Reactions of 2,3,4-Trichlorothiophene and Tetrachlorothiophene with Ethylmagnesium Bromide. Preparation of Trichloro-2-thienylmagnesium Bromide and 2,5-Bis(Bromomagnesium)-3,4-Dichlorothiophene

M. T. RAHMAN*

Department of Chemistry, Iowa State University, Ames, Iowa 50011 (U.S.A.)

Metal-hydrogen exchange between ethylmagnesium bromide and 2,3,4-trichlorothiophene in THF gives trichloro-2-thienylmagnesium bromide in at least 86% yield. Similarly, metal-halogen exchange between tetrachlorothiophene and ethylmagnesium bromide produces trichloro-2-thienylmagnesium bromide in 84% yield. The reaction of two and a half equivalents of ethylmagnesium bromide with 2,3,4-trichlorothiophene yields a mixture of trichloro-2-thienylmagnesium bromide (40%) and 2,5-bis(bromomagnesium)-3,4-dichlorothiophene (41%). The Grignard reagents were characterised by converting them into the corresponding known trimethylsilyl derivatives and carboxylic acids.

RECENTLY we have reported the reactions of tetrachlorothiophene[1] and 2,3,4-trichlorothiophene[2] with metallic magnesium. Our interest here is to report the reactions of these polychlorothiophenes with ethylmagnesium bromide. The reactions of tetrachlorothiophene with alkyllithium reagents[3,4] and of 3,4-dichlorothiophene with both alkyllithium and -magnesium reagents[5] have been described previously.

Experimental

The reactions were carried out under a positive pressure of dry, oxygen-free nitrogen. The ethereal solvents were dried over sodium-wire and distilled prior to use from sodium-benzophenone ketyl. Magnesium turnings were from the Mallinckrodt Chemical Works. Tetrachlorothiophene - was obtained commercially and used without further purification. IR spectra were determined as mujol mulls using a Perkin-Elmer Model 21 spectrophotometer. Glc analyses were carried out on an F and M Model 500 Gas Chromatograph using a $4' \times \frac{1}{4}''$ column packed with 15% Silicone Gum Rubber on Chromosorb W (60-80 mesh). The yields were based on the starting amounts of 2,3,4-trichlorothiophene and tetrachlorothiophene. The temperatures quoted are uncorrected.

Preparation of 2,3,4-trichlorothiophene :

2,3,4-Trichlorothiophene was prepared as before[2] by the acid hydrolysis of trichloro-2-thienylmagnesium halide[1]. 2,3,4-Trichlorothiophene prepared in this way had the following constants: b.p. 76.5°/10 mm, n_D^{19} 1.5862 (cited[10] : b.p. 209.6°, n_D^{20} 1.5861).

Reaction of 2,3,4-trichlorothiophene and tetrachlorothiophene with ethylmagnesium bromide :

(a) With 1.2 equivalents of ethylmagnesium halide :

To a solution of 2,3,4-trichlorothiophene (2.35 gr, 12.5 m moles) in THF (50 ml) at ca, 35° was added ethylmagnesium bromide[11] (15.0 m moles) in ether (2 ml) over a period of 1 min. After 15-20 minutes of stirring at 35° an aliquot was withdrawn and reacted with an excess of chlorotrimethylsilane. Glc (n-tetradecane as an internal standard) showed that (trichloro-2-thienyl)trimethylsilane[1] was formed in approximately 24% yield. The reaction mixture was further stirred for 8 hr at room temperature (ca. 27°) and the yield of the silylated derivative in a second aliquot was 86%. No 2,5-bis (trimethylsilyl)-3,4-dichlorothiophene or (3,4-dichloro-2-thienyl)trimethylsilane was formed even on a glc detectable amount. Carbonation of the resulting Grignard reagent and subsequent work-up gave trichloro-2-thiophenecarboxylic acid (2.2 gr, 74%), m.p. 224-226° (cited[12] : 224°), identical (mixed m.p. and ir) with a sample prepared by the carbonation of trichloro-2-thienyllithium[3].

Under similar conditions when tetrachlorothiophene was used in place of 2,3,4-trichlorothiophene, the reaction seemed to be complete in 4 hr and the yield by glc (n-tetradecane as an internal standard) of (trichloro-2-thienyl)trimethylsilane was 84%, subsequent to derivatization with chlorotrimethylsilane.

(b) With 2.5 equivalents of ethylmagnesium bromide :

This experiment was conducted exactly as above

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* Present address : Department of Chemistry, University of Dacca, Dacca-2, Bangladesh.

except that in this case 2.5 equivalents of ethyl-magnesium bromide was used and the reaction mixture was stirred at room temperature for 24 hr. Then an excess of chlorotrimethylsilane was added and the mixture stirred for a further period of 12 hr. A glc analysis (with n-tetradecane as an internal standard) indicated that (trichloro-2-thienyl)-tri-methylsilane[1] (40%) and 2,5-bis(trimethylsilyl)-3,4-dichlorothiophene[1] (41%) were formed. There were also formed a few trace products, but these were not identified.

