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ALYLATION OF ALLYLIC CYCLOHEXENYL ESTERS WITH TRIALKYLALUMINUM REAGENTS. A REGIO AND STEREOCHEMICAL STUDY

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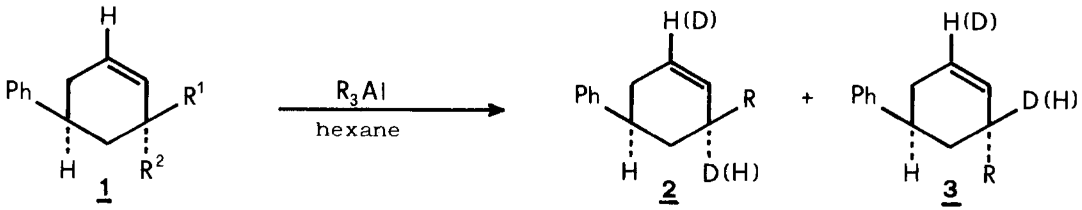
Abstract. Regio and stereochemistry of the title reaction appear to be strongly influenced by the nature of both organometallic and allylic reagents. The results are discussed in view of the intervention of ion-pair intermediates.

The alkylation of allyl acetates with organoaluminum reagents has been recently developed as an exceptionally mild procedure[1] and carbocationic intermediates were recognised to intervene in the alkylation of allyl, benzyl and cyclopropylmethyl acetates.[2] We wish to report that the outcome of the reaction is strongly influenced by the nature of the allylic system, leaving group, aluminum reagent and by the leaving group orientation.

The cyclohexenyl esters 1a-1d,[3] 4a, 4b, 5a and 5b[4] were alkylated on 1 mmole scale by treatement with 2 molar equivalents of organoaluminum reagent, in hexane, under nitrogen, according to the Table. The products 2a, 3a, 6a, 7a, 6b and 7b were identified by comparison with authentic samples.[3,4] The cis and trans isobutylderivatives 2b and 3b (obtained as 98:2 and 19:81 mixtures) were characterized by analytical and spectral (IR, ^{1}H NMR, MS) data; cis and trans configurations were attributed by ^{1}H NMR[3,5] after catalytic hydrogenation into the corresponding 1-isobutyl-3-phenylcyclohexanes. Product composition and yields were determined by GLC[6] while the extent of α/γ-substitution in the reactions of 1a-1d was obtained by evaluating the abundance of the vinylic protons relative to the aromatic protons through careful integration of their NMR signals. The results are reported in the Table.

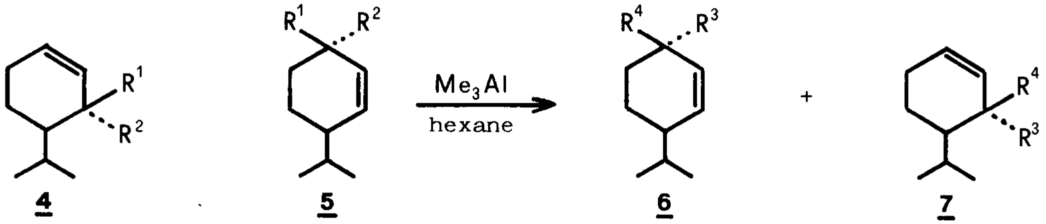
The reaction of acetates 1a, 1b and benzoates 1c, 1d with Me_3Al shows a high degree of stereoselectivity[7] with preference of the trans product, in accordance with the mechanism suggested by Oshima,[2] involving as intermediate an allylic cation attacked by the nucleophile from the less hindered side.

When iBu_3Al is used, on the contrary, the reaction becomes stereo-



a) R^1 = $OCOCH_3$ R^2 = D
b) R^1 = D R^2 = $OCOCH_3$
c) R^1 = OCOPh R^2 = D
d) R^1 = D R^2 = OCOPh

a) R = CH_3
b) R = CH_2-$CH(CH_3)_2$

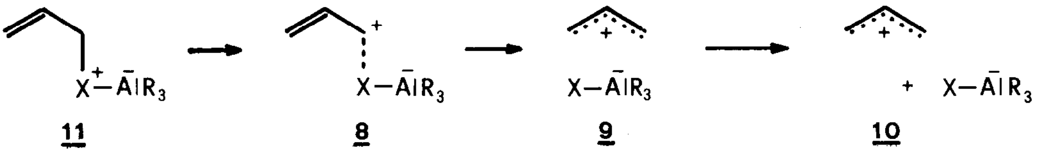


a) R^1 = $OCOCH_3$ R^2 = H
b) R^1 = H R^2 = $OCOCH_3$

a) R^3 = CH_3 R^4 = H
b) R^3 = H R^4 = CH_3

specific with preference for *syn*-substitution and even regiospecific with preference for γ-substitution for the *trans* esters 1b and 1d. Finally, the reaction of isomeric acetates 4a, 4b and 5a, 5b with Me_3Al shows only a little preference for the *syn*, γ-substitution.

