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Addition Compounds of Alkali Metal Hydrides. 27. A General Method for Preparation of the Potassium 9-Alkoxy-9-boratabicyclo[3.3.1]nonanes. A New Class of Stereoselective Reducing Agents

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The reaction in tetrahydrofuran of potassium hydride with representative *B*-alkoxy-9-borabicyclo[3.3.1]nonanes (*B*-OR-9-BBN) containing alkoxy groups with increasing steric requirements was examined in detail to establish the generality of this synthesis of the corresponding potassium 9-alkoxy-9-boratabicyclo[3.3.1]nonanes (K9-OR-9-BBNH) and the stereoselectivities of these new reagents for the reduction of cyclic ketones. For R = Me and *n*-Bu, the reactions with potassium hydride are very fast, almost instantaneous, even at 0 °C. However, the products are unstable and rapidly undergo redistribution, even in the presence of excess potassium hydride. Moderately hindered alkoxy derivatives, R = 2-Pr and 2-Bu, react somewhat slower (1 h at 0 °C and 25 °C, respectively) and the products are stable to redistribution. More hindered alkoxy derivatives, R = *t*-Bu, *t*-Am, Thx, require 24 h at 25 °C. Even more hindered alkoxy groups, R = 3-ethyl-3-pentyl and 2,4-dimethyl-2-pentyl, require even longer reaction times and higher temperatures. All reagents show high stereoselectivities in the reduction of cyclic ketones, with the stereoselectivities generally increasing with increasing steric requirements of the alkoxy substituent. The thexyl derivative appears especially favorable, with the byproducts of the reaction readily removed from the reaction mixture.

Among the common alkali metal hydrides, LiH, NaH, and KH, potassium hydride has been established as possessing exceptional ability to transfer hydride to organoboranes, producing the corresponding trialkylborohydrides,[2] exceptionally powerful reducing agents,[3] and to trialkoxyboranes,[2,4] producing the corresponding trialkoxyborohydrides, very mild, highly selective reducing agents.[5]

A systematic study of the rates of reaction of potassium hydride with trialkylboranes of increasing steric requirements has been reported.[2b] The reaction proceeds readily in tetrahydrofuran (THF) at 25 °C to give the corresponding potassium trialkylborohydrides. Even some highly hindered trialkylboranes react smoothly under these conditions (eq 1).

$$KH + R_3B \xrightarrow[25\ °C]{THF} KR_3BH \qquad (1)$$

Recently we described a general procedure for the preparation of potassium trialkoxyborohydrides by the reaction of trialkoxyboranes with potassium hydride in THF.[4b] Except for the trimethoxy and triethoxy derivatives, which undergo rapid redistribution, the more hindered derivatives are quite stable in THF, providing the solutions are maintained over a small excess of potassium hydride (eq 2).

$$KH + (RO)_3B \xrightarrow{THF} K(RO)_3BH \qquad (2)$$

Our original experience in attempting to synthesize potassium dialkylmonoalkoxyborohydride, $KR_2R'OBH$, had been discouraging because of rapid disproportionation of the products. The stabilizing effect of excess potassium hydride and of 9-BBN as a dialkylboryl group encouraged us to examine the synthesis of the potassium 9-alkoxy-9-

(1) Postdoctoral research associate on Grant ARO DAAG-29-79-C-0027, supported by the United States Army Research Office.

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Table I. ^{11}B NMR Spectra and Physical Properties of *B*-(Alkoxy)-9-borabicyclo[3.3.1]nonane (*B*-Alkoxy-9-BBN)

B-alkoxy-9-BBN[a]	^{11}B NMR chemical shift,[b] δ	bp, °C (torr)	n^{20}_D
B-methoxy-9-BBN	56.6	37–38.5 (0.31)	1.4791
B-isopropoxy-9-BBN	55.3	52–53 (0.11)	1.4670
B-*n*-butoxy-9-BBN	56.5	106–107 (5)	1.4628
B-*sec*-butoxy-9-BBN	55.3	104–105 (6.7)	1.4670
B-*tert*-butoxy-9-BBN	55.5	58–59 (0.25)	1.4630
B-(2-methyl-2-butoxy)-9-BBN	55.7	110–112 (4)	1.4696
B-(2,3-dimethyl-2-butoxy)-9-BBN	55.1	95–96 (1.3)	1.4785
B-(3-ethyl-3-pentoxy)-9-BBN	55.3	129–130 (4)	1.4801
B-(2,4-dimethyl-3-pentoxy)-9-BBN	56.0	144–145 (5.5)	1.4750

