[Chem. Pharm. Bull. 21(10)2187—2194(1973)]

UDC 547.546'572.1.02.03

Mechanism of the Color Reaction of Active Methylene Compounds with 1,3,5-Trinitrobenzene Derivatives. V.[1] A New Type and the Meisenheimer Type Coloring Matters of the Janovsky Reaction of Acetophenone and 1,3,5-Trinitrobenzene[2]

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(Received February 5, 1973)

Two main coloring matters were isolated in crystalline forms from an aqueous reaction mixture of acetophenone and 1,3,5-trinitrobenzene under the Janovsky conditions. One of them was the Meisenheimer type compound, sodium salt of II. The other was a new compound and the structure was determined as sodium salt of diphenacyltrinitrocyclohexenide anion III (Chart 3). The spectral behavior of these coloring matters was compared with that of the reaction mixture and the color reaction of acetophenone and TNB under the aqueous Janovsky conditions was discussed.

In the previous paper of this series,[4] mechanisms of the color reactions of cyclohexanone, and acetophenone, with 1,3,5-trinitrobenzene (TNB) under the conditions of the spot test procedure for active methylene compounds[5] were discussed by isolating the Meisenheimer type and the bicyclic type compounds. The present paper describes the structure of a new type coloring matter produced along with the Meisenheimer type compound under the conditions of the Janovsky reaction[6] of acetophenone and TNB, where a large excess of the ketone is used, and discusses its role in the reaction in correlation with the Meisenheimer type compound.

Result and Discussion

Absorption spectra of the alkaline reaction mixture of acetophenone and TNB under the Janovsky conditions are shown in Fig. 1. Immediately after the addition of sodium hydroxide to an aqueous dimethylformamide (DMF) solution of acetophenone and TNB, a spectrum with a maximum at 455 nm and broad shoulder around 530 nm appeared (within 1 sec) (Fig. 1, 1—2) and the spectrum rapidly (within 60 sec) changed to new one with a maximum at 515 nm (Fig. 1, 6). The new absorption band remained almost unchanged for 1 hr (Fig. 1, 7). The

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1) Part IV: T. Kabeya, K. Kohashi, Y. Ohkura, and T. Momose, *Chem. Pharm. Bull.* (Tokyo), **21**, 2168 (1973).

2) This forms "Organic Analysis LXXXVIII." A part of this paper was presented at IUPAC International Congress on Analytical Chemistry, Kyoto, Apr. 1972. Part LXXXVII: 1).

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4) K. Kohashi, Y. Ohkura, and T. Momose, *Chem. Pharm. Bull.* (Tokyo), **21**, 118 (1973).

5) T. Momose, Y. Ohkura, and K. Kohashi, *Chem. Pharm. Bull.* (Tokyo), **11**, 301 (1963).

6) J.V. Janovsky and L. Erb, *Ber.*, **19**, 2155 (1886); J.V. Janovsky, *ibid.*, **24**, 971 (1891). For reviews, see T. Nambara, *Bunseki Kagaku*, **13**, 184 (1964); E. Buncel, A.R. Norris, and K.E. Russell, *Quart. Rev.*, **22**, 123 (1968).

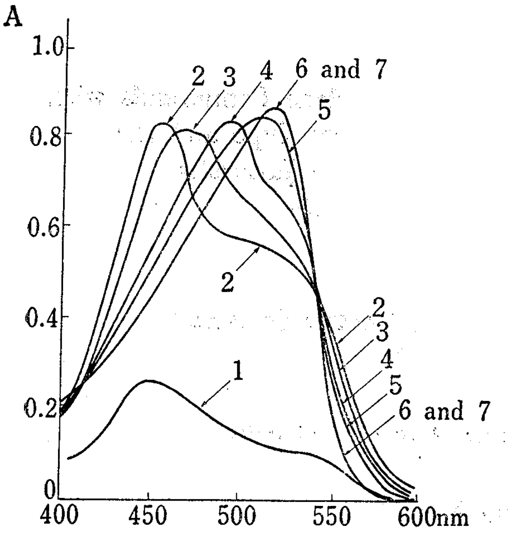
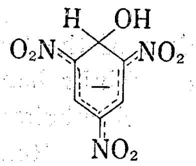


