a) Reaction with Red Phosphorus and Halogen: To a mixture of I (255 mg) and red phosphorus (20 mg) in a 5 ml round-bottomed flask fitted with a reflux condenser holding a calcium chloride tube was added iodine (272 mg) at room temperature. The mixture was heated on an oil bath at 150° for 30 min. After purification, the yield of 2-phenylethyl iodide-1-^{14}C was 378 mg (78.0%).

b) Reaction with Phosphorus Trihalide: In a 5 ml two-necked flask with a reflux condenser holding a calcium chloride tube and a separatory funnel was placed II (122 mg). With stirring, the vessel was heated on an oil bath maintained at 150°. Phosphorus tribromide (298 mg) was added dropwise to it. After its addition, the mixture was allowed to stand at 150° for 1 hr. The yield of 2-phenylethyl bromide-1-^{13}C was 139 mg (89.5%).

Degradation to Benzoic Acid——A mixture of 2-phenylethyl iodide (382 mg), $KMnO_4$ (965 mg) and 1% NaOH solution (17 ml) was refluxed for 3 hr, and then MnO_2 precipitated was removed by filtration. The filtrate was acidified with conc. HCl. After removal of the precipitate resulted, the solution was concentrated *in vacuo* to give benzoic acid, 159 mg (79.7%). This product was repeatedly recrystallized and sublimed until a constant specific activity was obtained.

Acknowledgement We thank Dr. M. Kaneda for the preparation of several raw materials and Mrs. Y. Tamura for her technical assistance.

[Chem. Pharm. Bull. 25(5)1103—1106(1977)]

UDC 547.546-033.03.04 : 546.33-36.03.04

Mechanism of the Color Reaction of Active Methylene Compounds with 1,3,5-Trinitrobenzene Derivatives. VIII.[1] Interaction of Mono- and Dihydroxylated Species (1:1 and 1:2 Complexes) derived from 1,3,5-Trinitrobenzene and Hydroxide Ion with Acid

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(Received July 26, 1976)

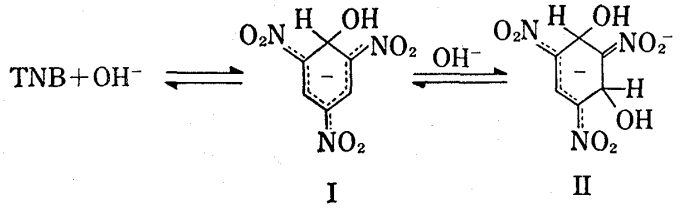
By use of stopped flow rapid scan spectrophotometric technics, it was demonstrated that the backward reaction from dihydroxylated anion (1:2 complex) derived from 1,3,5-trinitrobenzene with sodium hydroxide to monohydroxylated anion (1:1 complex) did not occur when the alkaline solution of 1,3,5-trinitrobenzene was neutralized or acidified with acids.

Keywords——1,3,5-trinitrobenzene; 1,3,5-trinitrobenzene monohydroxylated anion; 1,3,5-trinitrobenzene dihydroxylated anion; absorption spectral changes with time; stopped flow rapid scan analyser

In the improved sensitive method of detecting active methylene compounds with 1,3,5-trinitrobenzene (TNB),[3] the alkaline color reaction mixtures were neutralized with sodium dihydrogen phosphate solution in order to diminish the intensive red color of excessive TNB and to intensify and stabilize the colors produced by the reactions of active methylene compounds with TNB in alkaline medium. In the previous study on the color reaction of acetophenone with TNB by use of stopped flow rapid scan spectrophotometric technics,[1] it was reported that 1:1 complex (I) and 1:2 complex (II) shown in Chart 1 were succes-

1) Part VII: K. Kohashi, T. Kabeya, and Y. Ohkura, *Chem. Pharm. Bull.* (Tokyo), **25**, 50 (1977).
2) Location: *Maidashi, Higashi-ku, Fukuoka.*
3) T. Momose, Y. Ohkura, and K. Kohashi, *Chem. Pharm. Bull.* (Tokyo), **11**, 301 (1963).

sively formed from TNB and sodium hydroxide prior to the formation of stable coloring matters from TNB and acetophenone.



