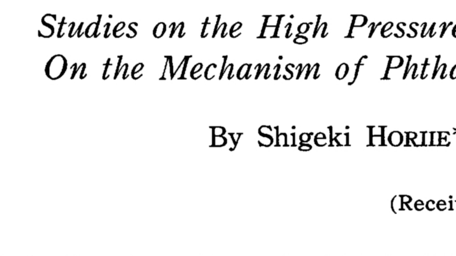
Studies on the High Pressure Reaction of Carbon Monoxide. IV. On the Mechanism of Phthalimidine and Indazolone Formation

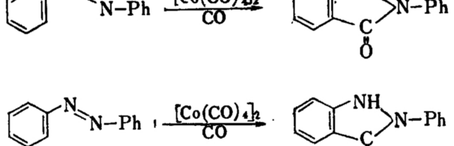
By Shigeki HORIIE* and Shunsuke MURAHASHI

(Received July 3, 1959)

Both the formation of phthalimidines and of indazolones from Schiff bases or azocompounds are considered formally to be the same type of reactions, in which one molecule of carbon monoxide was incorporated into, and then underwent ring closure.



The formation of quinazolons from indazolone is considered to proceed via the reaction of ring enlargement, and has to be considered as another type of reaction and will be mentioned later.



In view of avoiding confusion arising from by-products formation, the reaction of Schiff base was preferably chosen as the subject of this investigation because of the simplicity of the reaction—in the latter case the only reaction product was phthalimidine. From an experiment with Schiff base in continuous run, there could be observed the formation of a complex compound, which was soluble in benzene and was appreciably stable. It was shown in the previous reports that both in the cases of Schiff bases and azobenzenes the more electronegative the "C=N" or "N=N" bond is, the easier the reaction proceeds. These observations seem to indicate that some relation could exist between the ease of complex formation and the feasibility of reaction, and if this argument holds true, the two alternative methods of thinking on the attachment of catalyst on the reactive center of the substrate might be conceivable.

a) The one is that complex formation gives rise to the attachment of cobalt carbonyl across the π-bond of C=N or N=N. In this case a steric requirement

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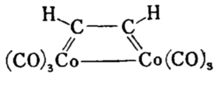
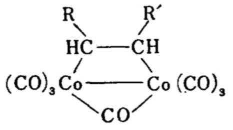
* Present address: Institute of Scientific and Industrial Research, Osaka Univ., Sakai, Osaka.

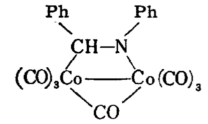
should necessarily be considered as was reported by Wender et al. in the case of oxo-synthesis. They observed the formation of a definite complex¹⁾ from acetylene and cobalt carbonyl of the following constitution and, from this fact they postulated the same kind of complex formation by oxo-reaction, when olefins and cobalt carbonyl were reacted II²⁾,

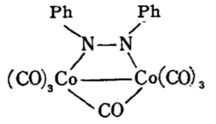

(I)


(II)

and they reasonably explained the observed differences of reaction velocity on various olefins on the steric ground, which inevitably affects the ease of intermediate complex formation.

If the same arguments are accepted in the authors' case, the intermediate complex would be such as III or IV, and marked steric effect might well be consiedered when Schiff bases or azocompounds were subjected to the experiment.


(III)


(IV)

On this account, the authors have compared the velocity of phthalimidine formation reaction, taking benzaldehyde-anil, acetophenone and benzophenone-anil as reactants, and the results are illustrated in Fig. 1. There has been no difference on the velocity and no sterically hindered effect of the phenyl group was discernible. Hence, the formation of this type of complex III would hardly be acceptable.

