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

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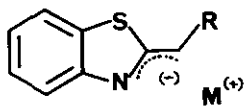
Abstract - Bis(2-benzothiazolyl)alkanes have been prepared via cross-coupling of 2-chlorobenzothiazole with benzothiazolylalkylmagnesium bromide.

As reported in a previous paper[1] 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.[2]

Metallated species of the type (A), easily available from 2-alkylbenzothiazoles,[3,4] 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 3, which are useful fluorimetric reagets[5] and lubricating oil antioxidants.[6] Bis(2-benzothiazolyl)alkanes are normally prepared from o-aminobenzenethiol and dicarboxylic acids in polyphosphoric acid at 150°C.[7]

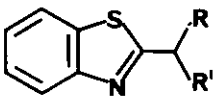


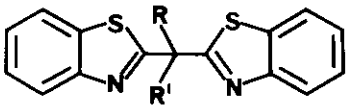
(A)

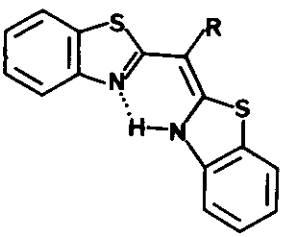
Reflux the 2-methylbenzothiazole 1a (1 mole) overnight with 2-chlorobenzothiazole (1 mole) in tetrahydrofuran (THF) in the presence of n-butylmagnesium bromide (1.5 moles), and quenching with aqueous ammonium chloride afforded a mixture of some *unreacted 1a and a new product that was characterised as 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.[8] In all cases appreciable amuonts of the unreacted starting 2-alkylbenzothiazole were recovered.

It appears to be likely that the formation of the above-mentioned bis(2-benzothi-

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_Ei'-like mechanism.[9] Subsequent elimination would produce the cross-coupled products 3, as shown in the Scheme.





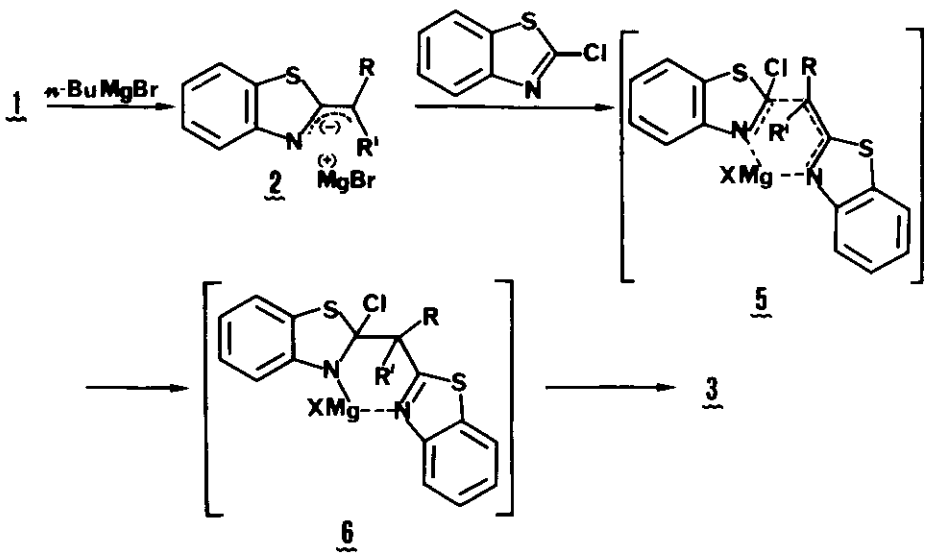


1a: R = R' = H
1b: R = H; R' = Me
1c: R = H; R' = Et
1d: R = R' = Me
1e: R = H, R' = Pr^n
1f: R = H; R' = Ph

3a: R = R' = H
3b: R = H; R' = Me
3c: R = H; R' = Et
3d: R = R' = Me
3e: R = H; R' = Pr^n
3f: R = H; R' = Ph

4a: R = Et
4b: R = Pr^n
4c: R = Ph

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,[9] 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-benzothiazolyl)alkanes 3 in deuteriochloroform ($CDCl_3$) 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-benzothiazolyl)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 $MgSO_4$ 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-benzothiazolyl)-methane 3a. IR, ^1H- and ^{13}C-NMR and physical data for 3a-e and 4a-e are given in ref. 10.

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REFERENCES

1) F. Babudri,S. Florio, L. Ronzini, and M. Aresta, Tetrahedron, 39, 1515 (1983).
2) S. Florio, E. Epifani, and G. Ingrosso, Tetrahedron, 40, 4527 (1984).
3) E.J. Corey and D.L. Boger, Tetrahedron Lett., 5 (1978).
4) F. Babudri, F. Ciminale, and S. Florio, Tetrahedron Lett., 25, 2051 (1984).
5) R. Douglas Earl and B.K. Afghan, Anal. Chim. Acta, 44, 115 (1969); R.R. Trenholm and D.E. Ryan, ibid., 32, 317 (1965).
6) C. Rai and J.B. Braunwarth, Chem. Abstr., 62, 1500e (1965).
7) J.J. D'Amico, J. Org. Chem., 26, 3434 (1961).
8) The bis(2-benzothiazolyl)phenylmethane 3f was obtained as the enamine form 4c.
9) E.A. Hill, J. Organomet. Chem., 91, 123 (1975).

10) 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 3c and 4a were separated by column chromatography on silica gel using acetone/petroleum ether (1/9) 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.

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_2O), 7.2-8.1 (m, 8H); ^{13}C-NMR (CDCl), δ 6.8, 36.1, 78.9, 121.0, 122.2, 124.4, 125.2, 135.2, 151.5, 174.2.

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 3e and 4b were separated by column chromatography on silica gel using acetone/petroleum ether (1/4) 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.

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_2O), 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_2O), 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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