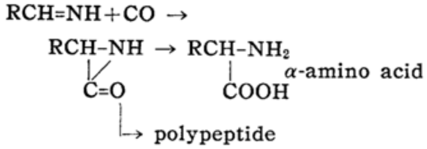
Studies on the High Pressure Reaction of Carbon Monoxide. I. On the Reactions of Schiff Bases and Azocompounds with Synthetic Gas

By Shunsuke MURAHASHI and Shigeki HORIIE*

(Received July 3, 1959)

From considerations of the chemical formula, it might be conceivable that if an addition of carbon monoxide to the double bond of Schiff base could occur, there are possibilities of synthesizing α-amino acid on hydrolysis of the addition products with water or peptide with a restricted quantity of water, as indicated below:

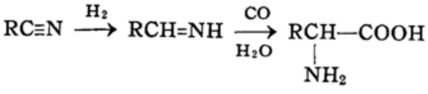


$$RCH{=}NH + CO \rightarrow \underset{C=O}{RCH{-}NH} \rightarrow \underset{COOH}{RCH{-}NH_2}\ \alpha\text{-amino acid}$$
$$\rightarrow \text{polypeptide}$$

The following work was undertaken in the light of such a consideration.

It is well known that the reduction of nitrile proceeds to amine via éte intermediate of Schiff base, and that cobalt carbonyl is able to catalyze oxo-reaction, and furthermore it also catalyzes hydrogenation of aldehyde to alcohol in the presence of carbon monoxide and hydrogen.

On such an account the authors attempted to prove the possibility of obtaining amino acid or polypeptide directly from nitriles.



$$RC{\equiv}N \xrightarrow{H_2} RCH{=}NH \xrightarrow[H_2O]{CO} \underset{NH_2}{RCH{-}COOH}$$

At the time when the authors started the work, chemical reaction of nitriles under an oxo-condition had not been explored and so benzonitrile and benzylcyanide were subjected to the present examination. The experiments resulted only in giving a small quantity of amines (mixtures of primary and secondary ones) and it revealed that reduction of nitrile would be very difficult to be realized and no reaction product was obtained in which carbon monoxide had been involved. Therefore, the authors have turned the subject to the Schiff base itself and studied to see whether the reaction in this case would take place, giving α-amino acid or peptide as was postulated above.

The general conditions adopted for the experiments are as follows: Catalyst, cobaltcarbonyl; Solvent, benzene or benzene-alcohol (1:1); Gas, $CO+H_2$ (1:1), 200 atm.; Reaction temperature, 120~130°C.

The results with Schiff bases were shown in Table I which shows conclusively that a reduction of C=N double bond had occured and no reactions were found in which carbon monoxide has participated.

The reduction proceeded very smoothly and did not present any marked difference even when the reactions were carried out at varied conditions, i. e. pressure, temperature and reaction time. As to the effect of reaction medium it was found, that the reaction was faster and began at a somewhat (10~20°C) lower temperature when alcohol-benzene mixture (1:1) was used instead of aromatic hydrocarbons.

Benzaldehyde phenylhydrazone did not give any definite result with synthetic gas. The authors, then, studied the reaction of synthetic gas on double bond having nitrogen atom, such as the N=O and N=N-group as well as C=S double bond.

Nitrobenzene and azobenzene was allowed to react with carbon monoxide and was ascertained to give aniline as a principal product. Hydrazobenzene was also subjected to this reaction for reference and it was confirmed that aniline was again the principal product. In all cases the authors found the formation of a considerable quantity of diphenylurea, as shown in Table II.

Thus, it has been confirmed that the four kinds of bond, C=N, N=N, C=S and N=O were all reduced by synthetic gas in the presence of cobalt carbonyl catalyst. The formation of urea derivatives observed in all cases except for the compound involving C=S linkage is

---

* Present address: Institute of Scientific and Industrial Research, Osaka Univ., Sakai, Osaka.

