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ORGANIC SYNTHESES BY MEANS OF METAL COMPLEXES—VI[1]

REACTIONS OF ANILINES, CARBON TETRACHLORIDE AND CARBON MONOXIDE

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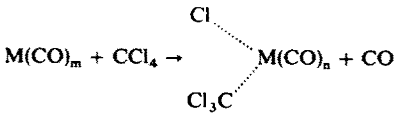
Abstract—Reactions of anilines, carbon tetrachloride and carbon monoxide catalyzed by dicobalt octacarbonyl, cyclopentadienylmolybdenum tricarbonyl dimer and molybdenum hexacarbonyl have been studied. *p*-Amino-N,N'-diphenylbenzamidine was obtained by the reaction of aniline and carbon tetrachloride. 3-Aryl-4(3H)-quinazolinones and 3-aryl-2,4(1H, 3H)-quinazolinedione were formed with substituted anilines depending on reaction conditions and nature of the substituents.

METAL carbonyls and their derivatives are useful for organic synthesis such as carbonylation reactions and have wide scientific and industrial application.[2] In many catalytic reactions of dinuclear metal carbonyls, the metal–metal bond is cleaved homolytically by reaction with covalent molecules such as hydrogen or halogen as a first step. We have studied the reaction of CCl_4 with dinuclear metal carbonyls, expecting the cleavage of the metal–metal bond with concomitant cleavage of C—Cl bond.

$$M - M + CCl_4 \rightarrow M\text{-}Cl + M\text{-}CCl_3$$

The reaction of CCl_4 with $Co_2(CO)_8$ to form $Co_3(CO)_9CCl$ is known, and intermediate formation of the species $CCl_3Co(CO)_4$ and $ClCo(CO)_4$ has been postulated.[3] Mononuclear metal carbonyls are also capable of cleaving a C—Cl bond in the following way.[4]



$$M(CO)_m + CCl_4 \rightarrow \begin{matrix} Cl \cdots \\ \quad M(CO)_n \\ Cl_3C \cdots \end{matrix} + CO$$

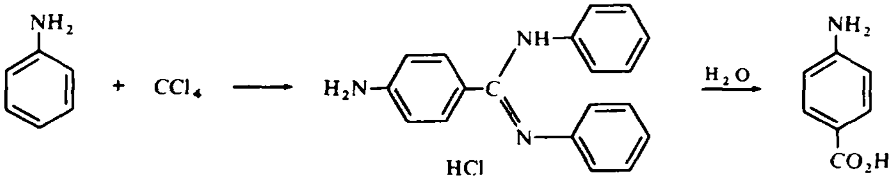
These C—Cl bond cleavages may generate Cl and CCl_3 radicals. These radical species seem to be different in reactivity from usual free radicals, because coordination or interaction with metal carbonyls may cause some modifications of reactivity. Thus somewhat different reactions may be expected using metal carbonyls as catalysts in the presence of CCl_4. We have indeed found that addition reactions of CCl_4, CO and olefins proceed smoothly to give chlorinated acyl chlorides.[1]

Extension of this catalytic system to amines was attempted. In the presence of metal carbonyls, strong coordination of the amines and radical species with metallic moieties is expected, and unique reactions may occur. New reactions of anilines have been discovered, and are presented in this paper.

RESULTS AND DISCUSSION

If an N—H hydrogen of anilines is extracted by the radical species formed from the reaction of CCl_4 and a metal carbonyl, formation of a nitrogeneous radical and migration of the radical center to the *ortho* or *para* position of the aromatic ring is expected. Once the aromatic radical is formed, attack by CO on the ring and subsequent formation of an aminobenzoic acid derivative is possible. The reaction of aniline, CCl_4 and CO in the presence of dinuclear metal carbonyls was carried out with this in mind.

Upon reaction a mixture of amine hydrochlorides, including aniline hydrochloride, was obtained. These were converted to free amines and the unreacted aniline was recovered. In addition, a solid amine identified as *p*-amino-N,N'-diphenylbenzamidine (I) was isolated. As expected, (I) was hydrolyzed with HCl to give *p*-aminobenzoic acid in a high yield.



I

In this reaction only the *p*-substituted amidine was obtained, no *ortho* or *meta* isomer was detected. It was found that the formation of the amidine is possible in the absence of CO; the reaction takes place even under N_2. Both mononuclear metal carbonyls, $Mo(CO)_6$ and $Cr(CO)_6$, and dinuclear metal carbonyls, $Co_2(CO)_8$ and $[CpMo(CO)_3]_2$, can be used as catalysts, $Mo(CO)_6$ seems to be the best. Under appropriate conditions, the amidine was obtained in above 90% yield. The results of the reactions are summarized in Table 1.

