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126. Tetsuzo Kato and Yutaka Yamamoto: Studies on Ketene and its Derivatives. X.*1 Reaction of Diketene with Schiff Base.

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In earlier papers of this series,[1,2] we have reported the reaction of diketene with a C=N double bond in a heterocyclic system such as pyridine, quinoline and isoquinoline to form so-called Wollenberg's compound (I),[3,4] as shown in Chart 1. If this reaction is applicable to other C=N double bonds in an aliphatic system, a new method of synthesizing heterocyclic compounds would be expected. Recently, Oda, *et al.*[5] reported the reaction of diketene with a Schiff base such as N-benzylidene-*tert*-butylamine to give an adduct of m.p. 108~109°. The structure for this compound was given as a cyclic compound, 1-*tert*-butyl-2-phenyl-4,6-piperidinedione (II). The structural assignment was made on the basis of its elemental analyses, dinitrophenylhydrazone formation, positive ferric chloride color test, and infrared absorption spectrum. In the case where N-benzylideneaniline was used as the Schiff base, the desired adduct was not isolated as a crystalline substance.

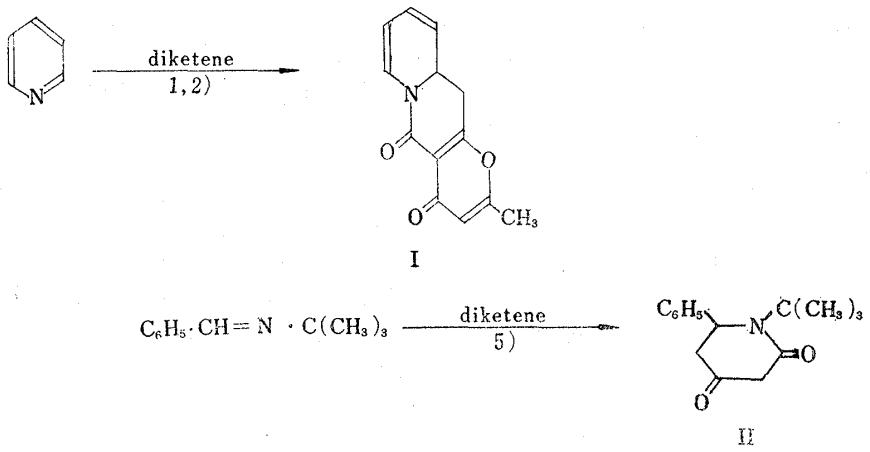

Chart 1.

When this reaction was re-examined in our laboratory in an effort to obtain a sample of II for study in a series of piperidine compounds, the results obtained were at variance with those reported by Oda. Similar treatment of N-benzylideneaniline with diketene as in the case of N-benzylidene-*tert*-butylamine afforded an adduct of m.p. 120~121° (IIIa). Furthermore, the adduct, m.p. 108~109°, obtained from N-benzylidene-*tert*-butylamine is not 1-*tert*-butyl-2-phenyl-4,6-piperidinedione (II), but N-*tert*-butyl-2-benzylideneacetoacetamide (IIIb). The evidence for this structural assignment is the subject of the present paper.

Following the procedure reported by Oda for the reaction of diketene with N-benzylideneaniline and N-benzylidene-*tert*-butylamine, we obtained crystalline compounds, m.p.

*1 Part IX. T. Kato, H. Yamanaka, F. Hamaguchi: Yakugaku Zasshi, **85**, 45 (1965).
*2 Kita-4, Sendai, Miyagi-ken (加藤鉄三, 山本 豊).
1) T. Kato, T. Kitagawa, Y. Yamamoto: Yakugaku Zasshi, **83**, 267 (1963).
2) *Idem*: *Ibid.*, **84**, 874 (1964).
3) O. Wollenberg: Ber., **67**, 1675 (1934).
4) J. Berson, W. Jones: J. Am. Chem. Soc., **78**, 1625 (1956).
5) R. Oda, S. Takashima, M. Okano: Bull. Chem. Soc., **35**, 1843 (1962).

