Ruthenium Complex Catalyzed Synthesis of Diamino Compounds from α,ω-Diols and Secondary Amines

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α,ω-Diols react with secondary amines in the presence of a catalytic amount of ruthenium catalyst at 180 °C to give diamino compounds in good to excellent yields. The yield of diamino compound was affected by the molar ratio of α,ω-diol to secondary amine. The reaction is affected by the nature of the phosphorus ligands employed and the effectiveness of the added ligand is completely different depending on the chain length of the α,ω-diol. The reaction between ethylene glycol and primary amine in the presence of a catalytic amount of ruthenium catalyst gave 1,4-disubstituted piperazine.

Introduction

Synthesis of diamino compounds from readily available starting materials have recently received some attention[1]. The usual method of synthesis from dihalo compounds are not always applicable, especially for molecules of biological interest[2]. Both diamino compounds and their derivatives chelate with metal ions[3].

We have recently developed ruthenium complex catalyzed N-methylation[4], N-alkylation[5], N-heterocyclization of amines[6-8], where the ruthenium complex efficiently activates alcohol functionalities to give nitrogen compounds.

This paper deals with the catalytic synthesis of diamino compounds, using transition metal complexes. The ruthenium complex catalyzed reaction between α,ω-diol and secondary amino to give the corresponding diamino compounds.

Results and Discussion

Secondary amines (1) reacted with α,ω-diols (2) in the presence of a catalytic amount of a ruthenium complex to give diamino compounds (3) in good to excellent yields (eq. 1).

Table 1. Effect of Reaction Conditions on the Synthesis of 1,2-Dipiperidinoethane from Piperidine and Ethylene Glycol[a]

Run	[Amine]/[E.G][b]	Temp., °C	Product yield/%[c]
1	4.0	180	86
2	3.0	180	86(79)[d]
3	2.5	180	73
4	2.0	180	61
5	3.0	150	37
6	3.0	120	8
7	1.0	180	71[e]
8	0.67	180	51[e]
9	0.50	180	30[e]
10	0.33	180	trace[e]

[a]Ethylene glycol(1.1 m*l*, 20 mmol), $RuCl_3$-H_2O(52 mg, 0.2 mmol), dioxane (10 m*l*), reaction time 5h. [b]Molar ratio of piperidine to ethylene glycol. [c]Determined by GLC based on the amount of ethylene glycol used. [d]Isolated yield. [e]Determined by GLC based on the amount of piperidine used.

Table 2. Solvent Effect in the Synthesis of 1,2-Dipiperidinoethane from Piperidine and Ethylene Glycol[a]

Run	Solvent	Product yield/%[b]
2	dioxane	86(79)[c]
11	diglyme	83
12	1,3-dimethyl-2-imidazolidinone	70
13	1-methyl-2-pyrrolidinone	57
14	N,N-dimethylformamide	20
15	acetonitrile	8
16	dimethylsulfoxide	0

[a]Piperidine(5.9 m*l*, 60 mmol), ethylene glycol(1.1 m*l*, 20 mmol), $RuCl_3 \cdot nH_2O$(52 mg, 0.2 mmol), solvent (10 m*l*), at 180 °C, 5h. [b]Determined by GLC based on the amount of ethylene glycol used. [c]Isolated yield.

$$R_1R_2NH + HO-(CH_2)_n-OH \xrightarrow[n=2,3,4,5]{[Ru]} R_1R_2N-(CH_2)_n-NR_1R_2 \quad (1)$$

1 2 3

Detailed effects of the reaction conditions were examined with piperidine and ethylene glycol as the substrates (Table 1). The yield of the product, 1,2-dipiperidinoethane, was considerably affected by a molar ratio of piperidine to ethylene glycol (runs 1-4, 7-10). The highest yield was realized above the molar ratio of 3.0 (runs 1 and 2). The lower molar ratios drastically reduced the yield of 1,2-dipiperidinoethane (runs 7-10). The reaction required a temperature higher than 160 °C. At 120 °C, the conversion of ethylene glycol was low and the yield of 1,2-dipiperidinoethane was considerably reduced (run 6).

The yield was affected by the solvent employed (Table 2). The highest yield was realized in dioxane (run 2). The reaction proceeded in similarly in diglyme, 1,3-dimethyl-2-imidazolidinone and 1-methyl-2-pyrrolidinone. The reactions were considerably supressed in N,N-dimethylformamide, acetonitrile, and dimethylsulfoxid which seemed to interact strongly with transition metal center (runs 14-16)[9].