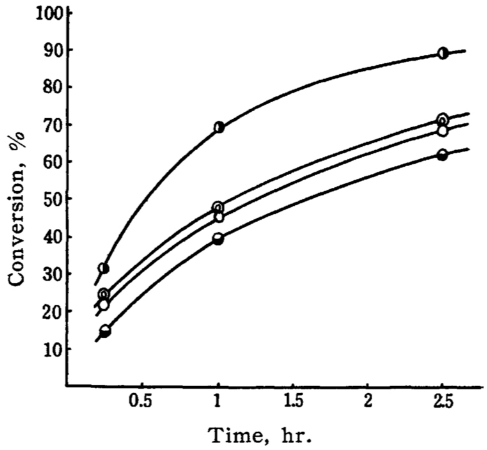
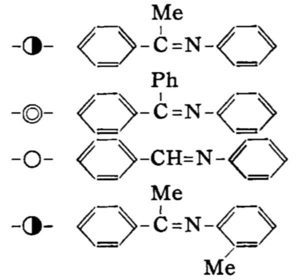
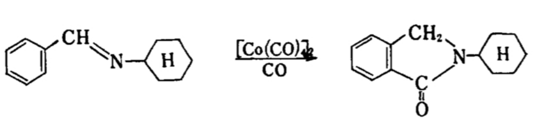


Fig. 1. Reactions of acetophenone-anil and benzophenone-anil with carbon monoxide.



Concn. of Schiff bases: 0.55 millimol/cc.
Concn. of $[Co(CO)_4]_2$: 0.03 millimol/cc.
Pressure of CO : 150 atm.
Solvent : benzene
Reaction temp. : 230°C

b) An alternative way of thinking would be that, an attachment of cobalt carbonyl takes place on the lone pair of nitrogen, which gives rise to the formation of a complex, acting as an intermediate for the reaction. Such consideration seems to explain much better the experimental facts which are described below. Although in the case of benzalcyclohexylamine gave in good yield phthalimidine as shown in formula below, benzyl cyclohexylamine did not give rise to phthalimidine, but only gave *N*-formyl compound by the treatment with carbon monoxide in the presence of cobalt catalyst, under the same condition. Recently, Wender and his collaborators³⁾ also observed the formation of formyl compounds by the reaction of dimethylamine or piperidine with carbon monoxide, in the presence of cobalt carbonyl catalyst.



In those cases it seems to be appropriate to postulate that an intermediate

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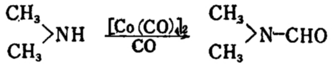
1) H. W. Sternberg, H. Greenfield, R. A. Friedel, J. Wotiz, R. Markby and I. Wender, *J. Am. Chem. Soc.*, **76**, 1457 (1954).

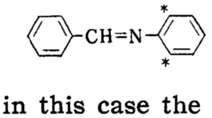
2) I. Wender, S. Metlin, S. Ergun, H. W. Sternberg and H. Greenfield, ibid., **78**, 5401 (1956).

3) H. W. Sternberg, I. Wender, R. A. Friedel and M. Orchin, ibid., **75**, 3148 (1953).



$$(CH_3)_2NH \xrightarrow[CO]{[Co(CO)_4]_2} (CH_3)_2N\text{-}CHO$$

formation of a complex occurred resulting from the coordination of the lone pair of the nitrogen atom with cobalt carbonyl, which in turn stabilized to yield formyl compound. Then, as a possible mechanism for the formation of phthalimidine and indazolone, the same argument would be worth while for consideration and for experimentation.



That is, in this case the initial step of the reaction is the coordination of cobalt carbonyl and nitrogen atom of anil bond CH=N, and the steric effect of ortho-position, which are marked with asterisks, would become very influential to the reaction. Thus, several *o*-substituted anils were subjected to the reaction so as to see whether the steric effect of the substituents was operative. The results of the experiments were illustrated in Fig. 2, where the effect caused by the methyl or ethyl substituent group were visualized in percentage of conversion of anils to phthalimidines, which were followed by the reaction time. It was expected mono-ortho-substituted anil yields lower conversion than unsubstituted one and ortho-dimethyl substituted anil would exhibit a still lesser conversion

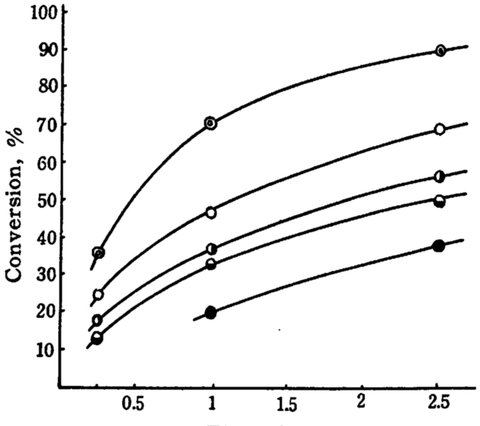
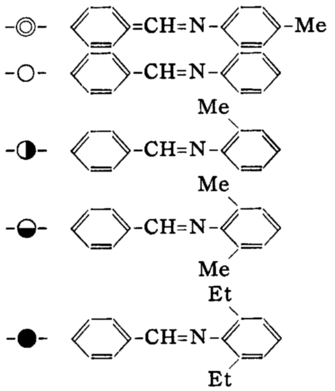


Fig. 2 Reactions of substituted benzaldehyde-anil and carbon monoxide.



