in the present investigation supports Jenkin's view. From the knowledge of ionisation constants of 2-chloro-3-nitro and 2-chloro-4-nitrobenzoic acids it is likely that the former should have a low rate compared to its *ortho* isomer. However, from the experimental observation it is found that 2-chloro-3-nitrobenzoic acid decarboxylates at a higher rate than 2-chloro-4-nitrobenzoic acid. This is due to the fact that the halogen atom in the 2-chloro-3-nitrobenzoic acid is bent out of the plane of the ring by the large groups on either side of it and thus is prevented from attaining the planar configuration necessary for the mesomeric effect. Since, the nitro group is *para* to carboxyl group, in 2-chloro-4-nitrobenzoic acid, such a steric effect is improbable and results in a low rate. A comparison of the enthalpies and entropies of activation of the two isomers is a further evidence for the proposed S_E1 mechanism. Although the inductive effect of the chlorine is the predominant factor, it is superimposed by the mesomeric effect to a greater extent in 4-chloro-3-nitrobenzoic acid. The net effect arising from the combination of these two increases the C–C bond strength and results in higher enthalpy of activation than its *ortho* isomer. This seems to be the reason for the low rate observed in the 4-chloro-3-nitrobenzoic acid.

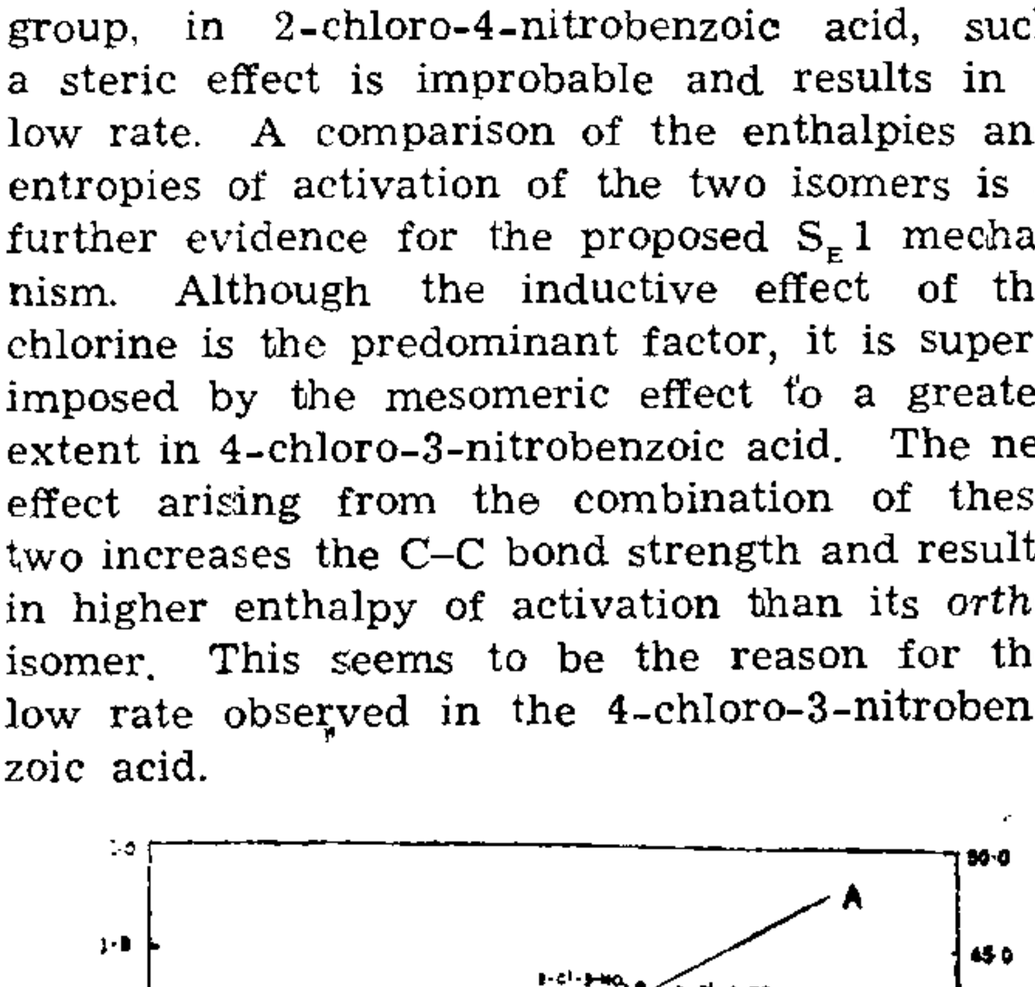

FIG. 1. A, Plot of log *k vs.* log K ; B, Plot of H^* *vs.* S^*.

The plot of log *k* against log K gave a linear relationship as in Fig. 1, A with a slope of + 0·27 suggesting that the decarboxylation is facilitated by electron withdrawing groups, a characteristic of the S_E1 mechanism.[8] The other plot, Fig. 1, B, ΔH^* against ΔS^* also reveals that all these acids follow a similar mechanism except *o*- and *p*-chlorobenzoic acids and the isokinetic temperature is calculated as 509° K.

