Table I. Results of Trialkylboron Studies

Run no.	Metal	Concentration, M: Initial metal	Concentration, M: Initial trialkylboron	Contact time, days	% metal reacted/24 hr
85A	K	3.0×10^{-3}	5.2×10^{-2}[a]	7	5.8
74A	Na	9.0×10^{-3}	7.3×10^{-2}[a]	19	5.3
47A	Na	1.6×10^{-2}[c]	1.6×10^{-1}[b]	25	3.2
9D	K	4.3×10^{-2}[d]	1.5×10^{-1}[b]	7	3.4
7A	Na	2.1×10^{-2}[c]	7.8×10^{-2}[b]	31	...[e]
91A	Na	3.6×10^{-2}[d]	4.2×10^{-2}[b]	8	0.9

[a] Trimethylboron. [b] Triethylboron. [c] Estimated from conductance. [d] Determined from hydrogen evolution. [e] Not estimated but solution was not faded.

Using conductance data reported by Kraus[7] and Smith,[3] concentration *vs.* time data were calculated. In all of the studies, metal concentration *vs.* time plots yielded straight lines indicating zero-order kinetics.

It can be seen in Table I that a minimum of 0.85% to a maximum of 5.8% of metal reacted per day in any run. Only in run 74A did the solution completely decolorize, indicating complete reaction of the metal, after 19 days. In all other runs the solutions remained blue for the contact times listed in Table I, at the conclusion of which the runs were terminated. An attempt was made following run 91A to recover the unreacted triethylboron as follows. After 8 days, the run was discontinued and the ammonia was distilled out of the reaction vessel through an acetone–Dry Ice trap and condensed in a liquid nitrogen trap. The triethylboron which remained in the reaction vessel and acetone–Dry Ice trap was next distilled into a tared vial which was sealed off and reweighed. (An interesting observation was made during this distillation. The mixture of unreacted triethylboron and sodium took on a red color while warming upon melting of the sodium. The red color faded after several minutes. A red flash was observed in another run when the reaction vessel was heated with a flame, and again the red color faded only slowly. It seems that the red color may be due to a sodium complex, but its nature was not investigated.) From a 0.199-g sample of triethylboron, 0.171 g was recovered after a single distillation. The recovery of 86% of the starting compound after 8 days indicates that little, if any, reaction had occurred according to eq 2.

To compare our results with those of Smith and Kraus[1] and Holliday and Thompson,[2] we might first point out that Smith and Kraus also reported that trimethylboron reacts with sodium amide in liquid ammonia according to the equation

$$(CH_3)_3BNH_3 + NaNH_2 \longrightarrow (CH_3)_3BNH_2Na + NH_3 \quad (4)$$

In the experiment reported by Holliday and Thompson,[2] a large excess of potassium was used and the amount of hydrogen obtained was in agreement with eq 5,

$$M + NH_3 \longrightarrow MNH_2 + 0.5H_2 \quad (5)$$

in which M is an alkali metal. On the other hand, in studying reaction 1, Smith and Kraus[1] used equivalent amounts of sodium and trimethylboron. Under these conditions, the hydrogen obtained will be in agreement with both eq 1 and 5. Furthermore, it has been shown that carefully prepared alkali metal–ammonia solutions are stable for up to several months[6] and decompose only slowly according to eq 5 which is autocatalytic,[8] while an unstable alkali metal–ammonia solution rapidly produces amide ions.[8,9]

In our experiments, excess amounts of trimethylboron or triethylboron failed in all cases but one to bleach metal–ammonia solutions even after long contact periods, and concentration *vs.* time data could be best fitted to zero-order kinetics. We conclude, therefore, that the mechanism for reaction 2 is eq 5 and 4, the rate depending on the stability of the solution to reaction 5, and that the ammonia coordination compounds of both trimethyl- and triethylboron are not reduced by sodium and potassium in liquid ammonia.

Acknowledgment. This work was supported by the National Science Foundation. The authors thank Mr. Norder for his cooperation.

(7) C. A. Kraus, *J. Am. Chem. Soc.*, 43, 749 (1921).

(8) R. E. Cuthrell and J. J. Lagowski, *J. Phys. Chem.*, 71, 1928 (1967).

(9) W. L. Jolly and C. J. Hallada in "Solvent Systems," T. C. Waddington, Ed., Academic Press Inc., New York, N. Y., 1965, p 37.