TABLE I. REACTION OF SYNTHETIC GAS WITH BENZALDEHYDEANILS

Anil	Solvent	Reaction temp., °C	Reaction time, min.	Product	Yield, %
$C_6H_5N{=}CHC_6H_5$	B	135	110	$C_6H_5NHCH_2C_6H_5$	80
$C_6H_5N{=}CHC_6H_5$	A B	120	60	$C_6H_5NHCH_2C_6H_5$	79
$p\text{-}ClC_6H_4N{=}CHC_6H_5$	B	150	70	$p\text{-}ClC_6H_4NHCH_2C_6H_5$	79
$p\text{-}ClC_6H_4N{=}CHC_6H_5$	A B	130	130	$p\text{-}ClC_6H_4NHCH_2C_6H_5$	81
$p\text{-}MeC_6H_4N{=}CHC_6H_5$	B	140	90	$p\text{-}MeC_6H_4NHCH_2C_6H_5$	82
$p\text{-}MeC_6H_4N{=}CHC_6H_5$	A B	120	60	$p\text{-}MeC_6H_4NHCH_2C_6H_5$	80
$p\text{-}MeOC_6H_4N{=}CHC_6H_5$	B	130	60	$p\text{-}MeOC_6H_4NHCH_2C_6H_5$	83
$p\text{-}MeOC_6H_4N{=}CHC_6H_5$	A B	120	50	$p\text{-}MeOC_6H_4NHCH_2C_6H_5$	82
$p\text{-}NO_2C_6H_4N{=}CHC_6H_5$	B	130	80	$p\text{-}NO_2C_6H_4NHCH_2C_6H_5$	80
$p\text{-}NO_2C_6H_4N{=}CHC_6H_5$	A B	120	70	$p\text{-}NO_2C_6H_4NHCH_2C_6H_5$	78

Catalyst, $[Co(CO)_4]_2$, 0.03 millimol./ml.; Solvent, B=benzene, AB=alcohol-benzene (1:1); Gas, CO(100 atm.)+H_2(100 atm.).

TABLE II. FORMATION OF DIPHENYLUREAS BY THE REACTION OF AZOBENZENES AND NITROBENZENE WITH SYNTHETIC GAS

	$C_6H_5NHCONHC_6H_5$ %	$R\text{-}C_6H_4NHCONHC_6H_5$ %	$R\text{-}C_6H_4NHCONHC_6H_4\text{-}R$ %
$C_6H_5NO_2$	5～ 6		
$C_6H_5N{=}NC_6H_5$	15～20		
$C_6H_5NH\text{-}NHC_6H_5$	25～30		
$p\text{-}ClC_6H_4N{=}NC_6H_5$	trace	5	3
$p\text{-}MeC_6H_4N{=}NC_6H_5$	trace	12	5

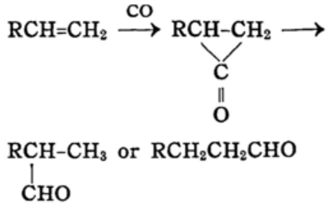
Reaction conditions are the same in Table I.

noteworthy, because it demonstrates, that some new kind of CO-reaction has occurred, and especially the fact that a formation of symmetrically substituted urea derivatives were observed from asymmetrically substituted azo-compounds was of special note.

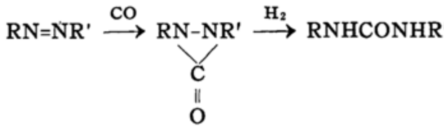
As the reaction appeared to be a new one, the authors planned further experiments so as to obtain more detailed information about the high pressure reaction of carbon monoxide.

Hydrazobenzene gave 50% yield of azobenzene under the similar condition, at the reaction temperature which was lower than that required for the reduction (80～90°C). From this experiment it could be postulated that urea could have formed from hydrazobenzene via azobenzene. However, the yields of diphenylurea were in all cases higher when hydrazobenzene was used instead of azobenzene. In the case of nitrobenzene, the formation of urea derivative was also observed and its formation could be interpreted by the intermediate formation of either hydrazobenzene or azobenzene.

In order to discuss the possible mechanism for the formation of urea derivative, one has to consider either 1) fission of hydrazo linkage followed by addition of CO, or 2) that the azo group remains without cleavage until CO is added across the double bond and then the -N-N- bond is subjected to fission by hydrogenolysis as will be shown below (Eq. 2). Eq. 1 was suggested earlier by W. Reppe1) as a possible mechanism of the oxo-reaction and the carboxylation of olefins. Accordingly one might propose Eq. 2 for the urea formation.



$$RCH{=}CH_2 \xrightarrow{CO} \underset{\underset{O}{\overset{\|}{C}}}{RCH\text{-}CH_2} \longrightarrow \underset{\underset{CHO}{|}}{RCH\text{-}CH_3} \text{ or } RCH_2CH_2CHO \qquad (1)$$



$$RN{=}NR' \xrightarrow{CO} \underset{\underset{O}{\overset{\|}{C}}}{RN\text{-}NR'} \xrightarrow{H_2} RNHCONHR' \qquad (2)$$

Since azobenzene is reduced for the most part to aniline, it would be an acceptable argument that the formation of urea could have resulted from the reaction of

---

1) W. Reppe, *Ann.*, **582**, 40 (1953).

aniline and carbon monoxide. Pino²⁾ discussed the possibility of formation of urea derivatives from two moles of aniline and one mole of carbon monoxide under a dehydrating condition, and Buckley³⁾ reported the formation of formylaniline by the reaction of aniline and carbon monoxide.