Under essentially similar conditions tetrachloro-thiophene in place of 2,3,4-trichlorothiophene in the above reaction gave (trichloro-2-thienyl)tri-methylsilane and 2,5-bis (trimethylsilyl)-3,4-dichloro-thiophene in 66 and 12% yield, respectively.

Reaction of thiophene with ethylmagnesium bromide :

To thiophene (4.2 gr, 0.8 mole) in THF (100 ml) was added ethylmagnesium bromide (0.96 mole) at room temperature and the mixture was stirred for 65 hr. The reaction products were carbonated and subsequent to work-up in the usual way there was obtained 0.3 gr, (3%) of an acid, m.p. 119-122°. 2-Thenoic acid melts[18] at 126.2 . Mixed m.p. with an authentic sample was 119-123°.

Results and Discussion

2,3,4-Trichlorothiophene (I) (x mole) undergoes a metalation reaction with ethylmagnesium bromide (1.2x mole) in THF to give trichloro-2-thienyl-magnesium halide (II) which subsequent to car-bonation affords trichloro-2-thiophenecarboxylic acid (III) in 74% yield. When the Grignard reagent, II, prepared as above, is treated with chlorotri-methylsilane it gives 2-(trimethylsilyl)trichloro-thiophene in 86% yield. Niether 2,5-bis(trimethyl-silyl)-3,4-dichlorothiophene (V) nor 2-(trimethyl-silyl)-3,4-dichlorothiophene (VI) was detected (by glc) to have been formed.

This indicated that metalation rather than metal-halogen exchange was the predominant course of the reaction. Metal-halogen exchange was, however, observed when tetrachlorothiophene (VII) (x mole) reacted with ethylmagnesium bromide (1.2x mole) in THF giving II which on trimethylsi-lylation gave IV in 84% yield.
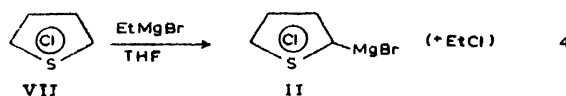

The readiness with which 2,3,4-trichlorothio-phene undergoes nuclear metalation reactions with a Grignard reagent contrasts with the difficulty in metalating thiophene itself. Thus, thiophene under-goes a metalation reaction with RMgX types only to the extent of less than 10% under extreme condi-tions viz. 160-170° for 1.75 hr in dimethylaniline[e], or to the extent of 3% under the conditions in which 2,3,4-trichlorothiophene is 74% metalated. This may indicate that the 5-hydrogen of 2,3,4-trichloro-thiophene is more acidic than either of the two ∝-hydrogens of thiophene. The greater reactivity of the 5-hydrogen of 2,3,4-trichlorothiophene towards RMgX types is probably due to the expected electronic effects of three nuclear chlorine atoms. This behaviour is reminiscent of the facile metalation reactions undergone by polyhalo-benzenes with organolithium reagents[7,8] or by pentafluorobenzene or polychloromethanes with organomagnesium reagents[7,9].

