Journal of Organometallic Chemistry
Elsevier Sequoia S.A., Lausanne
Printed in The Netherlands

REACTIONS OF ORGANOZINC COORDINATION COMPOUNDS II*. REACTIVITY WITH SECONDARY AMINES

SHOHEI INOUE AND YOSHIHIKO IMANAKA
Department of Synthetic Chemistry, Faculty of Engineering, University of Tokyo (Japan)

(Received July 29th, 1971)

SUMMARY

The reactivity of diethylzinc is much the same towards di-n-propylamine, diphenylamine, pyrrole, indole and carbazole, in spite of the differences in the acidities of the amines. *N,N,N',N'*-Tetramethylethylenediamine has an accelerating effect on the reaction of diethylzinc with pyrrole and derivatives, and 2,2'-bipyridine a similar but much larger effect on this reaction. These facts indicate the importance of the coordination of the amine to the organozinc complex in the reaction.

INTRODUCTION

We have reported previously[1] that the reaction of dialkylzinc with diphenylamine is considerably accelerated by the presence of an equimolar amount of aromatic nitrogen base such as 2,2'-bipyridine (Bipy), 8-dimethylaminoquinoline or pyridine. On the other hand, triethylamine and *N,N,N',N'*-tetramethylethylenediamine (TMEDA) exhibited no accelerating effect, and in order to explain the clear difference between Bipy and TMEDA we have suggested back donation from the zinc atom to Bipy in the dialkylzinc–Bipy complex as being an important factor in determining its reactivity with diphenylamine.

In the present studies, the reaction of diethylzinc with some secondary amines in the presence of Bipy, TMEDA and other complexing agents has been examined in order to obtain further insight into the acceleration mechanism.

RESULTS AND DISCUSSION

Reaction of diethylzinc with secondary amines

The reaction of equimolar quantities of diethylzinc and a secondary amine in toluene at 40° was followed by volumetric determination of the ethane evolved during the reaction:

$$=\text{N--H} + \text{Et}_2\text{Zn} \rightarrow =\text{N--ZnEt} + \text{EtH} \qquad (1)$$

As reported previously, the reaction of diethylzinc with diphenylamine is very

---

* For Part I see ref. 1.

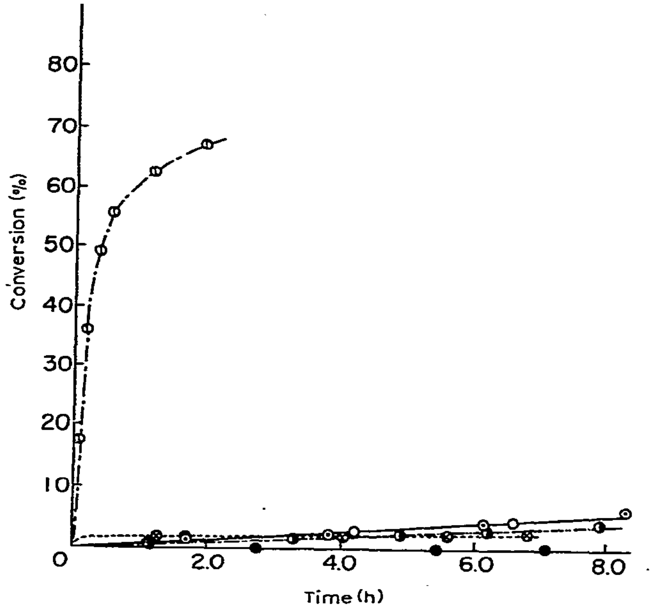


Fig. 1. Reaction of diethylzinc with secondary amines and ethanol. Equimolar reaction in toluene at 40°. Initial conc.: in the reaction of secondary amine, 0.30 *M*; in the reaction of ethanol, 0.075 *M*, ⦶, ethanol; ⊗, di-n-propylamine; ⊙, diphenylamine; ○, pyrrole; ◑, indole; ●, carbazole,

slow. The reaction with di-n-propylamine is however even slower, and since the reactivity is considered, at least in part, to be determined by the acidity of the amine (N–H), an examination of the reactivity of pyrrole, which has a greater acidity (p*K*a 16.5) than diphenylamine (p*K*a 23) or di-n-propylamine (p*K*a about 35, as expected from the value for ammonia) might be important. Interestingly, pyrrole showed low reactivity towards diethylzinc as illustrated in Fig. 1, whilst, in sharp contrast, ethanol with similar acidity (p*K*a = 18) reacted very rapidly with diethylzinc.