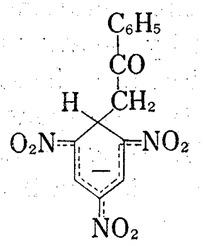
Fig. 1. Absorption Spectra of Alkaline Reaction Mixture of Acetophenone and TNB under the Janovsky Conditions

Equal volumes of the solution of TNB (1.0×10^{-4}M) and acetophenone (0.04M) in aq. 40% DMF and the aq. 40% DMF solution of NaOH (0.4M) were automatically mixed with a stopped-flow mixing system of a rapid scan spectrophotometer. The spectra of the mixture were recorded repeatedly after the periods (1, 4 msec; 2, 1 sec; 3, 3 sec; 4, 10 sec; 5, 30 sec; 6, 60 sec; 7, 60 min) against H_2O under computer control.



I

Chart 1



II

Chart 2

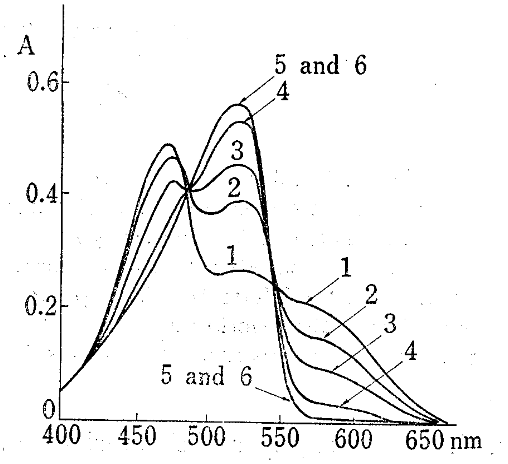


Fig. 2. Absorption Spectra of Neutralized Reaction Mixtures of Acetophenone and TNB under the Janovsky Conditions

To a mixture of 1.0 ml each of DMF solution of acetophenone (0.2M) and TNB (1.0×10^{-4}M), 1.0 ml each of H_2O and aq. 0.4% NaOH were successively added. The solution was kept at 25° for several periods (1, 15 sec; 2, 1 min; 3, 2 min; 4, 5 min; 5, 30 min; 6, 60 min) and neutralized with 1.0 ml of aq. 2.4% $NaH_2PO_4\cdot2H_2O$.

The spectra were measured against H_2O.

transient spectra (Fig. 1, 1—2)[7] were assigned to the formation of the anion I[8] (Chart 1).

On the other hand, when the reaction mixtures showing the absorption around 500 nm (Fig. 1, 5—7) were neutralized with sodium dihydrogen phosphate solution, it was observed

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[7] Under the present aqueous alkaline conditions, the influence of dimethylamine, which might be produced from DMF and sodium hydroxide, on the absorption intensity was negligible, though it was reported that TNB-dimethylamine complex (λ_{max}: 450 and 528 nm) was formed in the reaction of TNB and dimethylamine in dimethylsulfoxide (M.R. Crampton and V. Gold, *J. Chem. Soc.* (*B*), **1967**, 23).

[8] The formation of I by the action of aqueous alkali on TNB has been investigated spectrophotometrically by several workers[8a] and its sodium salt was isolated (C.A. Fyfe, M.I. Foreman, and R. Foster, *Tetrahedron Letters*, **1969**, 1521). Recently, the interaction between TNB and sodium hydroxide in the DMF-water system has been studied quantitatively (E.A. Symons and E. Buncel, *Can. J. Chem.*, **50**, 1729 (1972)). For reviews on the related anions formed in the reaction of TNB and base, see *a*) R. Foster and C.A. Fyfe, *Rev. Pure and Appl. Chem.*, **16**, 61 (1966); M.R. Crampton, *Adv. Phys. Org. Chem.*, **7**, 211 (1969); M.J. Strauss, *Chem. Rev.*, **70**, 667 (1970); T.N. Hall and C.F. Poranski, Jr., "The Chemistry of the Nitro and Nitroso Groups," Part 2, ed. by H. Fueer, Interscience (John Wiley & Sons), New York, 1970, p. 329; C.A. Fyfe, "The Chemistry of the Hydroxyl Group," Part 1, ed. by S. Patai, Interscience (John Wiley & Sons), New York, 1971, p. 51; *b*) A.T. Nielson, "The Chemistry of the Nitro and Nitroso Groups," Part 1, ed. by S. Patai, Interscience (John Wiley & Sons), New York, 1969, p. 349.

that the spectrum with a maximum at 465 nm and broad shoulder around 550 nm (Fig. 2, 1) changed with time of standing in the alkaline medium and finally became new one with a maximum at 515 nm (Fig. 2, 5—6). The new band remained unchanged for more than 3 hr, suggesting that the species responsible for the spectrum was stable.

