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REACTIONS OF SODIUM CYANOBOROHYDRIDE WITH BENZOTHIAZOLIUM AND Δ^2-THIAZOLINIUM CATIONS. FORMATION OF BENZOTHIAZOLINES, THIAZOLIDINES AND STABLE THIAZABOROLES

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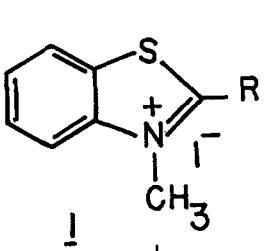
Abstract - Sodium cyanoborohydride reduction of benzothiazolium 1 and Δ^2-thiazolinium 2 cations give benzothiazolines 3 and thiazolidines 5 alongwith [[o-(disubstituted amino) phenyl] and 2-(dialkylamino) ethyl] thio] boranecarbonitriles (N-B) 4 and 6. Because of the heterocyclic structures formed through N→B coordination and consequent chirality, the latter species constitute mixtures of two diastereomers which are exceptionally stable to acid and base.

INTRODUCTION

The potential of benzothiazoline 3[1,2] and thiazolidine 5[3] derivatives as synthetic intermediates has prompted investigations on their procurement through reduction of benzothiazolium 1 and thiazolinium 2 cations, because the latter undergo a myriad of transformations at C-2 substituents[1,3a-c,4]. Sodium borohydride reductions of 1[1,5c] and 2[3c,5a,b] have quite often been accompanied by reductive cleavages to mercaptoethylamine[6] and o-aminothiophenol[5c,7] derivatives. Sodium cyanoborohydride[8], a mild reagent used for selective reduction of $>C=\overset{+}{N}<$ has not been employed for reduction[9] of the cations 1 and 2. Here, we report that 1 and 2 with sodium cyanoborohydride furnish the reduced products 3 and 5 alongwith [[o-(disubstituted amino) phenyl] and 2-(dialkylamino) ethyl] thio] boranecarbonitriles (N-B) 4 and 6 which exhibit N→B coordination and existence of an unprecedented heterocyclic structure (Scheme 1).



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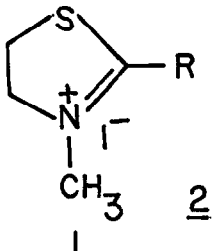
1a R = H
1b R = CH_3
1c R = C_6H_5

2a R = CH_3
2b R = C_6H_5



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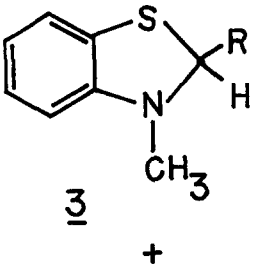

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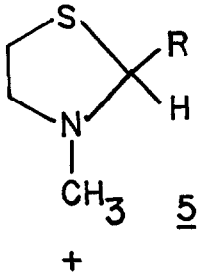
3a R = H
3b R = CH_3
3c R = C_6H_5

5a R = CH_3
5b R = C_6H_5



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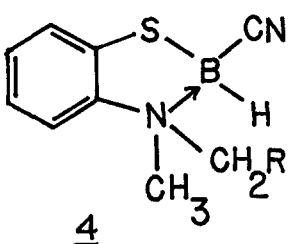
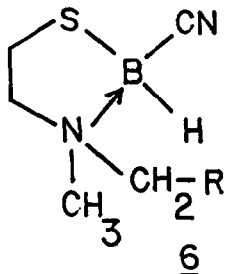
+



4

4a R = H
4b R = CH_3
4c R = C_6H_5

6a R = CH_3
6b R = C_6H_5



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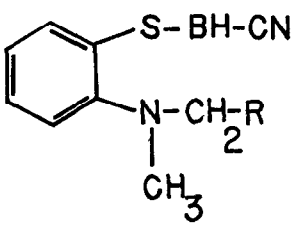

