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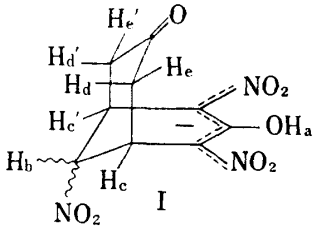
Isolation of a Bicyclic Compound from the Reaction of Acetone and Picric Acid

In the previous papers,[1,2] it was shown that a Meisenheimer type, a bicyclic type and a tetracyclic type compounds were formed as the main coloring matters of the reaction of acetone with a large amount of 1,3,5-trinitrobenzene in an alkaline medium. During the course of study on the mechanism of the color reaction between acetone and picric acid, a bicyclic compound was found to also be formed in the reaction. This communication deals with the preparation and structure of the compound and discusses its role in the Janovsky reaction.

The bicyclic compound was first obtained as yellow needles of mp 106° (Ia) (from methanol and ethyl acetate) in a relatively high yield (35%) by treating aqueous picric acid with a large amount of acetone in the presence of piperidine (molar ratio, 1:30:2). Ia [UV $\lambda_{max}^{aq.NaOH(10^{-4}-2M)}$ mμ: 236, 398, IR ν_{max}^{KBr} cm^{-1}: 3310 (broad, OH, hydrogen bonded), 1720 (C=O), 1543 and 1325 (NO_2)] was determined to have the formula of $C_{19}H_{31}O_8N_5$ by the elemental analysis (*Anal.* Calcd. for the formula: C, 49.93; H, 6.84; N, 15.33. Found: C, 50.12; H, 7.23; N, 15.16), which agreed with the composition of one piperidinium ($C_5H_{12}N$), one piperidine ($C_5H_{11}N$) and a bicyclic structural moiety (I) ($C_9H_8O_8N_3$). But, the bicyclic structure could not be confirmed by the nuclear magnetic resonance (NMR) spectrum because the intense signals due to piperidine and piperidinium protons veiled some signals to be ascribable to protons of I [NMR (dimethylsulfoxide-d_6) δ (ppm): 1.55 (broad singlet, piperidine $-CH_2$), 2.90 (broad singlet, piperidine $-CH_2$ adjacent to N), 8.00 (broad singlet, piperidinium –H), 2.35 (doublet, J=3.0 cps), 4.30 (poorly resolved quartet), 5.63 (triplet, J=3.0 cps)].

Ia was easily converted into yellow needles of mp above 300° (Ib) (from acetone) in 65% yield by treating it with a mixture of acetic anhydride and anhydrous sodium acetate at room temperature. Ib [IR ν_{max}^{KBr} cm^{-1}: 3436 (OH), 1728 (C=O), 1560 and 1322 (NO_2)] had the formula of $C_9H_8O_8N_3Na$ (elemental analysis. *Anal.* Calcd. for the formula: C, 34.95; H, 2.61; N, 13.59; Na, 7.44. Found: C, 35.38; H, 2.95; N, 13.71; Na, 7.07), suggesting that Ib was sodium salt of I. The NMR spectrum of Ib (Fig. 1) resembled that of the bicyclic compound (II) formed in the reaction of acetone and trinitrobenzene,[1] except that a singlet ascribable to hydroxyl proton, which disappeared on adding D_2O, was observed at δ 18.04 instead of a singlet at δ 8.51 in II. Furthermore, the results of spin-decoupling (Fig. 1) were entirely identical with those observed in the previous paper.[1] Thus, I was proved to be the anion having a structure written below.



I

The absorption spectrum of Ib showed the maxima at 241 and 398 mμ in a sodium hydroxide solution.

