

3-Alkylation of the Pyrrole Ring. III<sup>1</sup>

Sir:

With the exception of nitrosation of pyrroles<sup>2</sup> and the formation of 2-methyl-3-selenocyanatopyrrole from 2-methylpyrrole and selenocyanogen,<sup>3</sup> preferential substitution at the 3 position of the pyrrole ring is unknown, although widely investigated.<sup>4</sup> We find that pyrrolylmagnesium chloride in ethyl ether is alkylated with ethylene oxide at predominantly the 3 position yielding (39%)<sup>5</sup> 2-pyrrol-2-ylethanol (I) and 2-pyrrol-3-ylethanol (II) in a ratio of 1:3 (vpc).<sup>6</sup> Moreover, in tetrahydrofuran II is the only monoalkyl product (16%) that we have been able to isolate. The isomeric hydroxyethylpyrroles were identified by elemental analysis and spectral properties.<sup>7</sup> Also, lithium aluminum hydride reduction of II-tosylate gave 3-ethylpyrrole, which was identical with the Wolff-Kishner reduction product from 3-acetylpyrrole.<sup>1</sup>

The preference for 3-alkylation indicates that the reaction takes place *via* the epoxide and not by way of the possible intermediate di-2-chloroethoxymagnesium, from the reaction of the epoxide and magnesium-chlorine bond breaking in the Grignard reagent,<sup>10</sup> for the chlorohydrin derivative would be expected to favor 2-alkylation.<sup>8</sup> A rationale for our results, albeit not the only one, can be offered in terms of the relative solvating power of the ethers: tetrahydrofuran > ethylene oxide > ethyl ether,<sup>11</sup> and steric hinderance to intermolecular alkylation at the 2 position of the pyrrole ring due to ether molecules complexed with magnesium, which is bonded at the ring nitrogen.<sup>8a,12</sup> In ethyl ether, replacement of the solvent ligands by ethylene oxide and reaction of the complexed epoxide with the nearby 2 position of the pyrrole ring yield I. Models<sup>13</sup> show that the 3 position is too far away to become involved in this way, and instead reaction occurs at this position by a separate intermolecular mecha-

nism to form II. The stronger solvent tetrahydrofuran is not displaced from coordination with magnesium by ethylene oxide and as a result substitution does not occur at the 2 position, but takes place solely at the 3 position in this solvent.

Pyrrolylmagnesium bromide reportedly<sup>14</sup> reacts with ethylene oxide in ethyl ether-benzene to form I. Similarly, in the first step of the first claimed synthesis of the alkaloid hygrine, the same Grignard reagent with propylene oxide in ethyl ether was thought to yield 1-pyrrol-2-yl-2-propanol.<sup>15</sup> Both of these earlier reports now seem questionable.<sup>16</sup> However, pyrrolylmagnesium chloride apparently reacts with trimethylene oxide in ethyl ether to form 3-pyrrol-2-yl-1-propanol and 3-pyrrol-3-yl-1-propanol in a ratio of 4:1.<sup>17</sup>

(14) K. Hess, F. Merck, and C. Uibrig, *Ber.*, **48**, 1886 (1915).

(15) K. Hess, *ibid.*, **46**, 3113, 4104 (1913).

(16) After this communication was accepted for publication, the recent paper by F. Moll and H. Thoma, *Arch. Pharm. (Weinheim)*, **301**, 872 (1968), became available to us. These workers have found that the reaction with ethylene oxide in the Hess procedure does indeed yield I and II, in approximately equal amounts, as the major product and a small amount of the third possible isomer, 2-pyrrol-1-ylethanol.

(17) L. R. Kray and M. G. Reinecke, *J. Org. Chem.*, **32**, 225 (1967).