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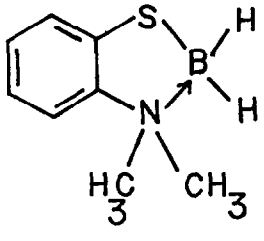

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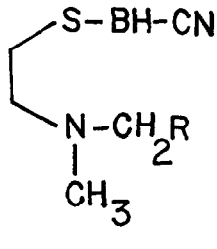


8

SCHEME 1

RESULTS AND DISCUSSION

Sodium cyanoborohydride reduction of 3-methylbenzothiazolium iodide 1a in anhydrous acetonitrile at various reaction temperatures formed 3-methylbenzothiazoline 3a (Table) and a product, m.p. 75°C. The latter was stable to both aqueous hydrochloric acid and sodium hydroxide and its i.r. spectrum showed absorptions at ν_{max} 2420, 2330 (B-H)[10,11a,b], 2150(C≡N) and 730-750 (B-N)[11c] cm^{-1}. Its molecular weight (M^+, 190) and elemental analysis indicated a molecular formula $C_9H_{11}BN_2S$. ^1H n.m.r. spectrum showed two singlets for methyl groups at δ 3.1 and 3.25, and in the ^{13}C n.m.r. spectrum also two methyl carbons appeared at different chemical shifts (δ 48.0 and 51.0) but cyano carbon could not be observed[12]. ^{11}B n.m.r. exhibited a doublet at δ -5.3 (J B-H = 124.5 Hz) depicting a tetrahedral geometry[13,14] around the boron atom. These data could be explained by the structure [[o-(dimethylamino)phenyl]thio]boranecarbonitrile (N-B) involving a nitrogen-boron coordination and formation of a heterocyclic structure 4a with a stable chiral boron atom and two diastereotopic N-methyl signals. The absence of any signal for tricoordinated boron in ^{11}B n.m.r. spectrum indicated that the tautomer 7, if present was in low concentration. Sodium borohydride reduction of 1a did not give 9 and formed o-(N,N-dimethylamino) thiophenol[15].

Table Reactions of benzothiazolium 1/thiazolinium 2 cations with sodium cyanoborohydride

1,2	Product(s)	Time of reaction(h)	Yield(%)[b](isolated)	
			3	4
1a	3a[a], 4a	4-5	41	47
1b	3b[a], 4b	4-5	34	43
1c	3c[a,c]	4	75	e
			5	6
2a	5a, 6a	3-5	25[d]	50
2b	5b, 6b	3	25[d]	55

a-Compared with authentic samples, b-On using CH_3OH or by running the reactions at -5°, or 0° or r.t. or under reflux no significant change was observed, c-Traces of 2-phenylbenzothiazole detected (tlc), d-Characterised by ^1H nmr, unstable in air, e-4c was not formed.

Even on using an excess of sodium cyanoborohydride in the reduction of 1a, only 3a and 4a were formed and 3a as such was also stable towards sodium cyanoborohydride. Consequently, formation of 4a did not involve

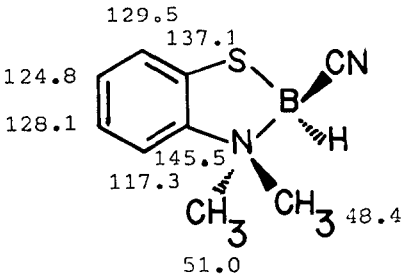
reaction of sodium cyanoborohydride with 3a. Monitoring of progress of reduction (t.l.c. and ^{1}H n.m.r.), showed initial formation of 3a, followed by 4a. Based on these observations, we argued that cyanoborane generated *in situ* during reduction of benzothiazolium cation to benzothiazoline 3, might be reacting with 3a to give 4a, in a manner analogous to the reactions of borane with benzothiazolines[13] or benzothiazoles where also ring cleavage and alternate ring formation[14] takes place. This mode of reaction is corroborated by the formation of 4a in the reactions of 3a performed with polymeric cyanoborane[10]. The extraordinary stability of 4a might be attributed to the presence of CN group which would make boron atom soft enough to form a strong bond with soft S and through electron withdrawl also facilitate coordination of N to B.

