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ORGANOZINC AND OTHER ORGANOMETALLIC COMPOUNDS DERIVED FROM *N,N*-DIETHYLBROMOACETAMIDE *

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Summary

The preparation of the zinc derivative (I) of *N,N*-diethylbromoacetamide in methylal has been investigated using NMR spectroscopy. The reagent I was used to replace reactive chlorine atoms in thionyl chloride and in organometallic compounds. Although the organozinc reagent would not alkylate transition metal halides, a corresponding organotin reagent could be used. Compound I added normally to the carbonyl group of aldehydes and ketones, but gave an unexpected product with phenyl isocyanate.

Introduction

Almost eighty years after Reformatsky [2] showed that β-hydroxy esters could be obtained when carbonyl compounds were treated with α-bromo ester and activated zinc, Curé and Gaudemar [3] prepared the organozinc intermediate from the α-bromo ester and zinc in methylal.

$$BrCH_2COX + Zn \xrightarrow{(MeOCH_2)_2} BrZnCH_2COX \qquad (X = OEt, NEt_2)$$

In the present paper an investigation into the preparation, structure and reactions of the product obtained from zinc and *N,N*-diethylbromoacetamide, together with the reactions of some related compounds is reported.

Results and discussion

The reaction between activated zinc and *N,N*-diethylbromoacetamide in methylal was monitored by sealing the reactants in an NMR tube in vacuo. The singlet at τ 6.10 due to the bromine linked methylene group in the amide start-

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* For a preliminary report see ref. 1.

ing material disappears within 2 h to be replaced by a singlet at τ 7.69. After 20 h, the latter has a slightly diminished intensity and an additional weak singlet is observed at τ 8.15. If the reaction is carried out in air the signal at τ 6.10 is again lost within 2 h and two singlets at τ 7.69 and τ 8.15 appear, the latter being the more intense. A plausible explanation for these observations is summarised in the following scheme.

$$\underset{\tau\ 6.10}{BrC\underline{H}_2CONEt_2} + Zn \rightarrow \underset{(I)\ \tau\ 7.69}{BrZnC\underline{H}_2CONEt_2} \xrightarrow{H_2O} \underset{\tau\ 8.16}{C\underline{H}_3CONEt_2} + ZnBrOH$$

It is assumed that traces of water are responsible for the slight hydrolysis observed in vacuo, while hydrolysis is substantial when air is admitted. After 2 h in vacuo integration shows that only a single organometallic product is present; it is possible that this is the bromine-free product II resulting from a rapid disproportionation of I. This possibility is discounted since when the reaction product is treated with 2,2′-bipyridyl the $ZnBr_2 \cdot$ 2,2′-bipy complex was obtained in only 28% yield and much higher yields would be expected if II is the sole organometallic product.

$$2\ BrZnCH_2CONEt_2 \rightarrow ZnBr_2 + \underset{(II)}{Zn(CH_2CONEt_2)_2}$$

Although ethylbromozinc acetate has been used to alkylate Group IVB elements in the series Ph_3MX (M = C, Si, Ge, Sn; X = halogen) [4] no systematic studies have been reported and it was decided to evaluate I as an organometallic reagent. Firstly it was shown that derivatives of silicon, germanium and tin

$$Ph_3MCl + BrZnCH_2CONEt_2 \rightarrow Ph_3MCH_2CONEt_2 + ZnBrCl$$

(M = Si, Ge, Sn)

were obtained in good yields. Only tetraphenyllead was obtained when the reaction was attempted with triphenyllead chloride. Even though an excess of the reagent was used only one chlorine atom in diphenyltin dichloride could be replaced giving $Ph_2Sn(Cl)CH_2CONEt_2$ (III). The most likely structure for III is a coordination polymer with 5-coordinate tin atoms and bridging amide groups. The coordination of the carbonyl amide group in III is indicated by the displacement of ν(C=O) from 1608 cm^{-1} in $Ph_3SnCH_2CONEt_2$ to 1575 cm^{-1} in III and also by its deshielding effect on the NMR signal from metal bound methylene group τ 6.90 for III compared with the following figures for the triphenyl compounds; τ values for $Ph_3MC\underline{H}_2CONEt_2$, M = Si 7.27, Ge 7.23, and Sn 7.37 (the order of these reflects the electronegativity differences in M). The Mössbauer parameters of III (δ 1.26 mm s^{-1}, Δ —3.04 mm s^{-1}) are consistent with a trigonal bipyramid with equatorial Sn—C bonds, O and Cl occupying axial positions [5,6].