120~121° and m.p. 112~113° respectively. Elemental analysis and molecular-weight determinations provided their empirical formulae as $C_{17}H_{15}O_2N$ and $C_{15}H_{19}O_2N$, respectively. The ferric chloride color test and 2,4-dinitrophenylhydrazone formationw ere positive. The infrared absorption spectra exhibited characteristic peaks at 3268, 1698 and 1629 cm^{-1} for $C_{17}H_{15}O_2N$ and 3257, 1695 and 1656 cm^{-1} for $C_{15}H_{19}O_2N$. The above data are in accord with those described by Oda.

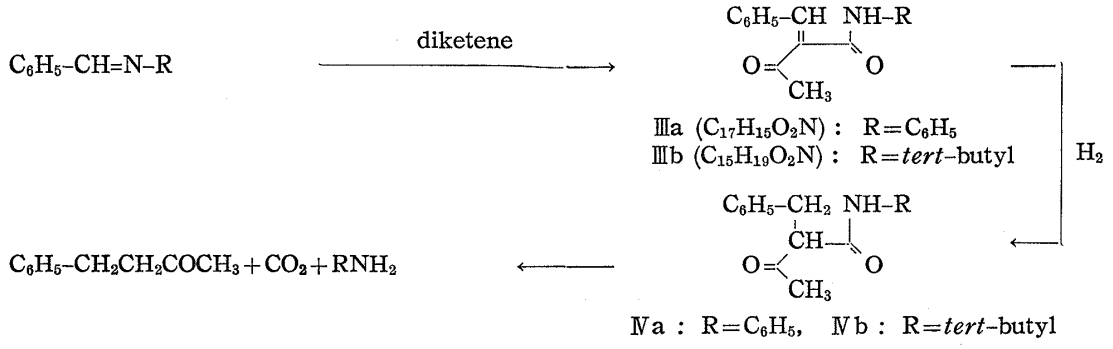

Chart 2.

Reduction of III over a palladium catalyst proceeded readily to give dihydro compounds (IVa and IVb). Hydrolysis of IV with 15% hydrochloric acid gave benzylacetone, carbon dioxide and the primary amine, aniline or *tert*-butylamine, as shown in Chart 2.

The results described above indicate that the Schiff base-diketene adduct has the structure of a 2-benzylideneacetoacetamide (III) rather than the six membered heterocyclic structure proposed by Oda, *et al.*

In order to confirm these structures, preparation of the 2-benzylideneacetoacetamides (III) and 2-benzylacetoacetamides (IV) was attempted by the procedure reported by Meyer and Pastour.[6] Accordingly, acetoacetanilide was treated with benzaldehyde in the presence of piperidine to give 2-benzylideneacetoacetanilide (IIIa).[6] The melting point of this sample was not depressed by admixture with the adduct obtained from the reaction of diketene with N-benzylideneaniline. Similarly, treatment of N-*tert*-butylacetoactamide with benzaldehyde gave N-*tert*-butyl-2-benzylideneacetoacetamide (IIIb) identical with the adduct obtained from diketene and N-benzylidene-*tert*-butylamine. Also, the 2-benzylacetoacetamides (IV) were prepared by the reactions of benzyl chloride with the corresponding acetoacetamides. The melting points of these samples were not depressed by admixture with the corresponding reduction products mentioned above.

Since the above facts leave no doubt that the Schiff base-diketene adducts are the 2-benzylideneacetoacetamides (III), assignment of the infrared absorption spectra of the adducts would be reasonably given as the following : 3268, 3257 (NH); 1698, 1695 (methyl ketone); 1629, 1656 (amide carbony) (λ_{max}^{KBr} cm^{-1}).*3

Although the details of the mechanism of the formation III remain obscure for the present, a probable mechanism is shown in Chart 3. It is well recognized that the resonance forms of diketene are limited to three (A, B and C). Though the formation of a four-membered cyclic adduct, such as V, has not been reported so far in the chemistry of diketene, a likely intermediate would be V, and the subsequent stage might well involve prototropy followed by fission of the C-N linkage in V to give III.

*3 Oda, *et al.* assigned these bands as the following : (Nujol, cm^{-1}) 3290 (OH), 1700 (ketocarbonyl), 1633 (lactam carbonyl).

6) A. Meyer, P. Pastour : Compt. rend., 228, 578 (1949).