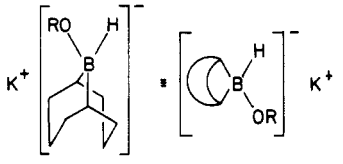
[a] Viscous liequids, very reactive toward air. [b] All chemical shifts are reported relative to $BF_3{\cdot}OEt_2$ with chemical shifts downfield from $BF_3{\cdot}OEt_2$ assigned as positive.

Table II. Reaction of Potassium Hydride with Representative *B*-Alkoxy-9-BBN in Tetrahydrofuran[a]

B-alkoxy-9-BBN	temp, °C	time	stability of K9-alkoxy-9-BBNH toward disproportionation at room temperature
B-methoxy-9-BBN	0	instantly	unstable
B-*n*-butoxy-9-BBN	0	instantly	unstable
B-isopropoxy-9-BBN	0	1 h	stable
B-*sec*-butoxy-9-BBN	25	1 h	stable
B-*tert*-butoxy-9-BBN	25	24 h	stable
B-(2-methyl-2-butoxy)-9-BBN	25	24 h	stable
B-(2,3-dimethyl-2-butoxy)-9-BBN	25	24 h	stable
B-(3-ethyl-3-pentoxy)-9-BBN	25	5 d	stable
B-(2,4-dimethyl-3-pentoxy)-9-BBN	reflux	>20 d	unstable[b]

[a] Solutions were 1.0 M in *B*-alkoxy-9-BBN and approximately 100% excess of potassium hydride utilized. [b] The product slowly underwent disproportionation in the refluxing THF during the long reaction period.

boratabicyclo[3.3.1]nonane (K9-OR-9-BBNH) (1) for possible examination of their stereoselective reducing characteristics.



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Indeed, we discovered that one of these compounds, R = Thx, possesses unusually favorable stereoselectivity in the reduction of cyclic ketones. Accordingly, we undertook to synthesize typical derivatives and to examine their stereoselectivities toward typical cyclic ketones.

Results and Discussion

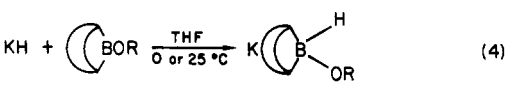
A representative series of *B*-alkoxy-9-BBN esters with increasing steric requirements of the R group were selected for the present study. These borinic esters were prepared by treating 9-BBN with a slight excess of the corresponding alcohols (eq 3). The ^{11}B NMR spectra and physical

(3)

properties of these borinic esters, freshly distilled from a small piece of potassium metal, are summarized in Table I.

Reaction with Potassium Hydride. The potassium 9-OR-9-BBNH derivatives (1) were prepared by adding the neat borinic ester to a vigorously stirred suspension of sufficient potassium hydride (free of oil) in THF to provide a 1.0 M solution of the product. The reactions were carried out either at 0 or 25 °C. Only in one very refractory case was it necessary to raise the temperature to 65 °C (refluxing THF). The course of the reaction was monitored by withdrawing aliquots of the clear reaction mixture at appropriate intervals of time and observing their ^{11}B NMR spectra. The results are summarized in Table II.

Variation in the Reactivity and Stability with the Alkoxy Group. The rate of reaction of *B*-OR-9-BBN with potassium hydride varies markedly with the steric requirements of the alkoxy group. Thus, the borinic esters containing the relatively unhindered methoxy and *n*-butoxy groups react with potassium hydride very rapidly, almost instantly, at 0 °C. With an increase in the steric requirements of the alkoxy group to isopropoxy and *sec*-butoxy, the reactions with potassium hydride are significantly slower, requiring 1 h at 0 °C and 1 h at 25 °C, respectively. Still more hindered alkoxy groups, such as *tert*-butoxy, *tert*-amyloxy, and thexyloxy (2,3-dimethyl-2-butoxy), decreased the rate of reaction and increased the reaction time to 24 h (eq 4).



