

animals were laparotomized on day 9–10 of pregnancy and the number of implantation sites and corpus lutea was recorded. The mean number of implantation sites and corpus lutea in the treated rats was calculated separately and the standard errors ( $\pm$  value) from mean value were calculated according to the following equation.

$$\text{Standard Error (S. E.)} = \sqrt{\frac{\sum d^2}{n(n-1)}}$$

where  $d$  is the difference from the mean and  $n$  is the number of observations i.e. number of rats tested per compound. The per cent effectiveness of the compounds tested for their anti-implantation activity was calculated in two ways.

(i) Incidence: The per cent effectiveness in terms of incidence of pregnancy

$$= \frac{\text{number of animals rendered infertile}}{\text{number of animals treated}} \times 100$$

(ii) Rate: The per cent effectiveness in terms of rate of pregnancy was calculated by comparing the mean number of implantations site found in the treated animals with that of the control.

**Early abortifacient activity<sup>7</sup>:** The compounds under investigation were prepared as suspension in gum acacia and an equal amount of distilled water to obtain a final concentration of 5 mg/ml and were fed orally on days 8–9 of pregnancy. Day 1 of pregnancy was designated when sperms were found in the vaginal smears of female albino rats (body weight  $200 \pm 10$  g) left overnight with males of proven fertility.

Following administration of the compounds, frank vaginal bleeding was taken as the index of the drug induced abortion of pregnancy. This was further confirmed by laparotomic observations of the uterus, 3–4 days after treatment. Based on the size and shape of the embryos as compared with the controls, the degree of abortifacient activity was graded as mild, midway and complete.

All the four tetrazine derivatives (1, 5, 6 and 9) which were screened for their anti-implantation activity were found inactive in terms of incidence of pregnancy. However, three tetrazine derivatives exhibited mild anti-implantation activity in terms of the rate of pregnancy. Compound no. 5 with a 3-methylimidazolyl substituent was found to possess 14.5% activity in terms of the rate of pregnancy while compounds no. 1 and 4 showed anti-implantation activity to the extent of 5.2% and 9.8% respectively.

All the four tetrazine derivatives (1, 2 and 5) which

were screened for their early abortifacient activity showed 33.3% activity. However the degree of resorption in animals aborted was complete in compounds 1 and 5. It was midway for compound no. 2 and mild for compound no. 3. In view of the limited data, the structure activity relationship could not be properly established.

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## KINETICS OF OXIDATION OF ACETOPHENONE OXIME BY 1-CHLOROBENZOTRIAZOLE