Table 1. Reactions of aniline with CCl_4[a]

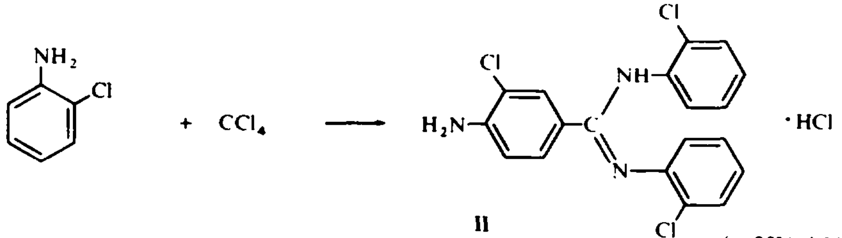
exp. No.	Catalyst	Pressure		Reaction temp	benzamidine hydrochloride I g (%)[b]
		carbon monoxide atm	nitrogen atm		
1	$Co_2(CO)_8$	50		150	12·59 (86·8)
2	$Co_2(CO)_8$		50	150	10·60 (73·3)
3	$[\pi\text{-}CpMo(CO)_3]_2$	50		150	12·98 (89·3)
4	$[\pi\text{-}CpMo(CO)_3]_2$	50		100	2·92 (20·9)
5	$Mo(CO)_6$	50		150	13·70 (94·5)
6	$Mo(CO)_6$	50		100	11·28 (77·8)
7	$Cr(CO)_6$	50		150	10·70 (73·8)
8	$Co_2(CO)_8$	150		150	6·53 (45·0)[c]

[a] Reactions carried out with aniline (25·0 g), CCl_4 (25 ml), catalyst (0·50 g). Reaction time: 16 hr

[b] Yield based on charged aniline

[c] 0·53 g of 3-phenyl-4(3H)-quinazolinone was also obtained

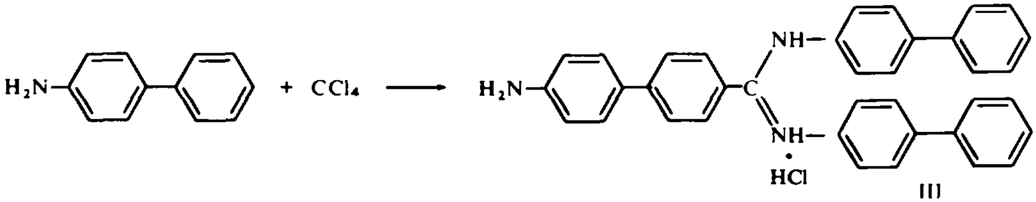
The effect of substituents on the benzene ring of aniline was then studied. The amidine (II) was isolated from *o*-chloroaniline in high yield using $Mo(CO)_6$.



II

(> 85% yield)

p-Phenylaniline behaved similarly giving 4′-amino-NN′-di-4-biphenylyl-4-biphenylcarboxyamidine (III) in 75% yield, showing that the migration of the radical proceeds through the benzene ring.



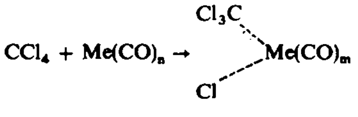
III

It should be noted that HCl was the only product of the hydrogen abstraction and no formation of $CHCl_3$ was observed.