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In the case of the 3-ethyl-3-pentoxy derivative, the reaction was considerably slower and a reaction time of 5 days at 25 °C was required to complete transfer of hydride. Finally, the 2,4-dimethyl-3-pentoxy derivative was even slower. This reaction required heating under reflux for more than 20 days to achieve completion.

Stability of Products. The stability of the products, 9-OR-9-BBNH (1) appears to vary strongly with the steric requirements of the alkoxy group. For R = Me and *n*-Bu, the products proved to be unstable toward redistribution, giving a mixture of potassium 9-boratabicyclo[3.3.1]nonane (2) and potassium 9,9-dialkoxybicyclo[3.3.1]nonane (3) (eq 5). Even the presence of excess potassium hydride, which successfully stabilized potassium triisopropoxyborohydride,[4a] failed to stabilize the methoxy and *n*-butoxy derivatives.

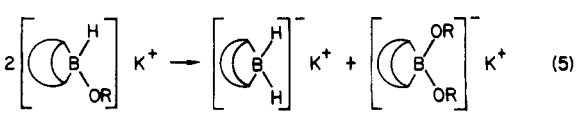

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Table III. Infrared and ^{11}B NMR Spectra of Potassium 9-Alkoxy-9-boratabicyclo[3.3.1]nonane (K9-Alkoxy-9-BBNH) in Tetrahydrofuran

K9-alkoxy-9-BBNH	IR		^{11}B NMR	
	$\nu_{(B-H)}$, cm^{-1}	$\nu_{(B-O)}$, cm^{-1}	chemical shift,[a] δ (multiplicity)	$J_{(B-H)}$, Hz
potassium 9-isopropoxy-9-BBNH	2010	1360	−1.5 (d)	69.5
potassium 9-*sec*-butoxy-9-BBNH	2000	1360	−1.8 (d)	71.4
potassium 9-*tert*-butoxy-9-BBNH	2000	1350	−1.6 (d)	68.1
potassium 9-(2-methyl-2-butoxy)-9-BBNH	2000	1350	−2.7 (d)	63.4
potassium 9-(2,3-dimethyl-2-butoxy)-9-BBNH	2000	1355	−2.8 (d)	60.3
potassium 9-(3-ethyl-3-pentoxy)-9-BBNH	2020	1350	−2.8 (d)[b]	69.3

[a] All chemical shifts are relative to $BF_3{\cdot}OEt_2$ with chemical shifts upfield from $BF_3{\cdot}OEt_3$ assigned as negative. [b] A broad singlet in the case of a more than 1 M solution.

Table IV. Stereoselective Reaction of Potassium 9-Alkoxy-9-boratabicyclo[3.3.1]nonane (K9-Alkoxy-9-BBNH) with Cyclic Ketones in Tetrahydrofuran at 0 and −25 °C[a,b]

ketone	temp, °C	R in K9-OR-9-BBNH					
		i-Pr	*sec*-Bu	*t*-Bu	*t*-amyl	*t*-hexyl	CEt_3[c]
2-methylcyclohexanone	0	99	98.5	95	97	98.5	96.5
	−25	99	98.5	98	97.5	99	98
3-methylcyclohexanone	0	73	80	83	84	90	86.5
	−25	79.5	82	89	86.5	90.5	85
4-methylcyclohexanone	0	68.5	74.5	78.5	77.5	85.5	81
	−25	72	75	80.5	80.5	86	81.5
4-*tert*-butylcyclohexanone	0	74	82	82.5	83	87	86.5
	−25	75	82	86.5	88	90	83.5
3,3,5-trimethylcyclohexanone	0	97	98.5	98.5	>99.9	>99.9	>99.9
	−25	99.5	99.9	>99.9	>99.9	>99.9	>99.9
norcamphor	0	92	91.5	95	97	95	97
	/25	94	93.5	95.5	98.5	96	97.5
camphor	0	96	97.5	93.5	93	97.5	98
	−25	98	98.5	93.5	93.5	98.5	95

[a] A 2:1 ratio for K9-alkoxy-9-BBNH:ketone was used. [b] The yields of alcohols were more than 98% and the figures are percentages of the less stable isomers. [c] Very slow heterogeneous reaction at −25 °C.