In this reaction, the catalyst precursor had a critical effect (Table 3). For ethylene glycol, $RuCl_3 \cdot nH_2O$ without added phosphorus ligands showed the highest activity (run 2). The catalytic activity was largely affected by the added phosphorus ligands. However, the addition of very bulky PCy_3[10] and a bidentate phosphorus ligand suppressed the catalytic

Table 3. Effect of Catalyst Precursor on the Synthesis of Dianino Compounds from α,ω-Diols and Piperidine[a]

Run	α,ω-diol	Catalyst	Product	Yield/%[b]
2	ethylene glycol	$RuCl_3 \cdot nH_2O$	1,2-dipiperidinoethane	86(79)[c]
17	ethylene glycol	$RuCl_2(PPh_3)_3$	1,2-dipiperidinoethane	66
18	ethylene glycol	$RuCl_2 \cdot nH_2O + 3PBu_3$	1,2-dipiperidinoethane	53
19	ethylene glycol	$RuCl_3 \cdot nH_2O + 3PCy_3$	1,2-dipiperidinoethane	3
20	ethylene glycol	$RuCl_3 \cdot nH_2O$ + 1.5dppe	1,2-dipiperidinoethane	7
21	1,3-propanediol	$RuCl_3 \cdot nH_2O$	1,3-dipiperidinopropane	68(59)[c]
22	1,3-propanediol	$RuCl_2(PPh_3)_3$	1,3-dipiperidinopropane	45
23	1,3-propanediol	$RuCl_3 \cdot nH_2O + 3pBu_3$	1,3-dipiperidinopropane	45
24	1,4-butanediol	$RuCl_3 \cdot nH_2O$	1,4-dipiperidinobutane	31
25	1,4-butanediol	$RuCl_2(PPh_3)_3$	1,4-dipiperidinobutane	45
26	1,4-butanediol	$RuCl_3 \cdot nH_2O + 3PBu_3$	1,4-dipiperidinobutane	86(81)[c]
27	1,5-pentanediol	$RuCl_3 \cdot nH_2O$	1,5-dipiperidinopentane	trace
28	1,5-pentanediol	$RuCl_2(PPh_3)_3$	1,5-dipiperidinopentane	16
29	1,5-pentanediol	$RuCl_3 \cdot nH_2O + 3PBu_3$	1,5-dipiperidinopentane	83(77)[c]
30	1,5-pentanediol	$RuCl_3 \cdot nH_2O + 3PEt_3$	1,5-dipiperidinopentane	81

[a] Piperidine(5.9 m*l*, 60 mmol), α,ω-diol(20 mmol), catalyst(0.2 mmol), dioxane (10 m*l*), at 180 °C, 5h. [b] Determinedby GLC based on the amount of α,ω-diol used. [c] Isolated yield.

Table 4. Syntheses of Diamino Compounds from α,ω-Diols and Amines[a]

Run	Amine	α,ω-diol	Cat.[b]	Product	Yield/%[c]
2	piperidine	ethylene glycol	A	1,2-dipiperidinoethane	79(86)
31	pyrrolidine	ethylene glyco.	A	1,2-dipyrrolidinoethane	79
32	morpholine	ethylene glycol	A	1,2-dimorpholinoethane	44
33	N-methylpiperazine	ethylene glycol	A	1,2-(N-methylpiperazino)ethane	64
21	piperidine	1,3-propanediol	A	1,3-dipiperidinopropane	59(68)
34	pyrrolidine	1,3-propanediol	A	1,3-dipyrrolidinopropane	56
35	morpholine	1,3-propanediol	A	1,3-dimorpholinepropane	59
36	N-methylpiperazine	1,3-propanediol	A	1,3-(N-methylpiperazino)propane	46
26	piperidine	1,4-butanediol	B	1,4-dipiperidinobutane	81(86)
37	pyrrolidine	1,4-butanediol	B	1,4-dipyrrolidinobutane	83
38	morpholine	1,4-butanediol	B	1,4-dimorpholinobutane	86
39	N-methylpiperazine	1,4-butanediol	B	1,4-(N-methylpiperazino)butane	72
29	piperidine	1,5-pentanediol	B	1,5-dipiperidinopentane	77(83)
40	pyrrolidine	1,5-pentanediol	B	1,5-dipyrrolidinopentane	79
41	morpholine	1,5-pentanediol	B	1,5-dimorpholinopentane	76
42	N-methylpiperazine	1,5-pentanediol	B	1,5-(N-methylpiperazino)pentane	68
43	diethylamine	ethylene glycol	A	N,N,N',N'-tetraethylethylenediamine	(19)
44	diethylamine	1,4-butanediol	B	N,N,N',N'-tetraethyl-1,4-diaminobutane	43