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Dept. of Chemistry, Osmania University, Hyderabad-7, *June* 12, 1970.

MRS. D. SITA MANIKYAM.
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2-SUBSTITUTED AMINOPROPIONAMIDOXIMES AND THEIR DERIVATIVES

AMINOACETAMIDOXIMES, having alkyl or aryl substituents on the nitrogen, have been reported[1] to possess fungicidal properties. 2-Arylaminopropionic acids and their amides have been claimed[2] to possess antidiabetic activity. So, the synthesis of 2-substituted aminopropionamidoximes and their carbamate derivatives was undertaken.

The 2-substituted aminopropionitriles required for our work were prepared by standard literature methods.[3] The nitriles were converted to the corresponding amidoximes in 40–60% yields by reacting them with hydroxylamine in aqueous ethanol. The oximes, on reaction with potassium cyanate, gave their O-aminocarbonyl derivatives. Compounds 4, 7 and 11 (Table I) have shown significant oral hypoglycemic properties, but they have also been toxic.

2 - o - Chloroanilinopropionamidoxime.—2 - o - Chloroanilinopropionitrile (4·5 g. ; 0·025 mole), hydroxylamine hydrochloride (1·75 g. ; 0·025 mole) and potassium carbonate (1·75 g. ; 0·013 mole) were refluxed in 80% ethanol (100 ml.) for 5 hours. The solvent was removed *in vacuo* ; the gummy residue was washed with ice-cold water and then chromatographed over

a 20" × 1·5" column of acid-washed alumina slurry-packed in benzene. The column was progressively eluted with benzene (400 ml.), benzene-ethanol (75%-25% ; 300 ml.), benzene-ethanol (50%-50% ; 300 ml. and ethanol (600 ml.) and 100 ml. fractions were collected. Fractions 2-4 gave 2-*o*-chloroanilinopropionitrile (2·3 g.) and fractions 11–14 gave 2·4 g. of the title product. It was crystallised from ethanol-benzene-hexane ; m.p. 69–70°.

