).[3] The urinary antibacterial activity was determined by serial tube dilution[4] or cup plate bioassay.[5] Following peroral dosing of the compound at 10 mg/kg to 4 rats as a suspension in 1% carboxymethylcellulose, the per cent of the dose excreted in rat urine over the 24-hr period was calculated as antibacterial equivalents of parent compound.

The antibacterial activity and urinary excretion data are presented in Table I. This series of compounds demonstrated a high order of *in vitro* antibacterial activity against *Escherichia coli*.

Although peroral administration of a number of the compounds in this series resulted in urinary excretion of antibacterial activity, only **8**, **9**, **10**, and **12** were excreted at levels higher than 15% of the administered dose (as antibacterial equivalents). High urine concentration of antibacterial activity often indicates potential usefulness of the compound as a urinary tract antibacterial agent. Based on the high level of excretion of activity in the urine and the *in vitro* antibacterial activity (MIC), **8** and **9** are considered to be the most active as urinary tract agents.

Experimental Section[6]

Materials.—The N-substituted ethylenediamines (**21**) used in the preparation of **2** were purchased or prepared as indicated: *N*-(2-hydroxyethyl)ethylenediamine,[7] *N*-(2-hydroxypropyl)ethylenediamine,[8] *N*-(3-hydroxypropyl)ethylenediamine,[9] *N*-(2-hydroxy-3-methoxypropyl)ethylenediamine.[10] For the preparation of **13** the prerequisite halide, 2-methoxyethyl chloride,[11] was synthesized by a literature method. All other intermediates were purchased from regular commercial sources.

1-(2-Hydroxyethyl)-3-[(5-nitrofurfurylidene)amino]-2-imidazolidinone (9).—Urea (204 g, 3.3 mol) and **21** (R = CH_2CH_2OH) (360 g, 3.46 mol) were heated under an air condenser; at 100° NH_3 evolved. The temperature was gradually increased to 230° over 2.75 hr in order to maintain the evolution of NH_3. The liquid was cooled to *ca.* 100° and poured into a large dish where it solidified to a gray solid to give 435 g (101%). The crude **2** (R = CH_2CH_2OH) (362 g, 2.78 mol) was dissolved in 2 *N* H_2SO_4 (7625 ml). The solution was cooled and kept at 5° while $NaNO_2$ (206 g, 3 mol) was added over 15 min. After stirring at <5° for 1.25 hr, Zn dust (420 g, 6.45 g-atoms) was added over 45 min at <20°. The mixture was stirred without cooling for 1 hr and filtered. The filtrate was divided into two portions. To the first portion (1945 ml) was added a solution of **3** (86 g, 0.61 mol) in 95% EtOH (600 ml). The mixture was cooled overnight and filtered. The crude solid material was washed with 50% aq EtOH and dried at 60° to yield 152 g of **9** as orange crystals, mp 194–195°.

In a similar manner, **10–12** were prepared from the appropriate N-substituted **21**.

(3) R. Freedman and R. E. Chamberlain, *Antimicrob. Ag. Chemother.*, **1967**, 502 (1968).

(4) B. Pitsch, T. Hebert, and W. F. Carey, *Antimicrob. Ag. Chemother.*, **1961**, 54 (1962).

(5) M. F. Paul, H. E. Paul, R. C. Bender, F. Kopko, C. M. Harrington, V. R. Ells, and J. A. Buzard, *Antibiot. Chemother. (Washington, D. C.)*, **10**, 287 (1960).

(6) The melting points were taken in an open capillary tube on a Mel-Temp melting point apparatus and are corrected. The physical constants of all the final products are listed in Table I. The analytical results for C, H, and N of the intermediates were within ±0.4% of the theoretical values.

(7) Purchased from Matheson Coleman and Bell.

(8) L. J. Kitchen and C. B. Pollard, *J. Org. Chem.*, **8**, 342 (1943).

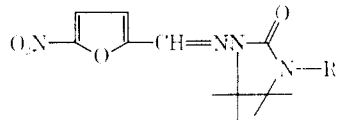
(9) A. R. Sorrey, C. M. Suter, and J. S. Buck, *J. Amer. Chem. Soc.*, **74**, 4102 (1952).

(10) H. Flores-Gallardo and C. B. Pollard, *J. Org. Chem.*, **12**, 831 (1947).

(11) D. E. Ames and R. E. Bowman, *J. Chem. Soc.*, 406 (1950).