I II

Chart 1

We newly found that when alkaline solution of TNB was neutralized with acidic solution, the resulting mixture showed unexpected rapid spectral changes, which could not be explained by the reversible equilibrium system shown in Chart 1. In the present paper, we show the absorption spectral evidence on this phenomenon and discuss the mechanism.

Results and Discussion

Immediately after mixing of TNB and sodium hydroxide, where both reagents were respectively dissolved in methanol-water (20: 80) mixture, the absorption band due to I with two maxima around 433 and 500 nm appeared (Fig. 1, a) and rapidly changed to a two-component band (Fig. 1, b—d). The band in Fig. 1, d did not change in shape and intensity for more than 30 min. One of the components is due to I and another due to II with a maximum around 490 nm. The ratio of I to II depended upon both sodium hydroxide concentration (*cf.*, Fig. 1, d and Fig. 2, a : The concentration ratio of sodium hydroxide to TNB in

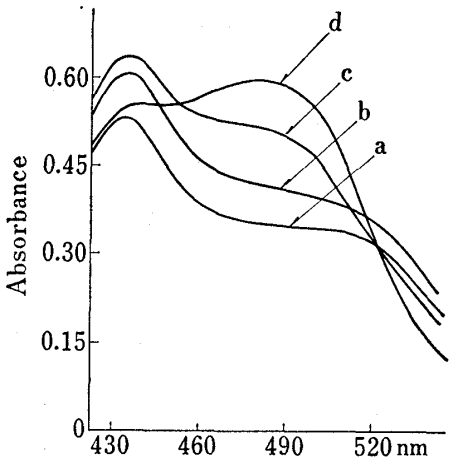


Fig. 1. Absorption Spectral Changes with Time of Mixture of TNB and Sodium Hydroxide in Methanol-Water (20:80)

Equal volumes of solutions of TNB (1×10^{-4} M) and NaOH (4%) in MeOH-H_2O (20: 80) were mixed. The spectra were recorded after the periods (a, 10 msec; b, 100 msec; c, 400 msec; d, 6.4 sec and 30 min) against MeOH-H_2O (20: 80).

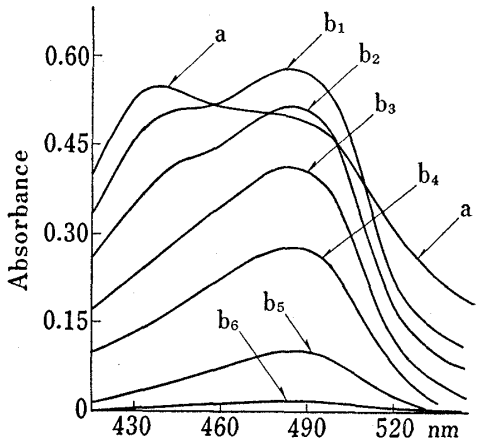


Fig. 2. Absorption Spectral Changes with Time of Mixture of TNB and Sodium Hydroxide on Neutralizing with Sodium Dihydrogen Phosphate in Methanol-Water (20:80)

a) One part of TNB (2×10^{-4} M) in MeOH-H_2O (20:80) and one part of NaOH (4%) in MeOH-H_2O (20:80) were mixed. The mixture was allowed to stand for 5 min and then diluted with equal volume of MeOH-H_2O (20:80). The spectrum was recorded after 6.4 sec against MeOH-H_2O (20:80).

b) Equal volumes of the mixture of TNB and NaOH in a) and a 10% solutions of NaH_2PO_4 $2H_2O$ in the MeOH-H_2O in a) were mixed. The spectra were recorded after the periods (1, 10 msec; 2, 50 msec; 3, 200 msec; 4, 1 sec; 5, 4 sec; 6, 8 sec) against MeOH-H_2O (20:80).

Fig. 1 was 2 times that in Fig. 2, a) and water content of the mixture.[4] When the mixture was neutralized with sodium dihydrogen phosphate solution, the colors due to I and II rapidly disappeared. The spectral changes with time followed by the stopped flow rapid scan analyser were shown in Fig. 2. The band due to I initially disappeared (Fig. 2, b_{1-2}), and then another band due to II decreased in intensity without change in its spectral shape (Fig. 2, b_{3-6}). The same spectral change as shown in Fig. 2 was also observed on acidifying the alkaline mixture with other acid solution (acetic, phosphoric or hydrochloric acid dissolved in methanol–water(20: 80) mixture).