When similar alkylations of triphenyltin halides were tried using the zinc derivative of bromoacetophenone ($PhCOCH_2ZnBr$) under a variety of conditions the only product was 1,4-diphenylbutan-1,4-dione which was obtained in yields of up to 75%. (cf. Ghera et al. [7] who obtained 32—40% of the same diketone by a related method.)

Attempts to use I to alkylate various transition metals were unsuccessful. Since α-functional groups bound to tin are very labile, alkylation of transition metals using the triphenylstannylamide were attempted. Tantalum pentachloride in chloroform, gave the dialkyltantalum trichloride; monitoring by TLC showed that the organotin compound was completely converted into triphenyltin chloride in 40 min at room temperature.

$$3\ Ph_3SnCH_2CONEt_2 + TaCl_5 \rightarrow (Et_2NCOCH_2)_3TaCl_2 + 3\ Ph_3SnCl$$

Compound I was used to replace the chlorine atoms in thionyl chloride by *N,N*-diethylamide groups and this reaction was extended to include related halogenozinc esters.

$$2\ XZnCHRY + SOCl_2 \rightarrow (YRCH)_2SO + 2\ ZnXCl$$

(X = Br, R = H, Y = $CONEt_2$; X = Br, R = H, Y = COOEt; X = Br, R = Y = COOEt)

We confirmed the observations of Curé and Gaudemar [8] that compound I adds normally to the C=O bond of aldehydes and ketones to give hydroxy amides by isolating the products shown in the following scheme:

$$PhCOR + BrZnCH_2CONEt_2 \rightarrow PhRC(OZnBr)CH_2CONEt_2 \xrightarrow{H_2O} PhRC(OH)CH_2CONEt_2 + Zn(OH)Br$$

(R = H, Me, Ph)

Reaction between the bromozinc amide (I) and phenyl isocyanate was abnormal: instead of the expected product from addition across the N=C bond only *N,N'*-diphenylsuccinamide could be isolated. A survey of related organozinc compounds showed that the halogenozinc nitrile and iodide behaved in the same manner.

$$XZnCH_2Y \xrightarrow[(2)\ aq\ NH_4Cl]{(1)\ PhNCO} PhNHCOCH_2CH_2CONHPh$$

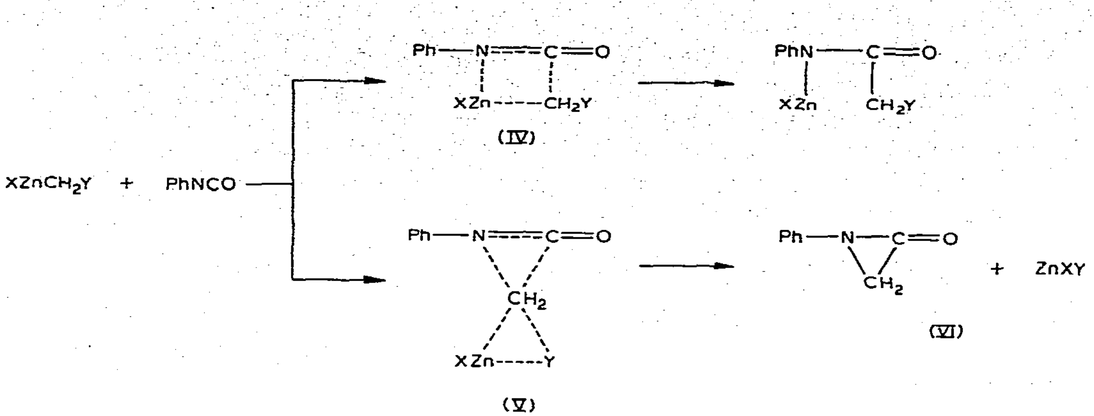
(X = Br, Y = $CONEt_2$; X = I, Y = CN; X = I, Y = I)