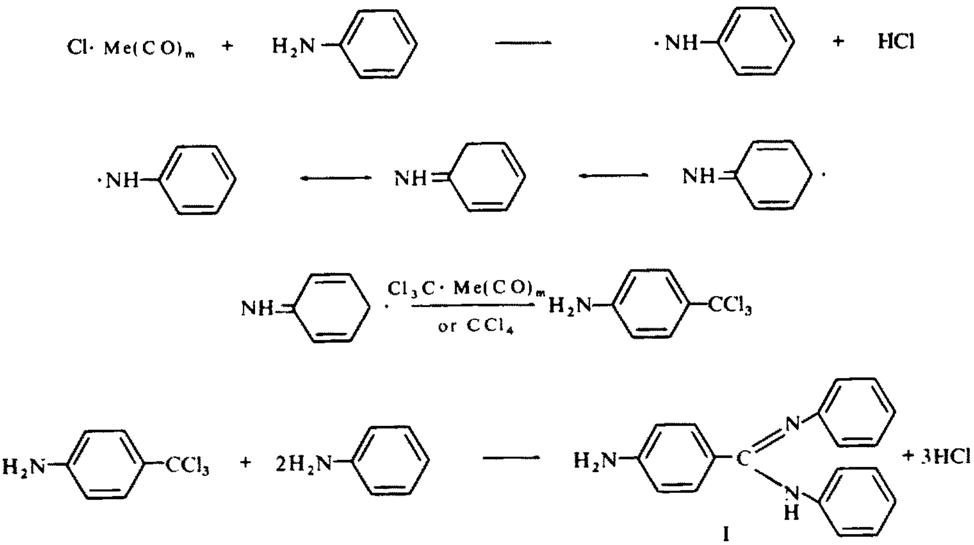
A possible mechanism of the amidine formation is shown below. The radical center at the *para* position formed by the migration of the nitrogeneous radical is attacked by CCl_4 or CCl_3 radical. The latter then reacts with anilines to give the amidine. Another possibility is the direct attack of CCl_3 free radical at the *para* position. however, this seems to be less likely by the following facts. Usually the attack of a free radical on an aromatic ring is non-selective and gives a mixture of *ortho*-, *meta*-, and *para* derivatives.[5] In the amidine formation the attack of CCl_3 is completely selective and no isomer was formed, suggesting that the reaction is different from the usual type. The reaction of aniline with CCl_4 was attempted by using $Fe(CO)_5$,[6] $[CpFe(CO)_2]_2$,[4] Cu_2O and benzoyl peroxide as catalyst, which are known to generate CCl_3 radicals from CCl_4. With these catalysts, no amidine formation took place and only resinous material was formed. Therefore, coordination or interaction of the radical species with the metal complex must have an important role in this highly selective amidine formation reaction, although it is difficult to clarify the real nature of the interaction of the radical species with the metal complexes.

$$CCl_4 + (Me(CO)_m)_2 \rightarrow Cl_3C\cdot Me(CO)_m + Cl\cdot Me(CO)_m$$

or

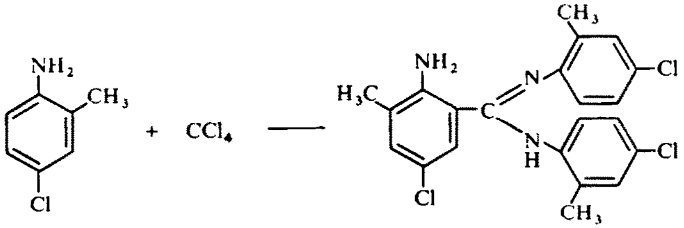


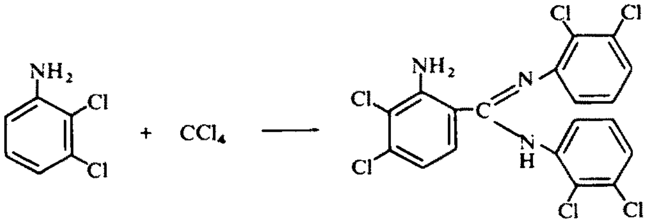
$$CCl_4 + Me(CO)_n \rightarrow \begin{matrix} Cl_3C \\ \quad\quad Me(CO)_m \\ Cl \end{matrix}$$



I

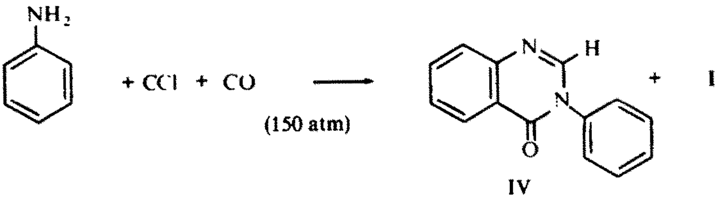
No *ortho* amidine was obtained with aniline itself. However, *o*-amidines were isolated by reaction of certain anilines blocked at both the *ortho* and *para* positions. For example, 4-chloro-*o*-toluidine and 2,3-dichloroaniline were converted into the corresponding *ortho*-amidine.





Since the amidines can be hydrolyzed easily to give aminobenzoic acids in high yields, this reaction constitutes a useful two step synthesis of various aminobenzoic acids.

