"CROSS-COUPLING" OF 2-CHLOROBENZOTHIAZOLE WITH BENZOTHIAZOLYLALKYL-MAGNESIUM BROMIDE: SYNTHESIS OF BIS(2-BENZOTHIAZOLYL)ALKANES

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Abstract - Bis(2-benzothiazolyl)alkanes have been prepared via cross-coupling of 2-chlorobenzothiazole with benzothiazolylalkylmagnesium bromide.

As reported in a previous paper, 2-halogenobenzothiazoles are reluctant to undergo "cross-coupling" reaction with alkyl and aryl Grignard reagents. For such a reaction nickel-complex activated Grignard reagents must be used. However, we recently have also disclosed that allylic Grignard reagents give clean "cross-coupling" with some 2-heterosubstituted benzothiazoles. Metallated species of the type (A), easily available from 2-alkylbenzothiazoles, are considered to be as aza-allyl organometallic reagents. Therefore we reasoned that they could be used for the "cross-coupling" with 2-chlorobenzothiazole to give the bis(2-benzothiazolyl)alkanes, which are useful fluorimetric reagents and lubricating oil antioxidants. Bis(2-benzothiazolyl)alkanes are normally prepared from o-aminobenzenethiol and dicarboxylic acids in polyphosphoric acid at 150°C.

Reflux the 2-methylbenzothiazole 1a (1 mole) overnight with 2-chlorobenzothiazole (1 mole) in tetrahydrofuran (THF) in the presence of n-butylmagnesium bromide (1.5 moles), and quenching with aqueous ammonium chloride afforded a mixture of some unreacted 1a and a new product that was characterised as the "cross-coupling" compound 3a. In a similar fashion 2-alkylbenzothiazoles 1b-f reacted with 2-chlorobenzothiazole and n-BuMgBr providing satisfactory yields of the bis(2-benzothiazolyl)alkanes 3b-f. In all cases appreciable amounts of the unreacted starting 2-alkylbenzothiazole were recovered.

It appears to be likely that the formation of the above-mentioned bis(2-benzothia-
azolylalkylmagnesium bromide 2, which, as aza-allyl Grignard reagent, may add to the C-N double bond of the 2-chlorobenzothiazole to give the benzothiazolebenzothiazoline derivatives 5 via the six-membered cyclic transition state 6 according to a $S_{E}$-like mechanism. Subsequent elimination would produce the cross-coupled products 3, as shown in the Scheme.

In accordance with the mechanism is the fact mentioned above that part of the starting material 2-alkylbenzothiazole is recovered unchanged. This is likely due to the competitive reversible condensation of 2 with 1. The condensation product, as reported, slowly goes back to the starting alkylbenzothiazole 1 during the workup of the reaction mixture.
It is worthy to note that some of the bis(2-benzothiazoly1)alkanes 3 in deuteriochloroform (CDCl₃) have been found to convert slowly to the enamine forms 4. The tautomers can be separated and isolated by column chromatography.

In summary, this paper describes a mild and new route to the useful bis(2-benzothiazoly1)alkanes 3 starting from easily or commercially available 2-alkylbenzothiazoles and 2-chlorobenzothiazole under basic conditions using n-BuMgBr.

EXPERIMENTAL

Reaction of 2-chlorobenzothiazole with 2-alkylbenzothiazole 1 and n-BuMgBr.

General procedure.

The reaction of 1a is described as an example. A THF solution of 0.87 N n-BuMgBr (8.7 ml, 7.5 mmole) was added dropwise to a stirred solution containing 1a (0.75 g, 5.01 mmole) and 2-chlorobenzothiazole (0.852 mmole) in 50 ml of dry tetrahydrofuran. The reaction mixture was refluxed until the disappearance of 2-chlorobenzothiazole (~8 h) and then cooled to room temperature and quenched with an aqueous solution of ammonium chloride. Extraction with ether (3 x 30 ml), drying over MgSO₄ and removal of the solvent under reduced pressure left a solid residue that was crystallised from petroleum ether (60-80°C boiling fraction) to give the bis(2-benzothiazoly1)methane 3a. IR, ¹H- and ¹³C-NMR and physical data for 3a-e and 4a-e are given in ref. 10.

