ORGANOBORON COMPOUNDS.

347. SYNTHESIS OF 9-ALKYL-1,2,3,4-TETRAHYDROACRIDINES FROM ANILS OF CYCLOHEXANONE AND NITRILES WITH THE AID OF ORGANOBORON COMPOUNDS

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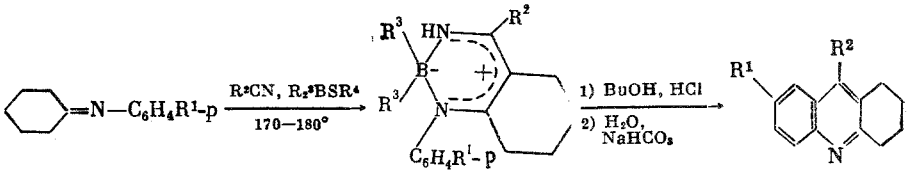
The formation of chelates of boron as intermediates is often utilized in organic chemistry. The simplest example is the synthesis of 1,3-diketones according to the Meerwein method by acylating ketones in the presence of BF_3 [1]. In the case of the synthesis of N-acylamidines from primary amides and nitriles with the aid of trialkylboranes, chelates, i.e., dialkylboryl acylamidinates, also form in an intermediate step [2]. In the present work we have made a thorough examination of the synthesis of 1,2,3,4-tetrahydroacridines from anils of cyclohexanone and aliphatic nitriles through dialkylboryl β-diiminates [3]:

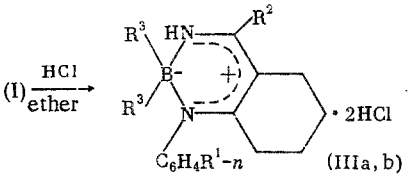


(Ia-d) (IIa-d)

$R^1 = H$, $R^2 = CH_3$, $R^3 = C_4H_9$(Ia), $R^1 = R^2 = CH_3$, $R^3 = C_4H_9$(Ib), $R^1 = Cl$, $R^2 = CH_3$, $R^3 = C_4H_9$(Ic), $R^1 = H$, $R^2 = C_3H_7$, $R^3 = C_3H_7$(Id) $R^1 = H$, $R^2 = CH_3$(IIa), $R^1 = R^2 = CH_3$(IIb), $R^1 = Cl$, $R^2 = CH_3$(IIc) $R^1 = H$, $R^2 = C_3H_7$(IId)

The anils of cyclohexanone are known to yield cyclohexenylaminodialkylboranes with alkylmercaptodialkylboranes [4, 5]. These products, in turn, add to nitriles to form dialkylboryl β-diiminates (I) [5, 6]. The synthesis of chelates of type I is best carried out in one step by heating a mixture of the anil of cyclohexanone, the nitrile, and the alkylmercaptoborane in an autoclave at 170-180°C. A number of boron β-diminates of type I containing aryl substituents on a nitrogen atom were obtained in this manner in a previous study [6].

It has previously been found that dialkylboryl β-diiminates, being weak bases, produce salts with strong acids [6, 7]. When an ethereal solution of HCl was applied to compounds of type I, salts of type III could be isolated in the form of colorless crystals containing 2 moles of HCl in the molecule (according to the data from elemental analysis):



(IIIa, b)

$R^1 = H$, $R^2 = CH_3$, $R^3 = C_4H_9$(IIIa); H, C_6H_5, C_4H_9(IIIb)

Interestingly enough, a number of β-diiminates synthesized from alkylphenylketiminoboranes form salts with HCl with a 1:1 composition having the structure of boronium salts [7]. The ability of β-diiminates of boron to react with HCl to form salts of variable composition is apparently related to the basicity of the ligand. In support of the hypothesis we can cite the fact that β-diiminate IV, in which weakly basic N-phenylbenzophenonediimine is the ligand, also produces unstable boronium salt V, which has a 1:1 rather than a 1:2 composition, with an excess of an ethereal solution of HCl:

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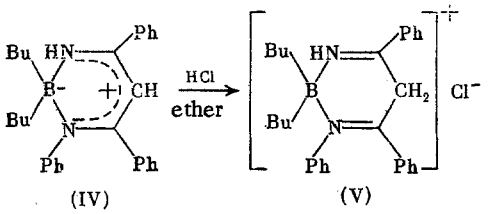
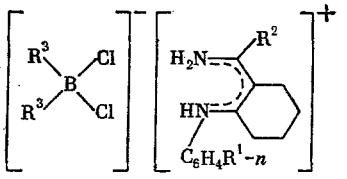


(IV) (V)

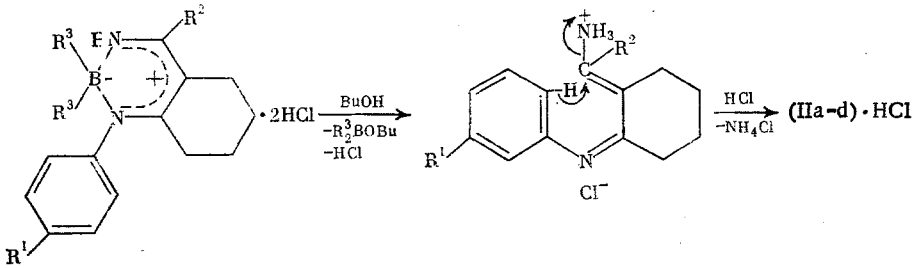
Because of the poor solubility of salts of type III in most organic solvents, the investigation of their structure is difficult. It may, however, be assumed that they have structure A



(A)

The free chelates can be recovered by applying a methanolic solution of $NaOCH_3$ or an aqueous solution of sodium carbonate to the salts of type III. The boiling of solutions of the salts of the dialkylboryl β-diiminates of type III in butanol or of the free chelates of type I in a butanolic solution of HCl results in the splitting off of the dialkylboryl group in the form of the butoxydialkylborane. Under these conditions the simultaneously formed β-diimine hydrochlorides undergo intramolecular cyclization (with the splitting off of NH_4Cl), in which the ortho proton of the phenyl group bound to the nitrogen participates. This yields 1,2,3,4-tetrahydroacridine hydrochlorides, which are converted into the free bases by the action of an aqueous solution of $NaHCO_3$.

This process is analogous to the cyclization of salts of N-aryl-β-diimines, which yields 2,3-substituted quinolines [8]:



The yield of the 1,2,3,4-tetrahydroacridines (IIa-IId) obtained in this manner is 30-60% (relative to the original anil). The crystalline compounds (IIa-IIc) and the liquid compound (IId) are highly soluble in most organic solvents. The structure of compounds IIa-IId was confirmed by the data from elemental analysis, as well as the IR, PMR, and mass spectra. The only known tetrahydroacridine among IIa-IId is 9-methyl-1,2,3,4-tetrahydroacridine (IIa), which was obtained by heating 9-hydroxymethyloctahydroacridine with P_2O_5 in xylene in [9], as well as by the condensation of o-aminoacetophenone with cyclohexanone [10].

The proposed method for the synthesis of tetrahydroacridines with the use of alkylmercaptoboranes is distinguished by the fact that it is based on the use of readily accessible starting compounds, viz., anils of cyclohexanone and nitriles.

In the literature there is information on the biological activity of a number of tetrahydroacridines with functional substituents in position 9 [11]. In this context the 9-alkyl-1,2,3,4-tetrahydroacridines synthesized are of definite interest from the point of view of the study of their physiological activity.

EXPERIMENTAL

The manipulations were carried out in an atmosphere of dry N_2 or Ar. The IR spectra were recorded on a UR-10 instrument (the data in the 1500-1700-cm^{-1} range are given), and the ^1H NMR spectra were recorded on a Varian DA-60-IL instrument. The anils of cyclohexanone [12] and the alkylmercaptodialkylboranes [13] were synthesized according to known methods.