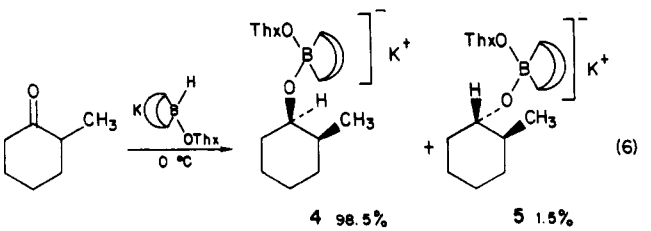
On the other hand, the more hindered alkoxy derivatives, R = *i*-Pr, *sec*-Bu, *t*-Bu, *t*-Am, Thx, and Et_3C, were very stable under nitrogen in THF at room temperature with or without added potassium hydride.

One exception was noted. The borinic ester, *B*-OR-9-BBN, R = 2,4-dimethyl-3-pentoxy, not only required exceptionally drastic conditions for the reaction with potassium hydride, >20 days at 65 °C (refluxing THF), but the product underwent redistribution as the reaction proceeded. Evidently the conditions required for the synthesis are too drastic for the product.

Infrared Spectra. Solutions of the potassium 9-alkoxy-9-BBNH in THF display typical absorptions in the IR. A strong, broad absorption is observed around 2000 cm^{-1}, attributed to the B–H stretching vibration, and a strong, sharp absorption around 1350 cm^{-1}, attributed to the B–O stretching vibration. These are similar to the characteristic absorption of B–H in trialkylborohydrides[2b,6] and of B–O in trialkoxyborohydrides.[4b] The results are summarized in Table III.

^{11}B NMR Spectra. The ^{11}B NMR spectra of the THF solutions of the stable borohydride derivatives, K9-OR-9-BBNH, exhibit clean doublets in the region slightly upfield from the standard, $BF_3{\cdot}OEt_2$. It should be pointed out that relatively high concentrations (>1 M) of compounds with bulky alkyl groups, such as K9-(3-ethyl-3-pentoxy)-9-BBNH, exhibit a broad singlet. This is a viscosity effect and the usual doublet is observed following dilution of the solution. The results are summarized in Table III.

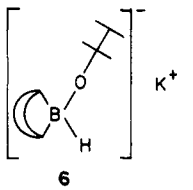
Stereoselectivities in the Reduction of Cyclic Ketones. A representative group of cyclic ketones was reduced by these new reagents at 0 and −25 °C in order to determine their stereoselectivities (eq 6). The results are summarized in Table IV.



4 98.5% 5 1.5%

All of the reagents showed an excellent stereoselectivity toward the monocyclic and bicyclic ketones examined. In general, the degree of stereoselectivity exhibits a close correlation with the size of the alkoxy substituent in the reagent (1). Only the 3-ethyl-3-pentoxy derivative fails to show a higher stereoselectivity anticipated from its slower rate of reaction with potassium hydride, presumably a consequence of large steric requirements of this alkoxy group.

Especially noteworthy is the thexyl derivative, potassium 9-(2,3-dimethyl-2-butoxy)-9-BBNH (**6**). This compound revealed the most favorable stereoselectivity of the compounds examined, exhibiting a stereoselectivity that is comparable to that shown by lithium tri-*sec*-butylborohydride.[3]



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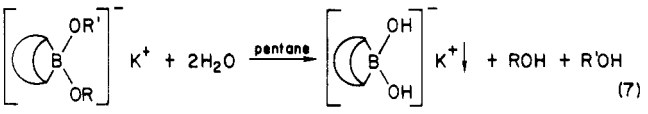
(6) Brown, H. C.; Krishnamurthy, S.; Hubbard, J. L. *J. Am. Chem. Soc.* **1978**, *100*, 3343.