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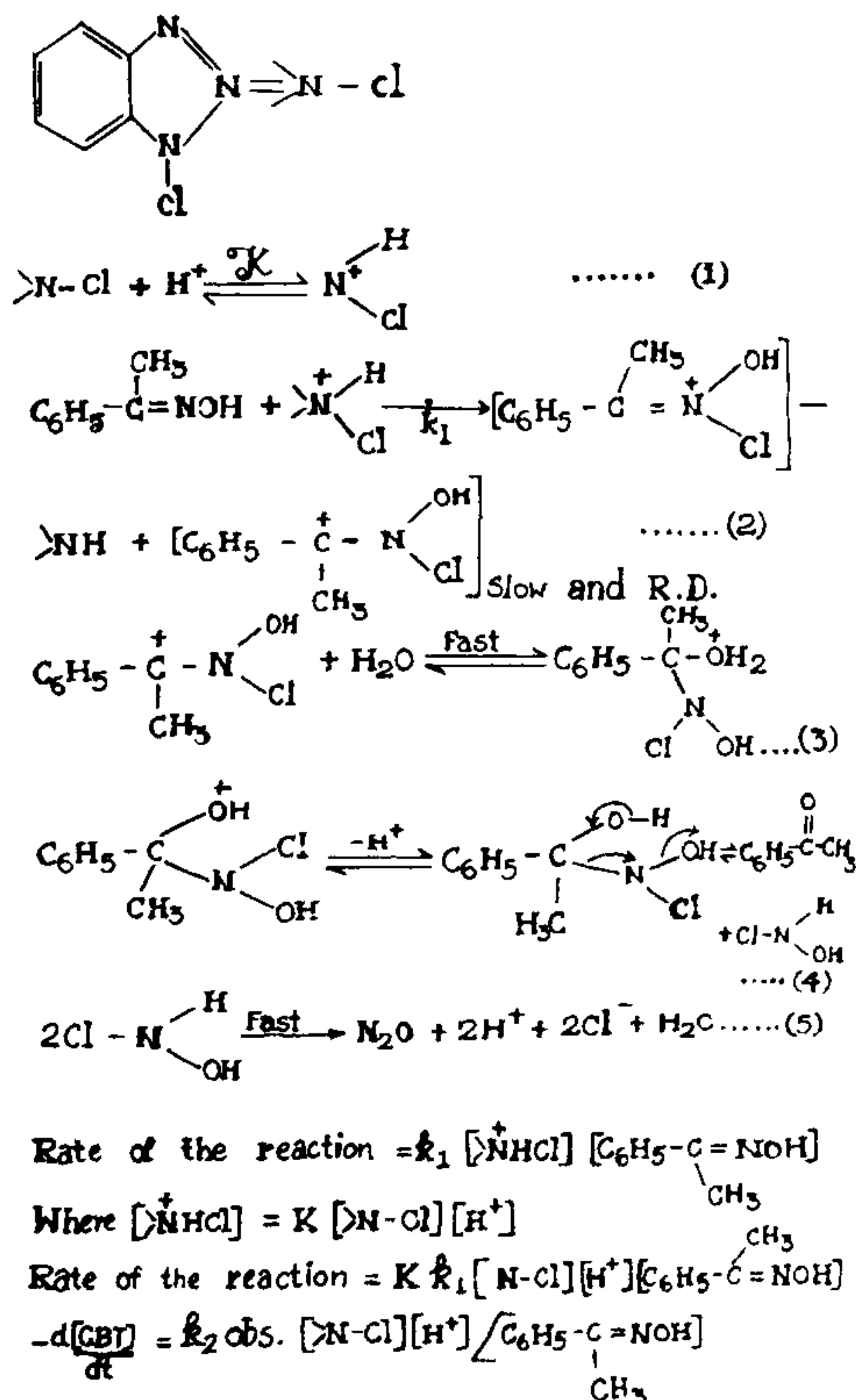
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A NUMBER of kinetic investigations on oxidation<sup>1–6</sup> and chlorination<sup>7–8</sup> of organic substrates like alcohols, ethers, hydrazo and organic sulphides by 1-Chlorobenzotriazole (CBT) have been reported. The oxidation of oximes typically acetophenone oxime and several substituted acetophenone oximes by CBT has been studied from the kinetic standpoint and the results are reported in this paper.

1-Chlorobenzotriazole was prepared as described by

Rees and Storr<sup>9-11</sup> and the purity was checked by iodometric assay. Acetophenone oxime and substituted acetophenone oximes (*p*-Cl, *p*-Br, *p*-CH<sub>3</sub> and *p*-OCH<sub>3</sub>) were prepared and purified by literature methods. The reaction was carried out in pseudo-first-order condition by always taking the substrate in excess. The experiment was carried out by mixing the substrate and oxidant in appropriate solvent mixture and the unreacted CBT was estimated iodometrically, using starch as indicator. The stoichiometry of the reaction was found to be 1:1. The final product was acetophenone through its DNP derivative (m.p.).

The reaction was total second-order, first-order with respect to CBT and first-order with respect to acetophenone oxime. The first-order dependence of CBT is revealed by the constancy of  $k_{obs}$  obtained from



Scheme -1.

the integrated first order equation. That reaction was first-order with respect to acetophenone oxime as evidenced from the constant  $k$  values.

The added H<sup>+</sup> ion increases the reaction rate (table 1) which also increases as the concentration of the added chloride ion increases (table 2). The effect of added neutral salt (NaClO<sub>4</sub>) is not significant. The effect of varying the composition of the binary solvent mixture of acetic acid and water has been studied. At 40, 45, 50 and 60% (v/v) aqueous acetic acid the rate constants were 4.24, 3.32, 2.85 and 2.01 × 10<sup>-4</sup> sec<sup>-1</sup> respectively.

The kinetics of oxidation of acetophenone oxime was studied at 30, 35, 40 and 45°C. The rate constants were 2.86, 5.02, 7.92 and 12.65 × 10<sup>-4</sup> sec<sup>-1</sup> respectively. The thermodynamic parameters were calculated at 303 K and the values of activation energy, activation enthalpy, activation entropy and free energy of activation were 90.98 KJ mol<sup>-1</sup>, 88.34 KJ mol<sup>-1</sup>, -185.15 JK<sup>-1</sup> mol<sup>-1</sup> and 55.57 KJ mol<sup>-1</sup> respectively.

