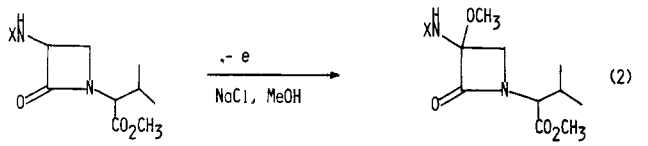
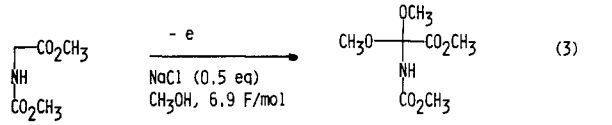


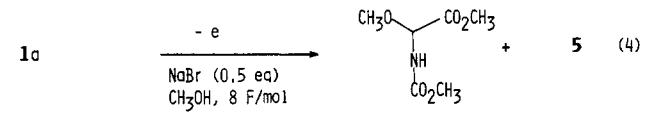
3a : X = CO_2CH_3 **4a** : 92 % (4.3 F/mol)
3b : X = CO_2CH_2Ph **4b** : 30 % (4.0 F/mol)

Although the oxidation of **1a** using NaCl resulted in the formation of α,α-dimethoxylated product (**5**) (eq 3),[7] the

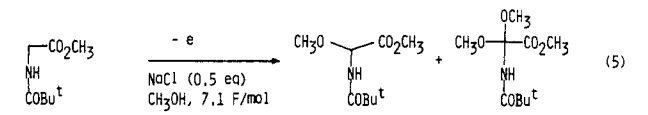


1a **5** 95 %

preparation of an α-monomethoxylated product (**2a** or **7**) could be accomplished by the use of NaBr (eq 4) or by changing the structure of the substrate from carbamate to bulky amide (**6**) (eq 5).[7]



2 66 % 26 %

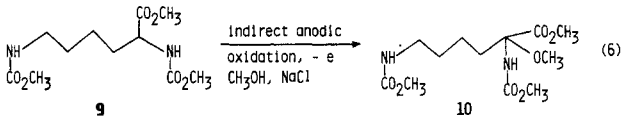


6 **7** 86 % **8** 11 %

The reaction conditions for this anodic α-methoxylation are simple and mild as exemplified below.

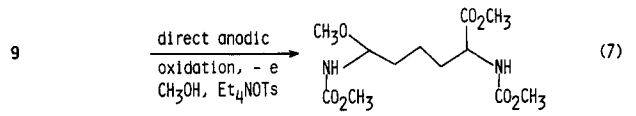
Into a cell equipped with platinum plate electrode (2 × 2 cm) was added a solution of *N*-(carbomethoxy)alanine methyl ester (**1b**) (4 mmol) in methanol (30 mL) containing sodium chloride (0.4 mmol). After a constant current of 0.1 A (terminal voltage 15 V) was passed through the solution for 10.8 h (10 F/mol of electricity) with external cooling in an ice–water bath, the solvent was removed in vacuo without heating and water was added to the residue. This mixture was extracted with CH_2Cl_2, and the extracts were dried with $MgSO_4$. Evaporation of CH_2Cl_2 gave *N*-(carbomethoxy)-α-methoxyalanine methyl ester (**2b**) as crystals (mp 94–95 °C) in 89% yield.

At least two mechanisms are conceivable for this α-methoxylation: (i) direct anodic oxidation of **1** and (ii) indirect oxidation of **1** with some oxidizing reagent anodically generated in situ. The anodic methoxylation of carbamates of aliphatic primary and secondary amines in methanol using tetraethylammonium *p*-toluenesulfonate (TEATS) as a supporting electrolyte has been shown[8] to proceed through the direct oxidation pathway. The transformation of **1b** to **2b**, however, was negligible under these conditions when using TEATS or sodium acetate as a supporting electrolyte (runs 10 and 11), whereas the methoxylation proceeded successfully in the presence of an alkali metal chloride or bromide. These facts suggest that **1** was oxidized indirectly by some active species such as Cl^+ (Br^+) or CH_3OCl (CH_3OBr)[9] that was generated by anodic oxidation of Cl^- (Br^-) in methanol. In fact, the anodic reaction of **9** in methanol containing NaCl gave selectively the α-methoxylated α-amino acid derivatives (**10**)[7] (eq 6), while the direct anodic methoxylation of **9** in