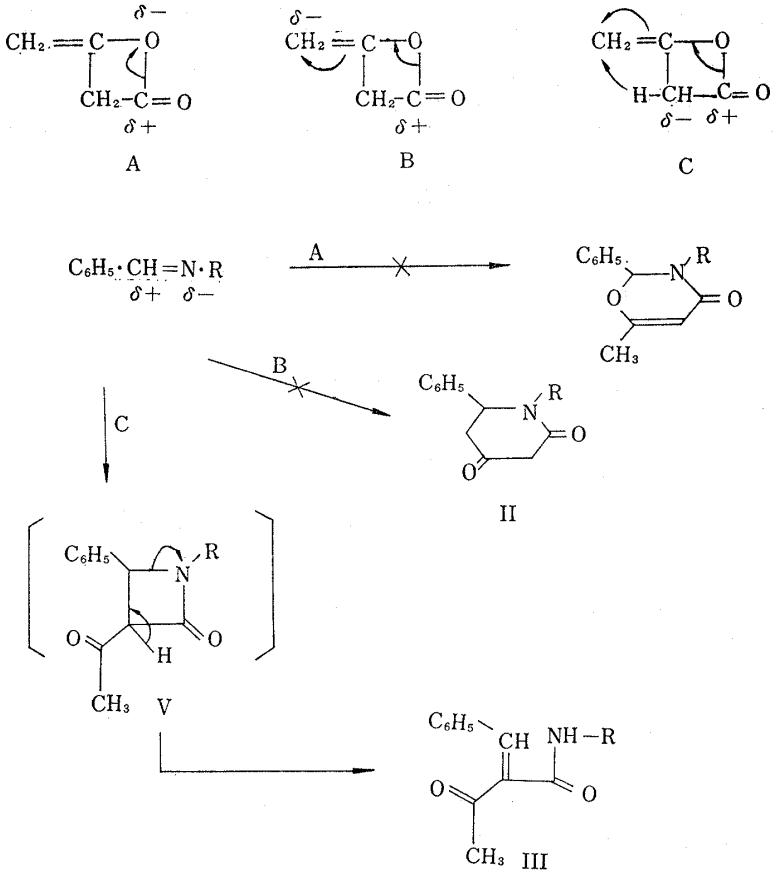

Chart 3.

Experimental

Reaction of Diketene with N-Benzylideneaniline——A solution of 5 g. (0.027 mole) of N-benzylideneaniline and 7 g. (0.083 mole) of diketene in 40 ml. of benzene was heated for 8 hr. under reflux. After evaporation of the solvent *in vacuo*, the syrupy residue was dissolved in ether and purified by alumina chromatography. The ether eluate after being concentrated and allowed to stand at room temperature afforded a crystalline solid which on recrystallization from ether-petr. ether gave pale yellow needles of m.p. 120~121°, undepressed with an authentic sample (IIIa). 0.6 g. (8%). *Anal.* Calcd. for $C_{17}H_{15}O_2N$ (IIIa): C, 76.96; H, 5.70; N, 5.28. Found: C, 77.02; H, 5.80; N, 5.25.

Reaction of Diketene with N-Benzylidene-*tert*-butylamine——According to the procedure reported by Oda, *et al.*,[5] the reaction of diketene (17.6 g.) with N-benzylidene-*tert*-butylamine (31 g.) gave 26 g. (55%) of N-*tert*-butyl-2-benzylideneacetoactamide (IIIb). Colorless needles from ether, m.p. 112~113°, undepressed on admixture with an authentic sample. *Anal.* Calcd. for $C_{15}H_{19}O_2N$ (IIIb): C, 73.44; H, 7.81; N, 5.71. Found: C, 73.83; H, 7.93; N, 5.97.

Reduction of 2-Benzylideneacetoacetanilide (IIIa)——A solution of 0.4 g. of IIIa in 20 ml. of MeOH was hydrogenated over 0.3 g. of 5% Pd-Norit catalyst. After 30 min., 40 ml. (1.2 molar equivalents) of hydrogen had been absorbed. The catalyst was filtered and the filtrate was taken to dryness. Recrystallization from ether-petr. ether afforded colorless needles of m.p. 100~101°, undepressed on admixture with an authentic sample (IVa) prepared by the method described below. 0.38 g. (95%). *Anal.* Calcd. for $C_{17}H_{17}O_2N$ (IVa): C, 76.38; H, 6.41; N, 5.24. Found: C, 76.02; H, 6.42; N, 5.12. IR ν_{max}^{KBr} cm^{-1}: 3289 (NH), 1721 (CH_3CO), 1653 (amide CO).

