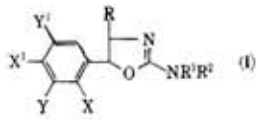
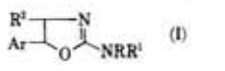
nervous system. Thus, 1.58 g. NaCN is treated with 5.7 g. Br in MeOH to give a soln. contg. BrCN, the soln. kept at ~5°, a soln. of 2.9 g. NaOAc and 7.44 g. 3,4,5-$(MeO)_3C_6H_2CH(OH)$-CH_2NH_2 in MeOH added at room temp., and the mixt. agitated 1.5 hrs. at room temp. to give 6.04 g. 2-amino-5-(3,4,5-trimethoxyphenyl) oxazoline, m. 181–3.5° (Me_2CO). Similarly prepd. are the following **I** (Y′ = R′ = R″ = H) (X, X¹, Y, R,



(I)

and m.p. given): Cl, Cl, H, H, 132–4°; H, H, H, Me, 154.5–6°; H, Cl, H, Et, —; MeO, H, H, H, 102–3°; H, MeO, H, H, 138–42°; H, H, $PhCH_2O$, H, 133–5°; H, H, OH, H, 170° (decompn.); H, Cl, H, H, 118–19°; Cl, H, H, H, 128–30°; H, CF_3, H, H, 97–100°; H, iso-Pr, H, H, 158–60°; H, MeO, MeO, H, 119–21°; H, CO_2Me, H, H, 158–9°; H, Br, H, H, —; H, F, H, H, —. **I** ($R^1 = R^2 = X = H$, R = Me, Y = X^1 = Y^1 = MeO), *cis*-2-amino-4,5-diphenyloxazoline, m. 216–17° (MeOH), and 2-amino-5-(3,4-methylenedioxyphenyl)-2-oxazoline, 178.5–80.5° (iso-PrOH), were also prepd. A soln. of 10.5 g. MeNHCONHCHMeCHPhOH in 100 ml. CH_2Cl_2 is cooled to 0°, a soln. of 3.9 ml. $SOCl_2$ in 20 ml. CH_2Cl_2 added, and the mixt. refluxed 30 min. to give 7.9 g. 2-methylamino-4-methyl-5-phenyl-2-oxazoline, m. 129–31° (C_6H_6-hexane). Similarly prepd. are the following **I** (X = Y = Y^1 = H) (R, R^1, R^2, X^1, and m.p. given): H, H, Ph, Cl, 148–50°; Me, H, Et, H, — (fumarate m. 146–7°); Me, H, Ph, H, 130–1°; Me, H, 1-$C_{10}H_7$, H, 181–2°; Me, Me, Me, H, — ($b_{0.75}$ 108–10°); H, Me, Me, Cl, — ($b_{0.5}$ 145°). BDPF

2-Aminooxazolines. McNeil Laboratories, Inc. **Belg. 628,803,** June 16, 1963, Appl. Feb. 22, 1963; 33 pp. 2-Amino-1-aryl-1-alkanols are cyclized with a cyanogen halide to give the title compds. which can be used as stimulants for the central nervous system. Thus, a mixt. of 56 g. NCBr in 400 ml. MeOH is added at room temp. to a soln. of 91.2 g. $PhCH(CH_2NH_2)OH.HCl$ and 87 g. NaOAc in 1500 ml. MeOH, the mixt. agitated 30 min., the alc. distd. *in vacuo*, the residue dissolved in H_2O, and the soln. neutralized with K_2CO_3 to give 62.5 g. 2-amino-5-phenyloxazoline, m. 136–8° (C_6H_6), λ (Nujol) 2.97, 5.87, 6.16, 6.67, 7.04, 7.44 μ. Similarly prepd. are the following **I** (R = R^1 = H) (R^2, Ar, and m.p. given): H, 3,4,5-$(MeO)_3$-



(I)

C_6H_2, 181–3.50 (Me_2CO); H, 2,4-$Cl_2C_6H_3$, 132–4° (C_6H_6); Me, Ph, 154.5–56° (C_6H_6); Et, *p*-ClC_6H_4, —; Me, 3,4,5-$(MeO)_3$-C_6H_2, —; H, *o*-$MeOC_6H_4$, 102–3° (CH_2Cl_2-methylcyclohexane); H, *p*-$MeOC_6H_4$, 138–42° (C_6H_6); H, *m*-$PhCH_2OC_6H_4$, 133–5° (C_6H_6); H, *m*-HOC_6H_4, 170° (decompn.); H, *p*-ClC_6H_4, 118–19° (C_6H_6); H, *o*-ClC_6H_4, 128–30° (C_6H_6-hexane); H, *p*-F_3C-C_6H_4, 97–100° (C_6H_6-petr. ether); H, *p*-iso-PrC_6H_4, 158–60° (C_6H_6-petr. ether); H, 3,4-$(MeO)_2C_6H_3$, 119–21° (EtOAc); H, 3,4-methylenedioxyphenyl, 178.5–80.5° (iso-PrOH); H, *p*-$MeO_2CC_6H_4$, 158–9° (CH_2Cl_2-ether); H, *p*-BrC_6H_4, —; H, *p*-FC_6H_4, —. Also prepd. were the following **I**:

R	R^1	R^2	Ar	m.p.
H	Me	Me	Ph	129–31° (C_6H_6-hexane)
H	Et	Me	Ph (1)	—
H	Ph	Me	Ph	130–1° (iso-PrOH)
H	Ph	H	*p*-ClC_6H_4	148–50° (iso-PrOH)
H	1-$C_{10}H_7$	Me	Ph	181–2° (iso-PrOH)
Me	Me	Me	Ph (2)	—
Me	Me	H	*p*-ClC_6H_4 (3)	—

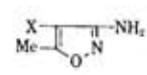
(1) fumarate m. 146–7° (iso-PrOH), (2) $b_{0.75}$ 108–10°, (3) $b_{0.5}$ 145°.

Similarly prepd. was *cis*-2-amino-4,5-diphenyloxazoline, m. 216–17° (MeOH). BDPF

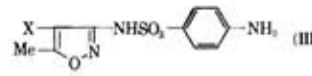
2-Amino-5-phenyloxazoline. McNeil Laboratories, Inc. **Fr. M2447** (Cl. A 61*k*, C 07*d*), May 4, 1964, Appl. Feb. 27, 1963; 9 pp. The title compd. was prepd. and could be used as a stimulant for the central nervous system and to decrease appetite. Thus, a soln. of 56 g. NCBr in 400 ml. MeOH was added at room temp. to a soln. of 91.2 g. $PhCH(CH_2NH_2)OH.HCl$ and 87 g. NaOAc in 1500 ml. MeOH, the mixt. agitated 30 min., the alc. distd. *in vacuo*, the residue dissolved in H_2O, the soln. neutralized, and the ppt. filtered off to give 73% 2-amino-5-phenyloxazoline, m. 136–8° (C_6H_6). BDPF

Methyl 5-methylisoxazole-3-carboxylate. T. P. Sycheva, Ya. G. Nekhlin, and M. N. Shchukina. **U.S.S.R. 160,274,** Jan. 16, 1964, Appl. Jan. 8, 1962. To 2.3 g. Na in 65 ml. abs. MeOH was added with stirring 11.8 g. $(CO_2Me)_2$ and 5.8 g. Me_2CO in 25 ml. abs. MeOH, the mixt. kept overnight, neutralized with concd. HCl, and treated with 8.9 g. $NH_2OH.HCl$. The whole was heated to boiling 3.5–4 hrs., the alc. distd., the residue cooled and basified (Na_2CO_3) to pH 8, and the ppt. dried ($CaCl_2$) to give the title compd., m. 89–90°, yield 46%. From *Byul. Izobret. i Tovarnykh Znakov* **1964**(3), 42. MDCL

Isoxazole derivatives of sulfanilamide. Hideo Kano, Masaru Ogata, and Haruo Nishimura (to Shionogi & Co., Ltd.). **U.S. 3,144,448** (Cl. 260–239.9), Aug. 11, 1964; Japan. Appl. Aug. 21, 1962; 5 pp. Chlorine gas was passed into a soln. of 3-amino-5-methylisoxazole (**I**) (1 part) in 5 parts AcOH for 0.5 hr. while cooling with H_2O. Aq. $Na_2S_2O_3$ was added, the mixt. shaken with $CHCl_3$, and the $CHCl_3$ layer washed with H_2O and dried. Removal of the solvent yielded 3-amino-4-chloro-5-methylisoxazole (**II**) (X = Cl), m. 89–91° (cyclohexane). Similarly



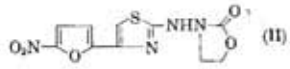
(II)



(III)

prepd. was **II** (X = Br), m. 77–8°. Solns. of 1.5 parts **I** in a small amt. of H_2O and 9 parts $HgCl_2$ in 200 parts hot H_2O were mixed, refluxed for 1 hr., and cooled to yield 4.5 parts **II** (X = ClHg), m. 223° (decompn.). A mixt. of 3.5 parts of the latter, 2.7 parts iodine, and 8 parts KI was stirred for 30 min., treated with $Na_2S_2O_3$, and extd. with $CHCl_3$. Removal of the solvent from the dried $CHCl_3$ layer yielded 0.8 part **II** (X = iodo), m. 104–5°. **II** (X = Br) was similarly prepd. To a soln. of 6 parts **II** (X = Cl) in a mixt. of 4 parts C_5H_5N and 20 parts C_6H_6 was added 11 parts *p*-acetamidobenzenesulfonyl chloride and the mixt. stirred for 2 hrs. at 50°. The C_6H_6 layer was decanted from the cooled soln. and H_2O was added to the residue to ppt. crystals. which were collected by filtration and heated with 10% NaOH on a H_2O bath for 1 hr. Acidification of the cooled mixt. yielded 3-sulfanilamido-4-chloro-5-methylisoxazole (**III**, X = Cl), m. 187–8° (EtOH). The following derivs. of **III** were similarly prepd. (X and m.p. given): Br, 183–4°; iodo, 209–10° (decompn.). I. Levi