[a] Amine(60 mmol), α,ω-diol(20 mmol), dioxane(10 m*l*1), at 180 °C, 5h. [b] Catalyst: A, $RuCl_3 \cdot nH_2O$ (0.20 mmol); B, $RuCl_3 \cdot nH_2O$(0.20 mmol) and PBu_3(0.60 mmol) [c] Isolated yield. Figures in parentheses show GLC yields.

activity considerably (runs 19 and 20).

We have reported no activity for this species with amines as substrates[4-8]. However, the reason for catalytic activity for $RuCl_3 \cdot nH_2O$ in the absence of phosphine additive is particularly noteworthy.

On the other hand, in the reaction of long chain diol such as 1,5-pentanediol, a drastic change in the catalytic activity was observed. In this case, $RuCl_3 \cdot nH_2O$ combined with PBu_3 showed the highest catalytic activity (run 29). Triethylphosphine (PEt_3) had the same effectiveness as PBu_3, since they have almost some basicity[12].

The yield of 1,5-dipiperidinopentane was influenced by the molar ratio of $PBu_3 \cdot nH_2O$. The highest yield was realized at the molar ratio of 2.0-3.0; the yield of 1,5-dipiperidinopentane was 67% at molar ratio of 1.0 under similar reaction conditions of run 29, 80% at 2.0. The higher molar ratio reduced the yield of the product; 63% at the ratio of 4.0, 39% at 8.0. The excess PBu_3 reduced the catalytic activity of $RuCl_3 \cdot nH_2O$, which seemed to coordinate strongly on metal center. However, at the ratio less than 0.5, the reaction did not proceed.

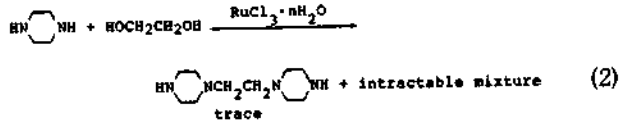
It is well-known that phosphorus (III) ligands modify or improve activities of transition-metal catalyst[14].

Under similar reaction conditions, rhodium and palladium complexes such as $RhCl(PPh_3)_3$, $RhH(PPh_3)_4$, $Pd(PPh_3)_4$, and $PdCl_2(PPh_3)_2$ showed low catalytic activities giving only

trace of diamino compounds with low conversion of the substrates.

Other representative secondary amines reacted with α,ω-diols in the same manner (Table 4). $RuCl_3 \cdot nH_2O$ acted most effectively as a catalyst for the short chain diols, while $RuCl_3 \cdot nH_2O$ combined with PBu_3 was an effective catalyst for more long chain diols. The short chain diamino compounds converted from the short chain diols is believed to behave like a phosphorus ligand, otherwise, the long chain diamino compounds obtained from the long chain diols does not behave like it. Morpholine and N-methylpiperazine could be used as the source of secondary amine for the synthesis of diamino compounds. However, from ethylene glycol and diethylamine, N,N,N',N'-tetraethylethylenediamine was obtained low yield in the presence of $RuCl_3 \cdot nH_2O$ catalyst (run 43). This phenomenon indicates that N-alkyl exchange reaction catalyzed by ruthenium complex[15].

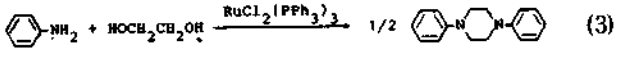
The reaction between piperazine and ethylene glycol gave 1,3-dipiperazinoethane in only trace yield despite the screening of the ruthenium catalyst system. The reaction gave only oligomeric intractable mixtures, whose molecular weights were 500-2000 according to GPC (eq. 2).