Concn. of Schiff bases : 0.55 millimol./cc.
Concn. of $[Co(CO)_4]_2$: 0.03 millimol./cc.
Solvent : benzene
Pressure of CO : 150 atm.
Reaction temp. 230°C

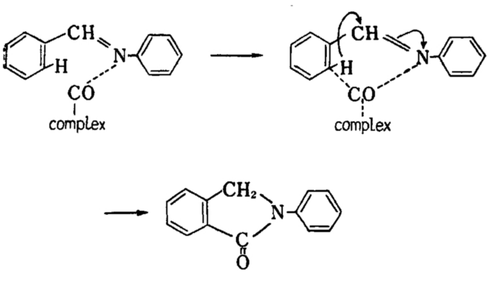
The experiment with *p*-methyl substituted anil has shown that methyl group had rather promoting effect, when it comes on para position, free from steric effect. The fact that in the case of ortho-substituted anil had shown marked low conversion in spite of having a methyl group of promoting action, shows that the steric effect is pronounced in these reactions. Hence it appeared as mentioned above, the primary step would be the addition of cobalt-carbonyl on the lone pair of nitrogen which is hindered by *o*-substituent of large steric requirement.

On the other hand, the reduction of a double bond of anils by means of synthetic gas and cobalt carbonyl go generally smoothly even if in the case where the substituents at the ortho position had shown to exhibit greatest resistance for the formation of phthalimidine, and no distinct steric effect was observed here.

The clear distinction of both reactions should indicate that the fundamental differences might exist in both reactions on the behavior of catalytic action. From the consideration above, the phthalimidine or indazolone formation can eventually be explained as follows.

1) Some kind of complex formation occurred at first between a lone pair of nitrogen atom of the anil or of azo-double bond, and here a steric effect was operative.

2) The formation of N-CO bond was then stabilized with the formation of a 5-membered ring with the carbon atom of benzene with simultaneous transfer of the hydrogen atom of ortho position of benzene to the unsaturated bond of C=N or N=N. Here the presence of such suitable acceptor of hydrogen atom was essential, and these might, side by side, have assisted the ring formation. In the case of benzyl cyclohexylamine as stated above, there is lacking such an accepting group and hence



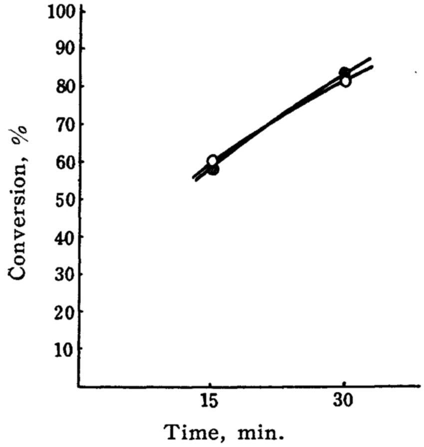
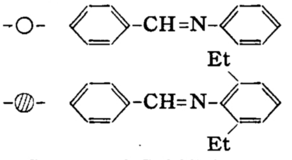


Fig. 3. Reduction of Schiff bases.



Concn. of Schiff bases : 0.5 mmol./cc.
Concn. of $[Co(CO)_4]_2$: 0.03 mmol./cc.
Pressure of synthetic gas : 180 atm.
$CO/H_2=1/1$
Solvent : benzene
Reaction temp. : 120°C

after the formation of the complex would stabilize by converting to formyl benzyl amine.

Concerning the formation of quinazolone from indazolone as the authors stated earlier, it is believed to have formed by a ring-enlargement reaction, and such a reaction, as far as the authors are aware, has not yet been described. A glance at this reaction seems to be similar to the reaction of the formation of diphenylurea from hydrazobenzene, but the mechanism of this enlargement is not yet fully understood.

