Pergamon

Tetrahedron Letters, Vol. 35, No. 2, pp. 297-300, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

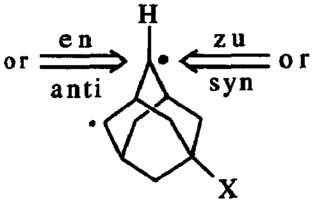
0040-4039(93)E0179-N

The Nature of Electronic Interactions Governing the Control of Π-Facial Selectivity in the Capture of 5-Substituted(X)-2-Adamantyl Radicals: Electrostatic *versus* Hyperconjugative Effects

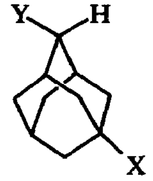
William Adcock*, Christopher I. Clark and Neil A. Trout
School of Physical Sciences, The Flinders University of South Australia,
Adelaide, South Australia, 5001

Abstract: An electrostatic rather than a hyperconjugative effect appears to be the dominant factor governing the control of Π-facial selectivity in the capture of 5-substituted(X)-2-adamantyl radicals.

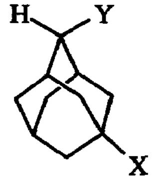
Recently, le Noble et al[1] reported that capture of the 5-phenyladamant-2-yl radical (1,X=C_6H_5), a species devoid of conformational and steric bias, occurs preferentially on the *zu* or *syn* face (58:42) i.e. dominant face preference which is *antiperiplanar* to the more electron-rich vicinal C-C bonds flanking C2. This result has been reconciled within Cieplak's transition-state hyperconjugation model.[1,2] Herein we report results from the trimethylstannylation of a series of (E)- and (Z)-2,5-dihaloadamantanes (2 and 3, respectively) which strongly suggests that hyperconjugation is unimportant as a factor governing the control of Π-facial selectivity in the capture of 5-substituted(X)adamant-2-yl radicals (1) and, moreover, that an electrostatic field model appears more appropriate for explaining the phenomenon.



1

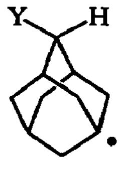


2

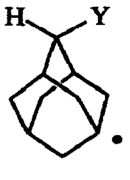


3

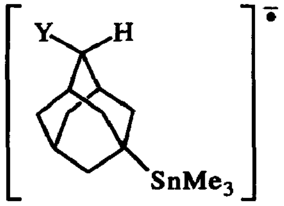
Product distributions for treatment of the chloro-iodo, bromo-iodo, and fluoro-bromo derivatives of 2 and 3 (X=I, Y=Cl; X=I, Y=Br; X=F, Y=Br) with Me_3SnLi in THF at 0°C in the absence and presence of dicyclohexylphosphine (DCPH) are listed in Table 1. An examination of the results reveals the following diagnostic traits of a free radical chain pathway for tin substitution (Scheme 1) as previously defined for 1,4-dihalobicyclo[2.2.2]octanes[3]: (i) the presence of DCPH (an excellent alkyl radical trap)[5] is able to divert the reactions from predominant tin substitution to mainly reduction products by trapping the initially formed radicals (1, X=F; 4 and 5, Y=Cl or Br). (ii) the presence of the ditin compounds in the case of the chloro-iodides



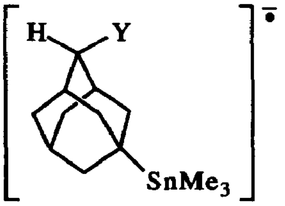
4



5



6



7

TABLE 1. Product Distribution Analysis of the Reaction between (E)- and (Z)-2,5-Dihaloadamantanes (2 and 3, respectively) and (Trimethylstannyl)lithium in THF[a]

entry No.	Compound	equiv. of Me_3SnLi	additive[d]	product distribution proportions, %[b,c]																extent of reaction, %
				Ad	1FAd	2ClAd	2BrAd	1SnAd	2SnAd	E 2Sn5F	Z 2Sn5F	E 2Cl5Sn	Z 2Cl5Sn	E 2Br5Sn	Z 2Br5Sn	E 2I5Sn	Z 2I5Sn	E 2Sn5Sn	Z 2Sn5Sn	
1	2; X=I, Y=Cl	1	none			20						68				3	3	3	3	76
2	2; X=I, Y=Cl	2	none			7		1	1			72						9	10	100
3	2; X=I, Y=Cl	2	DCPH			88						12								100
4	3; X=I, Y=Cl	1	none			55							41					2	2	56
5	3; X=I, Y=Cl	2	none			11			1				76					6	6	100
6	3; X=I, Y=Cl	2	DCPH			93							7							100
7	2; X=I, Y=Br	1	none				22	4						23		12	14	13	13	66
8	2; X=I, Y=Br	2	none				2	5	3					11				38	40	100
9	2; X=I, Y=Br	2	DCPH	8			70	7						3				6	6	100
10	3; X=I, Y=Br	1	none				25	3	1						27	6	8	15	15	61
11	3; X=I, Y=Br	2	none				9	2	3						24	3	3	28	28	94
12	3; X=I, Y=Br	2	DCPH	5			80	5							2			4	4	100
13	2; X=F, Y=Br	2	none		8					41	51									91
14	2; X=F, Y=Br	2	DCPH		44					25	31									92
15	3; X=F, Y=Br	2	none		2					43	55									100
16	3; X=F, Y=Br	2	DCPH		32					29	39									100

