

Several derivatives of *p*-chlorophenoxyacetic acid. N. A. Zakharova, N. V. Khromov-Borisov, and M. L. Indenbom. *Biol. Aktivn. Soedin., Akad. Nauk SSSR* 1965, 112-16(Russ). Derivs. of  $p\text{-ClC}_6\text{H}_4\text{OCH}_2\text{COR}$  (I, R = OH) (Ia) were prepd. and the pharmacol. properties of their HCl salts studied.  $\text{Na}_2\text{CO}_3$  (61 g.) was dissolved in 400 ml.  $\text{H}_2\text{O}$  and 108.8 g. (15% excess)  $\text{ClCH}_2\text{CO}_2\text{H}$  added in portions; addnl.  $\text{Na}_2\text{CO}_3$  was added to obtain pH near 7.  $p\text{-ClC}_6\text{H}_4\text{OH}$  (128.6 g.) in 350 ml.  $\text{H}_2\text{O}$  contg. 40 g. NaOH was added, the mixt. refluxed 8 hrs., cooled to  $80-5^\circ$ , and 100 ml. concd. HC ladded within 20-25 min. under const. stirring. The cryst. product (Ia), m.  $156-8^\circ$ , was converted to its acyl chloride (II), b<sub>12</sub>  $138-41^\circ$ ,  $n_D^{21}$  1.5489 by refluxing 1.5 hrs. with a 2.5-fold excess of  $\text{SOCl}_2$ . II (0.1 mole) in 50 ml.  $\text{C}_6\text{H}_5\text{Cl}$  and 0.1 mole of the 2nd compd. were warmed 1.5-3 hrs. at  $120-5^\circ$ , the residue was filtered off, and washed several times with  $\text{C}_6\text{H}_6$  and  $\text{Et}_2\text{O}$  to yield the cryst. HCl salts which on neutralization gave the free bases. The following I were prepd. (R, % yield, b.p./mm.,  $n_D^{23.5}$ , m.p. HCl salt given):  $\text{OCH}_2\text{CH}_2\text{N}(\text{CH}_3)_2$  (III), 67.2,  $180^\circ/9-10$ , 1.5160,  $140-2^\circ$ ,  $\text{OCH}(\text{CH}_3)\text{CH}_2\text{N}(\text{CH}_3)_2$  (IV), 70.5,  $173^\circ/8$  (m.  $35-7.5^\circ$ ), —,  $196-7^\circ$ ;  $\text{OCH}_2\text{CH}(\text{CH}_3)\text{N}(\text{CH}_3)_2$  (V), 52.5,  $153-4^\circ/2$ , 1.5141,  $136-40^\circ$ ;  $\text{NHCH}_2\text{CH}_2\text{N}(\text{CH}_3)_2$  (VI), 29.7, —, —,  $148-50^\circ$ ;  $\text{OCH}_2\text{CH}_2\text{N}(\text{C}_2\text{H}_5)_2$  (VII), 52.1,  $169-71^\circ/2-3$ , 1.5119,  $115-17^\circ$ ;  $\text{OCH}(\text{CH}_3)\text{CH}_2\text{N}(\text{C}_2\text{H}_5)_2$  (VIII), 64.0,  $161-3^\circ/3$ , 1.5066, hydroscopic;  $\text{OCH}_2\text{CH}(\text{CH}_3)\text{N}(\text{C}_2\text{H}_5)_2$  (IX), 33.6,  $174^\circ/4-5$ , 1.5074,  $81-3^\circ$ ;  $\text{NHCH}_2\text{CH}_2\text{N}(\text{C}_2\text{H}_5)_2$  (X), 50.8, —, —,  $112-14^\circ$ ;  $\text{SCH}_2\text{CH}_2\text{N}(\text{C}_2\text{H}_5)_2$  (XI), 39.6,  $186-7^\circ/3$ , 1.5492,  $151-3^\circ$ ; tropine (XII), 65.5,  $195^\circ/2-3$  (m.  $85-7^\circ$ ), —,  $194.5^\circ$ . III and VII had low toxicity showing faint local anesthetic and stimulating activity of the central nervous system. VI is similar to III and VII, but exhibits a high cholinolytic effect. X and XI show high toxicity and local action, but XI in 5 and 10% solns. exhibits an irritating action. IV, VIII, V, and IX also show increased activity; however, IV and VIII are somewhat more toxic and possess a higher local anesthetic action than V or IX. IX is similar to VII, but shows cholinolytic effects while XII shows strong action on the central nervous system. The above studies were done on the HCl salts.

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