From the difference in reactivity of diethylzinc towards pyrrole and ethanol, it is clear that the reactivity of diethylzinc towards an active hydrogen compound is not determined solely by the acidity of the latter. In addition, the coordination of the latter to the zinc atom must be very important; thus, in ethanol O→Zn coordination is possible, whilst in pyrrole the lone pair on the nitrogen atom is not readily available for N→Zn coordination since the nitrogen atom is included in the conjugated system of pyrrole. The reactivities of indole and carbazole were also very low, despite the fact that these amines are generally considered to have higher acidities than pyrrole. (Although p*K*a values for these amines (N–H) have not been reported, the p*K*a value for the conjugate acid (NH^+) of indole[2] is −2.4, that of pyrrole[3] being 0.4.)

With di-n-propylamine, strong N→Zn coordination might be expected, but the acidity of the N–H group is too low in this case for the reaction to be readily studied.

Effect of the complexing agent

As previously reported, the reaction of diethylzinc and diphenylamine is greatly accelerated by the presence of an equimolar quantity of Bipy. The second-order rate constant for this reaction (at 40° in toluene) as determined by ethane evolution (Eqn. 1) was $k=4.1\ \mathrm{l \cdot mole^{-1} \cdot h^{-1}}$, in agreement with the value obtained previously

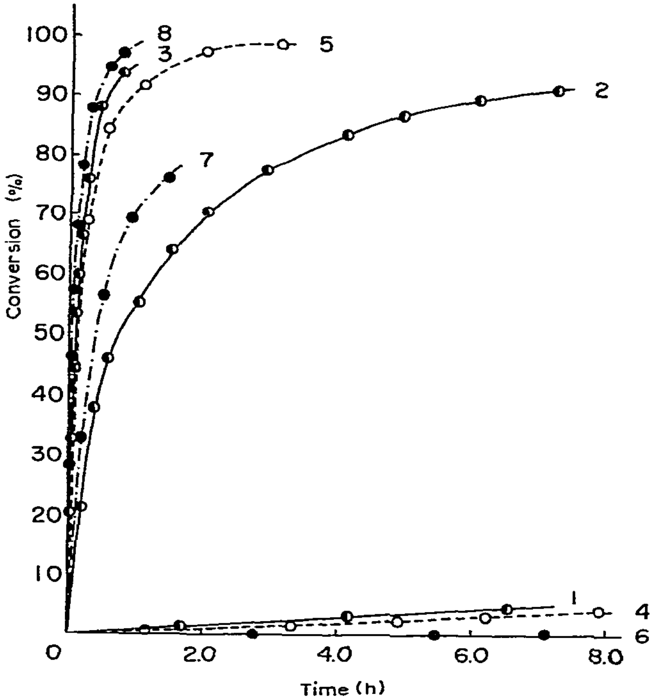


Fig. 2. Reaction of diethylzinc with pyrrole and derivatives. Equimolar reaction in toluene at 40°. Amine, complexing agent (1 mole ratio to zinc) and initial concentration: 1, pyrrole, none, 0.30 *M*; 2, pyrrole, TMEDA, 0.30 *M*; 3, pyrrole, Bipy, 0.075 *M*; 4, indole, none, 0.30 *M*; 5, indole, TMEDA, 0.075 *M*; 6, carbazole, none, 0.30 *M*; 7, carbazole, TMEDA, 0.05 *M*; 8, carbazole, Bipy, 0.02 *M*.

TABLE 1

SECOND ORDER RATE CONSTANT OF DIETHYLZINC–AMINE REACTION

Equimolar reaction in toluene at 40°. Equimolar ratio of complexing agent when used. Rate constant in $\mathrm{l \cdot mole^{-1} \cdot h^{-1}}$.