CO did not take part in the amidine formation. However, when the CO pressure was increased in the reaction of aniline with CCl_4, a small amount of product derived from CO attack on the *ortho* position of aniline was obtained (Table 1, No. 8). The product was identified as 3-phenyl-4(3H)-quinazolinone (IV).



IV

Interestingly, quinazolinones were obtained as main products in high yields with some substituted anilines, showing that substituents have a marked effect on the reaction course. A typical example is the reaction of *m*-chloroaniline and the results of the quinazolinone formation are shown in Table 2. A reaction temperature above 150° is necessary for quinazolinone formation. At 120°, urea derivatives were obtained; not formed by carbonylation, but probably by hydrolysis of a reaction intermediate.

TABLE 2. REACTIONS OF *m*-CHLOROANILINE WITH CCl_4 AND CO[a]

Catalyst	Carbon monoxide pressure atm	Reaction temp	quinazolinone g (%)[b]	recovered m-chloroaniline g
$Mo(CO)_6$	50	150	3·35 (38·4)	1·95
$Mo(CO)_6$	150	150	7·30 (823)	1·58
$Mo(CO)_6$	100	120	trace[c]	14·58
$[\pi\text{-}CpMo(CO)_3]_2$	100	150	6·97 (83·0)	3·03
$Co_2(CO)_8$	100	150	2·04 (29·0)	6·58
$Cr(CO)_6$	100	150	6·54 (79·6)	3·52

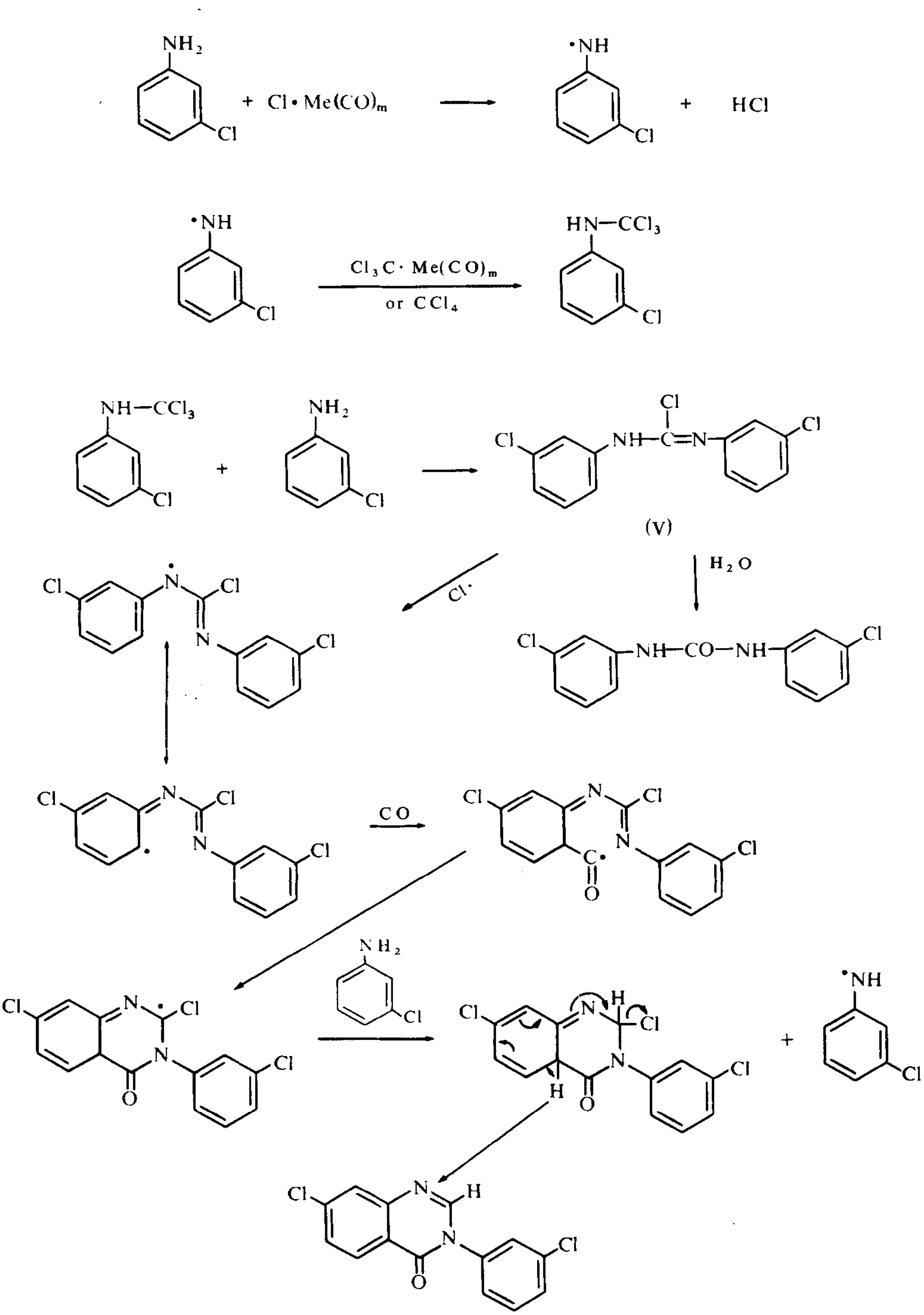
[a] Reactions were carried out with *m*-chloroaniline (25·0 g). CCl_4 (25 ml). catalyst (0·50 g). Reaction time: 16 hr