(2)

In a previous papar[5], we investigated the reaction of amines with alcohols. From the kinetic features of the reactions, the possible catalytic cycle which includes the nucleophilic attack of the amin on an aldehyde intermediate was proposed[5]. In the present reaction, a similar catalytic cycle is postulated.

The reaction between aromatic primary amine such as aniline and ethylene glycol gave 1,4-diphenylpiperazine in 73% isolated yield (eq. 3). Similar reaction between benzylamine and ethylene glycol also gave 1,4-dibenzylpiperazine in 78% isolated yield (eq. 4).



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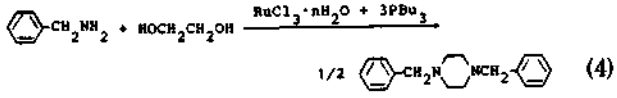

(4)

Experimental

The amines, ethylene glycol, 1,3-propanediol, 1,4-butanediol, 1,5-pentanediol, PBu_3, PEt_3, PCy_3, and the solvent were commercial materials and were purified by distillation before use. Diphenylphosphinoethane (dppe) was purcharsed from Alfa Division and used without further purification. $RuCl_3 \cdot nH_2O$ (mainly $n=3$) was purchased from Wako Pure Chemical Industries and used without further purification. $RuCl_2(PPh_3)_3$[16], $RhCl(PPh_3)_3$[17], $RhH(PPh_3)_4$[18], $Pd(PPh_3)_4$[19], and $PdCl_2(PPh_3)_2$[20] were prepared according to literature procedures.

General Reaction Procedure. A typical reaction of piperidine with ethylene glycol will be described here to exemplify the general reaction procedure. A stainless steel reactor (50 m*l*, Taiatsu Glass Industry, TVS-1, type) containing a glass liner was used. Under an orgon stream, dioxane (10 m*l*), piperidine (5.9 m*l*, 60 mmol), ethylene glycol (1.1 m*l*, 20 mmol), and $RuCl_3 \cdot nH_2O$ (52 mg, 0.20 mmol, 1.0 mol% based on ethylene glycol used) were added into the glass liner set in the reactor. After the reactor was sealed, an air purge was confirmed by four pressurization (10 atm)-depressurization sequences with argon. The reactor was heated to 180 °C in 30 min in the mantle heater and thermostated at this temperature with stirring for 5 h. The reaction was terminated by rapid cooling and the reactor was discharged. The product was isolated from clear dark brown solution by vacuum distillation and a flash column chromatography (hexane-aluminiumoxide 90, Merck, Art. 1076). 1,2-Dipiperidinoethane was isolated in 79% yield.

Analytical Procedure. All boiling points and melting point were uncorrected. The identification of products was made by ^1H-, ^{13}C-NMR, and elemental analysis. The ^1H- and ^{13}C-NMR spectra were recorded at 100 and 25.05 MHz, respectivery, with a JEOL JNM FX-100 spectrometer. Sample were dissolved in $CDCl_3$, and the chemical shift were expressed relative to Me_4Si as an internal standard. Elemental analyses were performed at Microanalytical Center of Kyoto University. The GLC analysis was made by Shimazu GC-4CM with a column (3 mm × 3 m) packed with Apiezon Grease L (10%) on Neopack 1A, 60-80 mesh. In some cases, the yields of product were determined by the internal standard method according to the calibration curve obtained for each product in a separate experiment. The fate of piperazine and ethylene glycol was ambiguous in the reaction for 1,2-dipiperazinoethane synthesis, so Gel-permeation chromatography (GPC) analysis was carried out. GPC were recorded on a Waters ALC/GPC 244 system equipped with Shodex GPC H-2002 column. The molecular weights were estimated according to calibration curves determined with standard polystyrenes.

1,4-diphenylpiperazine from aniline and ethylene glycol (eq. 3). A mixture of aniline (1.8 m*l*, 20 mmol), ethylene glycol (1.7m*l*, 30 mmol), $RuCl_2(PPh_3)_3$ (192mg, 0.2 mmol), and dioxane (10 m*l*) was stirred magnetically at 180 °C for 5 h under an argon atmosphere. A flash column chromatography (hexane-aluminium oxide 90, Merck, Art. 1076) of the reaction mixture gave 1,4-diphenypiperazine. Further vacuum distillation afforded the pure product (1.74g, 7.3 mmol) in 73% yield. bp. 100 °C (0.10 mmHg); white crystal; mp. 162-163 °C; ^1H-NMR (100 MHz) ($CDCl_3$) 3.33(s, 8H, $4CH_2$), 6.80-7.37(m, 10H, Ph); ^{13}C-NMR(25.05 MHz)($CDCl_3$) 49.5(t, $4CH_2$), 116.4(d), 120.3(d), 129.1(d), 150.8(s). Anal. Found: C, 80.59; H, 7.55; N, 11.60%. Calcd. for $C_{16}H_{18}N_2$: C, 80.64: H, 7.61; N, 11.75%.