On the other hand, bromozinc esters and phenyl isocyanate reacted normally to give the addition products.

$$BrZnCHRCOOEt \xrightarrow[(2)\ aq\ NH_4Cl]{(1)\ PhNCO} PhNHCOCHRCOOEt$$

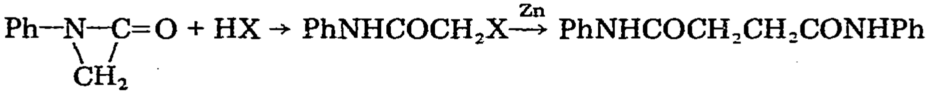
(R = H or COOEt)

This difference in behaviour may be rationalized by considering two alternative transition states for the reaction of a methylene—zinc compound, $XZnCH_2Y$, with phenyl isocyanate. Transition state IV leads to the normal addition product and this is the route followed by the zinc derivatives of ethyl bromoacetate and diethylbromomalonate. The methylene transfer reagent $IZnCH_2I$ would be expected to react via transition state V and it is postulated that $IZnCH_2CN$ and $BrZnCH_2CONEt_2$ also follow this route to give the α-lactam VI (compound VI is formed as an intermediate by the action of other



methylene transfer reagents such as diazomethane on phenyl isocyanate [9]). When VI is formed from I, methylene transfer would give $BrZnCONEt_2$ which would be rapidly hydrolysed to give diethylformamide and material exhibiting an intense singlet in the NMR at τ 1.4, characteristic of formamides was shown to be present.

A tentative proposal for a route for the conversion of VI into *N,N*-diphenylsuccinamide is as follows:



$$\underset{\text{(VI)}}{\underset{CH_2}{Ph{-}N{-}C{=}O}} + HX \rightarrow PhNHCOCH_2X \xrightarrow{Zn} PhNHCOCH_2CH_2CONHPh$$

(VI)

Adventitious hydrolysis of zinc halogen bonds would ensure the presence of hydrohalogenic acid HX and it is known [10] that α-lactams react rapidly at room temperature with protic reagents to give the halogenoacetamide.

Experimental

Details of the Mössbauer spectrometer have been described elsewhere [11]; the isomer shift refers to tin(IV) oxide. NMR spectra were measured using a Perkin—Elmer R12 60 MHz instrument. IR measurements were made with Perkin—Elmer 237 and 325 spectrometers. The reactions were monitored by thin layer chromatography [12]. Activated zinc supplied by B.D.H. Ltd. was used without further treatment.

Treatment of bromozinc N,N-diethylacetamide with 2,2'-bipyridyl

Activated zinc (3.2 g) was added to *N,N*-diethylbromoacetamide (1.94 g) in methylal (30 ml) and the mixture stirred until the surface of zinc blackened and then for a further hour. Unreacted zinc was removed by filtration, 2,2'-bipyridyl (1.3 g) in methylal (30 ml) added and the mixture boiled under reflux for 3 h. Filtration gave the 2,2'-bipyridyl complex of zinc dibromide (0.54 g, 28%) m.p. > 360°C (Found: C, 31.5; H, 2.4; N, 7.4. $C_{10}H_8Br_2N_2Zn$ calcd.: C, 31.5; H, 2.1; N, 7.35%).

Triphenylstannyl N,N-diethylacetamide

Activated zinc (4.26 g), methylal (30 ml), *N,N*-diethylbromoacetamide

(2.2 g) and a small crystal of iodine stirred until surface of zinc blackened and then for a further 20 min. Triphenyltin chloride (1.8 g) in methylal (30 ml) added, heated under reflux for 3 h. Excess reagent was decomposed with saturated aqueous ammonium chloride and the product extracted with benzene. After washing with water and drying (Na_2SO_4) the benzene was removed to give the product as an oily solid (1.4 g, 64%). This product was recovered unchanged from a silica chromatography column by elution with 1/1 ethyl acetate/light petroleum (Found: C, 61.8; H, 5.9; N, 3.5. $C_{24}H_{27}NOSn$ calcd.: C, 62.1; H, 5.9; N, 3.0%). IR (Nujol); ν (C=O) 1608 cm^{-1}; ν_s (Sn—Ph) 235 cm^{-1}, ν_{as} (Sn—Ph) 268 cm^{-1}, NMR ($CDCl_3$); Sn—$C\underline{H}_2$—CO singlet τ 7.37.