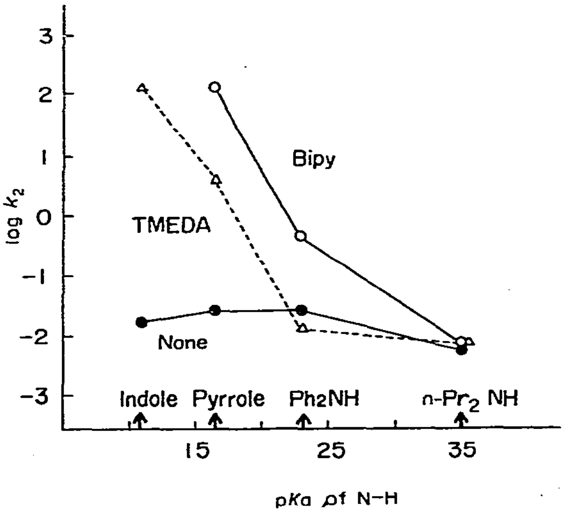
Amine	p*K*a	Complexing agent		
		None	TMEDA	Bipy
Di-n-propylamine	(35)[a]	$0.6 \cdot 10^{-2}$	$0.7 \cdot 10^{-2}$	$0.7 \cdot 10^{-2}$
Diphenylamine	23	$2.3 \cdot 10^{-2}$	$1.2 \cdot 10^{-2}$	$4.1 \cdot 10^{-1}$
Pyrrole	16.5	$2.3 \cdot 10^{-2}$	3.8	$1.2 \cdot 10^{2}$
Indole	(11)[b]	$1.7 \cdot 10^{-2}$	$1.2 \cdot 10^{2}$	not determined
Carbazole	—	$1.0 \cdot 10^{-2}$	7.9	$9.2 \cdot 10^{2}$

[a] Value for ammonia. [b] Assumed value from p*K*a value of the conjugate acid[3], on the basis of the linearity between p*K*a values of N–H and $NH_2^{\ominus}$ as determined in ammonia, aniline and pyrrole.

($k = 4.1$ l·mole^{-1}·h^{-1}, at 40° in benzene) by infrared spectroscopic determination of the N–H or Et–Zn–Et linkage.

In the reaction of diethylzinc with di-n-propylamine, no accelerating effect was exhibited in the presence of Bipy, TMEDA or *o*-phenanthroline. On the other hand, in the reaction with pyrrole and derivatives the complexing agent demonstrated a remarkable accelerating effect, as shown in Fig. 2.

TMEDA which is not effective in the reaction with diphenylamine[1], also showed an accelerating effect in reaction with pyrrole and derivatives. The effect of Bipy, however, was even greater than that of TMEDA in all cases. The second-order rate constants for these reactions are summarized in Table 1 and Fig. 3.



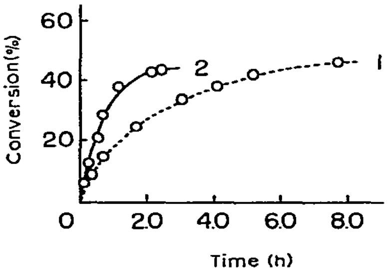


Fig. 3. Relation of second-order rate constant k_2 (l·mole^{-1}·h^{-1}) *vs.* p*K*a of amine in the reaction with diethylzinc. In absence or presence of complexing agent (TMEDA or Bipy).

Fig. 4. Equimolar reaction of diethylzinc with pyrrole in the presence of a half mole ratio of complexing agent. In toluene, initial conc. 0.075 *M*. 1, TMEDA, 40°; 2, Bipy, 0°.

Function of the complexing agent

In addition to TMEDA and Bipy, the accelerating effect of some other complexing agents was examined in the reaction between diethylzinc and diphenylamine or pyrrole.

In the reaction with diphenylamine, 4-methylpyridine exhibited an accelerating effect similar to that of pyridine[1], whilst 2,6-dimethylpyridine did not; the latter may be incapable of forming a complex with diethylzinc due to steric hindrance by the two methyl groups. *N,N*-Dimethylaniline and *N,N,N′,N′*-tetramethyl-*o*-phenylenediamine (TMOPDA) also showed no effect. TMOPDA, however, exhibited a similar effect to TMEDA in the reaction with pyrrole, thus demonstrating the importance of the coordinating nitrogen atom in the conjugated system for promoting an active complexing agent.