Two coloring matters were isolated in crystalline forms from the reaction mixture as described in Experimental. One of them was identical with sodium salt of the Meisenheimer type anion II⁹⁾ (Chart 2) (II Na) isolated in the previous paper.⁴⁾ An aqueous solution of II Na showed a characteristic visible absorption band with two maxima (the Meisenheimer band)⁴⁾⁸⁾⁹⁾ (Fig. 7, a), which was similar to that of the reaction mixture neutralized at an earlier time (*cf.*, Fig. 2, 1). Its alkaline solution (*cf.*, Fig. 6, 1) also showed the same band as that of the alkaline reaction mixture shown in Fig. 1, 6.

The other coloring matter was a new compound and showed a spectrum with a maximum at 515 nm when dissolved in the same solvent system as the reaction mixture (Fig. 5, b′ or c′), which was close similar to that of the reaction mixture in a prolonged reaction time as shown in Fig. 1, 7 or Fig. 2, 6. The infrared (IR) spectrum of the new compound is shown in Fig. 3. Absorptions at 1698 and 1680 cm^{-1} suggested the presence of two kinds of carbonyl group. Absorptions at 1600, 1580, 1450, 760, and 690 cm^{-1} were in fair agreement with those of monosubstituted benzene ring in acetophenone.^10a)^ Absorptions at 1550 and 1375 or 1350 cm^{-1} were assigned to those of nitro group. Absorptions at 1315, 1240 or 1215, and 750 cm^{-1} were assigned to those of nitronate anion group^10b)^ in the dinitropropenide function of TNB ring system.¹¹⁾ The data of the elemental analyses described in Experimental and the relative intensities of the signals in the nuclear magnetic resonance (NMR) spectrum (Fig. 4) were consistent with a formula of $C_{22}H_{18}O_8N_3Na$, which consisted of two molecules of acetophenone and one molecule of TNB. A structure of the compound was determined as sodium salt of diphenacyltrinitrocyclohexenide anion III¹²⁾ (III Na) (Chart 3), which might be considered to have a number of stereochemical forms.

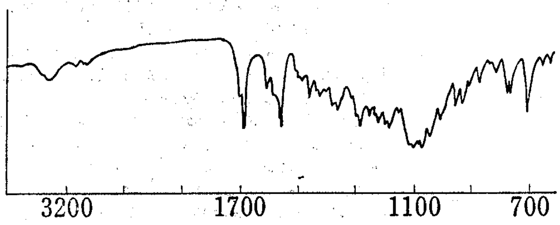

Fig. 3. IR Spectrum of III Na (KBr)

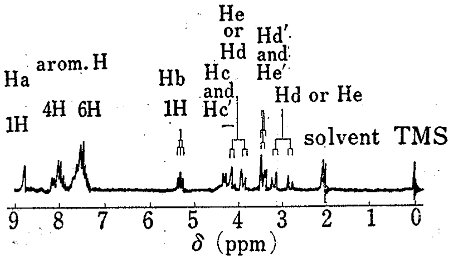

Fig. 4. NMR Spectrum of III Na (in acetone-d_6)

The NMR spectral assignments and analyses of the signals ranging from δ (ppm) 5.5 to 2.8 were made by the use of spin-decoupling and the computer simulation techniques described in Experimental. A singlet at δ 8.75 (1H) was assigned to the proton Ha on the dinitropro-

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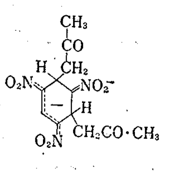
9) M. Kimura, *Yakugaku Zasshi*, **73**, 1219 (1953).

10) K. Nakanishi, "IR Absorption Spectroscopy (Practical)," Nankodo, Tokyo, 1960, *a*) Practical part p. 94; *b*) Qualitative part, p. 55.