[b] Yield based on consumed *m*-chloroaniline

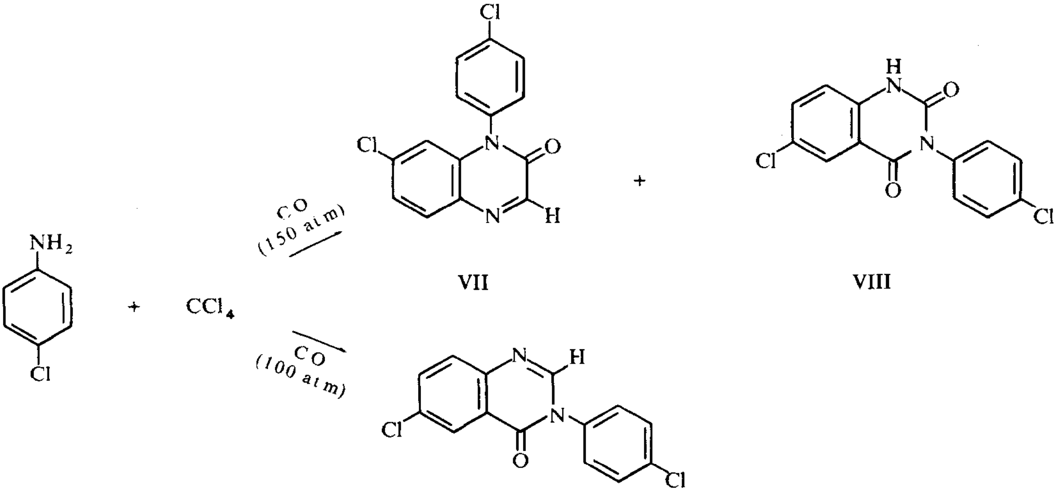
[c] 4·64 g of N.N'-(3-chlorophenyl) urea obtained

Although the mechanism of quinazolinone formation seems to be rather complicated, we propose the following tentative mechanism. With *m*-chloroaniline the *para* position is somewhat hindered and CCl_4 or $\cdot CCl_3$ attacks the nitrogeneous radical. Then the CCl_3 is attacked by another aniline, followed by elimination of HCl to give the chloroamidine (V). Hydrogen abstraction and migration of the free electron to the benzene ring allows CO attack at the *ortho* position followed by cyclization. The subsequent radical picks up hydrogen from fresh aniline to generate the free radical which initiates another catalytic cycle. The final step is elimination of HCl to give a quinazolinone ring.

Also 3,4-dichloroaniline and *m*-bromoaniline were converted into the corresponding quinazolinones. Somewhat complicated results were obtained with *p*-chloroaniline depending on the CO pressure. Below 100 atm., 6-chloro-3-(*p*-chlorophenyl)-4(3H)-quinazolinone (VI) was obtained (62%). However, when the pressure was raised to 150 atm., two other products were obtained. These were determined to be


NH₂
Cl
+ Cl • Me(CO)m
•NH
+ HCl
Cl₃C · Me(CO)m
or CCl₄
HN—CCl₃
NH—CCl₃
NH—C=N
(V)
H₂O
Cl·
NH—CO—NH
CO
N
C•
O
H

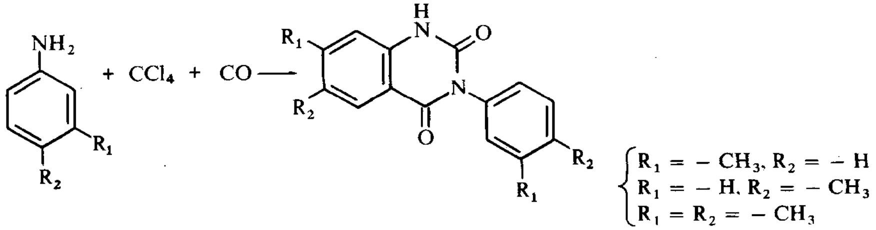
7-chloro-1-(*p*-chlorophenyl)-2(1H)-quinoxalinone (VII) and 6-chloro-3-(*p*-chlorophenyl)-2,4-(1H, 3H)-quinazolinedione (VIII).