1,4-dibenzylpiperazine from benzylamine and ethylene glycol (eq. 4). A mixture of benzylamine (2.2 m*l*, 20mmol), ethylene glycol(1.7m*l*, 30 mmol), $RuCl_3 \cdot nH_2O$(157 mg, 0.60 mmol), PBu_3(0.45 m*l*, 1.8 mmol), and dioxane (10 m*l*) was stirred magnetically at 180 °C for 5h under an argon atmosphere. A flash column chromatography(hexane-aluminium oxide 90, Merck, Art. 1076) of the reaction mixture gave 1,4-dibenzylpiperazine. The pure product (2.32g, 7.8 mmol) was obtained by further Kugel Rohr distillation in 78% yield. Kugel Rohr pot temp. 115 °C (0.10 mmHg); whith

crystal; mp 98 °C; ^{1}H-NMR(100 MHz)($CDCl_3$) 2.46(s, 8H, $4CH_2$), 3.49(s, 4H, $2CH_2$), 7.27(s, 10H, Ph); ^{13}C-NMR(25.05 MHz) ($CDCl_3$) 53.0(t, $4CH_2$), 62.9(t, $2CH_2$), 126.8(d), 128.2(d), 128.9(d), 138.1(s). Anal. Found: C, 81.14; H, 8.34; N, 10.43%. Calcd. for $C_{18}H_{22}N_2$: C, 81.16: H, 8.32; N 10.52%.

1,2-Dipiperidinoethane. Colorless oil; bp. 87 °C(2.0 mmHg); ^{1}H-NMR(100 MHz)($CDCl_3$) 1.25-1.78(m, 12H, $6CH_2$), 2.37(t, 8H, $4CH_2$), 2.43(s, 4H, $2CH_2$); ^{13}C-NMR(23.05 MHz)($CDCl_3$) 24.7(t, $2CH_2$), 29.1(t, $4CH_2$), 52.1(t, $4CH_2$), 62.4(t, $2CH_2$). Anal. Found: C, 73.27; H, 12.37; N, 14.15%. Calcd. for $C_{12}H_{24}N_2$: C, 73.41; H, 12.32; N, 14.27%.

1,2-Dipyrrolidinoethane. Colorless oil; bp. 76 °C(1.7 mmHg); ^{1}H-NMR(100 MHz)($CDCl_3$) 1.65-1,67(m, 8H, $4CH_2$), 2.23-2.42(m, 8H, $4CH_2$), 2.46(s, 4H, $2CH_2$); ^{13}-CNMR(25.05 MHz)($CDCl_3$) 23.4(t, $4CH_2$), 54.0(t, $4CH_2$), 61.7(t, $2CH_2$). Anal. Found: C, 71.29; H, 11.71; N, 16.60%. Calcd for $C_{10}H_{20}N_2$: C, 71.34; H, 11.98; N, 16.65%.

1,2-Dimorpholinoethane. Colorless oil; bp. 64 °C(1.2 mmHg); ^{1}H-NMR(100 MHz)($CDCl_3$) 2.36(s, 4H, $2CH_2$), 2.45(t, 8H, $4CH_2$), 3.73(t, 8H, $4CH_2$); ^{13}C-NMR(25.05 MHz)($CDCl_3$) 53.8(t, $4CH_2$), 60.3(t, $2CH_2$), 66.9(t, $4CH_2$). Anal. Found; C, 59.91; H, 10.07; N, 13.91; O, 16.01%. Calcd. for $C_{10}H_{20}N_2O_2$: C, 59.97; H, 10.06; N, 13.99; O, 15.98%.