Experimental

1) Reactions of Schiff Bases and Carbon Monoxide. — *General procedure.* — A solution of 0.0275 mol. of Schiff base and 1.5 millimol. of dicobalt octacarbonyl in 50 ml. benzene was heated at 230°C under 150 atmospheric pressure of carbon monoxide. After the reaction, benzene solution was heated under atmospheric pressure in a water bath so as to decompose cobalt carbonyl and filtered. After removal of benzene by distillation and then under reduced pressure, the residue was analyzed.

On each run, conversions from Schiff base into phthalimidine was determined for every 15, 60 and 150 min.

(i) On benzaldehyde-anil. — Conversions (%) into 2-phenylphthalimidine were 22.9, 46.2 and 68.1, respectively.

(ii) On acetophenone-anil. — Conversions (%) into 2-phenyl-3-methylphthalimidine melted at 82°C were 31.5, 68.5 and 89.0, respectively.

Anal. Found: C, 80.29; H. 5.99. Calcd. for $C_{15}N_{13}ON$: C, 80.69; H, 5.87%.

(iii) On benzophenone-anil.— Conversions (%) into 2,3-diphenyl-phthalimidine melted at 196.5°C were 24.8, 48.6 and 70.2, respectively.

(iv) On acetophenone o-tolylimide.—Conversions (%) into 2-*o*-tolyl-3-methylphthalimidine melted at 108°C were 14.3, 10.0 and 63.5, respectively.

Anal. Found: C, 80.68; H, 6.15. Calcd. for $C_{16}H_{15}ON$: C, 80.98; H, 6.37%.

(v) On benzaldehyde p-tolylimide.—Conversions (%) into 2-*p*-tolylphthalimidine were 36.8, 69.9 and 87.9, respectively.

(vi) On benzaldehyde o-tolylimide.—Conversions (%) into 2-*o*-tolylphthalimidine were 18.2, 36.0 and 53.0, respectively.

(vii) On benzaldehyde o, o-xylidylimide. — Conversions (%) into 2-*o*, *o*-xylidylphthalimidine melted at 103°C were 14.5, 32.8 and 49.8, respectively.

Anal. Found: N, 5.85. Calcd. for $C_{16}H_{15}ON$: N, 5.90%.

(viii) On benzal-o, o-diethylaniline.—Conversions (%) into 2-*o*, *o*-diethylphthalimidine melted at 140°C were 18.6 and 35.9, respectively.

Anal. Found: N, 5.02. Calcd. for $C_{18}H_{19}ON$: 5.28%.

2) Reactions of Benzylcyclohexylamine and Carbon Monoxide.—A solution of 5 g. of benzylcyclohexylamine and 1 g. of dicobalt octacarbonyl in 45 ml. of benzene was heated at 230°C under 140 atmospheric pressure of carbon monoxide to give 1.6 g. (28.1%) of benzylcyclohexylformylamine boiling at 135~140°C/3 mmHg.

Anal. Found: N, 5.99. Calcd. for $C_{14}H_{13}ON$: N, 6.63%.

3) Reaction of Schiff Base and Water Gas.—*General procedure.*—A solution of 0.025 mol. of Schiff base and 1.5 millimol. of dicobalt octacarbonyl in 50 ml. of benzene was heated at 120°C under 180 atmospheric pressure of synthetic gas (CO : H=1 : 1).

A benzene solution obtained was hydrolyzed with 4 N sulfuric acid. Benzaldehyde liberated was determined by the method of Bennett and Salamon[4] (hydroxylamine) to get the amount of unreacted Schiff base.

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[4] C. T. Bennett and M. S. Salamon; *Analyst*, 52, 693 (1927).

The percentage conversions of benzal compound to benzyl compound were estimated from the value of Schiff base remaining after 15 and 30 min. in each run.

(i) On benzaldehyde-anil. — Conversions (%) from benzaldehyde-anil into benzylaniline were 59.8 and 80.0, respectively.

(ii) On benzal-o, o-diethylaniline.—Conversions (%) from benzal-*o*, *o*-diethylaniline into benzyl-*o*,*o*-diethylaniline were 58.0 and 81.9, respectively.

Department of Chemistry
Faculty of Science
Osaka University
Nakanoshima, Osaka