Other complexing agents examined and shown to have little or no effect were: benzalaniline, 4,4′-dichlorobenzalaniline, 1,2-dimethoxyethane, methyl furfuryl ether, thiophene and ethylene-bis(diphenylphosphine).

In order to elucidate the function of the complexing agent the reaction of diethylzinc with pyrrole was studied in the presence of a half mole ratio of TMEDA or Bipy. As shown in Fig. 4, the conversion reached a plateau value at 50%. Since TMEDA or Bipy forms a stable complex with diethylzinc[4], the above observation indicates that diethylzinc reacts as this complex and that complexing agents of this sort are included in the product as such and not recycled as catalytic species. For example:

$$\mathrm{ZnEt_2 + TMEDA} \rightleftarrows \mathrm{ZnEt_2 \cdot TMEDA} \quad (2)$$

$$\mathrm{ZnEt_2 \cdot TMEDA + Pyrrole} \xrightarrow{-\mathrm{EtH}} \mathrm{EtZnPyrrolide \cdot TMEDA} \quad (3)$$

On the basis of equation (3), it is reasonable to postulate second-order kinetics for the reaction of diethylzinc and pyrrole in equimolar quantities in the presence of a half mole ratio of TMEDA and this is, in fact, demonstrated by the results depicted in Fig. 5.

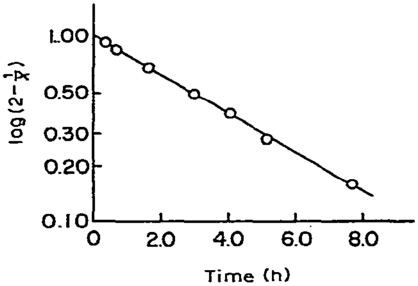


Fig. 5. Second order plot of diethylzinc/TMEDA/pyrrole (1/0.5/1) reaction. In toluene at 40°, initial conc. 0.075 *M*. $1-x$: extent of reaction.

The mechanism of the acceleration process.

As demonstrated by the results recorded in Table 1 and Fig. 3, acceleration in the system is very dependent upon the nature of the amine, although the reactivities of the amines with diethylzinc alone are much the same.

Bipy and TMEDA are known to form stable equimolar complexes with diethylzinc[4] in benzene solution ($K=3\cdot10^3$ and 10^5, respectively), and the observed enhancement of the reactivity is considered to be due to this complex formation (Eqns. (2) and (3)). For the diethylzinc–TMEDA complex, coordination by the strong base (p*K*a of TMEDA 8.97) will increase the nucleophilicity of the Et–Zn linkage so that the resulting complex will enhance reactivity towards amines of higher acidity.

The higher reactivity of the diethylzinc–Bipy complex is not solely due to the increased nucleophilicity of the Et–Zn bond, since the basicity of Bipy (p*K*a 4.12) is lower than that of TMEDA and also the strength of the coordination in the complex is much the same as that observed in the infrared spectra of these complexes[1]. For this reason, back donation from the zinc atom to Bipy (π-bonding)[4] must play an important role in this case, as has already been suggested for the reaction of diethylzinc with diphenylamine[1]. Such a back donation will decrease the electron density on the zinc atom and facilitate the coordination of the reacting amine to the zinc.

The difference in reactivity between Bipy and TMEDA complexes (see Fig. 3) must correspond to the magnitude of this back donation since such donation is not possible with TMEDA or TMOPDA complexes.

In conclusion, therefore, the reactivity of diethylzinc towards amines must be considered dependent upon three factors: (1) the acidity of the N–H bond of the amine, (2) the nucleophilicity of the Et–Zn bond, and (3) the coordination of the amine to zinc. With reference to the third of these factors, the high reactivity of pyrrole derivatives with diethylzinc–Bipy complex is worthy of note Although the coordination of the pyrrole nitrogen to diethylzinc is considered very weak, the amine nitrogen may in this case, be coordinated to the Bipy complex. Another possibility is that π-coordination occurs between the pyrrole derivative and the organozinc complex; no evidence for this latter suggestion has to date been obtained.