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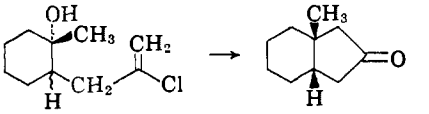
Intermediates for 16-Keto and A-Nor Steroids and Derivatives

Sir:

In our initial studies of cycloalkanone formation by intramolecular cyclization of β-chloroallyl groups with electrophilic centers, we succeeded in obtaining *cis*-8-methyl-2-hydrindanone.[1] This fact suggested that 2-



(β-chloroallyl)-1-tetralones could provide tricyclic ketones of potential utility in total synthesis of natural products such as 16-keto steroids and A-nor steroids containing *cis*-ring fusions in the hydrindanone portion of the molecule. Using 5- or 6-methoxy-1-tetralones (to allow further elaboration of cyclohexenones obtainable by Birch reduction) and introducing angular methyl groups (potentially C_{18} and C_{19}) by enolate alkylation (route a) or Grignard addition (route b), the following possibilities present themselves. We now wish to report that such synthetic sequences can be carried out in good over-all yield[2] beginning with commercially available 1-tetralones[3] when proper conditions are chosen for the crucial final cyclization.[4]

Monoalkylation of tetralones I and II was accomplished efficiently by using methylmagnesium carbonate[5] and 2,3-dichloropropene in dimethylformamide to

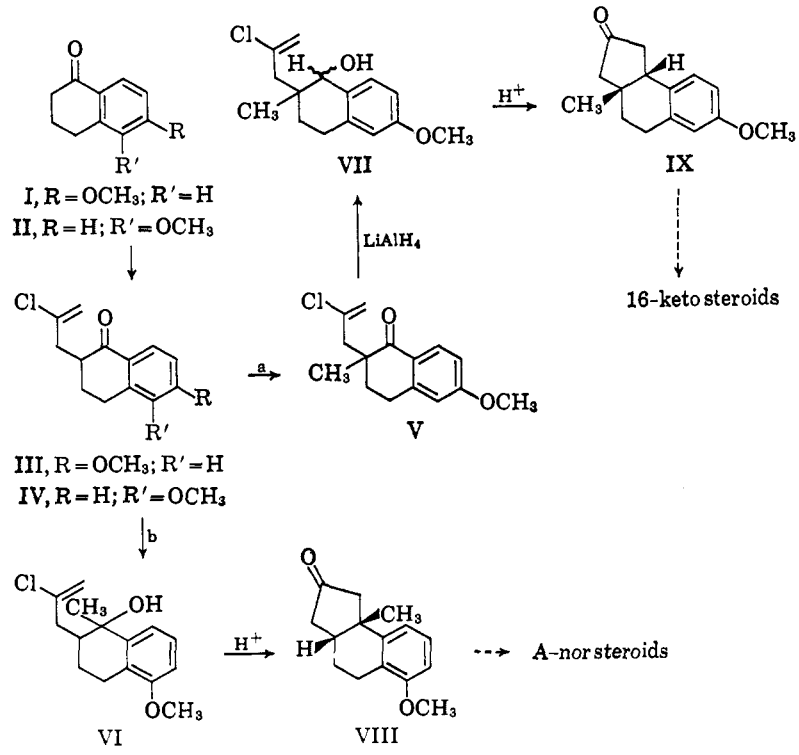
(1) P. T. Lansbury and E. J. Nienhouse, *J. Am. Chem. Soc.*, 88, 4290 (1966).

(2) All compounds gave satisfactory elemental analyses and consistent spectral properties (infrared, ultraviolet, and nmr).

(3) The routes described herein are considerably better than those conceivable beginning with 2-tetralones, which are also more costly.

(4) Reaction of VI and VII with acid can lead to simple dehydration (from VI) and/or hydrolysis of the β-chloroallyl group to an *uncyclized* acetone derivative. It appears that such compounds can be partially converted to tricyclic ketones VIII and IX, which may be the thermodynamic products (P. T. Lansbury and F. R. Hilfiker, unpublished observations).

(5) M. Stiles, *J. Am. Chem. Soc.*, 81, 2598 (1959).

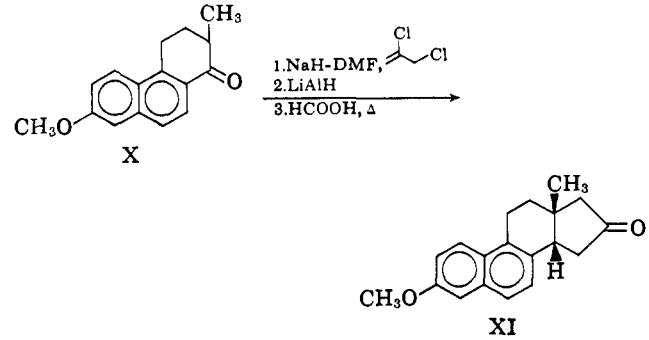


give 2-(β-chloroallyl)-1-tetralones III and IV in 87 and 79% yields, respectively. Ketone III, mp 55–56.5° (from petroleum ether, bp 30–60°), displayed infrared bands (Nujol mull) at 5.99 (>C=O) and 6.11 μ (>C=CH_2); similarly IV, mp 54–56.5° (methanol), had the corresponding infrared stretching absorptions at 5.96 and 6.11 μ.

