reagent, then *ca.* 1.5 l. of 10% sulfuric acid was added and the aqueous layer was re-extracted several times with ether. The combined organic layers were washed with sodium carbonate solution and water, dried and evaporated through a 25-cm. Vigreux column. Distillation of the residue through the same column furnished 313 g. (79%) of the chlorocarbinol, b.p. 67° (20 mm.), n^{26}D 1.4408 (this compound has previously been made by the reaction of β-chloropropionaldehyde with methylmagnesium iodide[7]; reported[7a] b.p. *ca.* 70° (13 mm.)). In addition a lower boiling fraction was obtained.

4-Chloro-2-butyl Acetate (III).—A solution of the chlorocarbinol (300 g.) in 300 cc. of ether and 360 cc. of pyridine was cooled in ice and 330 g. of acetyl chloride was added dropwise during 90 minutes with stirring and continued cooling. Stirring was continued for 5 hours at room temperature and the mixture was then set aside overnight. Ice and ether were added, the organic layer was washed with water, dilute hydrochloric acid, sodium bicarbonate and water, dried and distilled through the Vigreux column. The acetate had b.p. 70° (16 mm.), n^{25}D 1.4260, and weighed 395 g. (95%).

1,3-Butylene Oxide (IV).—An apparatus as described by Noller[5] incorporating a 25-cm. Vigreux column (ref. 5, Note 2) was used and the receiver was cooled in ice–salt. A mixture of 437 g. of solid potassium hydroxide and 40 cc. of water was placed in the reaction flask, which was heated to 150° in an oil-bath, and a few cc. of the acetate was added. Thereupon the mixture became liquid, and stirring was commenced. The acetate (total of 389 g.) was then added dropwise with vigorous stirring at such a rate as to keep the inside temperature at 140–150°, and that at the distillation head at 70–85°. The reaction was quite exothermic and the inside temperature was maintained by keeping the oil-bath at 120–140°. The distillate passed over at a rate of *ca.* 1 drop/second. After 3 hours the addition was complete, and the oil-bath was heated to 160° for a further 30 minutes. The distillate (186.5 g.) was dried over 40 g. of solid potassium hydroxide, whereupon a lower aqueous layer separated. The upper layer was dried over a further 20 g. of potassium hydroxide, decanted and distilled through the 25-cm. Vigreux column. The fraction (134 g.) with b.p. 55–70° was refluxed with 15 g. of sodium hydride for 1 hour to remove impurities, and was then refractionated. The oxide was obtained as a pleasant smelling liquid, b.p. 60–61° (762 mm.), n^{25}D 1.3894, and weighed 122 g. (66%) (reported[2] b.p. 59.4–59.7° (736 mm.), n^{20}D 1.3889).

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(7) (a) E. Fourneau and P. Ramart-Lucas, *Bull. soc. chim.*, [4] **25**, 364 (1919); (b) H. J. Backer and C. C. Bolt, *Rec. trav. chim.*, **54**, 68 (1935); (c) R. C. Elderfield, *et al.*, THIS JOURNAL, **68**, 1516 (1946).

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The Reaction of Tolylene Diisocyanate Dimer with Dibutylamine

BY J. H. SAUNDERS AND EDGAR E. HARDY

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Isocyanate dimers are of interest principally because they may exhibit isocyanate activity only at elevated temperatures, and because they may occur as impurities in isocyanates, especially in polyisocyanates. The reactions of phenyl isocyanate dimer have been studied qualitatively, as by Hofmann,[1] and Bayer[2] has reported that the dimer of tolylene diisocyanate (I) dissociates to the monomer at 150°. This dimer has been observed in this Laboratory to react with more than two equivalents of dibutylamine in refluxing toluene, in a modification of an analytical procedure for isocyanates.[3] To clarify further the chemistry of this dimer its reaction with di-*n*-butylamine in *o*-dichlorobenzene was studied briefly at 50–180°.