In methanolic medium, the band due to I also appeared with two maxima at 423 and 495 nm immediately after mixing of TNB and sodium hydroxide (Fig. 3, a). In this case, such change of band from I to II as shown in Fig. 1, was not observed perceptively, because the equilibrium between I and II (Chart 1) lay so far to the left in methanol[4] and the band due to II, if any present, would be covered with that due to I of high intensity. When the alkaline mixture was acidified with methanolic acetic acid solution, the band due to II was revealed with a maximum around 505 nm after the first disappearance of the band due to I and then decreased in intensity as shown in Fig. 3, b).

When the neutralized or acidified mixture was made alkaline with sodium hydroxide, the bands due to I and II appeared again in the medium of the methanol–water mixture and the band due to I in the medium of methanol.

Above observations indicated that the backward reaction from II to I did not occur and II directly changed to TNB without through I when the alkaline TNB solutions were neutralized or acidified in both methanol and methanol–water mixture.

Similar spectral changes to those observed in the reaction of alkaline TNB solutions with acids were also observed when aqueous methanol solutions of TNB and sodium sulfite, in which 1: 1 and 1: 2 complexes[5] occurred in the solutions, were neutralized with acid solutions as described above.

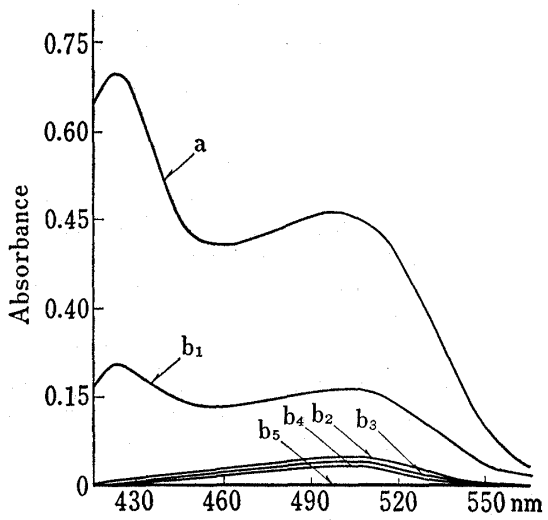


Fig. 3. Absorption Spectral Changes with Time of Mixture of TNB and Sodium Hydroxide on Acidifying with Acetic Acid in Methanol

a) One part of methanolic solution of TNB (2×10^{-4}M) and 1 part of methanolic solution of NaOH (4%) were mixed. The mixture was allowed to stand for 5 min and then diluted with the equal volume of MeOH. The spectrum was recorded after 10 msec of the dilution against MeOH.

b) Equal volumes of the mixture of TNB and NaOH in a) and methanolic solution of AcOH (3.5%) were mixed. The spectra were recorded after the periods (1, 1 msec; 2, 10 msec; 3, 40 msec; 4,320 msec; 5,640 msec) against MeOH.

Experimental

TNB was purified as previously described.[6] The other chemicals used were reagent grade and their solutions were prepared immediately before use. Rapid visible absorption spectral changes shown in the

4) Kinetic studies of the formation of I and II have been made: M.R. Crampton and M. El-Ghariani, *J. Chem. Soc.* (*B*), **1971** 1043; C.F. Bernasconi and R.G. Bergstrom, *J. Org. Chem.*, **36**, 1325 (1971); *idem*, *J. Am. Chem. Soc.*, **96**, 2397 (1974).