9 **10** 70 % (10 F/mol)

methanol containing TEATS took place at the position α to the ω-amino group, yielding only **11** (eq 7).[7]



11 51 % (12 F/mol)

Furthermore, Table I shows that the yields of **2b** are almost independent of the amount of NaCl (runs 1–4), suggesting that Cl^- is regenerated in the reaction system. Accordingly, a schematic diagram of this indirect α-methoxylation is shown in Figure 1, in which NaCl behaves as a mediator.[10]

The new methods reported in this paper are highly promising for the α-methoxylation of N-carbomethoxylated or N-acylated α-amino acid esters and α-amino β-lactams, since the reaction conditions are mild, operation is simple, and no oxidizing agents are necessary. The application of this method to more complicated β-lactams and free amino acids or esters is now in progress.

Registry No. **1a**, 70288-73-2; **1b**, 28819-00-3; **1c**, 41844-71-7; **1d**, 85235-39-8; **1e**, 85235-40-1; **2a**, 64356-73-6; **2b**, 85235-41-2; **2c**, 85235-42-3; **2d**, 85235-43-4; **2e**, 85235-44-5; **3a**, 85235-45-6; **3b**, 19789-85-6; **4a**, 85235-46-7; **4b**, 85235-47-8; **5**, 85235-48-9; **6**, 63974-28-7; **7**, 85235-49-0; **8**, 85235-50-3; **9**, 85235-51-4; **10**, 85235-52-5; **11**, 85235-53-6.

(8) For examples, see: (a) Shono, T.; Hamaguchi, H.; Matsumura, Y. *J. Am. Chem. Soc.* **1975**, *97*, 4264. (b) Shono, T.; Matsumura, Y.; Tsubata, K. *Ibid.* **1981**, *103*, 1172; (c) *Tetrahedron Lett.* **1981**, *22*, 2411; (d) *Ibid.* **1981**, *22*, 3249. (e) Shono, T.; Matsumura, Y.; Tsubataa, K.; Takata, J. *Chem. Lett.* **1981**, 1121.

(9) The oxidation of α-amino acid derivatives with *tert*-butyl hypochlorite has been known,[3] though this is not necessarily applicable for the large-scale preparation.

(10) For examples, see: (a) Shono, T.; Matsumura, Y.; Hayashi, J.; Mizoguchi, M. *Tetrahedron Lett.* **1979**, 165; (b) *Ibid.* **1979**, 3861; (c) *Ibid.* **1980**, *21*, 1867. (d) Shono, T.; Matsumura, Y.; Yamane, S.-i.; Kashimura, S.; *Chem. Lett.* **1982**, 565.

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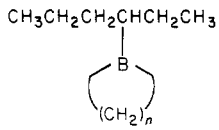
Unusually Slow Thermal Isomerization of Alkyldihaloboranes. A Highly Regio- and Stereospecific Synthesis of Alkyldihaloboranes from Labile Olefinic Structures

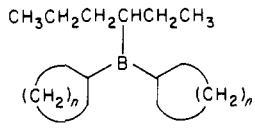
Summary: The thermal isomerizations of 3-hexyldihaloboranes were systematically examined at 150 °C in *o*-dichlorobenzene. The 3-hexylboranes derived from the hydroboration of *cis*-3-hexene with $HBCl_2{\cdot}SMe_2$ and $HBBr_2{\cdot}SMe_2$ are exceptionally resistant to thermal isomerization, a discovery of considerable importance for the regio- and stereospecific synthesis of alkyldihaloborane intermediates from highly labile olefinic structures.

0022-3263/83/1948-1389$01.50/0

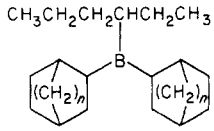
Sir: In our studies of the factors influencing the rate of the thermal isomerization of organoboranes, we employed a number of structurally defined 3-hexylboranes (such as **1–3**) that contain only carbon groups for all three valences



1, n = 2–4



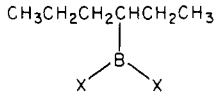
2, n = 2–5



3, n = 1,2

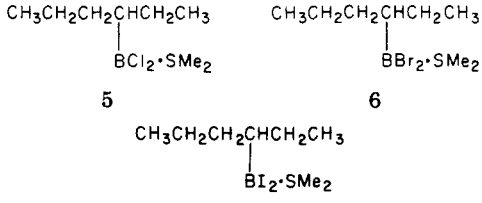
on boron. The results establish that increases in the steric crowding in the initial trialkylborane undergoing the thermal isomerization significantly accelerate the rate of isomerization and markedly improve the equilibrium boron distribution in favor of the 1-alkylboranes.[1-4]

Interestingly, all literature reports of the thermal isomerization of organboranes deal only with trialkylboranes.[5] Hence, nothing is known at present about the thermal isomerizaton behavior of organoboranes (such as **4**) containing heteroatom substituents.