VII VIII

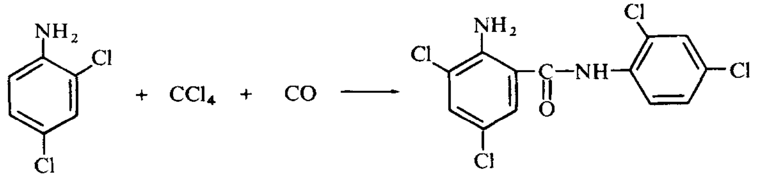
VI

Apparently the quinazolinedione (VIII) was formed by attack of two CO molecules and it is reasonable that this took place at higher CO pressure. The quinazolinedione was obtained as sole product when Me-substituted anilines were treated, although the yield was not high. Thus *m*- and *p*-toluidine and 3,4-xylidine gave the quinazolinediones.



The reactions described can give amidines, quinazolinones, quinazolinediones and quinoxalinone. Selectivity in forming these compounds is dependent on reaction conditions, especially CO pressure and the nature of the substituents. However, no systematic studies have been carried out to determine the influence of these factors on the selectivity.

Furthermore when 2,4-dichloroaniline was treated, the sole product obtained was 2-amino-2′,3,4′,5-tetrachlorobenzaniline (IX). The reason why the benzamide was obtained only in this case is unknown.



(IX)

EXPERIMENTAL

All experiments both in the presence and absence of CO were carried out using a glass tube equipped with a gas inlet capillary. The glass vessel was placed in an autoclave and the reaction carried out by shaking. Only typical procedures are shown below.

Reaction of aniline. Aniline (25 g). CCl_4 (25 ml). $Co_2(CO)_8$ (0·5 g) were mixed in the glass vessel and then placed in the autoclave. CO (150 atm) was introduced and the autoclave was shaken at 150° for 16 hr. The product was extracted with Et_2O. Evaporation gave 0·53 g 3-phenyl-4(3H)-quinazolinone (IV). m.p. 135–137° (recrystallized from MeOH). (Found: C. 75·73; H. 4·56; N. 12·69. $C_{14}H_{10}N_2O$ requires: C. 75·65; H. 4·54; N. 12·61%); IR (KBr. cm^{-1}): 1680 (CO—N). 1610. 780. 760 and 700. No N—H band. The IR was identical with that of an authentic sample.

The ether insoluble part was extracted with MeOH. evaporated. and 18·53 g of aniline hydrochloride obtained. The MeOH insoluble part (6·53 g. *p*-amino-N.N′-diphenylbenzamidine hydrochloride) was suspended in H_2O and made alkaline with Na_2CO_3 aq. Extraction with Et_2O and evaporation gave *p*-amino-N.N′-diphenylbenzamidine. m.p. 198–200° (recrystallized from acetone). (Found: C. 79·19; H. 5·98; N. 14·69; MW. 281. $C_{19}H_{17}N_3$ requires: C. 79·42; H. 5·96; N. 14·62; MW. 287); IR (KBr. cm^{-1}): 3390. 3310. 3190. 1630 (C═N). 1610. 1585. 855. 760. 750 and 695.

Hydrolysis of p-*amino*-N.N′-*diphenylbenzamidine.* The amidine (3·0 g) and conc. HCl (20 ml) were mixed in the glass vessel and heated in the autoclave at 160° for 16 hr with shaking. The product was made alkaline with NH_3 and aniline obtained, 1·25 g, b.p. 180–184. The residue was acidified with AcOH and *p*-aminobenzoic acid obtained as crystals. recrystallized from EtOH. m.p. 186–187°. 1·02 g.

Similarly. the following compounds wereobtained.