Reduction of N-*tert*-butyl-2-benzylideneacetoacetamide (IIIb)——Following the procedure described above, reduction of IIIb (0.7 g.) gave 0.55 g. of colorless needles (ether-petr. ether), m.p. 103~104°. *Anal.* Calcd. for $C_{15}H_{21}O_2N$ (IVb): C, 72.84; H, 8.56; N, 5.66. Found: C, 73.07; H, 8.56; N, 5.70. IR ν_{max}^{KBr} cm^{-1}: 3322 (NH), 1730 (CH_3CO), 1642 (amide CO).

Hydrolysis of 2-Benzylacetoactanilide (IVa)——A suspension of 0.45 g. of IVa in 17 ml. of 20% HCl was heated for 1.5 hr. under reflux. The gas, which was evolved, when absorbed into a $Ba(OH)_2$ solution gave a white precipitate of $BaCO_3$. After cooling, the reaction mixture was extracted with $CHCl_3$. From

the $CHCl_3$ extract, a colorless oil of b.p. 120~145°/13 mm. (bath temp.) was obtained. The IR absorption spectrum was identical in every respect with that of authentic benzylacetone, and its 2,4-dinitrophenylhydrazone showed no depression in melting point on admixture with an authentic sample of the 2,4-dinitrophenylhydrazone (m.p. 125~127°). The HCl soluble fraction was concentrated, then made alkaline with Na_2CO_3 and extracted with ether. The ether extract was heated with acetic anhydride to give colorless leaflets of m.p. 113~114°, undepressed on admixture with acetanilide.

Hydrolysis of N-*tert*-butyl-2-benzylacetoacetanilide (IVb)——When subjected to the procedure described above, Ⅳb (0.9 g.) afforded, after hydrolysis with 20 ml. of 15% HCl, CO_2, *tert*-butylamine and benzylacetone (0.5 g., 92.5%).

2-Benzylideneacetoacetanilide (IIIa)[6]——To a solution of 2.5 g. (0.014 mole) of acetoacetanilide and 1.5 g. (0.014 mole) of benzaldehyde in 30 ml. of absolute EtOH was added a few drops of piperidine. The reaction mixture was stirred for 6 hr. in an ice-NaCl bath. After evaporation of the solvent, the resulting residue was taken up into ether and purified by alumina chromatography. Concentration of the ether eluate gave a crystalline solid which after recrystallization from ether afforded pale yellow needles of m.p. 120° (lit. m.p. 119°),[6] undepressed on admixture with the adduct obtained in the reaction of diketene with N-benzylideneaniline.

N-*tert*-Butyl-2-benzylideneacetoacetamide (IIIb)——N-*tert*-butylacetoactamide (0.8 g.) and benzaldehyde (0.7 g.) when treated as above afforded 0.73 g. (50%) of Ⅲb, m.p. 112~114°.

2-Benzylacetoacetanilide (IVa)——Sodium metal (0.13 g.) was dissolved in 20 ml. of absolute EtOH, and then 1 g. of acetoacetanilide and 0.71 g. of benzyl chloride were added to this solution. The mixture was warmed on a steam bath for 4 hr. The reaction mixture, after being filtered from the precipitated NaCl, was concentrated to give a pale yellow residue, which was washed with petr. ether. From the petr. ether washings white crystals were obtained. Recrystallization from ether gave 2,2-dibenzylacetoacetanilide, m.p. 86~88°. *Anal.* Calcd. for $C_{24}H_{23}O_2N$: N, 3.92. Found : N, 4.00.

The petr. ether insoluble residue was dissolved in acetone, and purified by alumina chromatography to give a crystalline solid. Recrystallization from ether-petr. ether gave Ⅳa, m.p. 99~101.5°, undepressed on admixture with the reduction product above mentioned.

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Summary

The adduct obtained from the reaction of diketene with the Schiff base, N-benzylidene-*tert*-butylamine, is not a heterocyclic compound, 1-*tert*-butyl-2-phenyl-4,6-piperidinedione (Ⅱ), as proposed by Oda, *et al.*,[5] but N-*tert*-butyl-2-benzylideneacetoacetamide (Ⅲb). Similarly, the reaction of diketene with N-benzylideneaniline afforded 2-benzylideneacetoacetanilide (Ⅲa). The evidence for this structure assignment is described.

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