December, 1981] © *1981 The Chemical Society of Japan* NOTES *Bull. Chem. Soc. Jpn.*, *54*, *3867—3868 (1981)* 3867

Abnormal $LiAlH_4$ Reduction of 4,4-Diphenyl-3-cyano-2-methyl-2-pyrrolin-5-one

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(Received January 29, 1981)

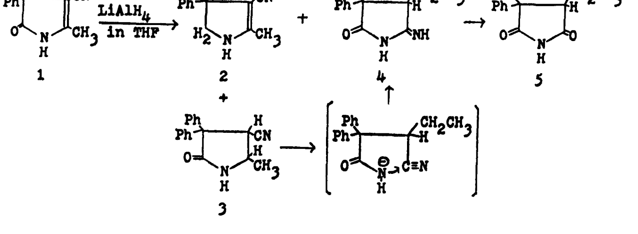
Synopsis. The reduction of 4,4-diphenyl-3-cyano-2-methyl-2-pyrrolin-5-one with lithium aluminum hydride yields three unexpected reduction products, together with the usual product.

We have recently reported[1)] that benzoins can be converted into 4,4-diaryl-3-cyano-2-methyl-2-pyrrolin-5-ones in good yields by a reaction with sodio-3-iminobutanenitrile in THF.

We now wish to report our results on the reduction of 4,4-diphenyl-3-cyano-2-methyl-2-pyrrolin-5-one (**1**) with $LiAlH_4$. Thus, **1** was treated with an excess of $LiAlH_4$ under anhydrous conditions, in THF. The expected compound (**2**) was formed in a minute amount; 3,3-diphenyl-4-cyano-5-methyl-2-pyrrolidinone (**3**) was a major product, along with **4** and **5** in about 5 and 3% yields respectively.

The molecular formula of **2** was deduced to be $C_{18}H_{16}N_2$ by means of the mass spectrum (M^+, *m/e* 260) and the elemental analysis. The IR spectrum of **2** displayed a strong NH absorption at 3300 cm^{-1} and C≡N at 2190 cm^{-1}. However, the IR spectrum lacked bands arising from the carbonyl group. Furthermore, in the ^1H NMR spectrum of **2**, the resonance for the methylene group appeared at δ 4.02 (s, 2H) as a sharp singlet, in addition to a singlet (3H, CH_3) at δ 2.00, a broad singlet (1H, NH) at δ 4.45, and a multiplet (10H, aromatic protons) at δ 7.27. All these results can be accommodated in the **2** structure. The molecular formula of **3** was deduced to be $C_{18}H_{16}N_2O$ by means of the mass spectrum (M^+, *m/e* 276) and by elemental analysis. The ^1H NMR spectrum of **3** showed the signal of methyl (δ 1.35, d, J=5 Hz) and two methine (δ 3.75, m, and 4.20, d, J=8 Hz) groups, in addition to a broad singlet (1H, NH) at δ 8.74 and a multiplet (10H, aromatic protons) at δ 7.30, which could be assigned to two phenyl groups. Decoupling experiments revealed that the multiplet observed at δ 3.57 is coupled to a proton at δ 4.20 with J=8 Hz and also to a methyl proton at δ 1.35 with J=5 Hz, showing the presence of the $CH_3\text{-}\overset{|}{C}H\text{-}\overset{|}{C}H\text{-}$ moiety. The presence of the carbonyl group was supported by the appearance of the characteristic carbonyl absorption at 1720 cm^{-1} in the IR spectrum. From these facts, the structure of **3** was assigned. The molecular formula of **4** was deduced to be $C_{18}H_{18}N_2O$ by means of the mass spectrum (M^+, *m/e* 278) and by the elemental analysis. The ^1H NMR spectrum of **4** showed the signals of methyl (δ 0.69), methylene (δ 1.52), and methine (δ 4.42) groups, in addition to two NH protons as a broad singlet at δ 6.95 and δ 8.05 and phenyl protons as a multiplet at δ 7.38. Decoupling experiments revealed that the multiplet protons observed at δ 1.52 are coupled to the methyl protons at δ 0.69 with J=7 Hz, and also to a methylene proton at δ 4.42 with J=7 Hz, showing the presence of a $-CHCH_2CH_3$ moiety. Irradiation at δ 1.52 changed the triplet at δ 0.69 into a singlet and the triplet at δ 4.42 into a singlet. Its IR spectrum exhibited absorption bands at 3300 (NH), 1770, and 1700 cm^{-1}. These absorptions suggested the presence of a $-CO\text{-}NH\text{-}\overset{|}{C}\text{=}NH$ moiety. All these results can be accommodated in the **4** structure. The molecular formula of **5** was also deduced to be $C_{18}H_{17}NO_2$ by means of the mass spectrum (M^+, *m/e* 279) and the elemental analysis. Compound **5** showed IR absorption bands at 3200, 1780, 1715, and 1500 cm^{-1}. These absorptions suggested the presence of a –CO–NH–CO– moiety. From these facts, the structure of **5** was assigned.