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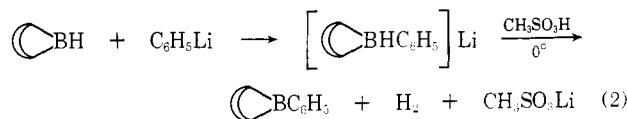
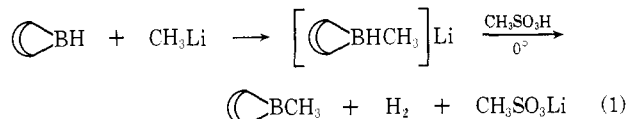
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### The Reaction of Ethyl Haloacetates and $\alpha$ -Bromo Ketones with B-Aryl-9-borabicyclo[3.3.1]nonanes under the Influence of Potassium *t*-Butoxide. A New Convenient Procedure for the $\alpha$ Arylation of Ketones and Esters

Sir:

Under the influence of potassium *t*-butoxide organoboranes react with ethyl bromoacetate,<sup>1</sup> ethyl dihaloacetates,<sup>2</sup> and various  $\alpha$ -bromo ketones<sup>3</sup> to give the corresponding esters,  $\alpha$ -halo esters, ethyl dialkylacetates, and  $\alpha$ -alkyl ketones. Application of the B-alkyl-9-borabicyclo[3.3.1]nonane derivatives<sup>4</sup> (B-alkyl-9-BBN) circumvented some of the difficulties encountered with the more hindered trialkylboranes<sup>2,3</sup> and greatly improved the utilization of the alkyl groups.<sup>5,6</sup>

We now wish to report that B-alkyl- and B-aryl-9-BBN may be readily synthesized from the corresponding organolithium derivatives and 9-BBN (eq 1 and 2).



(1) H. C. Brown, M. M. Rogić, M. W. Rathke, and G. W. Kabalka, *J. Am. Chem. Soc.*, **90**, 818 (1968).

(2) H. C. Brown, M. M. Rogić, M. W. Rathke, and G. W. Kabalka, *ibid.*, **90**, 1911 (1968).

(3) H. C. Brown, M. M. Rogić, and M. W. Rathke, *ibid.*, **90**, 6218 (1968).

(4) E. F. Knights, *ibid.*, **90**, 5280, 5281, 5283 (1968).

(5) H. C. Brown and M. M. Rogić, *ibid.*, **91**, 2146 (1969).

(6) H. C. Brown, M. M. Rogić, H. Nambu, and M. W. Rathke, *ibid.*, **91**, 2147 (1969).

(1) For the preceding report in this series see A. J. Castro, J. R. Lowell, Jr., and J. P. Marsh, Jr., *J. Heterocyclic Chem.*, **1**, 207 (1964).

(2) H. Fischer and H. Orth, "Die Chemie des Pyrrols," Part I, Akademische Verlagsgesellschaft M. B. H., Leipzig, 1934, p 104.

(3) L.-B. Agenäs and B. Lindgren, *Arkiv Kemi*, **28**, 145 (1967).

(4) (a) C. E. Griffin and R. Obrycki, *J. Org. Chem.*, **29**, 3090 (1964); (b) M. K. A. Khan, K. J. Morgan, and D. P. Morrey, *Tetrahedron*, **22**, 2095 (1966); (c) H. J. Anderson and S. J. Griffiths, *Can. J. Chem.*, **45**, 2227 (1967).

(5) Uncorrected for recoverable pyrrole.

(6) Carbowax 20M, Varian Aerograph Co., Walnut Creek, Calif.

(7) Isomeric pair, bp 161° (2 mm). *Anal.* Calcd for C<sub>5</sub>H<sub>9</sub>NO: C, 64.8; H, 8.16; N, 12.60. Found: C, 65.01; H, 8.30; N, 12.70. For I (vpc) ir: OH and NH 3.02, ring H in-plane deformations<sup>8a,9</sup> 8.96, 9.15  $\mu$ ; nmr (CDCl<sub>3</sub>, internal TMS): NH  $\tau$  1.00 (broad singlet), ring H-5 3.55 (multiplet), ring H-4 3.90 (multiplet), ring H-3 4.05 (multiplet), carbinol CH<sub>2</sub> 6.20 (triplet), ring-bonded CH<sub>2</sub> 7.20 (triplet), OH 7.95 (singlet), expected integrals. For II (vpc) ir:<sup>9</sup> OH and NH 2.99  $\mu$ ; nmr: NH 1.70 (broad singlet), ring H-2 and H-5 3.30 (multiplet), ring H-4 3.90 (multiplet), carbinol CH<sub>2</sub> 6.23 (triplet), ring-bonded CH<sub>2</sub> 7.27 (triplet), OH 7.97 (singlet), expected integrals.

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(9) Overlapping OH absorption prevents assignment of deformation bands in the region around 9.30–9.90  $\mu$ .<sup>8a</sup>

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