Triphenylsilyl N,N-diethylacetamide

Obtained in 70% yield as an oily solid by the same procedure as the tin compound (Found: C, 77.4; H, 7.5; N, 3.8. $C_{24}H_{27}NOSi$ calcd.: C, 77.2; H, 7.3; N, 3.8%). IR (film): ν (C=O) 1610 cm^{-1}. NMR ($CDCl_3$): $SiC\underline{H}_2CO$ singlet τ 7.27.

Triphenylgermyl N,N-diethylacetamide

Obtained in 65% yield as an oily solid by the same procedure as the tin compound (Found: C, 69.3; H, 6.5; N, 3.25. $C_{24}H_{27}NOGe$ calcd.: C, 68.9; H, 6.5; N, 3.4%). NMR ($CDCl_3$): $GeC\underline{H}_2CO$ singlet τ 7.23.

Chlorodiphenylstannyl N,N-diethylacetamide

Prepared from zinc (3.6 g), *N,N*-diethylbromoacetamide (4.6 g) and diphenyltin dichloride (2.0 g) using the same procedure as for the triphenyltin compound to give a solid product (1.56 g, 70%). Analytical specimen recrystallised from light petroleum had m.p. 134—135°C (Found: C, 52.2; H, 5.6; N, 2.9. $C_{18}H_{22}ClONSn$ calcd.: C, 51.2; H, 5.2; N, 3.3%). IR (Nujol): ν (C=O) 1575 cm^{-1}. NMR ($CDCl_3$): $SnC\underline{H}_2CO$ singlet τ 6.90.

1,4-Diphenylbutan-1,4-dione

Zinc (1.0 g), phenacyl bromide (1.94 g) and tetrahydrofuran heated under reflu for 3 h. Saturated aqueous ammonium chloride was added and the product extracted with ether. Evaporation of the dried ($MgSO_4$) solution gave the solid diketone (0.87 g, 75%). The analytical specimen obtained by crystallisation from light petroleum had m.p. 144.5—145.5°C (lit. [13] m.p. 144—145°C) (Found: C, 80.1; H, 6.2. $C_{16}H_{14}O_2$ calcd.: C, 80.6; H, 5.9%). IR (Nujol): ν(C=O) 1690 cm^{-1}. NMR ($CDCl_3$): methylene singlet τ 6.5. The same product was isolated when triphenyltin chloride or triphenyltin iodide was added to the reaction mixture before heating.

Tris(N,N-diethylacetamido)tantalum dichloride

Triphenylstannyl *N,N*-diethylacetamide (1.13 g), tantalum pentachloride (0.45 g) in chloroform (90 ml) was stirred for 40 min when it was shown by TLC that all of the tin compound had been converted to triphenyltin chloride. The solution was evaporated to dryness and the resulting solid extracted with light petroleum in a Soxhlet flask for 4 days. The product remained as an insoluble yellow solid (0.45 g, 94%) (Found: C, 35.5; H, 5.7; N, 7.1. $C_{18}H_{36}Cl_2N_3OTa$ calcd.: C, 36.4; H, 6.1; N, 7.1%). IR (DMSO): ν (C=O) 1608

TABLE 1

RESULTS OF THE REACTIONS OF ORGANOZINC REAGENTS WITH THIONYL CHLORIDE

α-Halogeno compound	Product (% yield)	n_D^{20}	Analysis (found (calcd. (%))			NMR ($CDCl_3$) τ ($SC\underline{H}_2$ or $SC\underline{H}$)
			C	H	N	
$BrCH_2CONEt_2$	$(Et_2NOCCH_2)_2SO$ (32)	1.5077	52.2 (52.1)	8.9 (8.8)	9.8 (10.1)	6.70
$BrCH_2COOEt$	$(EtOCOCH_2)_2SO$ (45)	1.4242	42.9 (43.2)	6.2 (6.3)		6.60
$BrCH(COOEt)_2$	$[(EtOCO)_2CH]_2SO$ (87)	1.4656	46.0 (45.9)	5.7 (6.1)		6.40

cm^{-1}. NMR (DMSO-d_6): ethyl (methylene) τ 6.8, ethyl (methyl) τ 9.0. $TaC\underline{H}_2CO$ τ 7.50.

