IMPROVED PROCEDURE FOR THE GENERATION OF ALLYL CATIONS FROM SIMPLE DIBROMO KETONES.
CHANGE OF MECHANISM ON REACTION WITH TRIETHYL BORATE AND ZINC. CYCLOADDITIONS
TO CONJUGATED DIENES.

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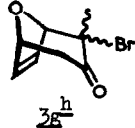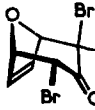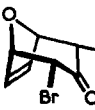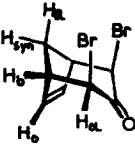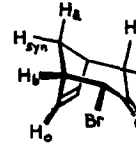
Several techniques are now available for generating allyl cations as reactive intermediates
of various cycloadditions. In addition to the silver salt route[1] which has permitted the
preparation of bicyclo[3.2.2]nona-6,8-dien-3-one from benzene and the 2-methoxyallyl cation[2],
one may use α,α -dihalo ketones in combination with suitable reducing agents such as zinc-
copper couple[3], nonacarbonyldi-iron[4] and also sodium iodide in the presence of copper.[5]
Presumably, each method has its merits which are emerging more clearly and which depend on the
lifetime of the required allyl cation intermediate, the nature of the added π component and
the stability of the final product.

We now report a novel variant which starts with a dihalo ketone, but is quite different from
previous approaches in that it involves a change of mechanism. The procedure does not require
highly reactive zinc-copper couple and seems advantageous for generating fairly reactive allyl
cations derived from dihalo ketones with a minimal number of terminal alkyl groups. An
illustrative experiment is the preparation of 2,2-dimethylbicyclo[3.2.1]oct-6-en-3-one (2a).
In a three-necked round-bottomed 500 ml flask equipped with a stirrer, dropping funnel and
efficient condenser are placed 16.5 g (0.25 g atom) zinc powder and 33 g (0.5 mole) cyclo-
pentadiene in dry tetrahydrofuran.   3-Bromo- 1-iodo-3-methyl-2-butanone (73 g, 0.25 mole)
and triethyl borate (50 ml, 0.3 mole) in dry tetrahydrofuran (50 ml) is added slowly with
stirring under a slow stream of nitrogen during 1-1.5 hr. The mixture is left overnight,
chilled with salt-ice mixture, and water (50 ml) is added slowly followed by concentrated
aqueous ammonia (200 ml, ca. 17% v/v) in order to dissolve the zinc salts. The aqueous layer
is extracted three times with 100 ml ether, the combined organic layer is washed once with
water, dried and the solvents are removed to give a crude mixture of products which is steam-
distilled in the presence of sodium hydroxide (p_H 10-11). The steam distillate contains some
dicyclopentadiene (ca. 10-15%) and the desired adduct 2a (23 g, 61 %), which can be purified
by chromatography on silica gel. Under the same conditions the primary-secondary dibromo
ketone 3, which in previous experiments with zinc-copper couple had failed to enter into
cycloadditions [5b] formed 3a + b and 3d + e respectively, with cyclopentadiene and furan
in addition to 3c and 3f. Furthermore, 1,1,3-tribromoacetone and cyclopentadiene gave at least
three adducts including a dibrominated bicyclic and 6c. As a further route to the known
bicyclics 5c and 6c we have also[4] used 1,1,3,3-tetrabromoacetone in combination with triethyl
borate and zinc and succeeded in isolating the tribrominated adduct 5a as well as 6b and
the cis-diaxial derivative 6a (cf. Table).

From previous experience with zinc-copper couple as reducing agent the formation of mono-

TABLE 1. CYCLOADDUCTS FROM THE REACTION OF SIMPLE BROMO KETONES
WITH TRIETHYL BORATE AND ZINC.

Dihalo Ketone [a]	Diene	Cycloadducts		Yield
		1a[b]　　1b[c]		78% [c] (1a 1b = 2.2.1)
		2a[b]		76% [c] 60-68% [d,e]
		3a[f]　3b[f]　3c	3c ir(CCl$_4$) 1734 cm^{-1} nmr(TMS,CCl$_4$)δ1.05(d,J=7Hz,3H) 1.75-2.95 (m,5H), 4.65 (d,J~3Hz,1H), 6.1 (m,2H)	3a+b 14% (3a 3b ~1.3 1) 3c 23% [g]
		3d[f]　3e[f]　3f	3f mp 55-56°, m/e 218,216, ir (CCl$_4$) 1737 cm^{-1}. 100MHz nmr (CCl$_4$) 1.04(d,J=7Hz,3H), 2.95 [d(J=4.5Hz) of q(J=7Hz,1H], 4.60 (d,J=4.5Hz,1H), 4.77(m,1H) 5.05 (m,1H), 6.4 (m,2H)	3d+e 10% [d] 3f 20% [d]
		3d + 3e + 3f + 3g[h]		3d+3e 9% 3f 23% 3g 14%
		5a　　5b[i]　　5c[i]	5a mp 102-104°,ir(CHCl$_3$) 1745 cm^{-1}. 100MHz nmr (CDCl$_3$) 5.15 (d of d,J= 1.5Hz,4.5Hz,1H), 5.30 (d,J=1.3Hz,1H), 5.42 (d,J=4.5Hz,1H), 6.66 (m,2H).	5a 2% [d] 5b 30% [d] 5c 2% [d]
		6a[k]　　6b　　6c[i]	6b ir(CHCl$_3$) 1748 cm^{-1} 100MHz nmr(CDCl$_3$) 2.12 (d,J=12.5Hz, H$_a$), 2.31 [d(J=12.5Hz) of t(J=5Hz), H$_{syn}$], 3.3(br s,2H$_b$), 4.73 (d,J=3Hz,2H$_\alpha$), 6.3 (br s,2H$_o$)	6a 10-12% [d] 6b 15-25% [d] 6c 2-8 % [d]

a   Prepared according to C.Rappe, *Arkiv Kemi*, <u>21</u>, 503 (1963) and ref. 3a.