Simplified Product Isolation. Hindered trialkylborohydrides, such as lithium tri-*sec*-butylborohydride and lithium and potassium trisiamylborohydride, are very valuable reagents, achieving stereoselectivities that appear almost unbelievable. Although these reagents are exceptionally useful for such reductions and have been widely applied, the reaction byproducts, tri-*sec*-butyl- or trisiamylborane, can cause difficulties with the isolation of the reduction product, the desired alcohol. A common solution is the oxidation of the organoborane at the end of the reduction with alkaline hydrogen peroxide. It is now a simple matter to separate the commonly less volatile alcohol product from *sec*-butyl or isoamyl alcohol.

The new reagent possesses a significant advantage in facilitating the recovery of the alcohol product. Controlled addition of water to the reaction mixture converts the 9-BBN moiety to the "ate" complex (eq 7). The THF solvent is removed and pentane is added. The "ate" complex precipitates.



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Indeed, we experienced no difficulty in isolating an 84% yield of *cis*-2-methylcyclohexanol in 98.5% isomeric purity following removal of the 9-BBN moiety from the reaction of 2-methylcyclohexanone with potassium 9-(2,3-dimethyl-2-butoxy)-9-BBNH (**6**) (eq 6), following treatment of the THF solution of the reaction products (**4**, **5**) with water (eq 7).

Conclusion

With the exception of the relatively unhindered alkoxy groups, such as methoxy and *n*-butoxy, and one highly hindered derivative, 2,4-dimethyl-3-pentoxy, the new reducing agents, potassium 9-alkoxy-9-boratabicyclo-[3.3.1]nonane (**1**) are readily prepared by treating the borinic esters, *B*-OR-9-BBN, with potassium hydride in tetrahydrofuran at 0 or 25 °C. Except for the three exceptions mentioned above, all of the potassium derivatives thus prepared are stable toward disproportionation, even in the absence of added potassium hydride.

The reagents reveal excellent stereoselectivity in the reduction of cyclic ketones at 0 and −25 °C. In the case of potassium 9-(2,3-dimethyl-2-butoxy)-9-boratabicyclo-[3.3.1]nonane (K9-OThx-9-BBNH), the stereoselectivity approaches that achieved with lithium tri-*sec*-butylborohydride but is not as high as that achieved with lithium trisiamylborohydride. However, the present reagent possesses a significant advantage, easy removal of the byproduct from the reaction mixture, facilitating recovery of the reduction product.

Experimental Section

General Methods. All glassware was dried in an oven, assembled hot, and cooled in a stream of dry nitrogen. All reactions were carried out under a nitrogen atmosphere. Special experimental techniques used in handling air-sensitive material are described in detail elsewhere.[7]

Materials. Tetrahydrofuran was dried over a 4-Å molecular sieve and distilled from benzophenone–sodium ketyl just prior to use. Potassium hydride was used as received from Alfa and was freed from the mineral oil according to the published procedure.[8] 9-Borabicyclo[3.3.1]nonane (9-BBN) was purchased from Aldrich Chemical Company and was used directly without further purification to prepare *B*-alkoxy-9-BBN. All of the *B*-alkoxy-9-BBN derivatives were distilled from a small piece of potassium metal.

Spectra. Infrared spectra were recorded on a Perkin-Elmer 700 spectrophotometer by using sealed liquid cells and the two-syringe technique.[7] ^{11}B NMR spectra were recorded with a Varian FT-80A instrument. The chemical shifts reported are in δ (ppm) relative to BF_3·OEt_2.

GLC Analyses. GLC analyses were carried out with a Varian Model 1400 FID chromatograph equipped with a Hewlett-Packard 3390A integrator/plotter. The alcohol products were analyzed with a 12 ft × 0.125 in. column of 15% THEED on a 100/120 mesh Supelcoport of 10% Carbowax 20M on 100/120 mesh Supelcoport. All GLC yields were determined by using a suitable internal standard and an authentic sample.