Reactions of organozinc reagents with thionyl chloride

The α-halogeno compounds were treated with zinc in methylal in a similar manner to that described previously, thionyl chloride was added to the organozinc reagent so that the ratio of α-halogeno compound to thionyl chloride was 2/1. The mixture was boiled under reflux for 3—6 h, excess reagent decomposed with saturated aqueous ammonium chloride and the products extracted with ether. The results are summarized in Table 1.

Reaction between bromozinc N,N-diethylacetamide and carbonyl compounds

To the organozinc reagent formed as before from *N,N*-diethylbromoacetamide and zinc in methylal was added a 0.5 *M* proportion of benzophenone and the mixture heated under reflux for 3 h. After addition of saturated aqueous ammonium chloride the mixture was extracted with benzene. Drying and evaporation gave *N,N*-diethyl 3-hydroxy-3,3-diphenylpropionamide as a colourless solid m.p. 87—88°C (88%) (Found: C, 76.6; H, 7.8; N, 4.75. $C_{19}H_{23}O_2N$ calcd.: C, 76.7; H, 7.8; N, 4.7%).

In a similar way $PhMeC(OH)CH_2CONEt_2$ (55%, n_D^{20} 1.521, lit. [8] 1.521) was obtained from acetophenone and $PhCH(OH)CH_2CONEt_2$ (61%, n_D^{20} 1.524, lit. [8] 1.524) from benzaldehyde having satisfactory spectral characteristics and analyses.

Reaction between organozinc reagents and phenyl isocyanate giving abnormal products

An equimolar quantity of phenyl isocyanate was added to the organozinc reagent from *N,N*-diethylbromoacetamide and zinc in methylal and the mixture heated under reflux for 3 h. Saturated aqueous ammonium chloride was added and the mixture extracted with benzene; drying and evaporation gave *N,N'*-diphenylsuccinamide which was recrystallised from ethanol (m.p. 226°C, lit. [14] 226°C) in 85% yield (Found: C, 71.6; H, 5.9; N, 10.6. $C_{16}H_{16}O_2N_2$ calcd.: C, 71.6; H, 6.0; N, 10.4%). IR (Nujol): ν (C=O) 1650 cm^{-1}, ν (N—H) 3340 cm^{-1}. NMR ($CDCl_3$): $C\underline{H}_2$ τ 6.9, $N\underline{H}$ τ 1.8. The same result was obtained when

THF was used instead of methylal as the reaction solvent.

When the organozinc reagent was made from methylene iodide in THF or from iodomethyl cyanide in THF the succinamide derivative was isolated in yields of 78% and 95% respectively.

Reaction between organozinc reagents and phenyl isocyanate giving normal products

The above procedure was repeated using the compound made from zinc and ethyl bromoacetate in methylal. In this case the product obtained was the ethyl ester of *N*-phenylmalonic acid monoamide (m.p., after crystallisation from ether, 36—37°C, lit. [15] m.p. 38—39°C) (Found: C, 64.1; H, 6.1; N, 6.9. $C_{11}H_{13}O_3N$ calcd.: C, 63.8; H, 6.3; N, 6.8%).

When the same reaction was carried out starting from diethyl bromomalonate the product $PhNHCOCH(COOEt)_2$, crystallised from ethanol, was obtained in 65% yield (m.p. 127—128°C, lit. [16] m.p. 124°C) (Found: C, 60.5; H, 6.3; N, 5.0. $C_{14}H_{17}O_5N$ calcd.: C, 60.2; H, 6.1; N, 5.0%). Both of these products showed the expected IR and NMR spectra.

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