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REFERENCES

8) The bis(2-benzothiazoly1)phenylmethane 3f was obtained as the enamine form 4f.
All of the products gave satisfactory elemental analysis. Yields are based on the converted 2-alkylbenzothiazole.

3a: yield 55%; mp 96-97°C from ethanol (lit. 96-97°C see ref. 9); $^1$H-NMR (CDCl$_3$, TMS int.), δ 5.0 (s, 2H), 7.4-8.3 (m, 8H); $^{13}$C-NMR (CDCl$_3$), δ 38.9, 121.6, 123.1, 125.3, 126.2, 135.8, 153.1, 165.6.

3b: yield 45%; oil; $^1$H-NMR (CDCl$_3$, TMS int.), δ 2.1 (d, 3H, J = 7 Hz), 5.2 (q, 1H, J = 7 Hz), 7.2-8.5 (m, 8H).

Tautomers 3b and 4a were separated by column chromatography on silica gel using acetone/petroleum ether (1:1) as eluent.

3c: yield 28%; oil; $^1$H-NMR (CDCl$_3$, TMS int.), δ 1.1 (t, 3H), 2.1-2.8 (m, 2H), 4.85 (t, 1H), 7.2-8.1 (m, 8H); $^{13}$C-NMR (CDCl$_3$), δ 12.2, 29.6, 51.5, 121.6, 123.2, 125.1, 126.1, 135.3, 151.9, 170.8.

3d: yield 48%; mp 132-134°C from ethanol; $^1$H-NMR (CDCl$_3$, TMS int.), δ 2.1 (s, 6H), 7.2-8.0 (m, 8H); $^{13}$C-NMR (CDCl$_3$), δ 29.4, 47.5, 121.5, 123.2, 125.1, 126.0, 135.5, 152.9, 176.6.

Tautomers 3d and 4b were separated by column chromatography on silica gel using acetone/petroleum ether (1:1) as eluent.

3e: yield 38%; oil; $^1$H-NMR (CDCl$_3$, TMS int.), δ 1.9 (t, 3H), 1.1-1.6 (m, 2H), 2.4 (q, 2H), 4.9 (t, 1H), 7.0-8.0 (m, 8H); $^{13}$C-NMR (CDCl$_3$), δ 14.0, 20.8, 38.2, 49.7, 121.6, 123.1, 125.2, 126.1, 135.3, 153.0, 171.0.

4a: yield 28%; oil; ir (NaCl), 3490 cm$^{-1}$ (NH); $^1$H-NMR (CDCl$_3$, TMS int.), δ 1.0 (t, 3H), 2.6 (q, 2H), 5.7 (s, 1H, exchange with D$_2$O), 7.2-8.1 (m, 8H); $^{13}$C-NMR (CDCl$_3$), δ 6.8, 36.1, 78.9, 121.0, 122.2, 124.4, 125.2, 135.2, 151.5, 174.2.

4b: yield 35%; oil; ir (NaCl), 3480 cm$^{-1}$ (NH); $^1$H-NMR (CDCl$_3$, TMS int.), δ 0.9 (t, 3H), 1.1-1.6 (m, 2H), 2.5 (t, 2H), 5.5 (s, 1H, exchange with D$_2$O), 7.1-8.0 (m, 8H); $^{13}$C-NMR (CDCl$_3$), δ 14.0, 16.8, 45.9, 79.6, 121.8, 123.1, 125.2, 126.1, 136.1, 152.3, 175.2.

4c: yield 65%; mp 148.5-149.5°C from ethanol; ir 3380 cm$^{-1}$ (NH); $^1$H-NMR (CDCl$_3$, TMS int.), δ 6.3 (s, 1H, exchange with D$_2$O), 7.3-8.3 (m, 13H); $^{13}$C-NMR (CDCl$_3$), δ 80.1, 121.8, 123.4, 126.1, 126.6, 128.5, 128.7, 136.1, 142.4, 152.2, 174.6.

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