4-Amino-3-chloro-N.N′-bis(*o*-chlorophenyl)benzamidine hydrochloride from *o*-chloroaniline. 4-Amino-3-chloro-N.N′-bis(*o*-chlorophenyl)benzamidine. m.p. > 250°. (Found: C. 53·36; H. 3·53; N. 9·87; Cl. 33·30). $C_{19}H_{14}N_3 \cdot HCl$ requires: C. 53·41; H. 3·55; N. 9·84; Cl. 33·20%).

4′-Amino-N.N′-di-4-biphenylyl-4-biphenylcarboxyamidine hydrochloride from 4-biphenylamine. 4′-Amino-N.N′-di-4-biphenylyl-4-biphenylcarboxyamidine hydrochloride. m.p. > 250°. (Found: C. 80·70; H. 5·40; N. 7·58; Cl. 6·49. $C_{37}H_{29}N_3 \cdot HCl$ requires: C. 80·48; H. 5·49; N. 7·61; Cl. 6·42%).

Reaction of m-*chloroaniline. m*-Chloroaniline (25·0 g). CCl_4 (25 ml). $Mo(CO)_6$ (0·5 g) were reacted with CO (100 atm) at 150° for 16 hr. The product was treated with $CHCl_3$. and *m*-chloroaniline hydrochloride (19·10 g) remained insoluble. The $CHCl_3$ was evaporated and the residue washed with MeOH. From the MeOH soluble part. *m*-chloroaniline (2·01 g) was recovered. Solid remained on a filter. 7·09 g (81·4%) was 7-chloro-3-(*m*-chlorophenyl)-4(3H)-quinazolinone. m.p. 189–191° (recrystallized from MeOH). (Found: C. 57·81; H. 2·82; N. 9·36; Cl. 24·60; MW. 283. $C_{14}H_8N_2OCl_2$ requires: C. 57·75; H. 2·78; N. 9·62; Cl. 24·36; MW. 291); IR (KBr. cm^{-1}): 3050. 1680. 1610. 1585. 870. 790 and 780.

By similar reaction of *p*-chloroaniline (CO pressure below 100 atm). *m*-bromoaniline. 3.4-dichloroaniline. corresponding quinazolinones were obtained.

6-Chloro-3-(p-chlorophenyl)-4(3H)-quinazolinone (VI). m.p. 230–231° (recrystallized from MeOH). (Found: C. 57·70; H. 2·79; N. 9·33; Cl. 24·28). $C_{14}H_8N_2OCl_2$ requires: C. 57·75; H. 2·78; N. 9·62; Cl. 24·36%).

7-Bromo-3-(*m*-bromophenyl)-4(3H)-quinazolinone. m.p. 208–210°. (Found: C. 44·23; H. 2·09; N. 7·19; Br. 42·35. $C_{14}H_8N_2OBr_2$ requires: C. 44·24; H. 2·13; N. 7·37; Br. 42·05%).

6.7-Dichloro-3-(3.4-dichlorophenyl)-4(3H)-quinazolinone. m.p. 246–248° (recrystallized from $CHCl_3$–MeOH). (Found: C. 46·57; H. 1·71; N. 7·55; Cl. 39·57. $C_{14}H_6N_2OCl_4$ requires: C. 46·70; H. 1·68; N. 7·78; Cl. 39·39%).

Reaction of p-*chloroaniline.* p-Chloroaniline (25·0 g). CCl_4 (25 ml). $Mo(CO)_6$ (0·5 g) were treated under a CO pressure of 150 atm. The products were extracted with $CHCl_3$. The $CHCl_3$ extract was separated by column chromatography (silica gel) and 7-chloro-1-(*p*-chlorophenyl)-2(1H)-quinoxalinone (VII). 5·43 g and 6-chloro-3-(*p*-chlorophenyl)-2.4-(1H. 3H)-quinazolinedione (VIII). 2·20 g obtained.

7-Chloro-1-(*p*-chlorophenyl)-2(1H)-quinoxalinone. m.p. 229–230·5° (recrystallized from MeOH). (Found: C. 57·90; H. 2·77; N. 9·33; Cl. 24·38. $C_{14}H_8N_2OCl_2$ requires: C. 57·75; H. 2·78; N. 9·62; Cl. 24·36%). IR (KBr. cm^{-1}): 1700 (CO—N). 1610. 885 and 830.

6-Chloro-3-(*p*-chlorophenyl)-2.4(1H. 3H)-quinazolinedione. m.p. > 260° (recrystallized from MeOH). (Found: C. 54·90; H. 2·64; N. 8·97; Cl. 23·30. $C_{14}H_8N_2O_2Cl_2$ requires: C. 54·74; H. 2·63; N. 9·12; Cl. 23·09%). IR (KBr. cm^{-1}): 3250 (NH). 1735. 1670 (CO—N—CO). 890 and 825. The IR was identical with that of an authentic sample.