11) K. Kohashi, Y. Ohkura, and T. Momose, *Chem. Pharm. Bull.* (Tokyo), **18**, 2151 (1970).

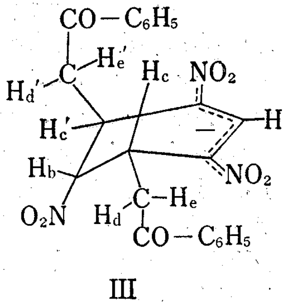
12) A diacetonyl-trinitrocyclohexenide anion IV (Chart 4) was postulated as a coloring matter formed in the reaction of acetone and TNB in an aqueous potassium hydroxide solution under the Janovsky conditions (A.Y. Kaminskii and S.S. Gitis, *J. Org. Chem.* (*USSR*), **2**, 1780 (1961); *Idem, ibid.*, **4**, 492 (1968)). Recently, tetraethylammonium salt of IV was isolated (I.M. Sosonkin, S.S. Gitis, A.Y. Kaminskii, V.A. Subbotin, and E.G. Kaminskaya, *J. Org. Chem.* (*USSR*), **7**, 2322 (1971)).



IV

Chart 4

penide function of TNB system.[13] Multiplets at δ 8.2—7.8 (4H) and 7.7—7.3 (6H) were assigned to the aromatic protons and were in fair agreement with those of acetophenone dissolved in the same solvent. A triplet centered at δ 5.42 (1H, J=4.5 Hz) was assigned to the proton Hb coupled to two magnetically equivalent protons Hc and Hc′, which appeared as multiplets at δ 4.5—4.2. The protons Hc and Hc′ also coupled to the geminal protons of phenacyl groups, respectively. Two phenacyl groups probably attach to ring carbons in a *trans* configuration with respect to one another. If they were mutually in a *cis* configuration, four phenacyl protons would be magnetically or sterically equivalent and would be expected to appear as more simple and symmetric signals than those observed. The four protons were tentatively assigned as shown in Fig. 4 and Chart 3.



III

Chart 3

Table I. Absorption Maxima of III Na and V Na in Various Solvents

Solvent	III Na λ_{max} (nm)	III Na ε	V Na λ_{max} (nm)	V Na ε
DMSO	518	40000	519	73500
DMF	515	51000	516	79300
Acetone	511	35000	512	68300
Ethanol	510	24000	512	41000
Methanol	500	20000	500	38000
Water	480	11000	480	18300

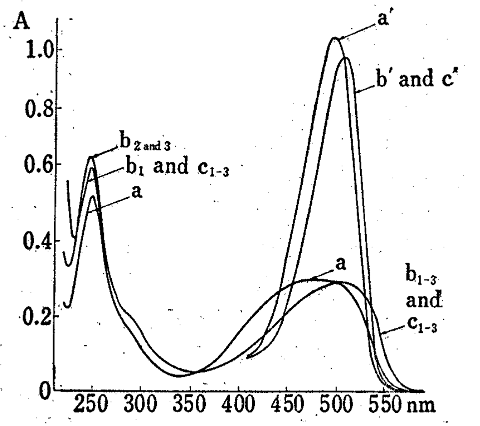


Fig. 5. Absorption Spectra of III Na in Alkaline and Neutralized Solutions

a) 2.0 ml of aq. solution of III Na (1.0×10^{-4} M) was diluted with 3.0 ml of H_2O.
a′) 2.0 ml of DMF solution of III Na (1.0×10^{-4} M) was diluted with 3.0 ml of H_2O.
b) To 2.0 ml of aq. solution of III Na in a), 2.0 ml of H_2O and 1.0 ml of aq. NaOH (1, 0.5; 2, 1.8; 3, 5.0%) were successively added.
b′) To 2.0 ml of DMF solution of III Na in a′), 2.0 ml of H_2O and 1.0 ml of aq. 0.5% NaOH were successively added. After being mixed well, the mixture was diluted with 1.0 ml of H_2O.
c) To each alkaline solution of III Na in b), 1.0 ml of aq. $NaH_2PO_4 \cdot 2H_2O$ (1, 2.0; 2, 7.2; 3, 20%) was added instead of H_2O.
c′) To 2.0 ml of DMF solution of III Na in a′), 1.0 ml each of H_2O, aq. 0.5% NaOH and aq. 2.0% $NaH_2PO_4 \cdot 2H_2O$ were successively added.
The spectra were measured against H_2O.