4, X = halogens, OR, SR, NR_2, etc.

Therefore, it appeared to be of considerable theoretical as well as possible practical interest to explore this virgin area. Accordingly, we prepared the 3-hexyldihaloboranes **5–7** and systematically examined their thermal isomerizations at 150 °C in o-dichlorobenzene[6] in order to precisely understand their thermal isomerization behavior.



5

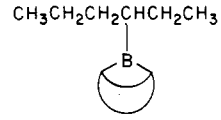
6

7

It is possible to prepare readily either the free 3-hexyldihaloboranes or their dimethyl sulfide adducts. Preliminary experiments established no significant difference in the rate of isomerization between 3-hexyldichloroborane and its dimethyl sulfide adduct or 3-hexyldibromoborane and its dimethyl sulfide adduct. Possibly, at the isomerization temperature, 150 °C, the adducts are dissociated. In any event, this observation simplified the study so that we could use either the 3-hexyldihaloborane or its dimethyl sulfide adduct, depending upon which compound is most readily prepared by established hydroboration procedures. In this discussion, for simplicity, we shall refer to the parent compound and not to the adduct.

The results for the thermal isomerizations of 3-hexyldihaloboranes **5–7** are summarized in Table I. (The isomeric distribution was established by oxidation to the corresponding alcohols, followed by GC analysis.)

3-Hexyldichloroborane (**5**) isomerizes approximately 45 times slower than 3-hexyldibromoborane (**6**) and nearly 4380 times slower than 3-hexyldiiodoborane (**7**) at 150 °C (Figure 1). So far, *B*-3-hexyl-9-borabicyclo[3.3.1]nonane (**8**) was the only 3-hexylborane that was known[7] to be exceptionally resistant to thermal isomerization ($t_{1/2}$ = 12 060 s) at 150 °C. Interestingly, 3-hexyldichloroborane (**5**) isomerizes approximately 22 times slower than *B*-3-hexyl-9-BBN (**8**, Table I).

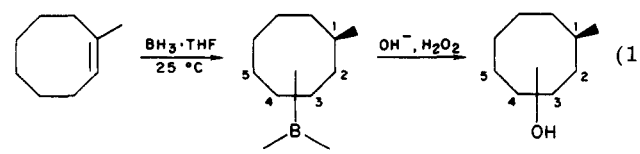


8

Further, while 3-hexyldiiodoborane (**7**) reaches equilibrium in thermal isomerization in 48 h and yields a boron distribution of 85% on C-1, 10% on C-2, and 5% on C-3, 3-hexyldibromoborane (**6**) does not attain equilibrium, even in 5 days. More interestingly, 3-hexyldichloroborane (**5**) fails to attain equilibrium, even in 15 days.

3-Hexyldichloroborane (**5**) was prepared[8] by the hydroboration of *cis*-3-hexene with $HBCl_2 \cdot SMe_2$ in the presence of the stoichiometric amount of BCl_3 in pentane at 0 °C, followed by addition of the stoichiometric amount of SMe_2. On the other hand, 3-hexyldibromoborane (**6**) and 3-hexyldiiodoborane (**7**) were prepared by the direct hydroboration of *cis*-3-hexene with $HBBr_2 \cdot SMe_2$[9] and $HBI_2 \cdot SMe_2$[9] (without using BCl_3), respectively, in CH_2Cl_2 at 40 °C for 4–5 h. The thermal isomerizations of the 3-hexyldihaloboranes were then conducted in *o*-dichlorobenzene at 150 ± 2 °C by using a thermowatch to maintain the temperature. At regular intervals of time, aliquots were withdrawn, oxidized by alkaline hydrogen peroxide, and analyzed by gas chromatography.[10]

The exceptionally slow rates of thermal isomerization of 3-hexyldichloroborane (**5**) and 3-hexyldibromoborane (**6**) suggested that $HBCl_2 \cdot SMe_2$ and $HBBr_2 \cdot SMe_2$ might be especially valuable for the hydroboration of labile olefinic structures such as 1-methylcyclooctene where an exceptionally facile thermal isomerization is often an undesired problem[11] (eq 1).