However, all the authors' tests with aniline and with formylaniline failed to show that the urea-formation is the result of the reaction of aniline and carbon monoxide.

An alternate mechanism would presumably be a fission of the azo-compound by means of carbon monoxide and hydrogen, leading to the primary formation of phenylisocyanate and aniline. However, the authors failed to isolate such an intermediate to prove this mechanism.

As another possibility, hydrazobenzene might well be accounted for the reaction. In this regard the authors will discuss it in later papers.

Experimental

1) **Reduction of Benzaldehydeanil with Synthetic Gas.** — Benzaldehydeanil (5 g.) was dissolved in 50 ml. of benzene or benzene-alcohol mixture (1:1) and charged in an autoclave of 100 ml. content made of 18-8 stainless steel together with cobalt carbonyl (1.0 g.). After replacement of air, the synthetic gas was compressed up to 200 atm. (CO, 100 atm. and H_2, 100 atm.). The autoclave was heated at 120∼130°C, when the pressure began to descend, and after completion of gas absorption it was allowed to cool. The content of the autoclave was heated in a flask on a water bath and after decomposition of the cobalt catalyst and filtration the filtrate was distilled in vaccuo, affording 4 g. of benzylaniline, m. p. 38°C, which was identified by the mixed melting point test with an authentic sample.

The essential feature of the experimental procedures are all the same as described above, and thus *p*-chloro, *p*-methyl-, *p*-methoxy- and *p*-nitro-benzaldehydeanil were subjected to examination. The results are given in Table I. The melting points and the boiling points all agree with the values described in the literatures. *p*-Nitrocompound was reduced under the present condition selectively at the anil double bond and the nitro group remained unchanged.

2) **Reaction of 3-Phenyl-2-thioxopropionic Acid and Carbon Monoxide.**—3-Phenyl-2-thioxopropionic acid (3 g.) in benzene (50 ml.) was allowed to react with carbon monoxide and hydrogen of 200 atm. in the presence of cobalt catalyst (1 g.) at 120∼130°C for 2 hr. No gas absorption was observed, but after cooling and degassing, it was found that hydrogen sulfide gas had formed. A definite product could not be isolated except 2-phenylpropionic acid amide melting at 102°C.

3) **Formation of Diphenylurea as a By-product in the Reaction of Azobenzene and Synthetic Gas.**—Azobenzene (5 g.) yielded 1.1 g. of diphenylurea (20% yield) in a form of a difficultly soluble product, which was recrystallized from alcohol.

4) **Urea Derivatives from *p*-Chloroazobenzene.**—*p*-Chloroazobenzene (5 g.) was treated as in exp. 1 and from the reaction product 0.6 g. (12%) of a mixture of urea compounds was obtained, and was separated into two parts: *p*,*p*'-dichlorodiphenylurea as the difficultly soluble part in alcohol in colorless prisms, m. p. 286°C (with decomposition), and as the soluble part *p*-chlorodiphenylurea in scaly crystals, m. p. 244°C.

Anal. Found: C, 56.66; H, 3.70; Cl, 25.20; N, 10.36. Calcd. for $C_{13}H_{10}Cl_2N_2O$: C, 56.93; H, 3.64; Cl, 25.26; N, 10.21%.

Anal. Found: C, 64.06; H, 4.64; Cl, 14.32; N, 11.55. Calcd. for $C_{13}H_{11}ClN_2O$: C, 64.19; H, 4.52; Cl, 14.40; N, 11.52%.

5) **Urea Derivatives from *p*-Methylazobenzene.**—*p*-Methylazobenzene (5 g.) was treated as in exp. 4 and from the filtrate of the reaction mixture a mixture (1.2 g., 22%) of urea was separated. From a difficultly soluble portion *p*,*p*'-dimethylphenylurea (0.3 g.) was obtained in colorless needles, m. p. 262°C and from the soluble portion *p*-dimethyldiphenylurea (0.7 g., 12%) was obtained, and further a small quantity of unsubstituted diphenylurea was obtained from the last portion of the soluble residue.

Anal. Found: C, 74.81; H, 6.70; N, 11.78. Calcd. for $C_{15}H_{16}N_2O$: C, 75.00; H, 6.66; N, 11.66%.

Anal. Found: C, 74.15; H, 6.20; N, 12.51. Calcd. for $C_{14}H_{14}N_2O$: C, 74.33; H, 6.19; N, 12.38%.

Department of Chemistry
Faculty of Science
Osaka University
Nakanoshima, Osaka

---

2) P. Pino and C. Paleari, *Gazz. Chim. Ital.*, 81, 646 (1951); *Chem, Abstr.*, **46**, 7063 (1952).

3) G. D. Buckley and N. H. Ray., *J. Chem. Soc.*, **1949**, 1151.