2,3-Dimethylbenzothiazolium iodide 1b and sodium cyanoborohydride furnished, 2,3-dimethylbenzothiazoline 3b and [[o-(ethylmethylamino)phenyl] thio]boranecarbonitrile (N-B) 4b (M^+, 204). The latter on t.l.c. showed two closely placed spots which could not be isolated. The ^{1}H n.m.r. of this mixture showed double signals each for N-CH_3 (δ 3.0 and 3.2) and N-CH_2CH_3 (t, 1.25, 1.29 and q, 3.5, 3.52), and in ^{13}C n.m.r. spectrum each carbon exhibited two signals. Evidently, the two constituents of the mixture are diastereomers due to two chiral centers at B and N.

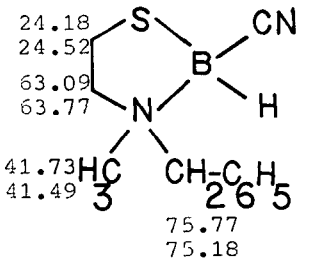
A variable temperature ^{1}H n.m.r. experiment with compound 4b (in DMSO-d_6) did not show coalescence of the signals for the methyl or ethyl groups in the mixture of diastereomers[16] A and B, (see Scheme 2), upto 185°C. Only some shifting of the signals, approaching each other, was observed. These results indicate that the energy of the ring opened form >24 Kcal above that of cyclised. Furthermore, the diasteromeric ratio remains constant even at 185°C. These facts show the high stability of the boron heterocycles depicted here.

1c with sodium cyanoborohydride furnished 2-phenyl-3-methylbenzothiazoline 3c alongwith traces of 2-phenylbenzothiazole. The lack of formation of 4c may be attributed to stability of 3c and its nonreactivity towards cyanoborane.

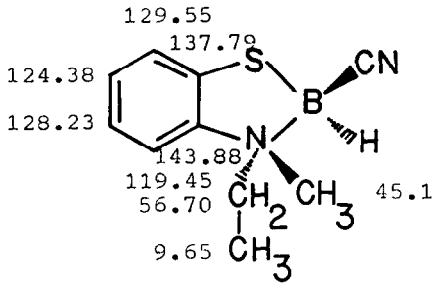
2,3-Dimethyl- Δ^2-thiazolinium iodide 2a and 2-phenyl-3-methyl- Δ^2-thiazolinium iodide 2b with $NaCNBH_3$ furnished 2,3-dimethylthiazolidine 5a and 2-phenyl-3-methylthiazolidine 5b alongwith [[2-(methylamino)ethyl]thio] boranecarbonitrile (N-B) 6a and [[2-(benzylmethylamino)ethyl]thio]borane-carbonitrile (N-B) 6b. The latter 6a, 6b again existed as heterocyclic species and mixtures of two diastereomers are evident from their spectral data (vide experimental).