The dialkylboryl β-diiminates (Ia-Id) were synthesized according to the method in [6] by heating a mixture of the anil of cyclohexanone, the alkylmercaptodialkylborane, and the nitrile (10-15% excess) in an autoclave at 170-180°C under 9-10 atm. All the β-diiminates of type I were purified by washing with absolute CH_3OH and recrystallization or distillation. The synthesis of Ia and Ic has been described in [6]. Compounds Ib and Id were obtained in an analogous manner. Their constants fit those presented in [5, 6].

9-Alkyl-1,2,3,4-tetrahydroacridines (IIa-IId)

A solution of 0.12 mole of HCl in 20-30 ml of abs. C_4H_9OH was added to a solution of 0.05 mole of I in 40-50 ml of abs. C_4H_9OH. Then the C_4H_9OH was distilled off in a vacuum, and the residue was filtered (in the case of IIa, the filtration was carried out immediately after the boiling). The solid residue on the filter (a mixture of NH_4Cl and 1,2,3,4-tetrahydroacridine hydrochloride) was washed with ether and then transferred to a flask with 50-60 ml of CCl_4. It was next treated with 70-80 ml of a saturated aqueous solution of $NaHCO_3$. The aqueous layer was extracted with CCl_4, and the combined extract was dried over $MgSO_4$. After the removal of the solvent in a vacuum, the crystalline compounds (IIa-IIc) were recrystallized, and the liquid compound (IId) was distilled.

A compound with the formula R_2BOBu (R = C_3H_7, C_4H_9) was isolated from the filtrate by distillation and identified by physicochemical methods.

9-Methyl-1,2,3,4-tetrahydroacridine (IIa). Yellow crystals, mp 68°C (from cyclohexane) [10], 30% yield. IR spectrum (CCl_4, ν, cm^{-1}): 1500, 1570, 1585, 1619. PMR spectrum (CCl_4, δ, ppm): 2.04 (s, 9-CH_3), 1.35-1.83 (m, 2-CH_2 and 3-CH_2), 2.21-2.99 (m, 1-CH_2, 4-CH_2), 6.90-7.87 (m, aromatic protons). Mass spectrum: m/e 197 (M^+). Salt of IIa with HCl, mp 278-279°C (from CH_3CN) [10].

7,9-Dimethyl-1,2,3,4-tetrahydroacridine (IIb). Yellow crystals, mp 76-77°C (from isopentane), 60% yield. Found: C 85.44; H 8.17; N 6.52%. Calculated for $C_{15}H_{17}N$: C 85.26; H 8.11; N 6.63%. IR spectrum (CCl_4, ν, cm^{-1}): 1512, 1575, 1593, 1639. PMR spectrum (CCl_4, δ, ppm): 2.10 (s, 9-CH_3), 2.32 (s, 6-CH_3), 1.38-1.87 (m, 2-CH_2, 3-CH_2), 2.42-3.03 (m, 1-CH_2, 4-CH_2), 6.97-7.7 (m, aromatic protons). Mass spectrum: m/e 211 (M^+).

7-Chloro-9-methyl-1,2,3,4-tetrahydroacridine (IIc). Colorless crystals, mp 64-66°C (from isopentane), 35% yield. Found: C 72.21; H 6.20; N 6.19; Cl 15.89%. Calculated for $C_{14}H_{14}NCl$: C 72.56; H 6.09; N 6.04; Cl 15.30%. IR spectrum (CCl_4, ν, cm^{-1}): 1489, 1568, 1582, 1609. PMR spectrum (CCl_4, δ, ppm): 2.15 (s, 9-CH_3), 1.60-1.90 (m, 2-CH_2, 3-CH_2), 2.41-3.05 (m, 1-CH_2, 4-CH_2), 7.12-7.76 (m, aromatic protons).

9-Propyl-1,2,3,4-tetrahydroacridine (IId). Yellowish oil, bp 160-161°C (1.5 mm), n_D^{20} 1.6040, 43% yield. Found: C 85.07; H 8.45; N 6.53%. Calculated for $C_{16}H_{19}N$: C 85.27; H 8.51; N 6.22%. IR spectrum (CCl_4, ν, cm^{-1}): 1500, 1565, 1588, 1620, 1690. Mass spectrum: m/e 225 (M^+).