Further alkylation of the enolate from III (sodium hydride in dimethylformamide) with methyl iodide gave an 85% yield of V, showing infrared carbonyl absorption (neat) at 5.98 μ and the C_2CH_3 as a singlet at 1.22 ppm in the nmr.[6] Reduction of V to VII (mixture of diastereomers) was accomplished in over 95% yield with ethereal lithium aluminum hydride. Brief treatment (0° for 10 min, then quenching in ice water) of VII (mp 90–94° from 30–60° petroleum ether; infrared bands due to O–H at 2.90 μ and terminal methylene at 6.11 μ) with 90% sulfuric acid yielded (44%) the oily tricyclic ketone IX[2] (semicarbazone mp 206–208° (C_2H_5OH)) whose infrared spectrum (neat) indicated cyclopentanone-type carbonyl stretching at 5.74 μ and disappearance of the OH and terminal methylene bands in VII. The nmr spectrum[6] of IX showed resonances at 1.14 ppm (three-proton methyl singlet), 1.38–3.34 (nine aliphatic protons in complex envelope), 3.72 (three-proton methoxy singlet), and 6.43–7.22 ppm (three aromatic protons). Tetralone IV was allowed to react with methylmagnesium iodide to give the tertiary alcohol VI,[2] mp 88–92° (hexane), as a mixture of diastereomers (78% yield) showing infrared absorption at 2.99 and 6.11 μ.

Cyclization of VI proceeded to ketone VIII in 40% yield when performed with polyphosphoric acid at ~95° for 5 hr or in lower yield using 90% sulfuric acid. Chromatography of the cyclization mixture over alumina afforded oily VIII, 2,4-dinitrophenylhydrazone mp 233–234° (benzene), which displayed the expected infrared carbonyl band at 5.74 μ (neat). The nmr spectrum of VIII showed a three-proton singlet at 1.43 ppm (CH_3), a complex envelope at 1.65–2.92 ppm (nine aliphatic protons), a three-proton singlet at 3.79 ppm (OCH_3), and three aromatic protons at 6.52–7.34 ppm.

Subsequent transformations of VIII and IX can provide entries to A-nor steroids functionalized at C_2 and 16-keto steroids, respectively.[7] A specific 16-keto steroid synthesis incorporating the above approach (as in V → VII → IX) is provided by the three-step conversion of 1-keto-2-methyl-7-methoxy-1,2,3,4-tetrahydrophenanthrene (X) to *cis*-3-methoxy-16-equilenone (XI),[8] mp 168.5–170°, mmp 168–170°. Carbinol cyclization with refluxing formic acid (30 min) led to XI in ~60% yield. This result, coupled with the previous synthesis of *cis*-8-methyl-2-hydrindanone,[1]



(6) All spectra were run in chloroform-*d* solution with internal TMS on the Varian A-60 spectrometer. Chemical shifts are reported in parts per million downfield from TMS.

(7) Typical total syntheses which could be adapted in transforming VIII and IX are discussed in L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, Chapters 15, 16, and 19. Previous approaches for converting 17-keto to 16-keto steroids (*trans* C/D ring fusion) are given by J. E. Bridgeman, E. R. H. Jones, G. D. Meakins, and J. Wicha, *Chem. Commun.*, 898 (1967), and D. Varec and J. Jacques, *Bull. Soc. Chim. France*, 67 (1965), and references cited therein.

(8) A. L. Wilds and W. J. Close, *J. Am. Chem. Soc.*, **69**, 3079 (1947); our sample of XI had ir and nmr spectra identical with those of an authentic sample furnished by Professor Wilds.

strongly supports the *cis*-fused structures for VIII and IX.

Acknowledgment. We are grateful to Professor A. L. Wilds for generous samples of X and XI and to the U. S. Army Research Office (Durham) for partial financial support.

(9) Alfred P. Sloan Foundation Fellow, 1963–1967.
(10) From State University College at Oneonta, N. Y., supported by NSF Grant No. GY-2430 for summer research participation for college teachers in chemistry, 1966–1967.