On the other hand, the reaction mixture of aqueous picric acid with acetone had another absorption spectrum (λ_{max} mμ: 407, 490) under the conditions of Janovsky reaction[3] in the early stage of the reaction. But the spectrum changed to have a maximum at 398 mμ when the reaction was continued for a longer time (2 hours). The resulting spectrum well agreed with that of Ib in the alkaline solution. The thin-layer chromatographic separation [adsorbent, Wakogel-B5; solvent system, ethanol–water–28% aqueous ammonia (10:5:1)] of the reaction mixture gave two main spots. One of them, a yellow and larger spot, was located

1) K. Kohashi, Y. Ohkura and T. Momose, *Chem. Pharm. Bull.* (Tokyo), **18**, 2151 (1970).
2) K. Kohashi, Y. Ohkura and T. Momose, *Chem. Pharm. Bull.* (Tokyo), **19**, 213 (1971).
3) M. Kimura, *Pharm. Bull.*, **3**, 81 (1955).

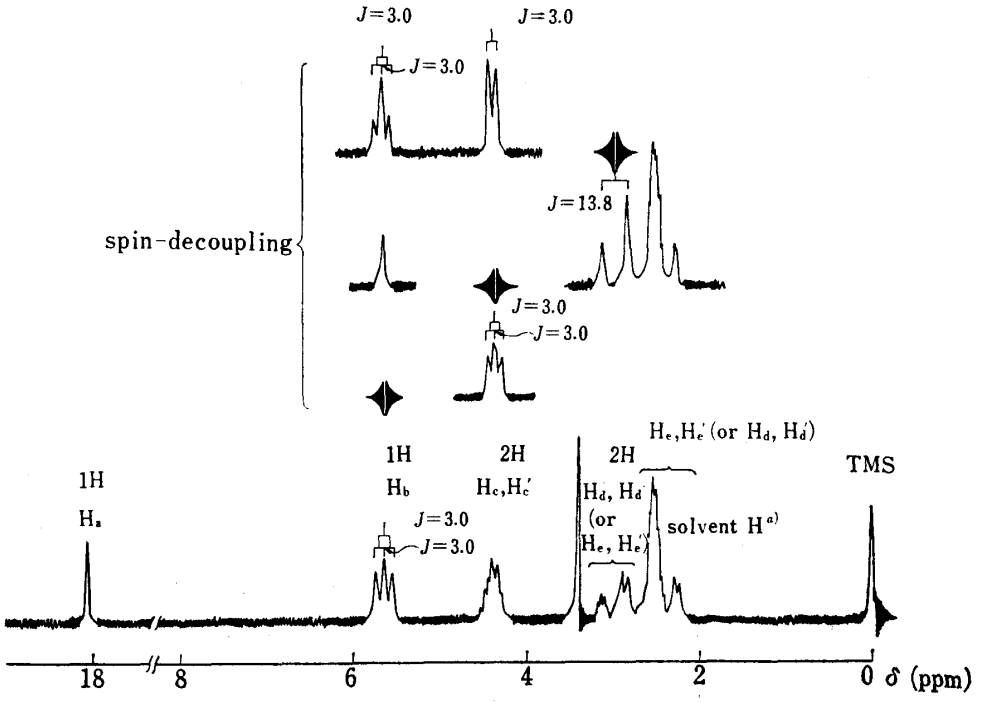


Fig. 1. The NMR Spectrum of Ib and the Results of Spin-Decoupling (Dimethylsulfoxide-d_6)

a) This signal might veil a part of the signals due to He and He' (or Hd and Hd'). *b*) *J* is expressed in cps.

at *Rf* value of 0.52, and identified with Ib by the overlapping method in the development. Furthermore, the water extract of the spot showed an identical absorption spectrum to Ib. These evidences clearly explained that Ib was produced as a main coloring matter in the reaction. It is important to note that such bicyclic compound as I is formed even in the aqueous Janovsky reaction.

Details of the study on I will be published in the near future, and the investigations of role of I in the reaction of acetone with a large amount of picric acid are now going on.

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6-Chloro-5-cyclohexylindan-1-carboxylic Acid (TAI-284), a New Antiinflammatory Agent

In the present communication we wish to report the synthesis and biological activity of a new antiinflammatory agent, 6-chloro-5-cyclohexylindan-1-carboxylic acid (TAI-284) (I), which has a simplified steroidal structure and reserves an interesting steric requirement for the activity.