It is known[2)] that an amide, on reduction with $LiAlH_4$, is converted in a good yield into a corresponding amine. For example, in THF at 65 °C, 5,5-dimethyl-2-pyrrolidinone is reduced to 2,2-dimethylpyrrolidine in a 67—79% yield. However, the similar reaction of **1** failed to give 3,3-diphenyl-4-cyano-5-methyl-2,3-dihydropyrrole (**2**) as a main product. The considerable difficulty in the reduction of the carbonyl group may be explained by the steric hindrance given by the adjacent two phenyl groups. It is interesting to note that $LiAlH_4$ reduces the double bond of **1**,[4)] in spite of the fact that it does not reduce ethylenic or acetylenic hydrocarbons.[3)] The formation of **4** can be explained by the process initiated by the cleavage of the $N\text{-}C_5$ bond of **3** and the attack of the nitrogen anion[5)] on the carbon atom of the cyano group, followed by the addition of a proton at the $C\text{=}N^-$ group. Additionally, the hydrolysis of **4** affords **5**. With the proper control of the amount of $LiAlH_4$, *N*,*N*-disubstituted amide is known[5)] to be susceptible to the cleavage of the –CO–NH– bond. However, the formation of an amine and an aldehyde on the reduction of an amide is induced by the addition of the hydride anion to the carbonyl. The present reduction differs from this type of cleavage in that the C–N bond is directly attacked by the hydride. In support of this explanation, two compound, **4** and **5**,[7)] were obtained, in 13 and 8% yields respectively, by the reduction of **3** with $LiAlH_4$ in THF.



Experimental

All the melting points are uncorrected. The infrared spectra were measured on a JASCO IRA-2 Diffraction Grating

Infrared Spectrometer. The NMR spectra were determined on a JNM-4H-100 spectrometer instrument, using TMS as the internal reference. The MS spectra were taken by using a JEOL-JMS-O1SG-2 mass spectrometer.

Materials. 4,4-Diphenyl-3-cyano-2-methyl-2-pyrrolin-5-one was prepared according to the procedure described in a previous paper.[1] Lithium aluminum hydride was used without further purification. The solvents were purified by distillation.

*Reduction of **1** with Lithium Aluminum Hydride in THF.* A solution of 2.74 g (10 mmol) of **1** in 150 ml of THF was added, over a period of 2 h, to a stirred suspension of an excess of lithium aluminum hydride (1.52 g, 40 mmol) in 150 ml of THF at reflux under an atmosphere of nitrogen. After careful decomposition with cold water, the solution was concentrated to *ca.* 80 ml. To a solution this obtained we added 10% hydrochloric acid (30 ml). The mixture was allowed to stand overnight to give yellowish solids. The precipitated solids were filtered off and recrystallized from ethyl acetate–hexane to give **3** (78%); mp 224—226 °C. Found: C, 78.11; H, 5.99; N, 10.20%. Calcd for $C_{18}H_{16}N_2O$: C, 78.23; H, 5.86; N, 10.14%. MS 276 (M^+). IR (KBr) 3290 (NH), 2200 (C≡N), 1720 (C=O) cm^{-1}. ^1H NMR (DMSO-d_6) δ 1.35 (d, J=5 Hz, 3H, CH_3), 3.75 (m, 1H, CH), 4.20 (d, J=8 Hz, 1H, CH), 7.30 (m, 10H, aromatic H), 8.74 (bs, 1H, NH). The evaporation of the mother-liquor at room temperature, after the separation of the **3**, gave a solid residue which was fractionally recrystallized from hexane containing a small amount of ethyl acetate to give **2** (3%); mp 115—116 °C. Found: C, 82.69; H, 6.31; N, 10.56%, Calcd for $C_{18}H_{16}N_2$: C, 83.04; H, 6.20; N, 10.74%. MS 260 (M^+). IR(KBr) 3300 (NH), 2190 (C≡N), 1600 cm^{-1}. ^1H NMR($CDCl_3$) δ 2.00 (s, 3H,CH_3), 4.02 (s, 2H, CH_2), 4.45 (s, 1H, NH), 7.27 (s, 10H, aromatic H). The mother-liquors, after isolation of **2**, were evaporated at room temperature to give the crude **5**. The recrystallization of the crude material from ethanol give pure **5** (3%); mp 134—136 °C. Found: C, 77.48; H, 6.13; N, 4.98%, Calcd for $C_{18}H_{17}NO_2$: C, 77.48; H, 6.13; N, 5.01%. MS 279 (M^+). IR (KBr) 3200 (NH), 1780, 1715 cm^{-1}. ^1H NMR (DMSO-d_6) δ 0.92 (t, J=5 Hz, 3H, CH_3), 1.15 (m, 2H, CH_2), 3.65 (t, J=6 Hz, 1H, CH), 7.25 (m, 10H, aromatic H), 9.13 (bs, 1H, NH).

