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HIGHLY REGIOSELECTIVE REAGENTS FOR CONJUGATE REDUCTION OF ENONES, $HAl(Ot\text{-}Bu)_2$, $HAl(Oi\text{-}Pr)_2$, $HAl[N(i\text{-}Pr)_2]_2$ and HBI_2

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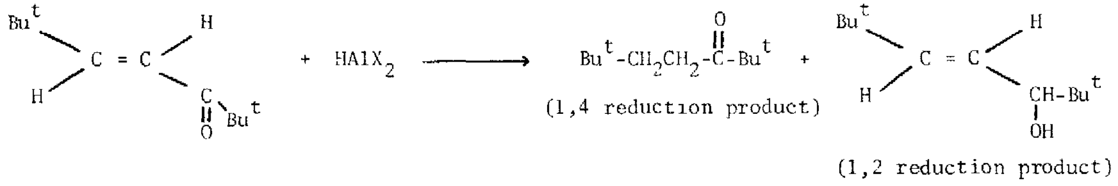
Recently, we reported that unusual regioselective conjugate reduction of enones can be effected by the reagent, $LiAlH_4$-CuI or its reactive species, H_2AlI.[1] Systematic studies on the haloalanes, H_nAlX_{3-n} (where n = 1 or 2 and X = I, Br, Cl) reveal that the steric effect of the X-group is the most important factor in determining this regioselectivity, i.e., $H_2AlI > H_2AlBr > H_2AlCl$.[2] This conclusion strongly suggested to us that we should investigate other alane derivatives containing bulky "X" groups, e.g., $HAl(i\text{-}Bu)_2$, $HAl[N(n\text{-}Bu)_2]_2$, $HAl[N(i\text{-}Pr)_2]_2$, HAl(Oi-P $HAl(Ot\text{-}Bu)_2$ and the boron derivatives containing a smaller central atom. We would like to report here excellent regioselectivity in the conjugate reduction of α,β-unsaturated ketones using $HAl(Oi\text{-}Pr)_2$, $HAl(Ot\text{-}Bu)_2$ and particularly $HAl[N(i\text{-}Pr)_2]_2$ and HBI_2.

Enone (I) was chosen as a representative enone for initial studies and the results are shown in Table I. The enone (I) was reduced by AlH_3 without specific selectivity (50:48) at a H^-:enone = 3 and with imporved regioselectivity (76:16) at H^-:enone = 1 (exp. 1 and 2). The



use of $HAl(i\text{-}Bu)_2$ (exp 3) results in greater regioselectivity (90:6) compared to AlH_3. Experiments 4-7 show that $HAl(Ot\text{-}Bu)_2$ is more selective than $H_2AlOt\text{-}Bu$ and that significantly greater selectivity is experienced at 0° compared to room temperature. Excellent regioselectivity (98:1) is observed for $HAl(Ot\text{-}Bu)_2$ at 0°, however the time required for complete reaction is long (12 hours). On the other hand, when $HAl(Oi\text{-}Pr)_2$ was allowed to react with I at 0° for 3 hours (exp. 9), 100% yield and 100% regioselectivity was observed. Although $HAl[N(n\text{-}Bu)_2]_2$ was

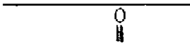
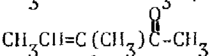
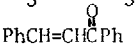
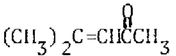
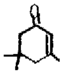
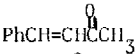
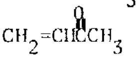
Table I. Reduction of 2,2,6,6-tetramethyl-trans-4-hepten-3-one (I) with $HAlX_2$ or HBI_2 Compounds.

Experiment	Alane or Borane	Mole Ratio Alane or Borane/Enone	Reaction Conditions	Enone Recovered	% Products[a]	
					1,4	1,2
1	AlH_3	1:1	0°, 1 hr.	0	50	48
2	"	1:3	0°, 1 hr.	8	76	16
3	$HAl(i\text{-}Bu)_2$	1:1	0°, 1 hr.	0	90	6
4	$H_2AlOt\text{-}Bu$	1:1	RT, 0.5 hr.[b]	0	88	11
5	"	1:1	0°, 0.5 hr.[b]	0	95	6
6	$HAl(Ot\text{-}Bu)_2$	2:1	RT, 4 hr.[b]	1	90	5
7	"	4:1	0°, 12 hr.[b]	0	98	1
8	$H_2AlOi\text{-}Pr$	1:1	0°, 3 hr.[c]	0	62	40
9	$HAl(Oi\text{-}Pr)_2$	2:1	0°, 3 hr.[c]	0	100	0
10	$H_2AlN(n\text{-}Bu)_2$	1:1	0°, 3 hr.[c]	0	81	19
11	$HAl[N(n\text{-}Bu)_2]_2$	4:1	0°, 6 hr.[c]	1	90	4
12	$H_2AlN(i\text{-}Pr)_2$	1:1	0°, 15 min.[d]	0	94	5
13	$HAl[N(i\text{-}Pr)_2]_2$	2:1	0°, 15 min.[d]	0	100	0
14	BH_3	1:1	0°, 0.5 hr.	0	78	11
15	"	1:3	0°, 2 hr.	0	94	7
16	H_2BI[e]	1:1	0°, 2 hr.	2	92	6
17	HBI_2[e]	4:1	RT, 9 hr	0	100	0

a. Yields are absolute based on initial ketone using an internal standard. All reactions were performed on 1 mmole scale. b. t-BuOH was added to AlH_3 dropwise and kept stirring 15 min. before use. c. Same procedure as (b) but 60 min. d. Same procedure as (b) but 3 hr. e. I_2/THF was added to BH_3 and kept stirring for 1 hr. at 0°C reasonably selective towards I (90:4), $HAl[N(i\text{-}Pr)_2]_2$ reduced I at 0° in 15 minutes in 100% yield and 100% regioselectivity (exp. 13). Furthermore, the enone I was reduced by HBI_2 in 100% regioselectivity and quantitative yield at room temperature, 9 hours (exp. 17)