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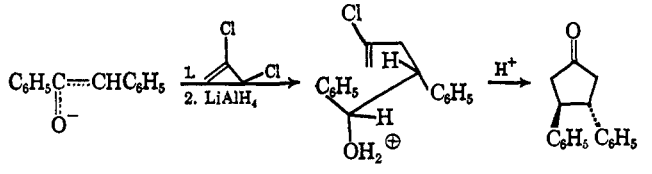
A Facile Entry into 3-Thianone and 3-Piperidone Ring Systems

Sir:

We have noted previously[1] the presence of electrophilic and nucleophilic sites in 2,3-dichloropropene (I) which can be used to advantage in compact reaction sequences with suitable bifunctional compounds (containing nucleophilic and potential electrophilic centers) to produce cycloalkanone rings, *e.g.*



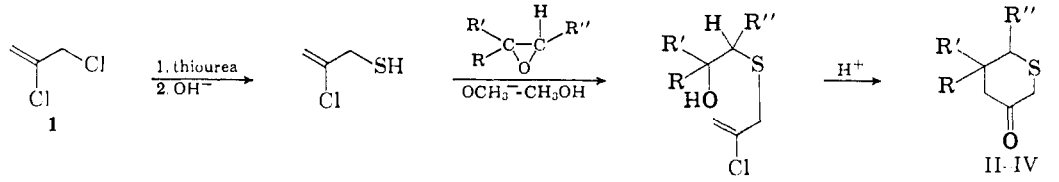
(1) P. T. Lansbury and E. J. Nienhouse, *J. Am. Chem. Soc.*, **88**, 4290 (1966).

In this communication we extend our cycloalkanone synthesis in novel fashion to heterosubstituted cyclohexanones[2] containing sulfur and nitrogen in place of C_3, compounds of substantial theoretical[3] and synthetic[4] interest, but not readily accessible.

In one variation, I can first be nucleophilically attacked by a species bearing the heteroatom to be incorporated at position 3 and the resultant derivative used to open an epoxide, which provides an alcohol for intramolecular cyclization.[1] This is illustrated in the preferred preparation of several 3-thianones[5] (Table I). Alternatively, I can be attacked by the nucleophilic derivative formed *after* epoxide cleavage, which appears to be the method of choice for constructing 3-piperidones. (Table II).

In the 3-thianone synthesis, the sodium salt of β-chloroallyl mercaptan[6] attacks the less substituted carbon of unsymmetrical epoxides predominantly (only one isomer was detected with isobutylene oxide and 1-methylcyclohexene oxide, whereas styrene oxide gave a 60:40 ratio of isomers VII and VIII). The acid-induced cyclization can proceed *via* episulfonium intermediates[7] as suggested by the exclusive generation

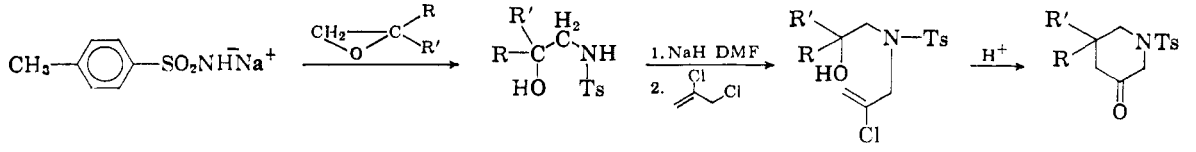
Table I



Compd	R	R′	R″	λ(C=O), μ	Cyclizing conditions	% yield[a]
II	C_6H_5	H	H	5.85 (neat)	Refluxing HCOOH, 90 min	54
III	CH_3	CH_3	H	5.86 (neat)	90% H_2SO_4, 0°, 20 min	90
IV	CH_3	—$(CH_2)_4$—		5.86 (neat)	90% H_2SO_4, 0°, 20 min	35

[a] For reactions using ~1 g of carbinol precursor in 25–30 ml of solvent.

Table II



Compd	R	R′	Mp, °C	λ(C=O), μ (Nujol)	Cyclizing conditions	% yield
V	C_6H_5	H	136–137	5.75	90% H_2SO_4, 0°, 10 min	50
VI	CH_3	CH_3	107–109[a]	5.77	90% H_2SO_4, 0°, 25 min	90

[a] Lit. mp 110° (R. F. C. Brown, V. M. Clark, and Lord Todd, *J. Chem. Soc.*, 2105 (1959)).

(2) All new compounds gave satisfactory elemental analyses and were further characterized by infrared and nmr spectroscopy.
(3) For example, possible transannular interactions of the heteroatom with the carbonyl group and the heteroatom effect on kinetic and equilibrium acidities at C_2 *vs.* C_5 are being explored by us.
(4) Lengthy sequences leading to substituted 5-methyl-3-piperidones for use in total syntheses of jervine, veratramine, and related Veratrum alkaloids have recently been reported by T. Masamune and W. S. Johnson and their coworkers (*J. Am. Chem. Soc.*, **89**, 4521, 4523 (1967)).
(5) The alternative epoxide opening by bisulfide ion followed by displacement upon I is poor because of substantial sulfonium salt formation in the S-alkylation step.
(6) Bp 56–57° (70 mm); 2,4-dinitrophenyl thioether derivative mp 67–68.5°; nmr SH at 2.02 ppm (triplet, J = 8 Hz), CH_2S at 3.5 ppm (doublet, J = 8 Hz), vinyl protons at 5.30 and 5.49 ppm (doublets, J = 2 Hz).