Reaction of m-*toluidine. m*-Toluidine (25·0 g). CCl_4 (25 ml). $Mo(CO)_6$ (0·5 g) were allowed to react under CO pressure (150 atm) at 150° for 16 hr. The product was extracted with $CHCl_3$. The $CHCl_3$ insoluble *m*-toluidine hydrochloride was recovered: 10·2 g. The $CHCl_3$ soluble part was purified by column chromatography to give 7-methyl-3-(*m*-tolyl)-2.4 (1H. 3H)-quinazolinedione. 2·31 g. m.p. > 260°. (Found: C. 72·04; H. 5·27; N. 10·47. $C_{16}H_{14}N_2O_2$ requires: C. 72·16; H. 5·30; N. 10·52%).

By the similar reactions of *p*-toluidine. 3.4-xylidine. corresponding quinazolinediones were obtained.

6-Methyl-3-(*p*-tolyl)-2.4 (1H. 3H)-quinazolinedione. m.p. > 260°. (Found: C. 72·02; H. 5·27; N. 10·47. $C_{16}H_{14}N_2O_2$ requires: C. 72·16; H. 5·30; N. 10·52%).

6.7-Dimethyl-3-(3.4-xylyl)-2.4(1H. 3H)-quinazolinedione. m.p. > 260°. (Found: C. 73·52; H. 6·05; N. 9·47. $C_{18}H_{18}N_2O_2$ requires: C. 73·45; H. 6·16; N. 9·52%).

Reaction of 2.3-dichloroaniline. 2.3-Dichloroaniline (25·0 g). CCl_4 (25 ml). $Mo(CO)_6$ (0·5 g) were reacted under CO pressure (100 atm) at 150° for 16 hr. The product was washed with $CHCl_3$. The $CHCl_3$ insoluble part was washed with H_2O leaving 2-amino-3.4-dichloro-N.N'-bis(2.3-dichlorophenyl)benzamidine hydrochloride. 8·68 g (70·7%). The hydrochloride was dissolved in MeOH. and made free benzamidine with KOH. 2-Amino-3.4-dichloro-N.N'-bis(2.3-dichlorophenyl)benzamidine. m.p. 172–174°. (Found: C. 46·15; H. 2·23; N. 8·50; Cl. 43·12; MW. 483 (acetone). $C_{19}H_{11}N_3Cl_6$ requires: C. 46·18; H. 2·25; N. 8·51; Cl. 43·06: MW. 494). IR (KBr. cm^{-1}) 3460. 3380. 1645. 800. 790 and 780.

By a similar reaction of 4-chloro-*o*-toluidine. 2-amino-5-chloro-N.N'-bis(4-chloro-*o*-tolyl)-*m*-toluamidine hydrochloride was obtained.

2-Amino-5-chloro-N.N'-bis(4-chloro-*o*-tolyl)-*m*-toluamidine hydrochloride m.p. 265–267°. (Found: C. 56·54; H. 4·52; N. 8·65; Cl. 29·99. $C_{22}H_{20}N_3Cl_3 \cdot HCl$ requires: C. 56·30; H. 4·52; N. 8·96; Cl. 30·22%).

Reaction of 2.4-dichloroaniline. 2.4-Dichloroaniline (25·0 g). CCl_4 (25 ml). $Mo(CO)_6$ (0·5 g) were reacted with CO (100 atm) at 150° for 16 hr. The product was treated with $CHCl_3$ leaving the insoluble 2.4-dichloroaniline hydrochloride (16·28 g). The $CHCl_3$ solution was evaporated. and the residue washed with MeOH. From the MeOH soluble part. 7·13 g of 2.4-dichloroaniline was recovered. The MeOH insoluble part was 2-amino-2'.3.4'.5-tetrachlorobenzanilide (IX). 6·65 g. m.p. 175–177° (from acetone). (Found: C. 44·69; H. 2·12; N. 7·93; Cl. 40·75; MW. 349 ($CHCl_3$). $C_{13}H_8N_2OCl_4$ requires: C. 44·60; H. 2·31; N. 8·00; Cl. 40·52%; MW. 350). IR (KBr. cm^{-1}): 3460. 3290. 3160. 1675. 860 and 825.

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