TABLE I

$$R_1\text{-}NHCH_2CH_2\text{-}C(=N\text{-}O\text{-}R_2)(\text{-}NH_2)$$

No.	R_1	R_2	m.p. °C.*	Nitrogen % Found	Nitrogen % Calc.
1	Phenyl ..	H : 2 HCl†	180-82	16·45	16·67
2	Benzyl ..	H : 2 HCl†	181–83	15·95	15·80
3	Phenylethyl ..	H : 2 HCl	180-82	15·32	15·00
4	Cyclohexyl ..	H	114–15	22·79	22·71
5	*o*-Chlorophenyl	H	69–70	19·37	19·67
6	,, ..	H : 2 HCl	195–96	14·31	14·67
7	,, ..	$CONH_2$	59-60	21·62	21·83
8	*m*-Chlorophenyl	H	79-80	19·81	19·67
9	,, ..	H : 2 HCl	189–90	14·79	14·67
10	,, ..	$CONH_2$	84–85	21·63	21·83
11	*p*-Chlorophenyl	H : 2 HCl	170-72	14·74	14·67
12	,, ..	$CONH_2$	112–13	21·58	21·83
13	*o*-Tolyl ..	H : 2 HCl	188-90	15·64	15·80
14	,, ..	$CONH_2$	89–90	23·49	23·73
15	*m*-Tolyl ..	H : 2 HCl	193–94	15·45	15·86
16	*p* Tolyl ..	H	82–83	21·61	23·76
17	,, ..	H : 2 HCl	187–88	15·59	15·80
18	,, ..	$CONH_2$	68–70	23·54	23·73
19	*o*-Anisyl ..	H	91–92	20·34	20·09
20	,, ..	$CONH_2$	59–60	22·41	22·22
21	*m*-Anisyl ..	H : 2 HCl	182-84	14·63	14·89
22	,, ..	$CONH_2$	109–10	23·23	22·22
23	*p*-Anisyl ..	H	92-93	20·06	20·09
24	,, ..	$CONH_2$	123-24	22·53	22·22

* All melting points are uncorrected. † Halogen estimation corresponded to 2 HCl.

O-Aminocarbonyl-2- o *- chloroanilinopropion-amidoxime.*—To a cold solution of 2-*o*-chloroanilinopropionamidoxime (1·8 g. ; 0·01 mole) in dilute hydrochloric acid (10 ml. ; 2 N) was added a solution of potassium cyanate (0·9 g. ; 0·011 mole). After 10 minutes at 5°, the reaction solution was rendered neutral with ammonia. The resulting gummy mass gradually solidified ; it was crystallised from acetone-benzene-hexane ; m.p. 59–60°.

The rest of the compounds in Table I were similarly prepared.

Sarabhai Res. Centre, S. SOMASEKHARA.
Wadi Wadi, D. M. DESAI.
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EFFECT OF PARAOXON ON THE SOMATOSENSORY EVOKED POTENTIALS IN THE RAT

THE transmitter function of acetylcholine in the cerebral cortex has been the subject of many investigations. Application to the cortex of drugs that influence cholinergic synapses gave results that were often contradictory and difficult to interpret.[3] Another approach to the cortical cholinergic mechanisms has been made by studying the effect of topically applied cholinomimetic drugs on the somatosensory evoked potentials. Bhargava[1] has shown that the cortical application of artificial cerebrospinal fluid (CSF) containing various concentrations of acetylcholine increases the amplitude of the repetitive after-discharges of the somatosensory cortex, whereas they do not influence the short latency positive-negative primary complex of the cortical evoked potentials. It appears that the short latency primary evoked potential is not cholinergic, as Mitchell[4] has shown that under chloralose anaesthesia acetylcholine output is greatly reduced while the initial positive-negative potential is increased. It seems that the activity of cholinoceptive units rather manifests itself in potentials of longer latency (*i.e.*, repetitive after-discharges).

The present experiments were undertaken to study the effect of cortical application of paraoxon (an irreversible inhibitor of cholinesterase) on the somatosensory evoked potentials, and to find out the cholinergic component of the cortical evoked potentials. The study may throw more light on the intra-cortical cholinergic mechanisms.

In rats (CFE strain from Carworth, Europe) lightly anæsthetised with pentobarbitone, the technique of Bhargava and Meldrum[2] was employed to record the averaged somatosensory evoked potentials. Computer derived averages of 32 consecutive somatosensory evoked potentials from both cortices, in response to the