Table II shows the results of the reactions of these new reagents with a series of ketones. The three alanes $HAl(Ot\text{-}Bu)_2$, $HAl(Oi\text{-}Pr)_2$ and $HAl[N(i\text{-}Pr)_2]_2$ reacted to give 94% regioselectivity with enones I-IV. Since $HAl[N(i\text{-}Pr)_2]_2$ and HBI_2 gave 100% regioselectivity when allowed to react with the same enones, further studies were carried out just with these two reagents. In the reaction of HBI_2 with enones V-X quantitative yields of conjugate reduction product were observed except in the cases of the cyclic ketones. On the other hand, $HAl[N(i\text{-}Pr)_2]_2$ gave excellent results except in the case of enones V and IX in addition to the cyclohexenones VI and VII. However, $HAl[N(i\text{-}Pr)_2]_2$ gave excellent results with cyclopentenone (X) whereas HBI_2 was ineffective with this compound.

Table II. Reduction of Enones II-X with $HAlX_2$ Reagents at 0° and HBI_2 at Room Temperature in THF

	Ratio of 1,4 to 1,2 Reduction				
	$HAl(i\text{-}Bu)_2$	$HAl(Ot\text{-}Bu)_2$	$HAl(Oi\text{-}Pr)_2$	$HAl[N(i\text{-}Pr)_2]_2$	$HBI_2{}^b$
 $CH_3CH{=}CH\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH_3$ (II)	8:90	94:5	95:2	100:0	95:0
 $CH_3CH{=}C(CH_3)\overset{O}{\overset{\|}{C}}\text{-}CH_3$ (III)	18:81	90:6	96:4	100:0.5	96:0
 $PhCH{=}CH\overset{O}{\overset{\|}{C}}Ph$ (IV)	63:35	98:0	97:2	100:0.5	95:0
 $(CH_3)_2C{=}CH\overset{O}{\overset{\|}{C}}CH_3$ (V)	-	-	-	6:0	98:0
 (VI)	-	-	-	23:72	5:0
 (VII)	-	-	-	0:0	15:0
 $PhCH{=}CH\overset{O}{\overset{\|}{C}}CH_3$ (VIII)	-	-	-	96:0	98:0
 $CH_2{=}CH\overset{O}{\overset{\|}{C}}CH_3$ (IX)	-	-	-	41:45	95:0
 (X)	-	-	-	94:1	11:0

a. $HAl(Ot\text{-}Bu)_2$:enone = 6, $HAl(Oi\text{-}Pr)_2$:enone = 6, $HAl[N(i\text{-}Pr)_2]_2$:enone = 4, $HAl(i\text{-}Bu)_2$:enone = 2. b. HBI_2:enone = 8, 20 hours, room temperature.

Aluminum hydride was synthesized by the reaction of 100% H_2SO_4 with $LiAlH_4$ in THF.[3] The above reagents were prepared by simply adding the appropriate alcohol or amine to AlH_3 in THF in 1:1 or 2:1 molar ratio. Hydrogen was evolved during the addition and the reaction was complete within 15-30 minutes except the reaction involving $i\text{-}Pr_2NH$, in which case 3 hours reaction time was required. The $HAlX_2$ compounds studied were identified by their Al-H stretching frequency assignments;[4] $HAl(Ot\text{-}Bu)_2$, 1850 cm^{-1}; $HAl(Oi\text{-}Pr)_2$, 1845 cm^{-1}; $HAl[N(n\text{-}Bu)_2]_2$, 1820 cm^{-1}; $HAl[N(i\text{-}Pr)_2]_2$, 1810 cm^{-1}. In no case were the Al-H bands for AlH_3 or H_2AlX observed. Diborane in THF was purchased from Alfa Products. HBI_2 was made by adding I_2/THF to BH_3/THF at 0°, the ratio of H^-/B was 0.95-1.00. The reduction procedure is straightforward and similar to that reported previously for H_2AlI.[1,2] The enone was added to the reagent slowly at 0° or room temperature, then the reaction was monitored by removing aliquot samples periodically, quenched by H_2O, dried by $MgSO_4$ and analyzed by glc using an internal standard.

In conclusion, $HAl(Ot\text{-}Bu)_2$, $HAl(Oi\text{-}Pr)_2$, $HAl[N(i\text{-}Pr)_2]_2$ and HBI_2 have been found to be effective conjugate reducing agents. The alane, $HAl[N(i\text{-}Pr)_2]_2$ and the borane, HBI_2, gave excellent regioselectivity and quantitative yields of conjugate reduction products in nearly all cases studied except the cyclohexenones.

References

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