b   Ref. 3a. c Determined by glc. d Isolated yield after chromatography on silica gel. e 2,4-Dibromo-3-methyl-2-butanone instead of <u>2</u> as allyl cation precursor gave <u>2a</u> in 48-55% yield. f N.J.Turro, S.S.Edelson, J.R.Williams, T.R.Darling and W.B.Hammond, *J.Amer.Chem.Soc.*, <u>91</u>, 2283 (1969). g Determined by nmr, the separation of <u>3a</u> + <u>b</u> from <u>3c</u> on silica gel being poor. Reduction of the mixture with an excess of zinc in CH_3OH/NH_4Cl gave <u>3a</u> + <u>b</u> only. h Tentative assignment as this compound could not be isolated pure. <u>3g</u> showed a singlet at δ2.02 ppm (CH_3) and could be reduced to <u>3d</u> + <u>3e</u>. The adducts <u>3c</u>, <u>3f</u> and <u>3g</u> are quite unstable and turn brown within a short time on standing, especially in the presence of traces of acid and on exposure to oxygen. If the bromines are to be removed reductively it is advantageous to quench the reaction mixture first with methanol at $-60°$ and then to let it warm up with addition, if necessary, of further zinc and ammonium chloride. i Ref. 4.

j A.E.Hill, G.Greenwood and H.M.R.Hoffmann, *J.Amer.Chem.Soc.*, <u>95</u>, 1338 (1973).

k m/e 282, 280, 278, ir ($CHCl_3$) 1722 cm^{-1}. 100 MHz nmr ($CDCl_3$) 2.14[d($J_{gem}=12.5Hz$) of t($J_{H_{syn},H_b}=5Hz$) of t($J_{H_{syn},H_a}=2Hz$), H_{syn}], 3.02 (d,$J_{gem}=12.5Hz$, H_a), 3.14 [d($J_{H_b,H_{syn}}=5Hz$) of d($J_{H_b,H_a}=2Hz$), $2H_b$], 4.19 [d($J_{H_a,H_b}=2Hz$) of d($J_{H_a,H_{syn}}=2Hz$, $2H_a$], 6.19 (m,$2H_o$).

brominated cycloadducts (e.g. <u>3c</u> and <u>3f</u>) on using a dibromo ketone (<u>3</u>) [and of dibrominated adducts using 1,1,3-<u>tribromoacetone</u> as well as <u>tribrominated</u> <u>5a</u> from <u>tetrabromoacetone</u> (<u>5</u>)] is surprising. The most obvious explanation that the starting bromo ketones were accompanied by more highly brominated derivatives, could be easily discounted by nmr. Furthermore, a control experiment in the absence of diene gave no evidence for any disproportion, e.g.
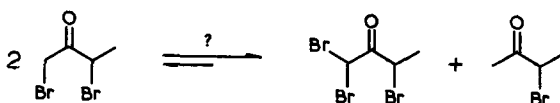
under the reaction conditions.

Significantly, the ditertiary dibromo ketone <u>7</u> which in earlier work with zinc-copper couple could be used as precursor par excellence towards zinc oxyallyl <u>8</u> [5b] did not react at all
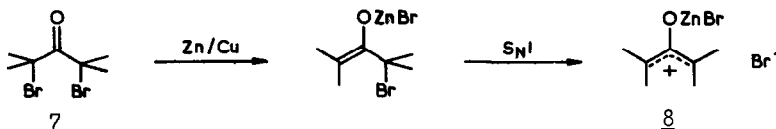
under the new conditions. Confirmatory evidence was provided by a competition experiment with <u>7</u> and the supposedly less reactive <u>2</u> in the presence of cyclopentadiene using triethyl borate and zinc, which gave the dimethylated bicyclic <u>2a</u>, but again no tetramethylated adduct.

A possible mechanistic sequence of the $(EtO)_3B/Zn$ reaction begins with enolization via loss of proton rather than reductive removal of bromine[6]. The postulated boron enolate 9[7] can ionize with intramolecular nucleophilic assistance by oxygen to the allyl cation 10, which combines with the conjugated diene. Consistently, the ditertiary dibromo ketone 7 which does not contain any protons α to the carbonyl group does not react under the modified conditions.
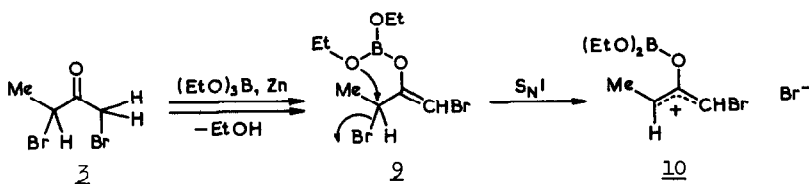
How is cis-diaxial 2,4-dibromobicyclo[3.2.1]oct-6-en-3-one (6a) being formed? An attractive possibility is that it arises from the exo, endo, exo-tribrominated bicyclic, the six-membered ring of which must be severely flattened. As a result the single bromine atom on the endo face of the molecule might well be most nearly axial and hence be removed selectively in the presence of zinc. It is striking that the nmr signal of methylene proton H_a in bicyclic 6a appears at 0.9 ppm downfield from the signal of H_a in the cis-diequatorial isomer 6b. It will be seen that the axial proton H_a in 6a is crowded by two exo bromine atoms and as a consequence, suffers van der Waals repulsion and deshielding.

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