

pK<sub>a</sub> VALUE OF PROTONATED 3,3-DIMETHYL-1-CYCLOBUTENE CARBOXYLIC ACID

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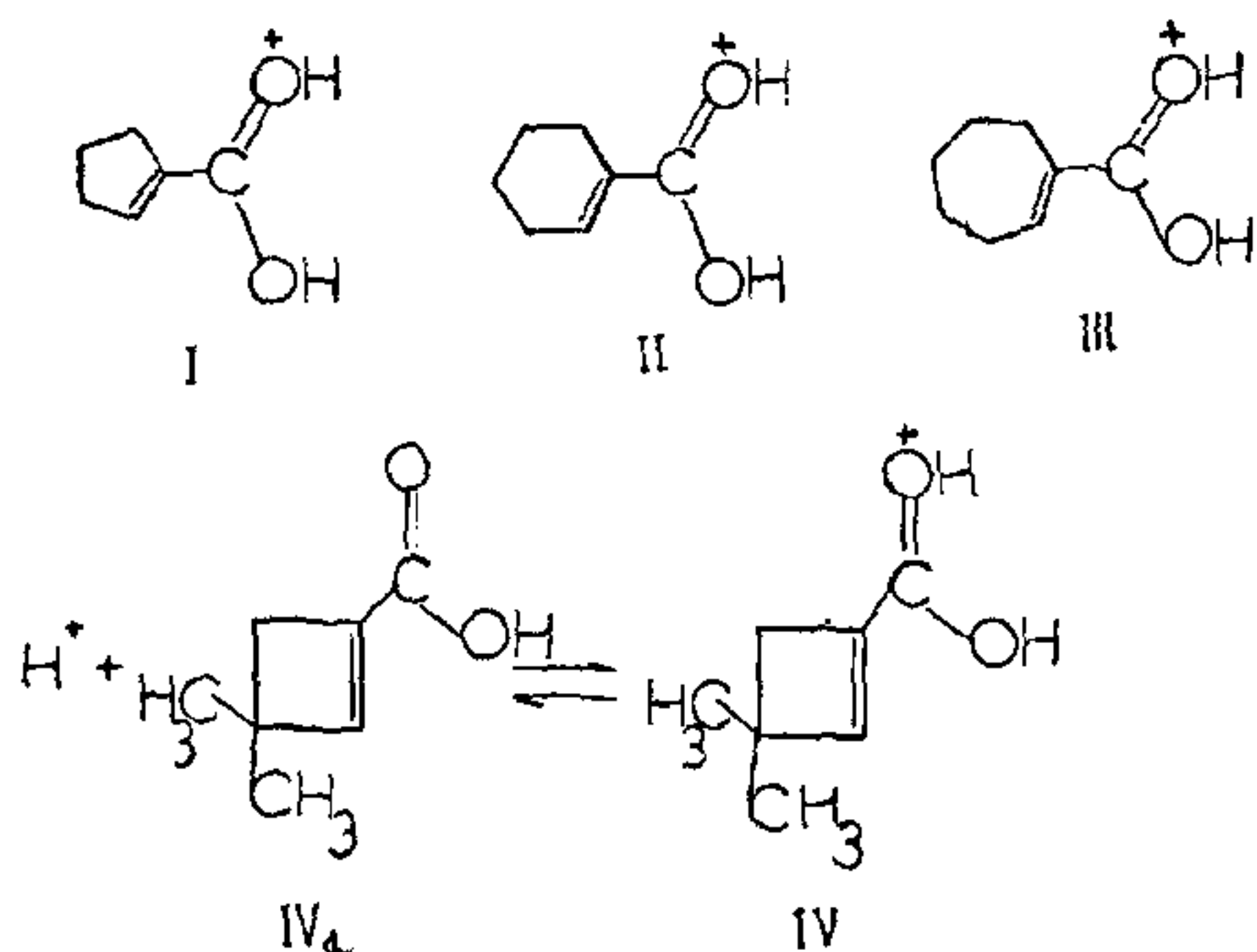
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## ABSTRACT

The pK<sub>a</sub> value of protonated 3,3-dimethyl-1-cyclobutene carboxylic acid has been found to be -4.10. The acidity of the protonated  $\alpha$ ,  $\beta$ -unsaturated acids can be arranged in the order of their ring size as follows: 4 > 5 > 6  $\sim$  7.