1,2-(N-Methylpiperazino)ethane. Colorless oil; bp. 87 °C(0.52 mmHg); ^{1}H-NMR(100 MHz)($CDCl_3$) 2.28(s, 6H, $2CH_3$), 2.38-2.52(m, 20H, $10CH_2$); ^{13}C-NMR(25.05 MHz)($CDCl_3$) 46.0(q. $2CH_3$), 53.3(t, $4CH_2$), 54.8(t, $4CH_2$), 59.1(t, $2CH_2$). Anal. Found: C, 63.49; H. 11.62; N, 24.79%. Calcd. for $C_{12}H_{26}N_4$: C, 63.67; H, 11.58; N, 24.75%.

1,3-Dipiperidinopropane. Colorless oil; bp. 68 °C(0.90 mmHg); ^{1}H-NMR(100 MHz)($CDCl_3$) 1.23-1.81(m, 14H, $7CH_2$), 24.6(t, $2CH_2$), 26.0(t, $4CH_2$), 29.6(t, CH_2), 51.9(t, $4CH_2$), 56.7(t, $2CH_2$). Anal. Found: C, 73.98; H, 12.47; N, 13.35%. Calcd. for $C_{13}H_{26}N_2$: C, 74.22; H, 12.46; N, 13.32%.

1,3-Dipyrrolidinopropane. Colorless oil; bp. 90 °C(2.5 mmHg); ^{1}H-NMR(100 MHz)($CDCl_3$) 1.28-1.86(m, 10H, $5CH_2$), 2.22-2.36(m, 12H, $6CH_2$); ^{13}C-NMR(24.05 MHz)($CDCl_3$) 23.4(t, $4CH_2$), 29.8(t, CH_2), 54.3(t, $4CH_2$), 56.9(t, $2CH_2$). Anal. Found: C, 72.46; H, 12.25; N, 15.29%. Calcd. for $C_{11}H_{22}N_2$: C, 72.47; H, 12.16; N, 15.37%.

1,3-Dimorpholinopropane. Colorless oil; bp. 74 °C(1.5 mmHg); ^{1}H-NMR(100 MHz)($CDCl_3$) 1.43(m, 2H, CH_2), 2.21(t, 4H, $2CH_2$), 2.47(t, 8H, $4CH_2$), 3.71(t, 8H, $4CH_2$); ^{13}C-NMR(25.05 MHz)($CDCl_3$) 30.1(t, CH_2), 53.4(t, $4CH_2$), 55.9(t, $2CH_2$), 67.1(t, $4CH_2$). Anal. Found: C, 61.47; H, 10.38; N, 12.94; O, 15.21%. Calcd. for $C_{11}H_{22}N_2O_2$: C, 61.65; H, 10.35; N, 13.07; O, 14.93%.

1,3-(N-Methylpiperazino)propane. Colorless oil; bp. 47 °C(0.38 mmHg); ^{1}H-NMR(100 MHz)($CDCl_3$) 1.46(m, 2H, CH_2), 2.31(s, 6H, $2CH_3$), 2.33-2.59(m, 20H, $10CH_2$); ^{13}C-NMR(25.05 MHz)($CDCl_3$) 30.7(t, CH_2), 45.8(q, $2CH_3$), 53.5(t, $4CH_2$), 54.7(t, $4CH_2$), 56.4(t, $2CH_2$). Anal. Found: C, 64.81; H, 11.81; N, 23.28%. Calc. for $C_{13}H_{28}N_4$: C, 64.95; H, 11.74; N, 23.31%.

1,4-Dipiperidinobutane. Colorless oil; bp. 63 °C(1.0 mmHg); ^{1}H-NMR(100 MHz)($CDCl_3$(1.21-1.80(m, 16H, $8CH_2$), 2.24-2.49(m, 12H, $6CH_2$); ^{13}C-NMR(25.05 MHz)($CDCl_3$) 23.9(t, $2CH_2$), 25.8(t, $4CH_2$), 27.4(t, $2CH_2$), 51.7(t, $4CH_2$), 53.2(t, $2CH_2$). Anal. Found: C, 75.04; H, 12.47; N, 12.44%. Calcd. for $C_{14}H_{28}N_2$: C, 74.94; H. 12.58; N, 12.48%.