***B*-(2,3-Dimethyl-2-butoxy)bicyclo[3.3.1]nonane (*B*-OThx-9-BBN).** The following procedure is representative. An oven-dried, 250-mL, round-bottom flask, equipped with a side arm, a condenser, and an adaptor, and connected to a mercury bubbler was cooled to room temperature under a stream of nitrogen and maintained under a static pressure of nitrogen. In the flask was placed 12.2 g (100 mmol) of 9-BBN and 30 mL of THF. A total of 10.73 g of 2,3-dimethyl-2-butanol (105 mmol) was added to the slurry of 9-BBN and THF dropwise while the mixture was stirred at room temperature. After completion of addition, the reaction mixture was brought to a gentle reflux to evolve all of the hydrogen (1 h). Evaporation of the solvent, followed by distillation from a small piece of potassium metal, yielded 20.0 g of pure *B*-OThx-9-BBN (89% yield): bp 95–96 °C (1.3 mm); n^{20}_D 1.4785; ^{11}B NMR δ 55.1 (neat). The results for other *B*-alkoxy-9-BBN are summarized in Table I.

Preparation of Potassium 9-(2,3-Dimethyl-2-butoxy)-9-boratabicyclo[3.3.1]nonane (K9-OThx-9-BBNH) in THF at Room Temperature. The following procedure is representative. An oven-dried, 100-mL, round-bottom flask with a side arm, a condenser, and an adaptor was attached to a mercury bubbler. The flask was flushed with dry nitrogen and maintained under a static pressure of nitrogen. To this was added 6.4 g of potassium hydride (160 mmol) as an oil suspension using a double-ended needle. The mineral oil was removed with THF (3 × 10 mL). To this pure potassium hydride was added 50 mL of freshly distilled THF. *B*-OThx-9-BBN (18 g, 80 mmol) was added slowly to the potassium hydride suspension in THF with vigorous stirring at room temperature. The reaction was monitored by withdrawing aliquots of the reaction mixture at appropriate time intervals and determining its ^{11}B NMR spectra. The ^{11}B NMR spectrum of the reaction mixture after 24 h at room temperature showed a clean doublet centered at δ −2.8 ppm (J_{BH} = 60.3 Hz), indicating the formation of pure K9-OThx-9-BBNH. An aliquot of the clear solution of the reagent was hydrolyzed in a THF–glycerine–2 N HCl mixture (1:1:1) and the hydrogen evolved was measured. This indicated the hydride concentration to be 0.92 M. The concentration of boron was estimated from the amount of cyclooctanediol produced by oxidation of an aliquot with $NaOH$–H_2O_2. A 0.93 M concentration of boron was indicated. The potassium content was measured as potassium hydroxide, after the solution of reagent was quenched with water. Titration with standard acid indicated the concentration of potassium ion to be 0.92 M. Therefore, a 1.00:1.01:1.00 ratio of K:B:H was established.

Stereoselective Reductions.[9] The reaction of 2-methylcyclohexanone with potassium 9-(2,3-dimethyl-2-butoxy)-9-BBNH is representative. In a 50-mL round-bottom flask was placed 2.2 mL of a 0.92 M solution of the reagent in THF (2.0 mmol in hydride). The flask was maintained at 0 °C with an ice–water bath. To this was added 1.0 mL of a 1.0 M solution of 2-methylcyclohexanone in THF. The reaction mixture was stirred at 0 °C for 3 h (3 days at −25 °C). The reaction was then quenched by addition of 2 mL of 2 N HCl and the aqueous layer saturated with anhydrous potassium carbonate. The GLC analysis of the

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(8) Brown, C. A. *J. Org. Chem.* **1974**, *39*, 3913.

(9) A preliminary Communication describing the high stereoselectivity achieved with K9-OThx-9-BBN has been published: Brown, H. C.; Cha, J. S.; Nazer, B. *J. Org. Chem.* **1984**, *49*, 2073.

organic layer revealed the presence of 100% 2-methylcyclohexanol containing 98.5% of the cis isomer. The results are summarized in Table IV.