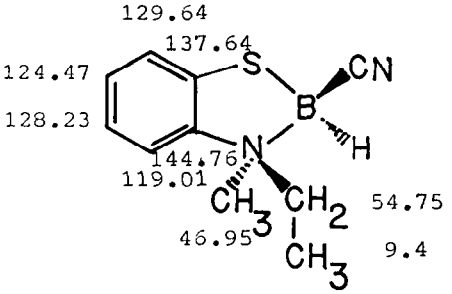
4a



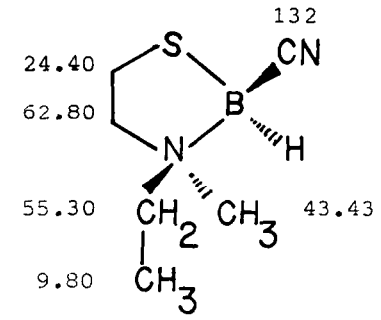
6b



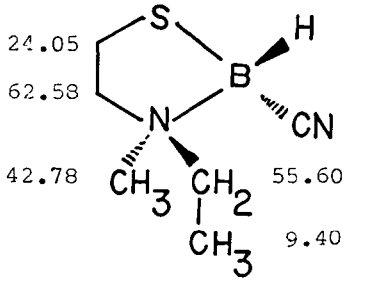
4b Isomer A 60%



4b Isomer B 40%



6a Isomer A 55%



6a Isomer B 45%

SCHEME 2

Taking advantage of the sensitivity of ^{13}C n.m.r. to steric effects, it was possible to deduce the configuration at boron and nitrogen of the mixture of 4b and 6a and to assign the signals of compounds 4a, 4b, 6a and 6b, as shown in Scheme 2.

Thus, $NaCNBH_3$ smoothly reduces $>C=\overset{+}{N}<$ of benzothiazolium and Δ^2-thiazolinium cations to their dihydroderivatives. The latter unlike with sodium borohydride are not reductively cleaved with sodium cyanoborohydride but cyanoborane generated *in situ* reacts with benzothiazolines or thiazolidines to form a stable thiazaborole type species.

EXPERIMENTAL

^1H n.m.r. spectra were recorded on a JEOL JNM PMX 60 MHz instrument. ^{13}C and ^{11}B n.m.r. were recorded on varian XL-100A (32.1 MHz) and JEOL FX-90Q (28.69 MHz) instruments using Me_4Si and $BF_3.Et_2O$ as standards. Mass spectra were obtained on a VG Micromass 7070 F instrument. I.r. spectra were recorded as KBr disc or neat film on Hungarian Spectromom 2000 and PYE UNICAM SP3-300 instruments.

1,3-Benzothiazolium and thiazolinium cations 1/2

3-Methylbenzothiazolium iodide 1a[2e], 2,3-dimethylbenzothiazolium iodide 1b[17], 3-methyl-2-phenylbenzothiazolium iodide 1c[18], 2,3-dimethyl-Δ^2-thiazolinium iodide 2a[19], and 3-methyl-2-phenyl-Δ^2-thiazolinium iodide 2b[5b] were prepared by reported methods.

General procedure for the reactions of 1 and 2 with $NaCNBH_3$

To a stirred suspension of 1 or 2 (0.01 mol) in anhydrous acetonitrile (dried over P_2O_5)(20-25 ml) at -5^oC, sodium cyanoborohydride (Aldrich) (0.0175 mol) was added portionwise. It was stirred for an additional period at the same temperature till the reaction was completed (t.l.c.). Water was added and the aqueous solution extracted with chloroform (3x50ml). Combined chloroform extracts were washed with cold water (2x50 ml), dried over anhydrous Na_2SO_4, concentrated and the residue chromatographed over silica gel G (60-120 mesh) using hexane, benzene, ethylacetate or their mixtures as eluents. The products formed are listed.

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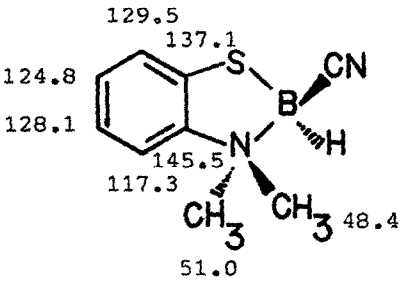
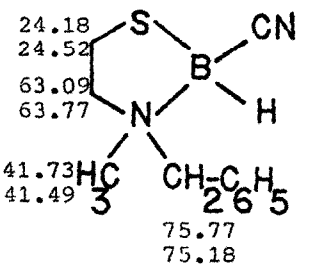
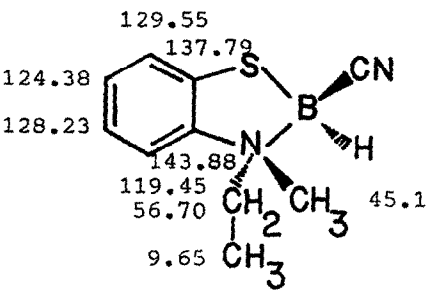
(b)-[[o-(Dimethylamino)phenyl]thio]boranecarbonitrile(N-B) 4a : m.p. 75^oC (hexane-benzene); R_f 0.55 (benzene/ethyl acetate : 10/4); IR(KBr) 2420,