III Na was soluble in water, methanol, ethanol, acetone, DMF and dimethylsulfoxide (DMSO), but insoluble in benzene, ether, chloroform and acidic solution (*e.g.*, diluted hydrochloric acid solution). The absorption maximum and intensity of III Na solution varied with solvents as shown in Table I. The same phenomenon was also observed in the solutions of sodium salt of the bicyclic type anion V (V Na)[11,14] shown in Chart 5. It is of interest to note that the absorption bands due to the dinitropropenide function of TNB ring system are affected in a similar way by the nature of the individual solvent.

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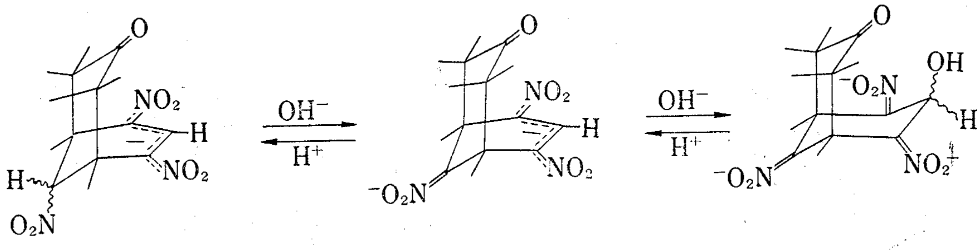
[13] The values of the chemical shifts of the corresponding protons fall within the range δ 8.9—8.3 for the 1,3,5-trinitrocyclohexadienide systems of the Meisenheimer type compounds[8a] and δ 8.6—8.2 for the dinitropropenide systems of the bicyclic type compounds (M.I. Foreman, R. Foster, and M.J. Strauss, *J. Chem. Soc.* (*C*), **1969**, 2112; M.J. Strauss, J.C. Jensen, H. Schran, and K. O'Conner, *J. Org. Chem.*, **35**, 383 (1970)).

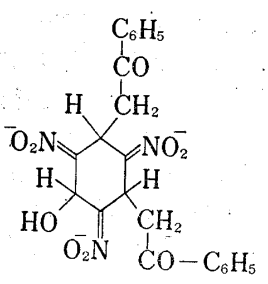
[14] K. Kohashi, Y. Ohkura, and T. Momose, *Chem. Pharm. Bull.* (Tokyo), **19**, 2065 (1971).



V Va Vb

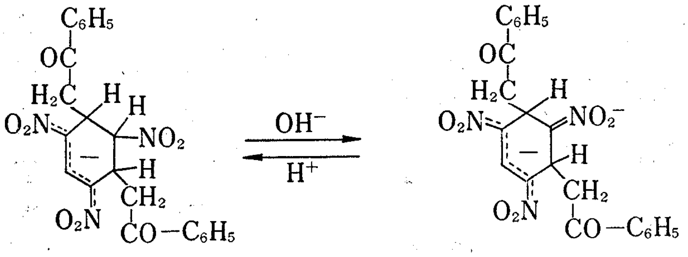
Chart 5

When sodium hydroxide was added to the aqueous solution of III Na, the maximum 480 nm (Fig. 5, a) shifted to 515 nm, which decreased slightly in intensity with higher ncentration of the alkali (Fig. 5, b), and the new band remained almost unchanged by the utralization (Fig. 5, c). This behavior was different from that of V Na, where the intensity the visible region was greatly decreased with increasing concentration of the alkali, and the itial intensity was recovered by the neutralization, as described in the previous paper.[11] is observation on V Na was already explained by equilibrium system as shown in Chart 5. the case of III Na, it might be considered that the dinitropropenide function of III, being ndwiched between two phenacyl groups, became stereochemically more stable than that V for the further attack of the alkali, and such an anion as IIIb (Chart 6) having the same nctional groups as Vb was difficult to be produced. However, it seemed reasonable to sume from the analogy to a common equilibrium between nitro and nitronate anion[8b] (*e.g.*, and Va) that III was also in equilibrium with IIIa[15] in an alkaline solution (Chart 7), though sible absorption spectral changes of III Na in alkaline and neutralized solutions were not served appreciably (Fig. 5, b and c or b′ and c′).