TABLE I

1-SUBSTITUTED 3-[(5-NITROFURFURYLIDENE)AMINO]-2-IMIDAZOLIDINONES



No.	R	Yield, %	Mp, °C	Formula[a]	Recryst solvent[d]	Minimal inhibitory concentration, μg/ml[e] Es-2[f]	% of dose excreted in rat urine in 24 hr[g]
1	H					0.4	5
5	CH_3	76	232–234	$C_9H_{10}N_4O_4$	A	0.4	6
6	$CH_2CH{=}CH_2$	53	194–195	$C_{11}H_{12}N_4O_4$	D	0.8	6
7	$CH_2C{\equiv}CH$	53	196–198	$C_{11}H_{10}N_4O_4$	C	0.4	4
8	CH_2OH	21	>200 (sinters)	$C_9H_{10}N_4O_5$	—	0.8	23
9	CH_2CH_2OH	82	199.5–201.5	$C_{10}H_{12}N_4O_5$	D	3.1	29
10	$CH_2CHOHCH_3$	55	194–196	$C_{11}H_{14}N_4O_5$	D	3.1	21
11	$CH_2CH_2CH_2OH$	97	195–197	$C_{11}H_{14}N_4O_5$	F	3.1	6
12	$CH_2CHOHCH_2OCH_3$	65	169–171	$C_{12}H_{16}N_4O_6$	A	3.1	24
13	$CH_2CH_2OCH_3$	54	156–157	$C_{11}H_{14}N_4O_5$	D	1.5	6
14	$CH_2CH_2OC_2H_5$	68	139.5–141	$C_{12}H_{16}N_4O_5$	B	6.3	8
15	CH_2CH_2Cl	57	195–196	$C_{10}H_{11}ClN_4O_4$[b]	H	1.5	3
16	CH_2CH_2I	25	189–191	$C_{10}H_{11}IN_4O_4$[c]	E	3.1	2
17	$CH_2CHClCH_3$	93	164.5–166	$C_{11}H_{13}ClN_4O_4$	I	3.1	4
18	$CH_2CH_2CH_2Cl$	34	163–164	$C_{11}H_{13}ClN_4O_4$	G	6.3	3
19	$CH_2CH_2N(CH_2CH_3)_2O\cdot HCl$	58	244–248 dec	$C_{14}H_{23}N_5O_5\cdot HCl$	—	3.1	13
20	NO	66	231.5–232 dec	$C_8H_7N_5O_5$	A	0.4	1

[a] The analytical results of these compounds were within ±0.4% of the theoretical value and were obtained for C, H, and N unless otherwise noted. [b] *Anal.* C, H, Cl. [c] *Anal.* C, H, I. [d] A, $MeNO_2$; B, *i*-PrOH; C, MeOH–$MeNO_2$; D, 95% EtOH–$MeNO_2$; E, DMF–H_2O; F, 95% EtOH–$MeNO_2$–Et_2O; G, MeOH; H, EtOH–MeCN; I, C_6H_6. [e] Lowest concentration of compound which prevents visible growth following 24-hr incubation at 37°. [f] The Norwich Pharmacal Company number: Es-2 = *Escherichia coli*. [g] Calculated on the basis of antibacterial equivalents; 10 mg/kg dose.

1-Benzylideneamino-2-imidazolidinone (4, R = H).—A solution of ethyleneurea (**2**, R = H) (252 g, 2.92 mol) in 2 *N* H_2SO_4 (8000 ml) was cooled to *ca.* 5°. $NaNO_2$ (202 g, 2.92 mol) was added in small portions over a period of 0.5 hr. During the addition the solution was kept at a temperature of 5–6°. The solution was stirred in an ice bath for an additional 3 hr and then Zn dust (440 g, 6.73 g-atoms) was added, in small portions, so that the temperature did not rise above 20°. The addition required 1.5 hr. The mixture was stirred in an ice bath for 1 hr and then at room temperature overnight. The excess Zn was filtered off and the filtrate was adjusted to a pH of 5 with AcONa (*ca.* 800 g). To the solution was added PhCHO (280 g, 2.64 mol) dissolved in 95% EtOH (2000 ml). The cloudy mixture was heated on the steam bath for 2 hr and then cooled. The solid was collected, washed with dil HCl, and then thoroughly with H_2O, dried at 60° to yield **4** (R = H) (373 g, 76%) mp 201–204°. Recrystallization of **4** from MeOH (charcoal) gave an analytical sample melting at 200–202°. *Anal.* ($C_{10}H_{10}N_3O$) C, H, N.