(1)

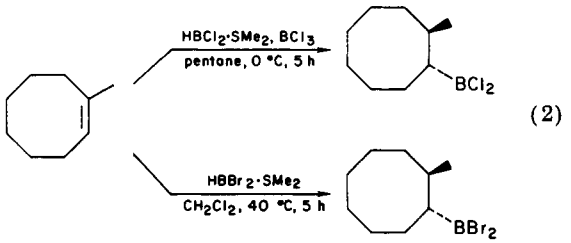
(1) Brown, H. C.; Racherla, U. S.; Taniguchi, H. *J. Org. Chem.* **1981**, *46*, 4313.
(2) Racherla, U. S.; Pai, G. G. *Heterocycles* **1982**, *18*, 285.
(3) Brown, H. C.; Racherla, U. S. *Organometallics* **1982**, *1*, 765.
(4) Brown, H. C.; Racherla, U. S. *J. Organomet. Chem.*, in press.
(5) (a) Hennion, G. F.; McCusker, P. A.; Ashby, E. C.; Rutkowski, A. J. *J. Am. Chem. Soc.* **1957**, *79*, 5190. (b) Brown, H. C.; Subba Rao, B. C. *Ibid.* **1959**, *81*, 6431. (c) Brown, H. C.; Zweifel, G. *Ibid.* **1960**, *82*, 1504. (d) Braun, J. C.; Fisher, G. S. *Tetrahedron Lett.* **1960**, *21*, 9. (e) Logan, T. J. *J. Org. Chem.* **1961**, *26*, 3657. (f) McCusker, P. A.; Rossi, F. M.; Bright, J. H.; Hennion, G. F. *Ibid.* **1967**, *32*, 450. (g) Sisido, K.; Naruse, M.; Saito, A.; Utimoto, K. *Ibid.* **1972**, *37*, 733. (h) Maruyama, K.; Terada, K.; Yamamoto, Y. *Ibid.* **1980**, *45*, 737.
(6) Alkyldihaloboranes react with etheral solvents such as Et_2O, THF, and diglyme. Hence the thermal isomerization of alkyldihaloboranes was conducted in *o*-dichlorobenzene.
(7) See ref 1.
(8) Brown, H. C.; Ravindran, N.; Kulkarni, S. U. *J. Org. Chem.* **1980**, *45*, 384.
(9) For preparation, see ref 8.
(10) Standard conditions used for the gas chromatographic separation of the hexanols: 10% Carbowax 1540 on Chromosorb W (1/8 in. × 12 ft) column; isothermal analysis at 70 °C; Varian 1200 Model gas chromatograph equipped with a flame ionization detector.
(11) (a) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 2544. (b) Brown, H. C.; Klimisch, R. L. *Ibid.* **1966**, *88*, 1430.

Table I. Results of the Thermal Isomerization of 3-Hexyldihaloboranes at 150 °C in o-Dichlorobenzene

organoborane	$t_{1/2}$,[a] s	time to attain equilibrium, h	organoborane composition, % 1-BX_2	2-BX_2	3-BX_2
$CH_3CH_2CH_2CH(CH_2CH_3)BCl_2 \cdot SMe_2$ (5)	262 800[b]	>360	0	68	32[c]
$CH_3CH_2CH_2CH(CH_2CH_3)BBr_2 \cdot SMe_2$ (6)	5 820[d]	>120	35	60	5[c]
$CH_3CH_2CH_2CH(CH_2CH_3)BI_2 \cdot SMe_2$ (7)	60	48	85	10	5
$CH_3CH_2CH_2CH(CH_2CH_3)B$ (8)	12 060	264	90	6	4[e]

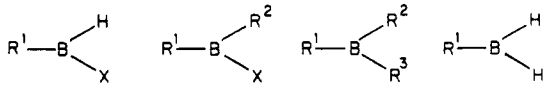
[a] Determined graphically from the kinetic data obtained in each case. [b] The corresponding SMe_2-free organoborane has a $t_{1/2}$ of 259 200 s and shows nearly the same boron distribution under identical isomerization conditions. [c] Not an equilibrium composition. [d] The corresponding SMe_2-free organoborane has a $t_{1/2}$ of 5460 s and shows almost the same boron composition under identical isomerization conditions. [e] See ref 1.