IIIb

Chart 6



III IIIa

Chart 7

On the other hand, when a DMF solution of II Na[16] was made alkaline with sodium hydroxide, the solution showed the spectrum with a maximum at 515 nm (*cf.*, Fig. 6, 1). However, the initial Meisenheimer band was recovered when the solution was neutralized with sodium dihydrogen phosphate (*cf.*, Fig. 7, b_1). This reversible change of spectrum has been explained by the equilibrium between II and IIa[4] (Chart 8). In this case, when a large amount of acetophenone was present and the reaction mixture was allowed to stand for more than 30 min, the resulting solution, which showed the band with a maximum at 515 nm (Fig. 6, 4), no longer reproduced the Meisenheimer band even if the solution was neutralized

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15) Attempts to measure a distinct NMR spectrum of III Na in aqueous sodium hydroxide solution were unsuccessful because of the broadening of signals. Therefore, direct NMR assignments of IIIa could not be carried out.

16) II Na was fairly unstable in water, as described in the previous paper,[4] but it was found to be more stable in DMF. Therefore, the DMF solution was used in the present work.

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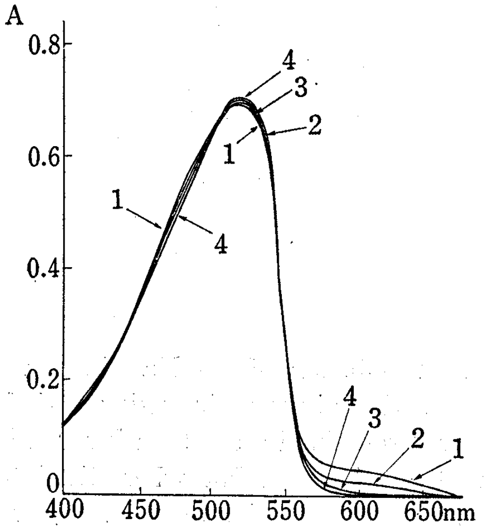

Fig. 6. Absorption Spectra of Alkaline Reaction Mixtures of II Na and Acetophenone

To a solution of 2.0 ml of aq. 50% DMF solution of II Na (1.0×10^{-4} M) and 1.0 ml of DMF solution of acetophenone (0.2 M), 1.0 ml of aq. 0.4% NaOH was added. The solution was kept at 25° for several periods (1, 15 sec; 2, 2 min; 3, 5 min; 4, 30 min) and diluted with 1.0 ml of H_2O.

The spectra were measured against H_2O.

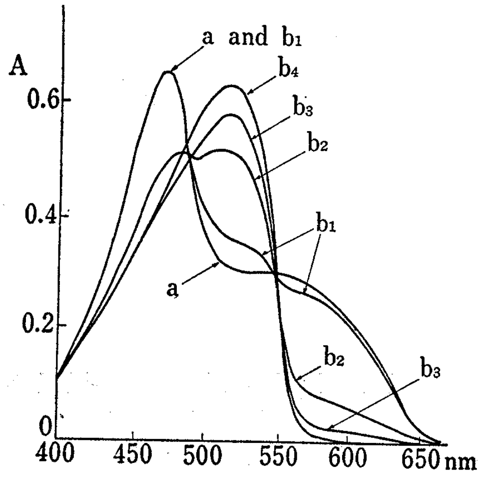

Fig. 7. Absorption Spectra of Neutralized Reaction Mixtures of II Na and Acetophenone

a) To 2.0 ml of aq. 50% DMF solution of II Na (1.0×10^{-4} M), 1.0 ml of DMF and 2.0 ml of H_2O were successively added.

b) To a solution of 2.0 ml of aq. 50% DMF solution of II Na (1.0×10^{-4} M) and 1.0 ml of DMF solution of acetophenone (0.2 M), 1.0 ml of aq. 0.4% NaOH was added. The mixture was kept at 25° for several periods (1, 15 sec; 2, 2 min; 3, 5 min; 4, 30 min) and neutralized with 1.0 ml of aq. 2.4% $NaH_2PO_4\cdot 2H_2O$.

The spectra were measured against H_2O.