Effect of Ethereal Solution of HCl on Dibutylboryl β-Diiminates Ia, Ib, and IV

A solution of 0.034 mole of HCl in absolute ether was added portionwise to 5.4 g (0.016 mole) of Ia in 30 ml of absolute ether. The mixture was stirred for 0.5 h. The precipitate formed was filtered, washed with absolute ether, and dried. As a result, 6.2 g of salt (IIIa) were obtained, the yield was 95%, and the mp was 218-221°C (with decomposition). Found: C 64.54; H 9.23; B 2.64; N 6.85; Cl 17.01%. Calculated for $C_{22}H_{37}BN_2Cl_2$: C 64.35; H 9.06; B 2.62; N 6.81; Cl 17.24%. IR spectrum (KBr, ν, cm^{-1}): 1495, 1598, 1635, 1702.

Salt IIIb was obtained in an analogous manner from Ib and an ethereal solution of HCl. The mp was >300°C (with decomposition), and the yield was 96%. Found: C 68.17; H 8.28; B 2.60; Cl 14.91%. Calculated for $C_{27}H_{39}BN_2Cl_2$: C 68.51; H 8.31; B 2.28; Cl 14.98%. IR spectrum (KBr, ν, cm^{-1}): 1495, 1582 sh, 1598, 1630, 1670.

Salt V was obtained by applying an ethereal solution of HCl to β-diiminate IV. The mp was 64-70°C (with decomposition), and the yield was 89%. Found: C 75.95; H 7.64; B 2.42; N 6.29; Cl 8.77%. Calculated for $C_{29}H_{36}BN_2Cl$: C 75.90; H 7.91; B 2.35; N 6.11; Cl 7.73%.

CONCLUSIONS

A method for synthesizing 9-alkyl-1,2,3,4-tetrahydroacridines from anils of cyclohexanone and nitriles through chelates, viz., dialkylboryl β-diiminates, has been developed.

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ORGANOBORON COMPOUNDS.

348. N-DIALKYLBORYLAMIDINES FROM N,N'-DISUBSTITUTED AMIDINES

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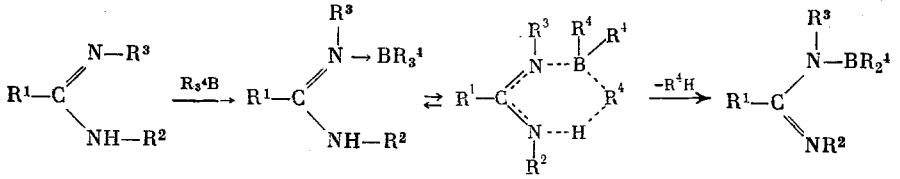
Amidines with a dialkylboryl group on one of the N atoms have high reactivities and are starting or intermediate compounds in the synthesis of cyclic coordination compounds of boron [1-3]. We have previously investigated dialkylborylamidines synthesized from asymmetric N,N-dialkylamidines [4]. As a continuation of those studies, in the present report we shall present the synthesis of the corresponding derivatives of N,N'-disubstituted amidines, viz., N-dialkylboryl-N,N'-dialkylamidines (DBDAA) and N-dialkylboryl-N-alkyl-N'-phenylamidines (DBAPhA), and examine several special features of the structure and chemical behavior of these compounds.

A simple method for the synthesis of DBDAAs and DBAPhAs is to react N,N'-dialkylamidines or N-alkyl-N'-phenylamidines with trialkylboranes. The reaction proceeds smoothly when a mixture of the compounds just indicated is boiled in THF (or in other solvents with a bp $\geqslant$ 50-60°C, viz., $CHCl_3$, C_6H_6, CH_3CN, etc.). The addition of an amidine to a trialkylborane results in the formation of a complex [1, 5], which decomposes upon heating into a dialkylborylamidine and a saturated hydrocarbon through a cyclic six-center transition state:



For the synthesis of DBDAAs and DBAPhAs we can also use the general method for obtaining compounds with a B—N bond from alkylmercaptodialkylboranes [6]:

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