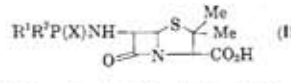
1-(2-Oxo-3-oxazolidinyl)thiourea. Frank F. Ebetino (to Norwich Pharmacal Co.). **U.S. 3,141,889** (Cl. 260–307), July 21, 1964, Appl. July 29, 1963; 1 p. A soln. of 0.6 mole 3-amino-2-oxazolidone and 0.67 mole KCNS in 125 ml. H_2O was treated with 50 ml. HCl and heated 1.5 hrs. on a steam bath to give 64% the title compd. (**I**), m. 195–6° (H_2O). A mixt. of 0.2



(II)

mole **I** and 0.2 mole bromomethyl 5-nitro-2-furyl ketone in 500 ml. of EtOH was refluxed 1 hr. with stirring to give 77% **II**, m. 170–3° (EtOH), which had antibacterial, anthelmintic, and antiprotozoal activity. H. A. Burch

Derivatives of 6-aminopenicillanic acid. Billie K. Koe (to Chas. Pfizer & Co., Inc.). **U.S. 3,144,444** (Cl. 260–239.1), Aug. 11, 1964, Appl. Sept. 27, 1960; 5 pp. A soln. of 8.97 g. *O*-(*p*-methoxyphenyl)phenylphosphonothioic chloride in 45 ml. Me_2CO is added slowly to a soln. of 6.48 g. 6-aminopenicillanic acid (**I**) and 6.0 g. $KHCO_3$ in 45 ml. H_2O and the soln. (pH 8) adjusted to pH 6 by the addn. of solid **I** and agitated for 5 hrs. The filtered mixt. is dild. with 400 ml. H_2O and extd. with Et_2O and then EtOAc at pH 5.5. The EtOAc soln. is washed with 0.5 vol. H_2O, dried (Na_2SO_4), adjusted to pH 8 with *N* methanolic KOH, and evapd. to dryness. The residue on trituration with Et_2O gave 6-[*O*-(*p*-methoxyphenyl)phenylphosphonamidothioyl]penicillanic acid (**II**, X = S, R^1 = Ph, R^2 = *p*-methoxyphenoxy). Similarly prepd. were the follow-



(II)

ing **II** (X, R^1, R^2 given): O, Ph, BuO: O, iso-Pr, EtO; O, Ph, β-chloroethoxy: O, Ph, *o*-ClC_6H_4O; S, Ph, EtO; O, Bu, BuO; O, Et, EtO; O, Ph, *o*-tolyloxy; S, Ph, PhO. These were obtained in the acid form as well as the Na and K salts. They are effective in treating a no. of gram-pos. and gram-neg. and penicillin-resistant infections in animals and man. I. Levi

Cycloaliphatic antimicrobial agents. Smith Kline & French Laboratories. **Brit. 959,054** (Cl. A 61*k*, C 07*d*), May 27, 1964; U.S. Appl. Jan. 31, 1961; 12 pp. Acylated derivs. of 6-aminopencillanic acid (**I**) and 7-aminocephalosporanic acid (**II**) are described. To a soln. of 350 ml. 3*M* ethereal MeMgBr and 150 ml. dry Et_2O at below 10° is added over 1.5 hrs. 132.2 g. PhCH:CHCHO with stirring under N. Treatment with 350 ml. 30% H_2SO_4 and distn. gives $PhCH{:}CHCH{:}CH_2$ (**III**). A mixt. of 59.6 g. **III**, 36 g. acrylic acid (**IV**), and 1 g. hydroquinone (**V**) is kept at room temp. 30 days to give solid 2-phenyl-3-cyclohexenecarboxylic acid (**VI**). Redn. of 45.3 g. **VI** in 150 ml. AcOEt with 0.5 g. PtO_2 and H at 50 lb./in.² gives 2-phenylcyclohexanecarboxylic acid. 2-Phenyl-3-cyclohexenecarbonyl chloride (**VII**) is prepd. by keeping 7.0 g. **VI** and 25 ml. $SOCl_2$ at room temp. 15 hrs. A soln. of 7.75 g. solid **VII** in 35 ml. acetone