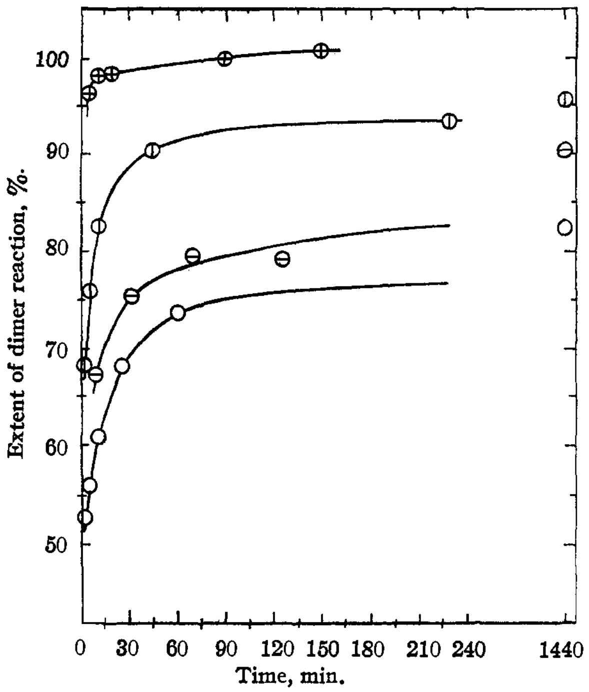
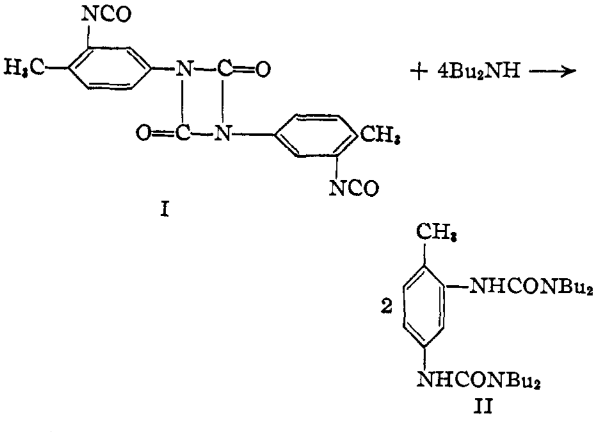


Fig. 1.—The reaction of tolylene diisocyanate dimer with dibutylamine: ○, reaction at 50°, 4:1 amine:dimer molar ratio; ⊖, 70°, 4:1 ratio; ⦶, 130°, 4:1 ratio, ⊕, 170–180°, 8:1 ratio.

The results are shown in Fig. 1. It is assumed that the first 50% of the reaction, which was very fast, corresponded to the reaction of the free isocyanate groups, and that further reaction took place at the dimerized groups. The dimer ring reacted at an appreciable rate, even at 50°, and reacted completely with 100% excess of amine in 1.5 hours at 170–180°. The reaction product gave an analysis in agreement with structure (II), and showed no depression of melting point with the reaction product from monomeric tolylene diisocyanate and dibutylamine.



These results show that isocyanate polymers may exhibit considerable activity in the analysis for isocyanates, and that dimers will not be completely unreactive at moderate temperatures in systems containing amines. It is likely that dimers will

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(1) A. W. Hofmann, *Ber.*, **4**, 246 (1871).

(2) O. Bayer, British Intelligence Objectives Subcommittee Final Report No. 719, July, 1946.

(3) S. Siggia and J. G. Hanna, *Anal. Chem.*, **20**, 1084 (1948).

be more stable in the presence of less reactive groups, such as hydroxyl.

Experimental

The dimer of 2,4-tolylene diisocyanate was prepared by mixing 1350 g. of dry pyridine and 1590 g. of the diisocyanate with stirring.[2] Some cooling was used to keep the temperature below 40°. After standing overnight the solid reaction mass was diluted with 3.5 liters of dry carbon tetrachloride, pulverized, filtered and dried in a vacuum desiccator. The dimer was recrystallized from chloroform, m.p. 155.4–155.7°, corrected.[4]

Anal. Calcd. for $C_{18}H_{12}O_4N_4$: C, 62.06; H, 3.47; N, 16.09. Found: C, 62.50; H, 3.75; N, 16.16.

The dimer was fairly stable toward atmospheric moisture.[2] After 48 hours exposure to the air the melting point was 4° lower than initially.

The reactions between the dimer and dibutylamine were performed in a dry 1-liter, 3-necked flask equipped with a sealed stirrer, thermometer and reflux condenser which was protected by a calcium chloride tube. The flask was immersed in a constant-temperature oil-bath. Redistilled technical *o*-dichlorobenzene which had been dried over calcium hydride was used as the solvent. The solvent (500 g). was added to the flask and was permitted to come to the bath temperature, when 25.0 g. (0.072 mole) of dimer was added. At zero time 37.6 g. (0.287 mole) of redistilled di-*n*-butylamine, neutralization equivalent 131, was added from a pipet. At intervals a sample of the reaction mixture was withdrawn and added to 25 ml. of 1.06 *N* hydrochloric acid, the mixture shaken, and the sample weight determined. Titration of the excess acid with 0.50 *N* sodium hydroxide solution to a brom phenol blue end-point permitted calculation of unreacted amine, and hence of unreacted dimer.

In the experiments at 50° 850 g. of solvent was required to dissolve the dimer. One experiment was performed in refluxing solvent (170–180°) with amine:dimer molar ratio of 8:1 to find the time required for complete reaction.