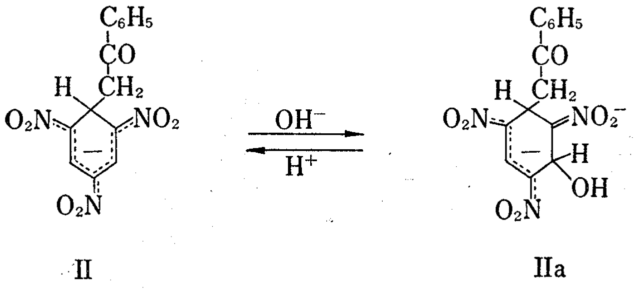

Chart 8

(Fig. 7, b_4). However, when the alkaline solutions showing the band with the maximum at 515 nm (Fig. 6) were neutralized at an earlier time than 30 min, the Meisenheimer bands were partly recovered as shown in Fig. 7,b_{1-3}. The changes of spectra shown in Fig. 7 were similar to those of the reaction mixtures of acetophenone and TNB under the Janovsky conditions as shown in Fig. 2. The irreversible new band observed in the reaction between II Na and acetophenone in the presence of sodium hydroxide was thought to be due to the formation of IIIa, which might occur *via* IIa.

On the basis of the above results, the reaction of acetophenone and TNB under the Janovsky conditions as described in the legend of Fig. 1 might be explained as follows (Chart 9).

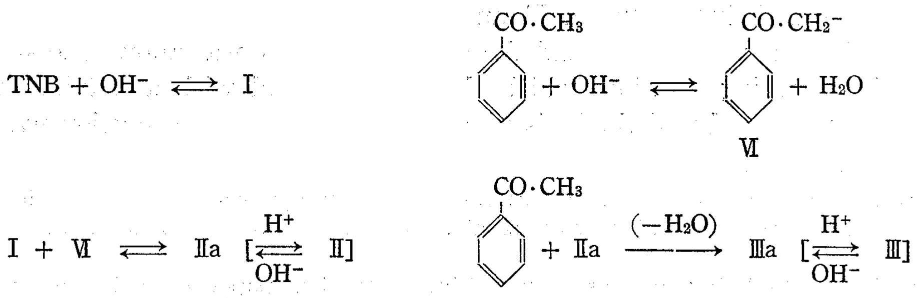

Chart 9

TNB and acetophenone react instantly with sodium hydroxide in aqueous medium to form I and phenacyl anion VI, respectively. Then, I and VI gradually combine to produce IIa.17) When a large amount of the ketone is present, it reacts with IIa to yield IIIa. The coloration of the alkaline reaction mixture7) could be ascribed to the formation of I in a very early stage of the reaction (Fig. 1, 1 and 2), then to IIa and IIIa (Fig. 1, 3—6) and finally to IIIa (Fig. 1, 7).

A similar type of explanation might be also applicable to the reactions of some other compounds such as *p*-bromoacetophenone, *o*-hydroxyacetophenone, acetaldehyde, propionaldehyde or *n*-butylaldehyde18) with TNB, because their reaction mixtures under the Janovsky conditions showed the same spectral changes as those of acetophenone.

Experimental19)

II Na and III Na——To a solution of acetophenone (5.0 g) and TNB (2.0 g) in DMF (50 ml), 50 ml of aq. 2% NaOH was added with stirring. After the mixture was left standing at 37° for 1.5 hr, 50 ml of aq. 20% $NaH_2PO_4 \cdot 2H_2O$ was added. Then, the solvent was removed *in vacuo*. The residue, dissolved in MeOH (30 ml) and filtered, was chromatographed on a column of neutral alumina (Merck Brockmann, activity II—III) and eluted with MeOH. Two main fractions were separated. The first eluate, fraction of dark purple color, was evaporated to dryness *in vacuo*. The residue was dissolved in a small amount of dry acetone and filtered. When an appropriate amount of ether was added to the filtrate, dark purple crystals were obtained. The crystals showed no melting point and exploded when ignited or heated rapidly. Yield, 0.5 g. Analytical data (elemental analyses, IR, NMR, Ultraviolet and Visible spectra) of this compound were identical with those of II Na, which was first prepared by Kimura.9) After the first eluate, II Na fraction, was removed, the orange fraction adsorbed over the whole column was eluted with MeOH. The eluate was evaporated to dryness *in vacuo*. The residue was dissolved in a small amount of dry acetone and filtered. When an appropriate amount of ether was added to the filtrate, bright orange crystals were obtained. Repeated recrystallizations from acetone–ether (1: 3) gave bright orange plates, which showed no melting point and exploded when ignited or heated rapidly. Yield, 1.0 g. *Anal.* Calcd. for $C_{22}H_{18}O_8N_3Na$: C, 55.58; H, 3.81; N, 8.83; Na, 4.84. Found: C, 55.67; H, 3.98; N, 8.81; Na, 4.50