THE basicity constant, *i.e.*, pK<sub>BH<sup>+</sup></sub> of weak organic bases using sulphuric acid medium has been the subject of intensive study for correlation of acidities with the substituent effects. Since resonance participation is more important in the ionic species than in the neutral molecule, the pK<sub>a</sub> value will be a measure of the stability of the protonated form relative to the unprotonated form.

In a recent communication<sup>2</sup>, we have reported the pK<sub>a</sub> values of protonated cyclic  $\alpha$ ,  $\beta$ -unsaturated carboxylic acids (I-III) and it was shown that the change in acidity is very much dependent on the ring size. We now wish to report the pK<sub>a</sub> value of protonated cyclobutene carboxylic acid derivative (IV).



## METHODS AND MATERIALS

3,3-Dimethyl-1-cyclobutene carboxylic acid was prepared using the procedure reported in the literature<sup>3</sup>, and was purified by vacuum distillation, b.p. 113-4°/1 mm. The compound became solid on keeping for some time and was further purified by recrystallization using *n*-hexane, m.p. 70° (lit. m.p. 70-71°). The percentage sulphuric acid w/w was determined by titrating against a standard base. The data of Hammett acidity functions *H*<sub>0</sub> and *H*<sub>A</sub> for a given percentage (w/w) of sulphuric acid are available in the literature<sup>4</sup>. The spectral measurements were carried using Cary-14R U.V. Spectrophotometer