These findings in terms of regio and stereochemistry suggest a more complex mechanism involving tight, asymmetric (8) and loose, symmetric (9) ion-pair intermediates[8] in addition to the allylic carbonium ion (10):



X = OCOR

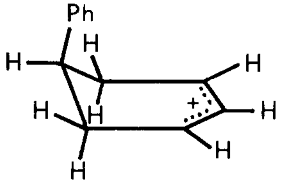
Table. Reaction of allylic esters with trialkylaluminum reagents in hexane

Ester	Reagent	T,°C	t,hr	Product composition				Yield	Substitution		
				2b	3b	2a	3a		syn/anti	α/γ	
1a	iBu$_3$Al	25	15	63	37			80	63:37	47:53	
1c	iBu$_3$Al	25	15	81	19			74	81:19	50:50	
1b	iBu$_3$Al	25	15	3	97			96	97:3	14:86	
1d	iBu$_3$Al	25	15	2	98			98	98:2	8:92	
1a	Me$_3$Al	-20	16			14	86	18	14:86	45/55	
1a	Me$_3$Al	25	3			23	77	75	23:77	47:53	
1c	Me$_3$Al	-20	16			14	86	37	14:86	35:65	
1c	Me$_3$Al	25	3			52	48	74	52:48	58:42	
1b	Me$_3$Al	-20	16			7	93	48	93:7	37:63	
1b	Me$_3$Al	25	3			8	92	96	92/8	26:74	
1d	Me$_3$Al	-20	16			9	91	52	91:9	32:68	
1d	Me$_3$Al	25	3			6	94	98	94:6	36:64	
				6a	6b	7a	7b			*	**
4a	Me$_3$Al	-20	16	4	60	6	30	92	90:10	33:67	60:40
4a	Me$_3$Al	25	3	7	48	22	23	97	71:29	32:68	76:24
4b	Me$_3$Al	-20	16	31	36	23	10	92	54:46	57:43	22:78
4b	Me$_3$Al	25	3	31	27	32	11	95	63:37	50:50	29:71
5a	Me$_3$Al	-20	16	5	46	5	43	92	89:11	52:48	50:50
5a	Me$_3$Al	25	3	6	37	19	38	97	75:25	50:50	79:21
5b	Me$_3$Al	-20	16	22	57	31	10	87	53:47	42:58	79:21
5b	Me$_3$Al	25	3	23	28	38	11	95	61:39	38:62	72:28

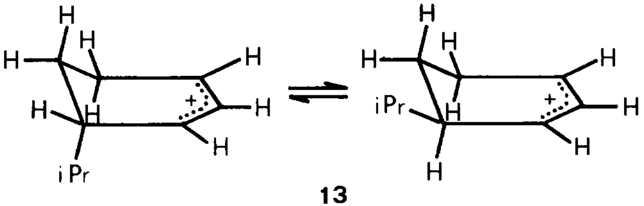
*) α/γ ratio for products of syn-substitution; **) α/γ ratio for products of anti-substitution.

In the absence of good external nucleophiles, the alkylation products should result from the direct collapse of the ion-pairs, with 8 leading probably to the syn,γ-substitution and 9 to the syn,α/γ-substitution, and/or attack of the carbonium ion (10) at the less hindered site.

Now a series of factors may be considered that influences the outcome of the reaction: i) Organoaluminum reagent: Me$_3\bar{A}$lOCOR is expected to be more stabilized than iBu$_3\bar{A}$lOCOR by both steric and electronic effects. Thus Me$_3$Al should promote more than iBu$_3$Al the intervention of a carbocation; ii) Leaving group: the positive charge induced at the carboxylate group of the adducts 11 can be delocalized by the phenyl group of the benzoates and its delivery to the allylic moiety is expected to be delayed in this case. Thus acetates 1a, 1c, rather than benzoates 1b,1d should promote formation of loose ion-pairs and carbocations in the reaction with iBu$_3$Al; iii) Nature of the allylic system: the allylic cation 12 related to the esters 1 is expected to be more stable than 13



12



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formed by the esters 4 and 5 since both 1,3-diaxial interactions and torsional strain are completely released only for 12. Thus esters 1, rather than 4 and 5, are expected to promote formation of the carbocation; in fact the reaction of *cis* and *trans* 1 with Me_3Al shows a strong preference for the *trans* product 3a, requiring the intervention of the common carbocation 12 while the acetates 4a, 4b and 5a, 5b show some preference for the *syn*,γ-substitution; iiii) *Leaving group orientation*: pseudoaxial leaving groups are expected to generate tight ion-pairs better suited for a *syn*,γ-substitution process. In fact the pseudoaxial esters 1b and 1d by reaction with iBu_3Al and 4a, 5a show more preference than their pseudoequatorial isomers for the *syn*,γ-substitution.

Maximum of *syn*,γ-substitution has been obtained for the reaction of benzoate 1d with iBu_3Al. It is interesting to observe that these circumstances, requiring minimum of positive charge transfer to the allylic moiety, suggest the intervention of a little polarized transition state which more closely resembles the intermediate of a cyclic synchronous process.

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6. 300 x .01" MBMA (Perkin Elmer) at 130° for products 2a and 3a; it is a pleseaure to acknowledge the skilful assistance of prof. Giovanna Ciranni for these analyses. 2 m x 2 mm i. d. 3% GAL on 60-80 mesh Chromosorb G at 180° for products 2b and 3b; 10 m x 2 mm i. d. 15% OV 275 on 100-120 mesh Chromosorb at 110° for products 6a, 6b, 7a and 7b. Nitrogen was used as carrier gas.
7. The terms stereospecific and stereoselective are used in the sense reported by E. L. Eliel, *Stereochemistry of Carbon Compounds*, McGraw-Hill, New York, 1962, 434-437. The terms regiospecific and regioselective are intended as proposed by H. L. Goering and V. D. Singleton, *J. Org. Chem.*, 1983, 48, 1531.
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