1,4-Dipyrrolidinobutane. Colorless oil bp. 66 °C(1.4 mmHg); ^{1}H-NMR(100 MHz)($CDCl_3$) 1.36-1.80(m, 12H, $6CH_2$), 2.27-2.52(m, 12H, $6CH_2$); ^{13}C-NMR(25.05 MHz)($CDCl_3$) 24.1 (t, $4CH_2$), 27.3(t, $2CH_2$), 54.0(t, $4CH_2$), 55.8(t, $2CH_2$). Anal. Found: C, 73.48; H, 12.28; N, 14.14%. Calcd. for $C_{12}H_{24}N_2$: C, 73.41; H, 12.32; N, 14.27%.

1,4-Dimorpholinobutane. Colorless oil; bp. 49 °C(0.53 mmHg); ^{1}H-NMR(100 MHz)($CDCl_3$) 1.31-1.52(m, 4H, $2CH_2$), 2.23-2.58(m, 12H, $6CH_2$), 3.70(t, 8H, $4CH_2$); ^{13}C-NMR(25.05 MHz)($CDCl_3$) 27.5(t, $2CH_2$), 53.5(t, $4CH_2$), 53.7 (t, $2CH_2$), 67.0(t, $4CH_2$). Anal. Found: C, 62.97; H, 10.68; N, 12.16; O, 14.19% Calcd. for $C_{12}H_{24}N_2O_2$: C, 63.12; H, 10.59; N, 12.27; O, 14.02%.

1,4-(N-Methylpiperazino)butane. Colorless oil; bp. 67 °C(0.32 mmHg); ^{12}H-NMR(100 MHz)($CDCl_3$) 1.32-1.54(m, 4H, $2CH_2$), 2.30(s, 6H, $2CH_3$), 2.23-2.61(m, 20H, $10CH_2$); ^{13}C-NMR(25.05 MHz)($CDCl_3$) 27.2(t, $2CH_2$), 46.1(q, $2CH_3$), 51.4(t, $4CH_2$), 51.8(t, $2CH_2$), 52.9(t, $4CH_2$). Anal. Found: C, 66.03; H, 11.87; N, 21.97%. Calcd. for $C_{14}H_{30}N_4$: C, 66.09; H, 11.89; N. 22.02%.

1,5-Dipiperidinopentane. Colorless oil; bp. 51 °C(0.47 mmHg); ^{1}H-NMR(100 MHz)($CDCl_3$) 1.20-1.72(m, 18H, $9CH_2$), 2.27-2.44(m, 12H, $6CH_2$); ^{13}C-NMR(25.05 MHz)($CDCl_3$) 23.1(t, $2CH_2$), 24.2(t, CH_2), 26.1(t, $4CH_2$), 30.8(t, $2CH_2$), 49.8 (t, $2CH_2$), 50.6(t, $4CH_2$). Anal. Found: C, 75.49; H, 12.71; N, 11.59%. Calcd. for $C_{15}H_{30}N_2$: C, 75.57; 12.68; N, 11.75%.

1,5-Dipyrrolidinopentane. Colorless oil; bp. 64 °C (0.82 mmHg); ^{1}H-NMR(100 MHz)($CDCl_3$) 1.21-1.80(m, 14H, $7CH_2$), 2.26-2.48(m, 12H, $6CH_2$); ^{13}C-NMR(25.05 MHz)($CDCl_3$) 24.1(t, CH_2), 24.3(t, $4CH_2$), 30.9(t, $2CH_2$), 49.7(t, $2CH_2$), 53.9(t, $4CH_2$). Anal. Found: C, 74.15; H, 12.47; N, 13.18%. Calcd. for $C_{13}H_{26}N_2$: C, 74.22; H, 12.46; N, 13.32%.

1,5-Dimorpholinopentane. Colorless oil; bp. 57 °C (0.46 mmHg); ^{1}H-NMR(100 MHz)($CDCl_3$) 1.18-1.64(m, 6H, $3CH_2$), 2.29-2.51(m, 12H, $6CH_2$), 3.70(t, 8H, $4CH_2$); ^{13}C-NMR(25.05 MHz) ($CDCl_3$) 24.3(t, CH_2), 30.7(t, $2CH_2$), 49.8(t, $2CH_2$), 53.6(t, $4CH_2$), 66.7(t, $4CH_2$). Anal. Found: C, 64.34; H, 10.83; N, 11.49; O, 13.33%. Calcd. for $C_{13}H_{26}N_2O_2$: C, 64.43; H, 10.81; N, 11.56; O, 13.20%.