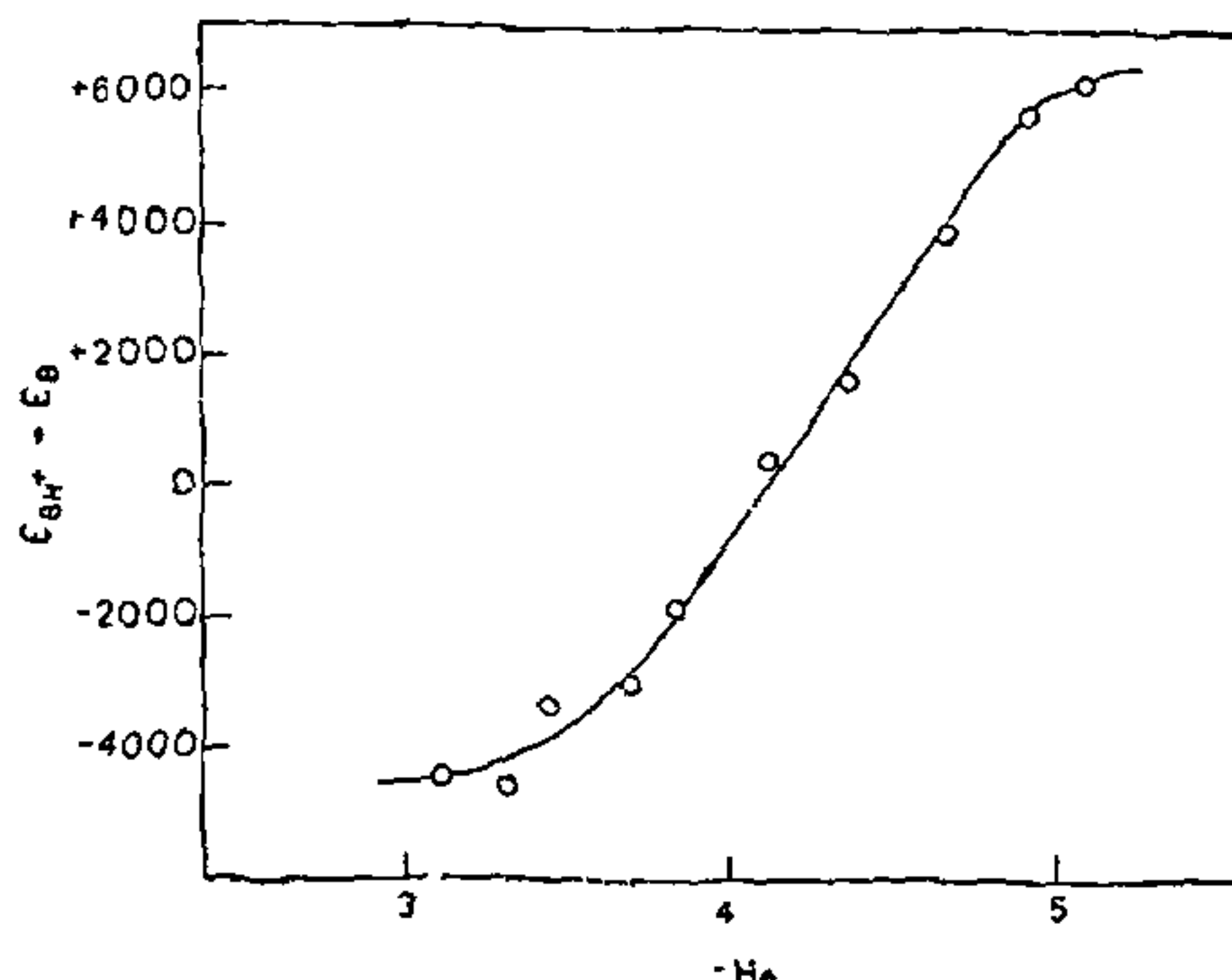


FIG. 1. pK<sub>a</sub> calculation using the procedure of Davis and Geissman<sup>5</sup> for protonated 3,3-dimethyl-1-cyclobutene carboxylic acid.

with a solvent blank as the reference. The pK<sub>a</sub> value has been determined using the procedure of Davis and Geissman<sup>5</sup> (Fig. 1) as described in our earlier paper<sup>2</sup>. In general, the concentration of the free base (B) and that of the protonated base (BH<sup>+</sup>) cannot be obtained directly from the spectra due to solvent effects. Various methods are known in the literature<sup>6,7,9</sup> for correcting solvent effects and we found the method described by Wang *et al.*<sup>10</sup> most satisfactory in the present studies. Accordingly we have plotted

$$\log [BH^+]/[B] \text{ i.e., } \log (\epsilon_{BH^+} - \epsilon)/(\epsilon - \epsilon_B) \text{ vs. } H$$

and the slopes are found to be 0.8 and 0.4 using *H*<sub>A</sub> and *H*<sub>0</sub> scales (Fig. 2) respectively. Similar to the other protonated cyclic acids, protonated cyclobutene carboxylic acid follows the *H*<sub>A</sub> and scale could be classed under the non-Hammett bases.

## RESULTS AND DISCUSSION

Simple cyclobutene carboxylic acid has been reported to be unstable and our own observations on the preparation of this compound further confirmed this. We, therefore, attempted the preparation of