Indeed, hydroboration of 1-methylcyclooctene either with $HBCl_2 \cdot SMe_2$ (in the presence of BCl_3) at 0 °C or with $HBBr_2 \cdot SMe_2$ (in the absence of BCl_3) at 40 °C cleanly affords *trans*-(2-methylcyclooctyl)dihaloboranes (≥99% pure)[12] in excellent yield[13] (≥98%) as shown in eq 2.



(2)

Although 9-BBN also hydroborates labile olefinic structures without significant thermal isomerization,[14] the present method offers a unique advantage in that the hydroboration products can be converted into a host of valuable borane intermediates (such as **9**–**12**) via the recently established hydridation[15] –stepwise hydroboration[16] procedures.



9 10 11 12

The present study points out for the first time that alkyldihaloboranes, which have recently emerged as valuable intermediates[17] in organic synthesis, can be obtained in a highly regio- and stereospecific manner, even from labile olefinic structures.

The precise reason for the unusually slow rates of thermal isomerization of 3-hexyldihaloboranes derived from $HBCl_2 \cdot SMe_2$ and $HBBr_2 \cdot SMe_2$ is still not understood. A final theoretical interpretation of these results would require presumably more detailed kinetic and mechanistic studies in this area.

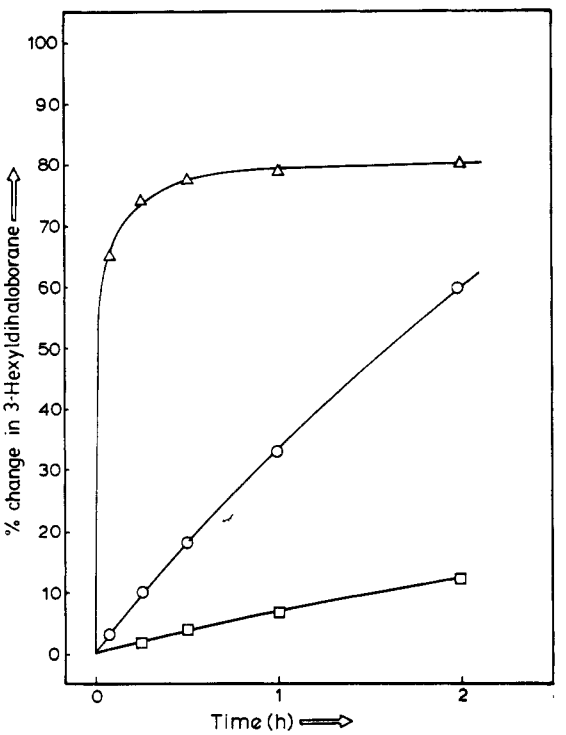


Figure 1. Comparison of the rates of thermal isomerization of 3-hexyldihaloboranes at 150 °C: (△) 3-hexyldiiodoborane (5), (○) 3-hexyldibromoborane (6), (□) 3-hexyldichloroborane (7).

(12) ^{11}B NMR spectrum of the methanolyzed sample in each case showed only a single peak at δ 31.0 corresponding to $RB(OMe)_2$. The stereochemistry of the hydroboration was found to be 100% trans by oxidation and GLC analysis.

(13) Isolated yield.

(14) Taniguchi, H.; Brener, L.; Brown, H. C. *J. Am. Chem. Soc.* **1976**, *98*, 7107.

(15) Brown, H. C.; Kulkarni, S. U. *J. Organomet. Chem.* **1981**, *218*, 299.

(16) Kulkarni, S. U.; Basavaiah, D.; Zaidlewicz, M.; Brown, H. C. *Organometallics* **1982**, *1*, 212.

(17) (a) Brown, H. C.; Basavaiah, D. *J. Org. Chem.* **1982**, *47*, 3806. (b) Brown, H. C.; Basavaiah, D.; Kulkarni, S. U. *Ibid.* **1982**, *47*, 3808. (c) Brown, H. C.; Basavaiah, D. *Ibid.* **1982**, *47*, 5407. (d) Brown, H. C.; Basavaiah, D. *Ibid.* **1982**, *47*, 754. (e) Brown, H. C.; Basavaiah, D.; Kulkarni, S. U. *Ibid.* **1982**, *47*, 172. (f) Brown, H. C.; Basavaiah, D. *Ibid.* **1982**, *47*, 1792. (g) Basavaiah, D. *Heterocycles* **1982**, *18*, 153. (h) Kulkarni, S. U.; Basavaiah, D.; Brown, H. C. *J. Organomet. Chem.* **1982**, *C1*, 225.

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