The kinetics of oxidation of substituted acetophenone oximes were studied (table 3) and the rate constants were analyzed by applying Hammett equation. A plot of log  $k_2/k_0$  vs  $\sigma$  gives a straight line ( $r = -0.990$ ) with the values of -0.77 and -1.05 at 303 K and 308 K indicating that the electron-releasing sub-

Table 1 Order dependence on added H<sup>+</sup> ion in the oxidation of APO by CBT

H <sup>+</sup> × 10 <sup>+3</sup> M	k <sub>1</sub> × 10 <sup>+4</sup> sec <sup>-1</sup>
3.00	3.21
4.00	4.38
5.00	5.64
6.00	7.10

[CBT] = 1.0 × 10<sup>-3</sup> M [APO] = 1.0 × 10<sup>-2</sup> M  
 50% HOAC-50% H<sub>2</sub>O. Temp. 30°.

Table 2 Order dependence on added Cl<sup>-</sup> ion in the oxidation of APO by CBT

Cl <sup>-</sup> × 10 <sup>+3</sup> M	k <sub>1</sub> × 10 <sup>+4</sup> sec <sup>-1</sup>
2.00	3.89
3.00	4.54
5.00	5.10
7.00	5.50

[CBT] = 1.0 × 10<sup>-3</sup> M [APO] = 1.0 × 10<sup>-2</sup> M  
 50% HOAC - 50% H<sub>2</sub>O. Temp. 30°.

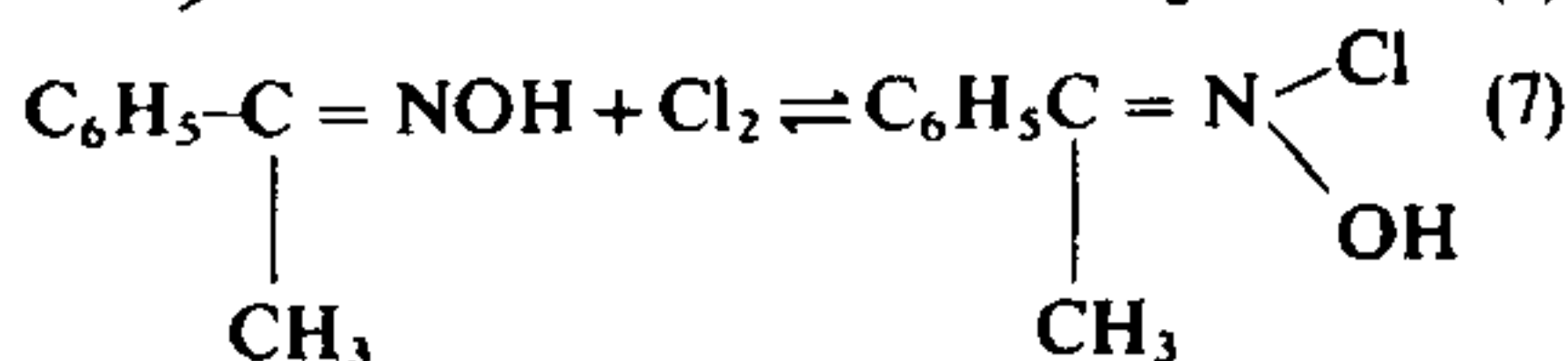
**Table 3** Effect of substituents in the oxidation of APO by CBT

	$k_t \times 10^4$ 303 K	$\text{sec}^{-1}$ 308 K
Acetophenone oxime	2.85	5.02
<i>p</i> -Chloroacetophenone oxime	2.07	2.17
<i>p</i> -Bromoacetophenone oxime	2.24	2.72
<i>p</i> -Methylacetophenone oxime	4.01	6.84
<i>p</i> -Methoxyacetophenone oxime	5.79	7.76

[CBT] =  $1.0 \times 10^{-3}$  M [oxime] =  $1.0 \times 10^{-2}$  M  
Solvent = 50% HOAc - 50% H<sub>2</sub>O.

stituents increase the reaction rate and the electron-withdrawing substituents decrease it.

In the presence of chloride ion the following mechanism is proposed in addition to scheme 1.



The protonated CBT reacts with Cl<sup>-</sup> to form free chlorine which reacts with acetophenone oxime at a faster rate and follows the steps 3, 4 and 5 as in scheme 1.