With two and a half equivalents of ethyl-magnesium bromide, tetrachlorothiophene in THF gives, subsequent to chlorotrimethylsilylation, IV and V in 66 and 12% yields, respectively. 2,3,4-Trichlorothiophene under similar conditions gives IV and V in 40 and 41% yields, respectively. The formation of V indicated that the di-Grignard reagent(VIII) was formed in at least 41% yield in the latter reaction.
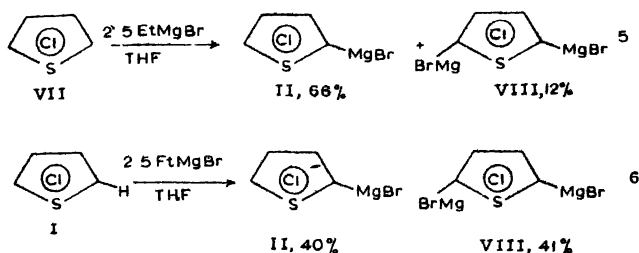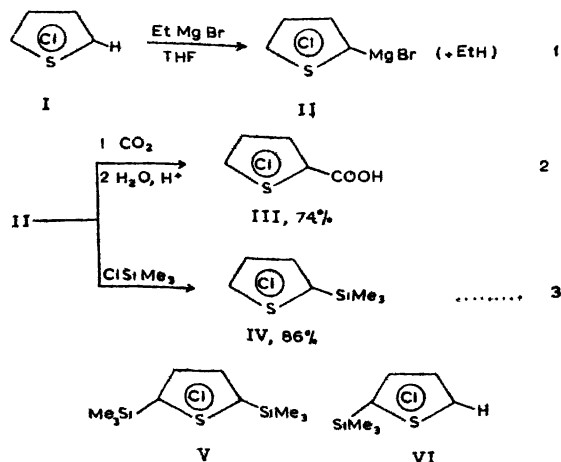
Since the metal-hydrogen exchange reaction is faster than the metal-halogen exchange (see reaction 1), the first step for the formation of the di-Grignard reagent, VIII, from I should be as described by reaction 1. The second step should be reaction 7 regardless of whether II is formed by reaction 1 or 4.
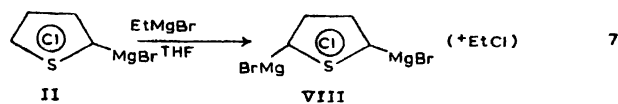
The lower yield of VIII *via* reaction 5 (i.e., steps 4 and 7) as compared to that *via* 6 (*i.e.*, steps 1 and 7) is probably because a large part of ethylmagnesium bromide is removed from the system by the latter's reaction with ethyl chloride under the reaction conditions. Ethyl chloride would be expected to be formed as one of the products in reactions 4 and 7. On the other hand, when VIII is formed *via* reaction 6, ethane is expected to be formed in the 1st step of the reaction (*i.e.*, reaction 1). Since ethane does not react with ethylmagnesium bromide, a large part of the remaining unreacted ethylmagnesium bromide should be available for reaction *via* pathway 7 to give the observed increased yield of VIII (in reaction 6).

The metal-halogen exchange of VII *via* reaction 4 is complete within 4 hr whereas that of II *via* reaction 7 is a much slower process and is largely incomplete even after 24 hr. This may indicate that the introduction of a — MgBr group in the thiophene nucleus deactivates the ring towards further Grignardation. This could explain why previous attempts[1] to prepare the di-Grignard reagent, VIII, were unsuccessful.

In conclusion we would like to emphasize that the reaction between ethylmagnesium bromide and 2,3,4-trichlorothiophene or between ethylmagnesium bromide and tetrachlorothiophene may serve as alternative[1] methods for the preparation of trichloro-2-thienylmagnesium halide. The reaction between 2.5 equivalents of ethylmagnesium bromide and one equivalent of 2,3,4-trichlorothiophene or tetrachlorothiophene to give the di-Grignard reagent, VIII, does not seem to have much synthetic utility for two reasons. Firstly, the yield of the di-Grignard reagent is poor. Secondly, in the reaction mixture, in addition to VIII, there will be present two other Grignard reagents which might be disadvantageous in ordinary synthetic work.

Acknowledgement

References

1. M. T. Rahman, M. R Smith, Jr., A. F. Webb and H. Gilman, *Organometal. Chem. Syn.*, 1970-1971, 1, 105.

2. M. T. Rahman and H. Gilman, *J. Indian Chem. Soc.*, 1976, 53, 269.

3. Milton R. Smith Jr. and Henry Gilman, *Organometal. Chem. Syn.*, 1971, 1, 265.

4. M. R. Smith Jr., M. T. Rahman and H. Gilman, *Organometal. Chem. Syn.*, 1971, 1, 295 ; I. Haiduc and H. Gilman, *Rev. Roum. Chim.*, 1970, 16, 805.

5. M. T. Rahman and H. Gilman, *J. Indian Chem. Soc.*, 1976, 53, 582.

6. F. Challenger and G. M. Gibson, *J. Chem. Soc.*, 1940, 305.

7. R. J. Harper, Jr., E. J. Soloski and C. Tamborski, *J. Org. Chem.*, 1964, 29, 2385.

8. C. Tamborski, E. J. Soloski and C. E. Dills, *Chem. Ind. (London)*. 1965, 2067 ; C. Tamborski and E. J. Soloski, *J. Organometal Chem.*, 1969, 20, 245.

9. H. Normant and J. Villieras, *Compt. Rend.*, 1965, 260, 4535. J. Villieras, *Compt. Rend.*, 1965, 261, 1876 ; T. Curvieigny and H. Normant, *Bull. Soc. Chim. Fr.*, 1964, 2000.

10. H. L. Coonradt, H. D. Hartough and G. C. Johnson, *J. Amer. Chem. Soc.*, 1948, 70, 2564.

11. A. I. Vogel, "A Text Book of Practical Organic Chemistry, 3rd Ed., Longmans, London, 1948, p. 258.

12. W. Steinkopf, H. Jacob and H. Penz, *Justus Liebigs Ann. Chem.*, 1934, 512, 136.

13. M. G. L. Voerman, *Recl. Trav. Chim. Pays-Bas*, 1907, 26, 297.