1-Methyl-3-[(5-nitrofurfurylidene)amino]-2-imidazolidinone (5).—Compound **4** (R = H) (95.0 g, 0.5 mol) was dissolved in DMF (*ca.* 2500 ml) and the system was swept with dry N_2. NaH (21.5 g, 0.5 mol), as a 56.6% dispersion in oil, was added and the mixture was stirred at near reflux temperature for 4 hr. The reaction mixture was cooled to room temperature. A solution of MeI (35 ml) in DMF was added and the reaction mixture was stirred at 40–45° for 4 hr. After standing at room temperature overnight, the DMF was removed under reduced pressure. The residue was treated with H_2O and filtered. The crude solid material was dissolved in H_2O (*ca.* 500 ml) and MeOH (*ca.* 100 ml). The solution was acidified (pH *ca.* 2) with concd HCl and heated on the steam bath for 10 min. A solution of **3** (39.0 g, 0.275 mol) in MeOH was added and the mixture was heated on the steam bath for 2 hr. The reaction mixture was cooled in an ice bath and filtered. The crude solid was washed with H_2O and dried at 65° yield **5** (74.0 g), mp 226–228°.

Similarly **6**, **7**, and **13** were prepared from **4** (R = H) using the appropriate halide (in most cases the bromide was used) in equimolar amounts. The alkylations were carried out at 70–90°.

1-Benzylideneamino-3-(2-hydroxyethyl)-2-imidazolidinone (23).—To a solution of **22** (R = CH_2CH_2OH) (5835 ml from the preparation of **9**) was added AcONa (450 g) to adjust the pH to 4–6. The cloudy mixture was heated to 40° and treated with PhCHO (212 g, 2 mol) dissolved in 95% EtOH (600 ml). After heating on a steam bath for 1.5 hr, the mixture was cooled and filtered. The white solid was washed with 2 × 200 ml of 25% EtOH and then with H_2O to yield **23** (364 g, 78%), mp 174–176°. An analytical sample was prepared by recrystallization from MeOH (charcoal), mp 178–179°. *Anal.* ($C_{12}H_{15}N_3O_2$) C, H, N.

1-Benzylideneamino-3-(2-chloroethyl)-2-imidazolidinone (24).—Compound **23** (340 g, 146 mmol) was added portionwise to $SOCl_2$ (680 ml), and the mixture was heated on a steam bath for 1 hr. After cooling, the solution was poured into a mixture of C_6H_6 (1700 ml) and Et_2O (1700 ml) and further cooled in the refrigerator. The solid was filtered and washed with Et_2O. The combined filtrates were cooled in the refrigerator to cause the pptn of more solid. The solids were combined and added to ice–H_2O, filtered, and slurried with more cold H_2O. The slurry was adjusted to pH 8 with satd Na_2CO_3 solution and filtered. The solid was washed with H_2O and dried at 60° to yield **24** (338 g, 92%), mp 106–107° One recrystallization from MeOH (charcoal) gave an analytical sample, mp 107–108°. *Anal.* ($C_{12}H_{14}ClN_3O$) C, H, N.

1-(2-Morpholinoethyl)-3-[(5-nitrofurfurylidene)amino]-2-imidazolidinone Hydrochloride (19).—A mixture of **24** (75.0 g, 0.3 mol), morpholine (52.0 g, 0.6 mol), and C_6H_6 (300 ml) was heated at reflux temperature for 7 hr. After cooling overnight at room temperature, the solid was filtered, washed with Et_2O and then with H_2O. The crude material was suspended in H_2O (250 ml) and acidified with 10% HCl. The suspension was filtered to remove any insoluble material; the filtrate was diluted with 10% HCl (155 ml). The solution was heated on a steam bath and **3** (42.0 g, 0.3 mol) was added. After heating for an additional 0.5 hr with occasional stirring, the mixture was cooled and extracted 6 times with $HCCl_3$. The H_2O layer was immediately filtered (before crystallization started) and cooled. The

solid was collected and dried at 110° to yield **19** (65.0 g), mp 245–250° dec.