NMR spectra were measured by a JEOL C-60H NMR Spectrometer using about 10% acetone-d_6 solution of the sample containing tetramethylsilane (TMS) as an internal standard. By the irradiation of the multiplet at δ 4.5—4.2 (assigned to Hc and Hc′), the triplet centered at δ 5.4 (assigned to Hb), the doublet centered at δ 3.85 (1H, J=6.0 Hz), two doublets centered at δ 3.2 and 2.9 (1H, J=6.0 Hz) (assigned to Hd or He (or Hd′ or He′)) became singlet, respectively, and the absorptions at δ 3.5 (singlet) and 3.38 (doublet) (assigned to Hd′ and He′ (or Hd and He)) became seemingly doublet.

Spectral analyses20) were carried out by using a 5 spin NMR Simulation Program run on the JEC-5 Spectrum Computer. The NMR parameters used for the computations were as follows: For 5 proton system of Hd, He, Hc, Hb, and Hc′ (or Hd′, He′, Hc′, Hb, and Hc), Hd (or Hd′)=208, He (or He′)=207, Hc (or Hc′)=262.5, Hb=324, and Hc′ (or Hc)=261 Hz; $J_{bc}=J_{bc'}=4.5$, $J_{ce(or\ c'e')}=7.2$, and $J_{cd(or\ c'd')}=5.5$ Hz. All other couplings were set to zero and the linewidth to 0.5 Hz. For 5 proton system of Hd′, He′, Hc′, and Hc (or Hd, He, Hc, Hb, and Hc′), Hd′ (or Hd)=240.1, He′ (or He)=181.5, Hc′ (or Hc)=261, Hb=324, and Hc (or Hc′)=262.5 Hz; $J_{c'd'(or\ cd)}=J_{c'e'(or\ ce)}=6$, $J_{bc}=J_{bc'}=4.5$, and $J_{d'e'(or\ de)}=17$ Hz. All other couplings were set to zero and the linewidth to 0.5 Hz. When the calculated spectra of above proton systems were combined, the resulting spectrum agreed very closely with the observed spectrum shown in Fig. 4.

Absorption spectra shown in Fig. 1 were measured by the automated stopped-flow system using a Hitachi RSP-2 Rapid Scan Spectrophotometer equipped with RSP-2 Sweep controller, Mixing controller, Mixing cell connected with Rapid flow generator, and Memoriscope. Other absorption spectra were measured by a

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17) Under the nonaqueous Janovsky conditions of TNB and acetophenone, it was reported that II was initially produced by the direct attack of VI to TNB.9)

18) Isolation of such type compound as III Na from the reaction mixture of TNB and aldehyde is now going on.

19) TNB and DMF were purified as previously described (T. Momose, Y. Ohkura, K. Kohashi, T. Tanaka, Y. Yano, and N. Itakura, *Rinsho Kensa*, 10, 747 (1966)).

20) In view of the symmetry of III, 7 protons (Hd, He, Hc, Hb, Hc′, Hd′, and He′) of III shown in Chart 3 were divided into two groups of 5 proton system and simulated.

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Hitachi 124 Spectrophotometer equipped with Hitachi 056 Recorder in a cell of 10 mm optical length. IR spectra were measured by a Nihonbunko DS 701-G Infrared Spectrophotometer in KBr pellets.

Acknowledgement The authors wish to thank Mr. H. Matsui and Miss Y. Soeda for the IR spectral measurements, Messrs. K. Ishimura and M. Shido for the elemental analyses, and Mr. Y. Tanaka for the NMR spectral measurements and the spectral analyses with the computations. Thanks are also due to the staff of the Scientific Instrument Application Laboratory, Naka works, Hitachi Co., Ltd. for their help with the rapid scan spectrophotometer.