A blank experiment showed that dibutylamine did not react appreciably with the solvent during 2.25 hours refluxing. It was also found that no hydrolysis of the dimer occurred during analysis. A mixture of 50 ml. of solvent and 1 g. of dimer was refluxed and added quickly to 25 ml. of acid. Titration after 25 minutes showed that no amine had been liberated by hydrolysis of the dimer.

The results at 0–240 min. and at 1440 min. are summarized in Fig. 1.

The product from a reaction between the dimer and dibutylamine in refluxing dichlorobenzene was obtained by vacuum distillation of the solvent. Repeated recrystallizations from hexane gave a white solid, m.p. 111.1–111.7°, corrected.

Anal. Calcd. for $C_{25}H_{44}O_2N_4$: C, 69.40; H, 10.25; N, 12.95. Found: C, 69.70; H, 10.37; N, 12.74.

From a reaction between monomeric tolylene diisocyanate and dibutylamine in benzene there was obtained a white solid, m.p. 111.1–111.6°, corrected. This solid showed no depression of melting point when mixed with the reaction product from the dimer and the amine, thus confirming structure II.

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(4) W. Siefken, *Ann.*, **562**, 75 (1949).

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Physical-chemical Studies on the Interaction of Surface-active Agents with Nucleoproteins. II[1]

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The ultracentrifuge studies of the Santomerse D–calf thymus nucleohistone system[2] have been extended to provide more information on the nature of complex formation in this system. The behavior of the components of the nucleohistone molecule, histone and nucleic acid, in Santomerse D solution, in the ultracentrifuge is reported here.

Experimental and Results

The nucleohistone, histone hydrochloride and tetrasodium nucleate were prepared as previously described.[2] All solutions containing Santomerse D were used for ultracentrifuge, viscosity and diffusion measurements immediately after dialysis was completed. All solvents contained 0.02 ionic strength phosphate buffer.

Ultracentrifuge Studies.—The experimental results with the customary optical rotor are summarized in Table I. "Schlieren" patterns of tetrasodium nucleate and histone hydrochloride sedimenting in buffer and in buffered Santomerse D solution are shown in Fig. 1.

TABLE I

SEDIMENTATION VELOCITY OF TETRASODIUM NUCLEATE AND HISTONE HYDROCHLORIDE

Solute	Concn., %	Solvent	s_{20}[a]
Tetrasodium nucleate	0.31	Water	4.23
	.155	Water	5.29
	.103	Water	6.34
	.000	Water	8.33[c]
	.31	0.35% Santomerse D	4.36
	.155	.35% Santomerse D	5.53
	.103	.35% Santomerse D	6.24
	.000	.35% Santomerse D	8.00[c]
Histone hydrochloride	0.22	Water	21.2,[b] 12.8[a]
	.32	0.35% Santomerse D	3.38
	.157	.35% Santomerse D	2.45
	.078	.35% Santomerse D	2.13
	.000	.35% Santomerse D	1.90[c]
Santomerse D	0.35	Water	0.89[d]

[a] Expressed in Svedberg units. [b] Fast moving components. The sedimentation constant of the slow moving component was too low for measurement. [c] Extrapolated value. [d] Obtained with Spinco Model E ultracentrifuge at 59,780 r.p.m.

To measure the amount of Santomerse D actually involved in complex formation, the experiments with the optical rotor were parallelled with a quantity type rotor[3]. The rotor was fitted with two plastic tube liners, each containing a stainless steel thimble which extended about half way to the bottom of the tube. The perforated bottom of the

TABLE II

BINDING OF SANTOMERSE D BY NUCLEOHISTONE, TETRASODIUM NUCLEATE AND HISTONE HYDROCHLORIDE FROM QUANTITY TYPE ROTOR EXPERIMENTS

Run	System[a]	Time, hr.	RCF, g's	Santomerse D in supernatant, %	Wt. fraction Santomerse D in complex
1	Santomerse D–nucleohistone	6	104,000	0.25	0.45[b]
2	Santomerse D–tetrasodium nucleate	6	104,000	.35	.00
3	Santomerse D–histone hydrochloride	12	129,000	.07	.64
4	Santomerse D	12	100,000	.16	

[a] Contains 0.35% Santomerse D with 0.02 ionic strength phosphate buffer, and 0.16% of second component listed. [b] Corrected for 0.03% nucleohistone remaining in the supernatant, as determined by micro-Kjeldahl nitrogen analysis. This result is in agreement with the previously reported[2] value obtained from area measurements.

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(1) Based on research carried out under contract between the Office of Naval Research and The Ohio State University Research Foundation.

(2) M. W. Renoll and Q. Van Winkle, THIS JOURNAL, **73**, 2504 (1951).

(3) R. W. G. Wyckoff and J. B. Lagsdin, *Rev. Sci. Instr.*, **8**, 427 (1937).