1-Benzylideneamino-3-(2-*p*-toluenesulfonyloxyethyl)-2-imidazolidinone (**25**).—Compound **23** (925 g, 3.97 mol) was added to a solution of C_5H_5N (10,280 ml, dried over KOH pellets) containing recrystallized TsCl (758 g, 3.97 mol). The addition required 30 min with the temperature at 0°. The reaction mixture was stored in the refrigerator for 48 hr. The product was collected, washed with H_2O and then with Et_2O, and dried at 60° to yield 955 g, mp 152–155°. The original filtrate was diluted with H_2O (50,000 ml) and cooled for 72 hr. Upon filtration, washing, and drying, an additional 231 g, mp 150–154°, was obtained. The total yield of **25** was 1186 g (77.6%). Recrystallization from $MeNO_2$ gave an analytical sample, mp 153–155°. *Anal.* ($C_{19}H_{21}N_3O_4S$) C, H, N.

1-(2-Ethoxyethyl)-3-[(5-nitrofurfurylidene)amino]-2-imidazolidinone (**14**).—Compound **25** (84.0 g, 0.22 mol) was added in small portions to a solution of abs EtOH (*ca.* 500 ml) and EtONa [prepared by the addition of NaH (10.4 g of 55.6% oil dispersion)]. The mixture was heated at reflux for 3 hr, filtered, and the solvent removed under reduced pressure. The residue was dissolved in aq MeOH and the solution was acidified (pH **1**) with concd HCl. After heating the solution on the steam bath for 10 min, a solution of **3** (30.6 g, 0.216 mol) in MeOH was added. The reaction mixture was heated on the steam bath for 2 hr, chilled in an ice bath, and filtered. The product was dried to yield 40.0 g, mp 138–140°.

1-(2-Iodoethyl)-3-[(5-nitrofurfurylidene)amino]-2-imidazolidinone (**16**).—A mixture of **25** (194 g, 0.5 mol), NaI (75 g, 0.5 mol), and DMF (2500 ml) was heated at 110–140° for 5 hr. The solution was cooled and diluted twofold with ice–H_2O. A brown ppt was collected, washed with H_2O, and dissolved in aq EtOH. The EtOH solution was acidified (pH **1**) with concd HCl and heated on the steam bath for 10 min. A solution of **3** (71 g, 0.5 mol) in 95% EtOH was added and the mixture was heated on the steam bath for 1 hr. The reaction mixture was cooled in an ice bath and filtered. The product was dried to yield 45 g of **16**, mp 186–188°.

1-(2-Chloroethyl)-3-[(5-nitrofurfurylidene)amino]-2-imidazolidinone (**15**).—Compound **9** (152 g, 0.57 mol) was added in small portions to $SOCl_2$ (400 ml). The resultant clear solution was heated at reflux for 30 min, cooled in an ice bath, and filtered. The solid was washed with C_6H_6 and the washings were added to the reaction filtrate to give a second crop of crystals. The total yield of **15** was 92.0 g, mp 184–185°.

In a similar manner **10** and **11** were chlorinated to yield **17** and **18**, respectively.

1-Hydroxymethyl-3-[(5-nitrofurfurylidene)amino]-2-imidazolidinone (**8**).—Compound **1** (60.0 g, 0.27 mol) was added to a refluxing solution of 5% aq CH_2O. The mixture was stirred at reflux for 5 min, filtered hot, and then stored in a refrigerator for 2 days. The precipitated orange plates were collected and washed with 1% CH_2O. The material was dried in a desiccator at room temperature to yield 14.4 g of **8**, mp 200° (sinters).

1-[(5-Nitrofurfurylidene)amino]-3-nitroso-2-imidazolidinone (**20**).—A suspension of **1** (112.0 g, 0.5 mol) in glacial AcOH (*ca.* 800 ml.) was stirred at room temperature while $NaNO_2$ (100 g) was added in small portions over a period of 1 hr. The bright orange suspension gradually changed to a bright yellow. The mixture was stirred for another 3 hr and filtered. The crude solid was washed with Et_2O and recrystd from $MeNO_2$ to yield 50.5 g, mp 228–229° dec. A second crop of material was obtained by concentrating the filtrate and cooling to give a total of 88.5 g.

