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A Novel Synthetic Use of Trialkyl(indol-2-yl)borate for a "One-Pot" Synthesis of [*a*]-Annelated Indoles

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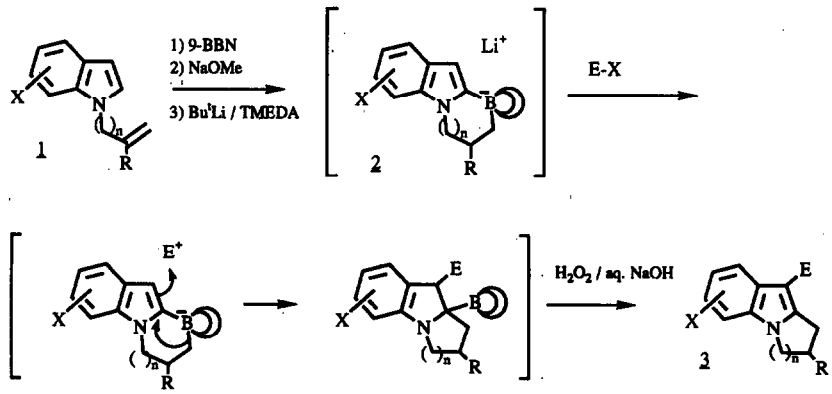
Key Words : [*a*]-Annelated indole; Cyclic trialkyl(indol-2-yl)borate; Lithiation; 1-Allyloxindole

Abstract : A novel one-pot procedure for [*a*]-annelated indole *via* cyclic trialkyl(indol-2-yl)borate is described.

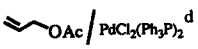
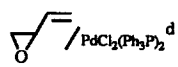
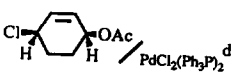
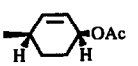
We have previously reported a palladium catalyzed process to [*b*]-annelated indole *via* trialkyl(indol-2-yl)borate, which involved an intramolecular 1,2-alkyl migration from boron to carbon promoted intramolecularly by π-allylpalladium complex.[1] There are no precedents of such use of the 1,2-alkyl migration, a very common sequence in organoborane chemistry,[2] for an intramolecular cyclization. In the course of our studies,[3] we have been concerning ourselves with exploration of additional synthetic potentialities of trialkyl(indol-2-yl)borate intermediate. Development of the methods for the construction of [*a*]-annelated indole nuclei has been the subject of numerous recent reports,[4] therefore, we herein demonstrate a concise procedure for [*a*]-annelated indole by way of cyclic trialkyl(indol-2-yl)borate (2) as a key intermediate.



Scheme 1

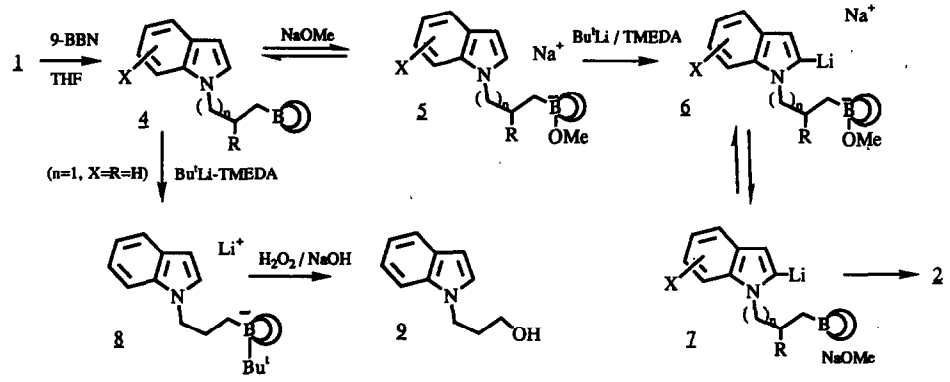
Cyclic trialkyl(indol-2-yl)borate (2) could be simply derived from readily available indole (1) *in situ*: [(1) hydroboration with 9-BBN (9-borabicyclo[3.3.1]nonane) (2) addition of NaOMe (3) lithiation with Bu^{t}Li-TMEDA (N,N,N',N'-tetramethylethylenediamine)]. Standard treatment of the resulted cyclic indolylborate (2) with alkaline hydrogen peroxide gave [a]-annelated indole (3; E=H). Various electrophiles (E-X), such as alkyl halides, allylic halides, π-allylpalladium complexes, also could promote the 1,2-alkyl migration in cyclic indolylborate (2), which allowed a simultaneous functionalization at 9-position in pyrrolo[1,2-a]indole nuclei (3; n=1) (Scheme 1). Table summarizes the results for the construction of [*a*]-annelated indole (3).