*Isolation of **4** from the Reduction Mixture of **1** with $LiAlH_4$ in THF.* The reduction was carried out in the same manner used the above reaction. After careful decomposition with water, the solution was concentrated to *ca.* 80 ml. The aqueous solution was extracted with ether; the ether extract was washed with water, dried over anhydrous $MgSO_4$, and filtered. After the removal of the solvent and several recrystallizations from ethyl acetate–hexane, we obtained 0.692 g of **3**. The aqueous solution was allowed to stand at room temperature until crystallization occurred. The recrystallization of the filtered solid product from ethanol gave **4** as colorless crystals in 5% yields; mp 289—291 °C. Found: C, 77.52; H, 6.58; N, 10.05%. Calcd for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.58; N, 10.05%. MS 278 (M^+). IR (KBr) 3300 (NH), 1770, 1700 cm^{-1}. ^1H NMR (DMSO-d_6) δ 0.69 (t, J=7 Hz, 3H, CH_3), 1.52 (m, 2H, CH_2), 4.42 (t, J=7 Hz, 1H, CH), 7.38 (bs, 10H, aromatic H), 6.95 (bs, 1H, NH), 8.05 (bs, 1H, NH).

*Reduction of **3** with Lithium Aluminum Hydride in THF.* A solution of 1.38 g (5 mmol) of **3** in 70 ml of THF was stirres, over a period of 2 h, into a suspension of an excess of $LiAlH_4$ (0.76 g, 20 mmol) in 70 ml of THF at reflux under an atmosphere of nitrogen. After careful decomposition with cold water, the volume of the solution was concentrated to *ca.* 35 ml. To the solution thus obtained we added 10% hydrochloric acid (13 ml). The mixture was allowed to stand overnight to give a yellowish, unreacted material as a solid. The solids were filtered off and recrystallized from ethyl acetate–hexane to give pure **3** (0.75 g). The evaporation of the mother-liquor at room temperature, after the separation of the **3**, gave a solid residue which was fractionally recrystallized from ethyl acetate–hexane to give **4** (13%); mp 289—291 °C. The mother-liquors, after the isolation of **4** were evaporated at room temperature to give the crude **5**. The recrystallization of the crude material from ethanol give pure **5** (8%); mp 134—136 °C.

The authors wish to thank Mr Mitsuo Takayama, Department of Pharmacology, Toho University, for the measurements of the mass spectra.

References

1) S. Akabori, M. Ohtomi, K. Takahashi, Y. Sakamoto, and Y. Ichinohe, *Synthesis*, **1980**, 900.

2) R. B. Moffet, *Org. Synth.*, Coll. Vol. 4, 355 (1963).

3) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," John Wiley and Sons (1967), Vol. 1, p. 592.

4) It is known that an α,β-unsaturated alcohol affords a complex with $LiAlH_4$ which, on decomposition with water, affords saturated alcohol; R. F. Nystrom and W. G. Brown, *J. Am. Chem. Soc.*, **69**, 2548 (1947); **70**, 3738 (1948); R. T. Gilsdorf and F. F. Nord, *J. Org. Chem.*, **15**, 807 (1956). It is also known that the lithium aluminum hydride reduction of the double bond of α,β-unsaturated ketone gave the corresponding saturated ketone; T. G. Halsall and M. Moyle, *J. Chem. Soc.*, **1960**, 1324; T. Anthonsen, P. H. McCabe, R. McCrindle, and R. D. H. Murray, *J. Chem. Soc., Chem. Commum.*, **1966**, 740.

5) F. Baumann, B. Bienert, G. Rasch, H. Vollmann, and W. Wolf, *Angew. Chem.*, **68**, 133 (1956).

6) F. Weygand and R. Mitau, *Chem. Ber.*, **89**, 301 (1955).

7) Compound **5** was also obtained in a 58% yield by the hydrolysis of **4** with dilute hydrochloric acid.