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### A NOVEL OBSERVATION ON THE REACTION OF 1,4-DIACETOXYBENZENE(III) WITH CERIUM(IV) AMMONIUM NITRATE

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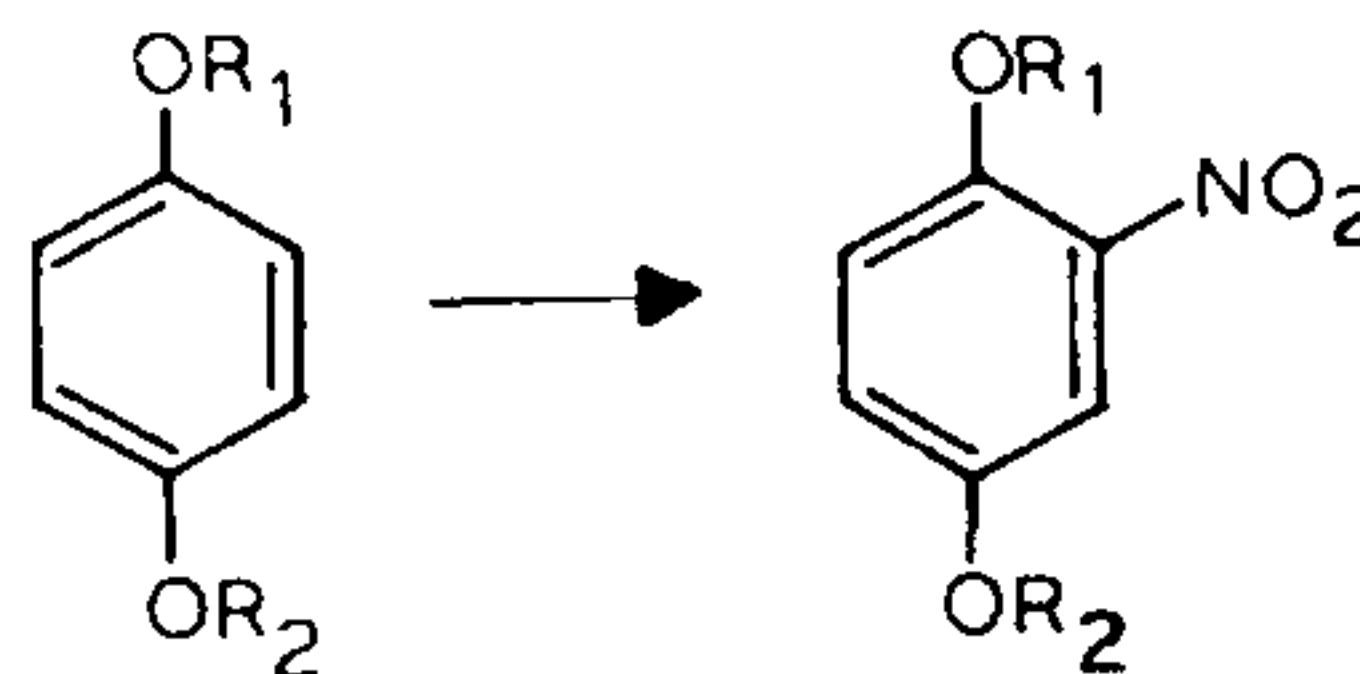
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IN continuation of our study on the reaction of phenolics induced by ceric ammonium nitrate (CAN)<sup>1,2</sup>, we have now studied the reactions of 1,4-dihydroxy; 1,4-dimethoxy; and 1,4-diacetoxybenzene with CAN. It is interesting to note that contrary to 1,4-dihydroxy and 1,4-dimethoxybenzenes where oxidation product is only quinone, no such oxidation product was obtained in 1,4-diacetoxybenzene, instead, nitro and deacetylated nitro products (IV and V) were obtained. This is the first report of nitration and deacetylation of diacetylbenzene using CAN as a reagent.

#### Experimental procedure

The phenol (1 g) was treated with CAN (2.2 g; 4 m mol) under conditions given in table 1. After the



- |     |                          |    |                                    |
|-----|--------------------------|----|------------------------------------|
| I   | $R_1 = R_2 = \text{H}$   | IV | $R_1 = \text{H}, R_2 = \text{OAc}$ |
| II  | $R_1 = R_2 = \text{OMe}$ | V  | $R_1 = R_2 = \text{H}$             |
| III | $R_1 = R_2 = \text{OAc}$ |    |                                    |