5) R.A. Henry, *J. Org. Chem.*, **27**, 2637 (1962); M.R. Crampton, *J. Chem. Soc.* (*B*), **1967** 1341; C.F. Bernasconi and R.G. Bergstrom, *J. Am. Chem. Soc.*, **95**, 3603 (1973); M.J. Strauss and S.P.B. Taylor, *ibid*, **95**, 3813 (1973); M.R. Crampton and M.J. Willison, *J. Chem. Soc. Chem. Comm.*, **1973** 215; M. Sasaki, *Chemistry Letters*, **1973, 205.**

6) T. Momose, Y. Ohkura, K. Kohashi, T. Tanaka, Y. Yano, and N. Itakura, *Rinsho Kensa*, **10**, 747 (1966).

figures were measured by a Union RA 1300 Stopped Flow Rapid Scan Analyser. After mechanical injection of equal volumes of two kinds of solutions into the reaction cell (optical path length of 1 cm) of the stopped flow apparatus circulated by thermostated H_2O at 25°, the absorption spectra in a range from 415 to 565 nm were recorded on the digital memory at appropreate time intervals and regenerated on an X–Y recorder.

Chem. Pharm. Bull. 25(5)1106—1108(1977)

UDC 547.896.04 : 547.655.1.04

A New Synthesis of 6,7-Benzomorphan[1]

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(Received July 26, 1976)

A new synthetic route to 6,7-benzomorphan has been developed. 2,2-Dimethyl-7-methoxy-3,4-dihydro-1(2*H*)-naphthalenone (**1**) was cyanomethylated, followed by $LiAlH_4$ reduction and a Wagner-Meerwein rearrangement, to give aminoethyl compound **3**. Treatment of **3** with bromine gave hydrobenz[*e*]indole **4**, which was rearranged to 9-methylene-6,7-benzomorphan **5**. Hydrogenation of the methylene gave 5,9α-dimethyl derivative **6**, from which 5,9α-dimethyl-2′-hydroxy-6,7-benzomorphan (**7**) was obtained.

Keywords——synthesis of benzomorphan; cyanomethylation of tetralone-1; Wagner-Meerwein rearrangement of 1,2,2-trialkyl-1-tetralol; stereospecific reduction of olefin; rearrangement of bromo-hydrobenz[*e*]indole to 6,7-benzomorphan

Many compounds possessing potent analgesic activity have been found from N-substituted 5,9-dimethyl-2′-hydroxy-6,7-benzomorphans, and among these, pentazocine is the one used clinically as a unique non-narcotic analgesic. 5,9-Dimethyl-2′-hydroxy(or methoxy)-6,7-benzomorphan, an important intermediate for the synthesis of the N-substituted derivatives, has been prepared by dealkylation of the N-methyl (von Braun cyanogen bromide procedure)[3] or the N-benzyl derivative (hydrogenolysis).[4] The dealkylation, however, would have been laborious. A more novel method for the synthesis of 6,7-benzomorphan, following the work of Belleau, *et al.*,[5] in which there was projected conversion of hydrobenz[*e*]indole to the 6,7-benzomorphan framework.

The synthesis of 5,9α-dimethyl-2′-hydroxy-6,7-benzomorphan (**7**) from 2,2-dimethyl-7-methoxy-3,4-dihydronaphthalen-1 (2*H*)-one (**1**)[6] is outlined in Chart 1. Cyanomethylation of the α-tetralone **1** with $LiCH_2CN$ gave the cyano alcohol **2**. Compound **2** was reduced with $LiAlH_4$, followed by a Wagner -Meerwein rearrangement with hydrochloric acid, to give 1-(2-aminoethyl)-1,2-dimethyl-1,4-dihydronaphthalene (**3**). It is worthy of note that the exo olefinic compound **3′** was obtained by treatment of **2** with hydrochloric acid for 2—3

1) This work was presented at the 96th Annual Meeting of the Pharmaceutical Society of Japan, Nagoya, April, 1976.
2) Location: *a) Hongo 13, Toyama; b) Hariwara-nakamachi 350–1, Toyama; c) Tawame 1076, Sakado-machi, Saitama.*
3) E.M. Fry and E.L. May, *J. Org. Chem.*, **24**, 116 (1959).
4) N.F. Albertson and W.F. Wetterau, *J. Med. Chem.*, **13**, 302 (1970).
5) I. Monkovic, T.T. Conway, H. Wong, Y.G. Perron, I.J. Pachter, and B. Belleau, *J. Am. Chem. Soc.*, **95**, 7910 (1973).
6) P.J. Hattersley, I.M. Lockhart, and M. Wright, *J. Chem. Soc.* (*C*), **1969**, 217.