EXPERIMENTAL

Reagents

Purification of reagents was usually undertaken in a nitrogen atmosphere.

Diethylzinc was purified by distillation in a nitrogen atmosphere, b.p. 49°/57 mm.

Di-n-propylamine was refluxed over barium oxide and distilled, b.p. 111°. Diphenylamine was recrystallized twice from n-hexane, m.p. 53–54°. Pyrrole was distilled over calcium hydride, b.p. 58°/52 mm. Indole was recrystallized twice from n-hexane, m.p. 52°. Carbazole was recrystallized twice from acetone, m.p. 245°. Ethanol was dried by distillation over magnesium ethoxide.

2,2'-Bipyridine was recrystallized twice from n-hexane, m.p. 70°. *N,N,N',N'*-Tetramethylethylenediamine was refluxed over calcium hydride and distilled, b.p. 121°. Pyridine, 4-methylpyridine and 2,6-dimethylpyridine were shaken with potassium hydroxide, refluxed over calcium hydride and distilled. *o*-Phenanthroline was obtained by the dehydration of the molten monohydrate *in vacuo* and subsequent recrystallization from n-hexane, m.p. 120–121°. *N,N*-Dimethylaniline was distilled over potassium hydroxide, refluxed over calcium hydride and again distilled.

N,N,N',N'-Tetramethyl-*o*-phenylenediamine (TMOPDA) was prepared by the reaction of *o*-phenylenediamine with trimethyl phosphate[5] at 200° for 2.5 h. After the addition of aqueous sodium hydroxide and extraction with chloroform, the extract was distilled. The distillate re-distilled over calcium hydride to give TMOPDA, b.p. 62°/3 mm.

Benzalaniline was obtained from the reaction of benzaldehyde with aniline, m.p. 50–51°. 4,4'-Dichlorobenzalaniline was similarly prepared, m.p. 113–114°. Methyl furfuryl ether was prepared by the reaction of sodium furfuryl alcoholate with trimethyl phosphate, b.p. 133–135° [6]. 1,2-Dimethoxyethane was refluxed over calcium hydride and distilled. Thiophene was shaken with potassium hydroxide and distilled over calcium hydride.

Reactions

Reactions were undertaken in a two-necked 100 ml flask equipped with a gas inlet and a three-way cock connected by means of a capillary tube with a gas burette sealed with mercury. Solvent, complexing agent and amine were introduced in the flask in the presence of a stream of dry ethane, the flask having previously been purged by a similar stream. Ethane was bubbled from the gas inlet into the solution until the latter was saturated as confirmed by no further absorption of ethane when the system was closed at the reaction temperature. The gas inlet was now replaced by a thermometer, diethylzinc added by means of a syringe through the three-way cock using positive nitrogen pressure and the system immediatedly closed. The reaction mixture was magnetically stirred and the volume of gas evolved determined by means of the gas burette and corrected for temperature, atmospheric pressure and the vapor pressure of the solvent. The gas was shown to be ethane by gas chromatography (silica gel column 1 m, 70°, H_2 40 ml/min). Equimolar quantities of diethylzinc, amine and complexing agent, with toluene as solvent at 40° were usually employed in the reactions studied.

ACKNOWLEDGEMENT

The authors are grateful to Professor Teiji Tsuruta for valuable discussions, and to Mr. Kazunori Furukawa for his contribution to some of the experimental work.

REFERENCES

1 S. Inoue and T. Yamada, *J. Organometal Chem.*, 25 (1970) 1.
2 G. Berti, A. D. Settimo and Segnini, *Gazz. Chim. Ital.*, 91 (1961) 571; *Chem. Abstr.*, 56 (1962) 9483 C.
3 G. M. Badger, *The Chemistry of Heterocyclic Compounds*, Academic Press, New York, 1961, p. 12.
4 J. G. Noltes and J. Boersma, *J. Organometal. Chem.*, 9 (1967) 1.
5 D. G. Thomas, J. H. Billman and C. E. Davis, *J. Amer. Chem. Soc.*, 68 (1946) 895.
6 R. Pummerer and W. Gump, *Ber. Deutsch. Chem. Ges.*, 56 (1923) 1004.