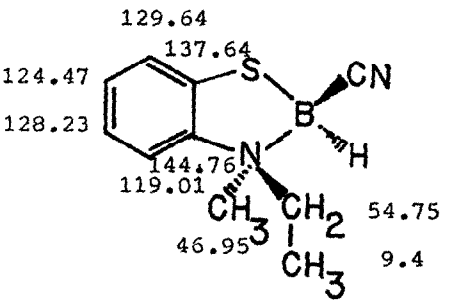
4a



6b



4b Isomer A 60%



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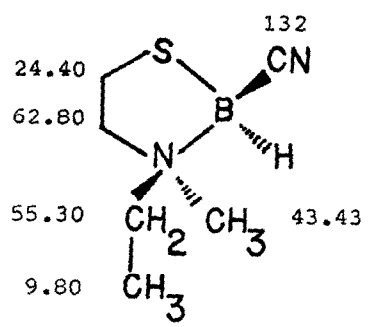
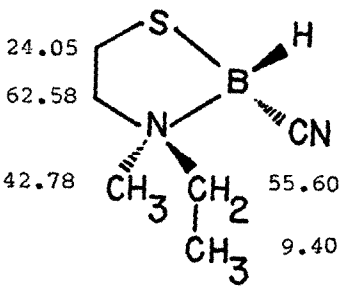


6a Isomer A 55%



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2330 (B-H), 2150(C≡N), 730-750(B-N) cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.1(3H, $N-CH_3$,s), 3.25(3H,$N-CH_3$,s), 7.1-7.55(4H, Ar-H,m); ^{13}C NMR ($CDCl_3$): δ 48.45, 50.99($N-CH_3$), 117.30, 124.78, 128.08, 129.54, 137.07 and 145.53, CN was not observed; ^{11}B NMR ($CDCl_3$): δ -5.3(d,J B-H=124.5Hz); Mass: $M^{+\cdot}$ m/z 190 (Found: C, 56.61; H, 5.67. $C_9H_{11}BN_2S$ requires C, 56.84; H, 5.78%).

Reduction of 1b: (a) - 2,3-Dimethylbenzothiazoline 3b : Oil[20b], R_f 0.3 (hexane); IR(neat): 3100, 2900, 1612 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.60(3H, CH_3, d, J = 6Hz), 2.85(3H, CH_3, s), 4.95(1H, CH, q, J = 6Hz), 6.00-7.90(4H, Ar-H, m); Mass: $M^{+\cdot}$ m/z 165.

(b)- [[o-(Ethylmethylamino)phenyl]thio]boranecarbonitrile(N-B) 4b: Oil, R_f 0.53 (benzene/ethyl acetate: 10/3); IR (neat): 2470, 2370, 2350 (B-H), 2247(C≡N), 750(B-N) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.25, 1.29(3H, CH_3, two triplets, J = 7Hz), 3.0, 3.2(3H, NCH_3 two singlets), 3.5(2H, CH_2, two quartets, J = 7Hz), 6.85-7.5(4H, Ar-H, m); ^{13}C NMR($CDCl_3$): δ 9.41/9.65 (CH_3), 45.10/46.95 ($N-CH_3$), 54.75/56.70(CH_2), 119.01/119.45, 124.37/124.47, 128.23, 129.54/129.64, 137.64/137.78, 143.88/144.75,CN was not observed; ^{11}B NMR ($CDCl_3$): δ -6.3(B-H , d, J B-H = 121.6Hz); Mass: $M^{+\cdot}$ m/z 204.