Table Formation of [*a*]-annelated indole (3) from indole (1)[a]

1		E-X	Yield(%)[b] of 3
n	X		
1	H	H_2O	38 (E=H, R=H)[c]
1	H	H_2O	62 (E=H, R=H)
1	H	H_2O	60 (E=H, R=Me)
2	H	H_2O	60 (E=H, R=H)
3	H	H_2O	40 (E=H, R=H)
1	5-Me	H_2O	60 (E=H, R=H)
1	5-OMe	H_2O	60 (E=H, R=H)
1	5-NO_2	H_2O	20 (E=H, R=H)
1	7-Me	H_2O	30 (E=H, R=H)
1	H	MeI	60 (E=Me, R=H)
1	H	ICH_2CN	25 (E=CH_2CN, R=H)
1	H		58 (E=-CH_2CH=CH_2, R=H)
1	H		56 (E=-CH_2CH=CH_2, R=H)
1	H		54 (E=-CH_2-CHOH-CH_2COOMe, R=H)
1	H		58 (E=-CH_2-CH=CH-CH_2OH, R=H)
1	H		52 (E=  , R=H)

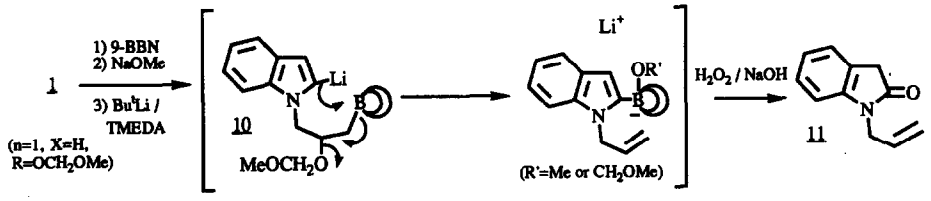
a) All products were fully characterized spectroscopically and elemental composition have been established by combustion analysis and/or high-resolution mass spectrometry. b) Isolated yield based on indole (1). c) Bu^{t}Li (1.2 eq) and TMEDA (1.2 eq) were used. d) Palladium catalyst (5 mol%) was used.

Treatment of alkylborane (4) with NaOMe , prior to the lithiation, was essential for the present one-pot procedure to be successful. Using the present condition except for the addition of NaOMe, alcohol (9) was obtained solely after an oxidation in 75% yield from indole (1; X=R=H, n=1), where the formation of tetraalkylborate (8) from Bu^tLi and alkylborane (4) thus became the preferred reaction pathway. As Scheme 2 plausibly shows, NaOMe serves as a tentative boron-protecting group *via* methoxyborate (5) formation upon the lithiation, which was followed by a series of sequences [formation of lithioindole (6), generation of alkylborane (7) through a slow equilibrium (6 ⇌ 7), and cyclization] leading to cyclic indolylborate (2).



Scheme 2

Moreover, an attempt was made to effect the cyclization with indole (1; X=H, R=OCH_2OCH_3, n=1); however, only 1-allyloxindole (11) [5] was isolated in 20 % yield upon workup. This result apparently suggests the involvement of unfavorable ß-elimination of borate in 10 (Scheme 3).



Scheme 3

We could illustrate an additional utilization of the 1,2-alkyl migration in trialkyl(indol-2-yl)borate for a one-pot formation of [*a*]-annelated indole.[6] Further studies on this new procedure will be reported in due course.

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5. Compound (11): IR(neat) 1708 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.55(s, 2H), 4.50(d, 2H, J=5.3Hz), 5.22 (dd, 1H, J=2, 10Hz), 5.24(dd, 1H, J=2, 17Hz), 5.84(tdd, 1H, J=5.3, 10, 17Hz), 6.82(d, 1H, J=7.8 Hz), 7.03(t, 1H, J=8Hz), 7.22-7.27(m, 2H). ^{13}C-NMR($CDCl_3$)δ: 35.7(t), 42.3(t), 108.9(d), 117.5(t), 122.3(d), 124.4(d), 127.7(d), 131.4(d), 144.3(s), 174.7(s).
6. The following procedure for the formation of 3 (R=X=H, n=1) is representative. After a mixture of indole.(1) (n=1, ,R=X=H) and 9-BBN (1.2 eq) in THF under an argon atmosphere was stirred for 1.5 h at room temperature, NaOMe (1.2 eq) was added, and the stirring was continued for 30 min. TMEDA (2.4 eq) and Bu^{t}Li (2.4 eq) were added at -30°C, then the whole was slowly raised to room temperature and stirred overnight. The reaction mixture was quenched with 10% aq. NaOH and 30% aq. H_2O_2 at 0°C. Ethyl acetate extraction, followed by drying over $MgSO_4$, concentration *in vacuo*, and silica gel chromatography with 100:1 hexane-ethyl acetate as an eluent gave 62% yield of 3 (R=X=H, n=1).[7]
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