Acknowledgments.—The authors gratefully acknowledge the aid of Mrs. Patricia Curtis, Mr. Frederick Abbott, Mr. Alexander Winterstein, and Mr. Benjamin Stevenson for the preparation of chemical intermediates, and of Mr. Leonard Bird for assistance in the syntheses. Compound 8 was prepared by Mr. Benjamin Stevenson. Mr. Grant Gustin and Mr. Marvin Tefft performed the microanalyses. Microbiologic data were obtained through the assistance of Mr. Patrick Moynihan. Miss Esther Nohle and Mr. Donald Humphrey assisted in obtaining the urinary excretion data.

Antimalarial Sulfilimines and Sulfoximines Related to Diaminodiphenyl Sulfoxide and Sulfone

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Received January 7, 1970

A series of sulfilimines I and sulfoximines II related in structure to 4,4′-diaminodiphenyl sulfone and sulfoxide were synthesized and tested for antimalarial activity (Table I). Compound **12** showed some slight activity in mice infected with *Plasmodium berghei*. The testing did not reveal activity in any of the other compounds.

I II

The sulfilimines were prepared from the known sulfides by reaction with various sodium *N*-chloroarene sulfonamides.[1] Sulfilimines unsubstituted on N appear to be hydrolytically unstable;[2] no attempt was made to prepare such compounds.

Experimental Section

Sulfilimines (**1,2,7,8,10,11,13,14,15**) were prepared from the sulfides by treatment with the appropriate sodium *N*-chloroarenesulfonamide.[2] A typical reaction is given below.

***S,S*-Di-*p*-acetylaminophenyl-*N*-benzenesulfonylsulfilimine** (**2**).—Chloramine B (2.67 g, 0.10 mol) in a 2:1 v/v dioxane–H_2O mixture (18 ml) was added all at once to 4,4′-diacetylaminodiphenyl sulfide (3.0 g, 0.10 mol) in a 2:1 v/v dioxane–H_2O (20 ml) mixture. The mixture was heated on a steam bath for 2 hr. The solvents were removed on a rotary evaporator and the residue dissolved in CH_2Cl_2–EtOAc. This solution was extracted with 5% aq NaOH, washed with H_2O, dried (Na_2SO_4), concd, and recrystd from Me_2CO: 3.0 g; 68%; mp 205°.

Sulfilimines (**3,4,5,6,9,12**) were prepared by the deacetylation of the corresponding acetylated sulfilimine. A typical reaction procedure is given below.

***S,S*-Di-*p*-aminophenyl-*N*-benzenesulfonylsulfilamine** (**3**).—*S,S*-Di-*p*-acetylaminophenyl-*N*-benzenesulfonylsulfilimine (**2**) (4.5 g) in 10% EtOH–NaOH (30 ml) was refluxed for 1 hr. The mixture was reduced in volume and poured into ice–water. The solid which pptd was collected by filtration, washed, dried, and recrystd from EtOH: 3.5 g; 94%; mp 197°.

***S*-Methyl-*S*-*p*-acetylaminophenyl-*N*-benzenesulfonylsulfoximine** (**16**).—*S*-Methyl *S*-*p*-acetylaminophenyl-*N*-benzenesulfonylsulfilimine (**8**) (10.0 g, 0.297 mol) was dissolved in dry C_5H_5N (100 ml) and $KMnO_4$ (3.4 g, 0.22 mol) and H_2O (0.2 ml) was added with stirring. After standing for 6 days at room temperature, the C_5H_5N was removed using a rotary evaporator and the residue treated with aq acidified $NaHSO_3$. The pptd white solid was collected by filtration and recrystd from EtOH: 7.5 g; 71%; mp 173°.

***S*-Methyl-*S*-*p*-acetylaminophenyl-*N*-*p*-acetylaminobenzenesulfonylsulfoximine** (**17**).—*S*-Methyl-*S*-*p*-acetylaminophenylsulfoximine (8.0 g, 0.038 mol) was dissolved in dry THF (400 ml). Na (1.0 g, 0.043 g-atom) was added in small portions to the refluxing solution. When no more Na dissolved, the clear solution was decanted into another flask and *p*-acetylaminobenzenesulfonyl chloride (7.0 g, 0.030 mol) was added. The mixture was refluxed for 45 min, cooled, and filtered. The filtrate was reduced in volume and poured into H_2O whereupon a solid precipi-

(1) A. Schöberl and A. Wagner in "Methoden der Organischen Chemie," Vol. 9, E. Muller, Ed., Georg Thieme Verlag, Stuttgart, 1955, Chapter 9.

(2) R. Appel and W. Büchner, *Chem. Ber.*, **95**, 849, 855 (1962).