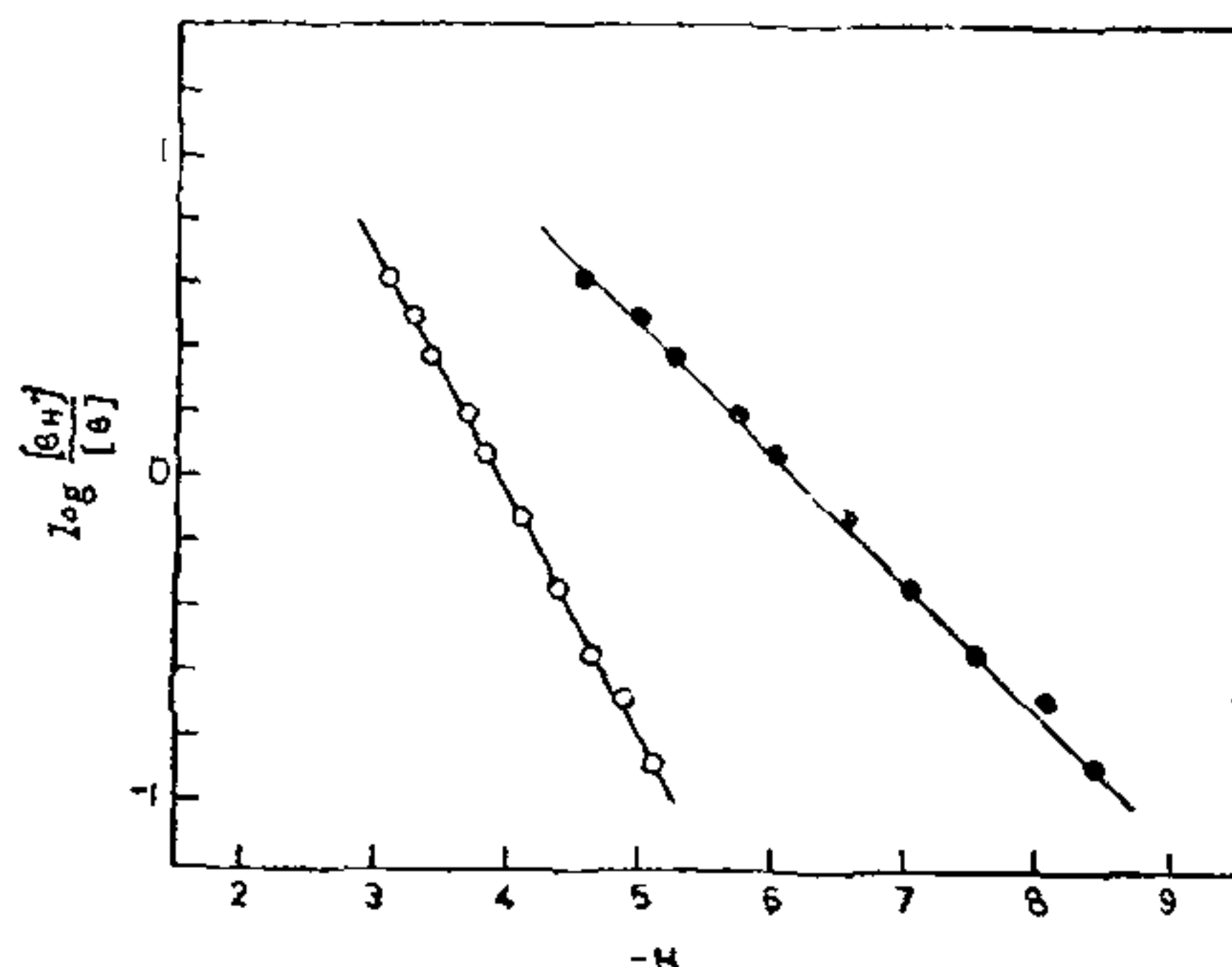


FIG. 2. Plot of  $\log [BH^+]/[B]$  vs. acidity of protonated 3,3-dimethyl-1-cyclobutene carboxylic acid.

O represent  $H_A$  and  $\bullet$  represent  $H_O$ .

3,3-dimethyl-1-cyclobutene carboxylic acid for comparison of acidities. The extra methyl groups at 3-position are unlikely to cause any changes in the conjugative ability of the double bond and, therefore, we have measured the acid strength of protonated 3,3-dimethyl-1-cyclobutene carboxylic acid which is quite stable in sulphuric acid solution.

The absorption maxima of IVa shifts from 254 to 214 nm, when the medium is altered from 95.32% sulphuric acid to water. The  $pK_a$  value was found to be  $-4.10$  and the acid IV seems to be stronger than the other protonated cyclic acids namely, cyclopentene, cyclohexene and cycloheptene carboxylic acids, whose  $pK_a$  values are  $-4.05$ ,  $-3.88$  and  $-3.84$  respectively. Other factors like solvation and the inductive effect of alkyl groups should have decreasing effect on the acid strength of the protonated species. Therefore, the increase in acidity in this

system suggests that the conjugative effect of the double bond is less in the four-membered ring system, compared to other cyclic systems. The protonated form (IV) is destabilized with respect to the free base (IVa), thereby shifting the equilibrium towards right  $IV \rightleftharpoons IVa$ . It appears, therefore, that the endo-double bond is preferred in the cyclobutene system and the acidity of the protonated cyclic  $\alpha, \beta$ -unsaturated cyclic acids can be arranged in terms of their ring size as  $4 > 5 > 6 \sim 7$ .

#### ACKNOWLEDGEMENT

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### A NEW METHOD FOR THE TOTAL SYNTHESIS OF 1-OXO-3-THIA-10-PHENYL-9-METHYL-9-AZA-1,2,3,4,9,10-HEXAHYDROPHENANTHRENE

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#### ABSTRACT

The synthesis of the tricyclic ketone, 1-oxo-3-thia-10-phenyl-9-methyl-9-aza-1,2,3,4,9,10-hexahydrophenanthrene (IX), starting with lepidine, is described, as a key intermediate for the total synthesis of the unknown 1-carbomethoxy-4-phenyl-5-methyl-4H, 5H, 10H-isoxazolo-[4,5-b] thiopyrano [4,3-c] quinoline (X).

#### INTRODUCTION

RECENT publications<sup>1-4</sup> point out that several steroidal analogues with replacement of D-ring of the normal steroid by an isoxazole or pyrazole ring

exhibit interesting biological properties. Encouraged by these findings, the total synthesis of the hitherto unknown tricyclic ketone (IX) was achieved with a view to converting it into the desired isoxazole derivative (X).