Product Isolation from a Preparative Run. In a larger-scale reaction, carried out to test the isolation procedure, 5.6 g of 2-methylcyclohexanone (50 mmol) was added dropwise as a neat liquid to 60 mL of the reagent solution in THF (55 mmol) at 0 °C. The reaction was complete in 1 h. The reaction mixture was then hydrolyzed with 2.5 mL of water for 0.5 h at room temperature. All THF was then pumped off by using an aspirator. Pentane (50 mL) was added to the residue. A white solid precipitated as the mixture was stirred. Fractional distillation of the solution following filtration gave 4.8 g (84% yield) of essentially pure 2-methylcyclohexanol, bp 166-168 °C (753 mm). GC examination revealed the presence of 98.5% cis- and 1.5% trans-2-methylcyclohexanol.

Acknowledgment. The support of this investigation by the United States Army Research Office (Grant ARO DAAG-29-82-K-0047) is gratefully acknowledged.

Synthesis of 4-, 5-, 11-, and 12-(Chloromethyl)benzo[*a*]pyrene[1]

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The previously unknown title compounds have been synthesized in excellent yields from the ethyl arylacetates **3a-d**. Formylation of **3a-d** allowed the isolation of formyl esters **4a-d** that were cyclized by a novel procedure utilizing dilute solutions (5-10%) of methanesulfonic acid in methylene chloride. The resulting benzo[*a*]pyrene ethyl esters were transformed to the target chloromethyl compound by reduction (LAH) followed by reaction with thionyl chloride. The overall yields obtained from esters **3a-d** ranged from 44% to 66%. These compounds can be used as immediate precursors of benzo[*a*]pyrenylmethyl carbocations which are believed to be relevant in certain carcinogenesis mechanisms.

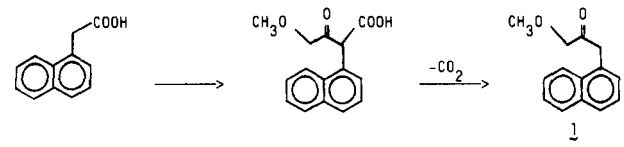
The synthesis of (chloromethyl)benzo[*a*]pyrenes has been an area of interest in our laboratories for several years since they can be used as arylmethyl carbocation precursors.[2-4] In some cases, these ionic species have been considered as possible "ultimate carcinogens".[5-7] These theories are a consequence of the consistent appearance of hydroxymethyl derivatives among the metabolites of many carcinogenic methylated polycyclic aromatic hydrocarbons (PAH).[8,9] For instance, the appearance of 6-(hydroxymethyl)benzo[*a*]pyrene as a metabolite of the potent carcinogens benzo[*a*]pyrene (B[*a*]P) and 6-methyl-B[*a*]P[10] and its role in the promotion of malignant tumors remains to be explained.

Assuming that arylmethyl carbocations are indeed ultimate carcinogens their immediate precursors should show significant tumorigenic activity, as has been shown to be the case in some specific cases.[11] It has also been shown by Dipple and co-workers that the carcinogenicity of a series of bromomethyl PAH's increased along with the stability of their corresponding carbocations.[12]

Since Cl^- has been found to be a good leaving group in the generation of B[*a*]P methyl carbocations and after considering all the findings mentioned above, the synthesis of (chloromethyl)-B[*a*]P in different regions of the B[*a*]P moiety was undertaken. The availability of these compounds, plus the 1-, 6-, and 10-(chloromethyl)-B[*a*]P (also synthesized in our laboratories)[2-4] would make possible a comprehensive study of the kinetics of B[*a*]P methyl carbocation formation. The values obtained can then be compared with both mutagenicity[13] and carcinogenicity data.

In the past, several research groups have shown interest in labeled (^{13}C and ^{14}C)[2,14] functionalized B[*a*]P's. We

Scheme I



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hoped to develop sequences that could be successfully adapted to the production of B[*a*]P's labeled with C-13 at the methylene carbon from available ^{13}C-labeled starting materials such as K*CN and CH_3*COOEt. These labeled compounds can be used to study the selectivity of B[*a*]P methyl carbocations in their reactions with different nucleophiles.[15]

Results and Discussion

Efforts to correlate the electronic density and reactivity of the K region (positions 4, 5 and 11, 12) and the bay

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