Reduction of 1c : 3-Methyl-2-phenylbenzothiazoline 3c : m.p. 115°C (acetonitrile)[21], R_f 0.73 (benzene); IR(KBr): 3100, 2900, 1610 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.30(3H, $N-CH_3$,s), 5.65(1H, CH, s), 6.00-7.50(9H, Ar-H, m).

Reduction of 2a :(a) - 2,3-Dimethylthiazolidine 5a: Oil, R_f 0.45(benzene/ethyl acetate : 10/4); IR(neat): 3200, 2850 cm^{-1}; ^1H NMR($CDCl_3$); δ 1.5(3H, CH_3, d, J = 6Hz), 2.65(3H, NCH_3, s), 2.8-3.7 (4H, 2xCH_2, m), 4.6(1H, CH, q, J = 6Hz).

(b)-[[2-(Ethylmethylamino)ethyl]thio]boranecarbonitrile(N-B) 6a: Oil, R_f 0.5 (ethyl acetate); IR(neat): 2460(B-H), 2220(C≡N), 720, 770(B-N)cm^{-1}; ^1H NMR($CDCl_3$): δ 1.34, 1.4(3H, CH_3, two triplets, J = 7Hz, 2.8, 2.9(3H, $N-CH_3$, two singlets), 2.5-3.0(4H, 2xCH_2, m), 3.24(2H, CH_2, two quartets, J = 7Hz); ^{13}C NMR($CDCl_3$): δ 9.40/9.79(CH_3), 24.05/24.40(CH_2), 42.77/43.42, ($N-CH_3$), 55.30/55.60(CH_2CH_3), 62.58/62.79(CH_2), 132 (br, CN); ^{11}B NMR ($CDCl_3$): δ -8.46(B-H, d, J B-H = 117.22 Hz); Mass: $M^{+\cdot}$ m/z 156.

Reducation of 2b: (a) - 3-Methyl-2-phenylthiazolidine 5b: Oil, R_f 0.39 (benzene); IR(neat): 2900 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.2(3H, NCH_3, s), 2.6-3.5(4H, 2xCH_2,m), 4.8(1H, CH, s), 7.0-8.0(5H, Ar-H, m).

(b)-[[2-(Benzylmethylamino)ethyl]thio]boranecarbonitrile (N-B)6b : Oil, two spots on tlc, R_f 0.33, 0.57 (benzene/ethyl acetate: 10/4); IR(neat):

2440 (B-H), 2200 (C≡N), 725-760(B-N) cm^{-1}; ^1H NMR($CDCl_3$): δ 2.7, 2.85(3H, N-CH_3, two singlets), 2.8-3.5(4H, 2xCH_2, m), 4.3, 4.4(2H, N-$CH_2C_6H_5$, two singlets), 7.1-7.85(5H, Ar-H, m); ^{13}C NMR($CDCl_3$): δ 24.18/24.52(S-CH_2), 41.49/41.73(N-CH_3), 63.09/63.77(N-CH_2), 75.18/75.77($CH_2C_6H_5$); ^{11}B NMR ($CDCl_3$): δ -7.0(B-H, d, J B-H = 127.5Hz); Mass: $M^{+\cdot}$ m/z 218.

Reaction of cyanoborane and 3a

A solution of 3a (500 mg) in anhydrous acetonitrile (7ml) was added with stirring at ambient temperature to acetonitrile solution of polymeric cyanoborane obtained from sodium cyanoborohydride (1g)[10]. After 24 hrs, water (20 ml) was added and mixture was extracted with chloroform (2x40 ml). The extract was dried (anhydrous Na_2SO_4), solvent was removed and residue was chromatographed over silica gel G (60-120 mesh) using benzene/ethyl acetate (90/10) as eluent to isolate 4a (188 mg, 30%) identical (i.r., n.m.r., mmp.) with authentic sample.

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