1,5-(N-Methylpiperazino)pentane. Colorless oil; bp. 77 °C(0.44 mmHg); ^{1}H-NMR(100 MHz)($CDCl_3$) 1.19-1.71(m, 6H, $3CH_2$), 2.30(s, 6H, $2CH_3$), 2.33-2.57(m, 20H, $10CH_2$); ^{13}C-NMR(25.05 MHz)($CDCl_3$) 24.2(t, CH_2), 30.7(t, $2CH_2$), 46.0(q, $2CH_3$), 49.4(t, $2CH)_2$, 53.8(t, $4CH_2$), 54.1(t, $4CH_2$). Anal. Found: C, 67.03; H, 11.97; N, 20.68%. Calcd. for $C_{15}N_{32}N_4$: C, 67.12; H, 12.01; N, 20.68%.

N,N,N′,N′-Tetraethylethylenediamine. Colorless oil; bp. 77 °C(4.8 mmHg); ^{1}H-NMR(100 MHz)($CDCl_3$) 1.02(t, 12H, $4CH_3$), 2.48(s, 4H, $2CH_2$), 2.53(q, 8H, $4CH_2$); ^{13}C-NMR(25.05 MHz)($CDCl_3$) 14.9(q, $4CH_3$), 49.0(t, $4CH_2$), 61.2(t, $2CH_2$). Anal. Found: C, 69.71; H, 14.01; N, 16.18%. Calcd. for $C_{10}H_{24}N_2$: C, 69.70; H, 14.04; N, 16.26%.

N,N,N′,N′-Tetraethyl-1,4-butanediamine. Colorless oil; bp. 55 °C(0.86 mmHg); ^{1H}-NMR(100 MHz)($CDCl_3$) 1.01(t, 12H, $4CH_3$), 1.31-1.42(m, 4H, $2CH_2$), 2.30-2.55(m, 12H, $6CH_2$); ^{13}C-NMR(25.05 MHz)($CDCl_3$) 14.8(q, $4CH_3$), 27.1(t, $2CH_2$), 48.9(t, $4CH_2$), 53.6(t, $2CH_2$). Anal. Found: C, 71.86; H, 14.11; N, 13.83. Calcd. for $C_{12}H_{28}N_2$: C, 71.93; H, 14.09; 13.98.

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Theoretical Studies on the Gas-Phase Pyrolysis of Esters The effect of α- and β-methylation of Ethyl Formates[1]

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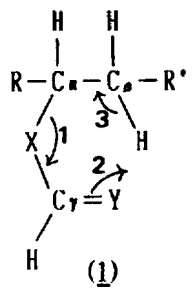
The gas-phase thermolysis reactions of α- and β-methylated ethyl formates, Y = CH-X-$CHR_1CH_2R_2$ where X = Y = O or S and R_1 = R_2 = H or CH_3, are investigated theoretically using the AM1 method. The experimental reactivity order is reproduced correctly by AM1 in all cases. The thermolysis proceeds through a six-membered cyclic transition state conforming to a retro-ene reaction, which can be conveniently interpreted using the frontier orbital theory of three-species interactions. The methyl group substituted at C_α or C_β is shown to elevate the π-HOMO of the donor fragment (Y = C) and depress the σ^*-LUMO of the acceptor fragment (C_β-H), increasing the nucleophilicity of Y toward β-hydrogen which in turn increases the reactivity. The two bond breaking processes of the C_α-X and C_β-H bonds are concerted but not synchronous so that the reaction takes place in two stages as Taylor suggested. The initial cleavage of C_α-X is of little importance but the subsequent scission of C_β-H occurs in a rate determining stage.

Introduction

The gas-phase thermal decomposition reaction of esters has been studied extensively.[2] Taylor[2a] proposed a fairly detailed picture of the transition state (TS) for pyrolysis of ethyl esters, (1): the TS has a six-membered cyclic structure in which electrons move in a cyclic manner, not at precisely the same time but sequentially as numbered in (1) so that C_β is less electron rich than C_α is electron deficient.

There is, however, still a controversial problem of the rate determining step; some investigators interpreted their data in favor of the C_α-O bond polarization[2a] whereas some in favor of the cleavage of the C_β-H bond[2i-2j] as the rate determining process. Experimentally monomethylation at the α-



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