a. In a typical reaction, Me_3SnLi (2 mole equivalent) in tetrahydrofuran (prepared by reacting hexamethylditin (0.67 g, 2.08 mmol) in anhydrous THF (5 ml) with lithium (8.32 mmol) at 0°C under argon for 5 hrs) was added dropwise to a well-stirred solution of the 2,5-dihaloadamantane (ca. 200 mg; 1 mole equivalent) in THF (10 ml) maintained at 0°C under N_2. After allowing the reaction mixture to warm to room temperature and then to stir for a further 30 minutes, the reaction was quenched with a saturated aqueous ammonium chloride solution before being extracted with CH_2Cl_2. After drying (Mg SO_4), the solvent was removed in vacuo to afford the reaction product mixture which was analysed by VPC and NMR (^{13}C and ^{119}Sn) in order to characterize and determine the relative proportion of products. b. The VPC product proportions (%) were determined by comparison of electronically integrated peak areas, giving errors to about 2-3%. Peak areas were not corrected for appropriate response factors. c. Ad ≡ adamantane; Sn ≡ $SnMe_3$. d. DCPH = dicyclohexylphosphine (10 mole equivalent).

constitutes powerful evidence for the S$_{RN}$1 like pathway (Scheme 1) since the chloro-tin derivatives, being relatively inert towards Me_3SnLi, are not intermediates in their formation. (iii) the significant presence of the iodo-tin compounds in the product mixtures of the chloro- and bromo-iodides is perplexing in terms of a non-chain radical process but clearly intelligible in terms of the pathway outlined in Scheme 1.[3,4]

Scheme I[a-e]

$$XC_mH_nY + Me_3Sn^- \longrightarrow XC_mH_n^\bullet + Y^- + Me_3Sn^\bullet \tag{step 1}$$
$$XC_mH_n^\bullet + Me_3Sn^- \longrightarrow [XC_mH_nSnMe_3]^{\overset{-}{\bullet}} \tag{step 2}$$
$$[XC_mH_nSnMe_3]^{\overset{-}{\bullet}} + XC_mH_nY \longrightarrow XC_mH_nSnMe_3 + XC_mH_n^\bullet + Y^- \tag{step 3}$$
$$[XC_mH_nSnMe_3]^{\overset{-}{\bullet}} \longrightarrow X^- + {}^\bullet C_mH_nSnMe_3 \tag{step 4}$$
$$XC_mH_nY + {}^\bullet C_mH_nSnMe_3 \rightleftharpoons YC_mH_nSnMe_3 + XC_mH_n^\bullet \tag{step 5}$$
$${}^\bullet C_mH_nSnMe_3 + Me_3Sn^- \longrightarrow [Me_3SnC_mH_nSnMe_3]^{\overset{-}{\bullet}} \tag{step 6}$$
$$[Me_3SnC_mH_nSnMe_3]^{\overset{-}{\bullet}} + XC_mH_nY \longrightarrow Me_3SnC_mH_nSnMe_3 + XC_mH_n^\bullet + Y^- \tag{step 7}$$
$${}^\bullet C_mH_nSnMe_3 + SH \longrightarrow Me_3SnC_mH_{n+1} + S^\bullet \tag{step 8}$$
$$2Me_3Sn^\bullet \longrightarrow Me_3SnSnMe_3 \tag{step 9}$$

[a] m=10, n=14 ; X= Cl or Br ; Y= I. [b] Li^+ is understood to be present as the counter ion. [c] For expedience, the radical-halide ion adduct is understood to occur prior to steps 1, 3, and 7. [d] The tin reagent is given as being monomeric for pictorial clarity. However, it should be remembered that its state of aggregation is unknown. [e] Solvent = SH.

The major focus of this paper is the stereochemical outcome (*en* or *zu* face preference, see 1) of the capture (steps 5 and 6; Scheme 1) of the intermediate 5-trimethylstannyladamant-2-yl radical (1,X=$SnMe_3$) which is mainly formed as a result of fragmentation (step 4, Scheme 1) of the appropriate halo-tin radical anions (6 and 7, Y=Cl or Br) and, as well, by dissociative electron transfer between the initially formed bromo- and iodo-tin compounds (2 and 3; Y=Br or I, X=$SnMe_3$) and Me_3Sn^-.[6] Note that the epimeric ditin and iodo-tin mixtures obtained from the respective chloro- and bromo-iodides (Table 1) are all, within experimental error, 50:50 (E:Z). Thus, with respect to electronic control of Π-facial diastereoselectivity, the powerful σ-electron donor Me_3Sn group is clearly an ineffectual bystander! This is a most surprising and profound result given the dramatic effect of (E)-5-Me_3Sn on the stability and behaviour of the adamant-2-yl carbocation.[7] It was expected that this double hyperconjugative effect would also prevail in the corresponding radical species, although to a lesser degree, to enforce a significant *en* face preference.[8] We can only conclude that the much favoured Cieplak hyperconjugative model[1,2] for rationalising Π-facial selectivity in the current circumstances is seriously flawed.

Finally, it can be seen (Table 1) that stannylation of the epimeric fluoro-bromides (2 and 3; X=F, Y=Br) give essentially the same product mixture (entries 13 and 15). It is therefore clear that the products are formed from a common intermediate, namely, the 5-fluoroadamant-2-yl radical (1,X=F). This is confirmed by the results of stannylation in the presence of DCPH (entries 14 and 16). The modest *zu* face preference (E/Z = 44/56) observed for the capture of this radical species by Me_3Sn^- suggests an electrostatic steering effect is operative as a consequence of the polarity of the *fluorine* substituent (σ_F = 0.40).[9] In this light the aforementioned outcome of the Me_3Sn group ($\sigma_F \sim 0$)[10] becomes intelligible in terms of an electrostatic field model as does the result reported[1] for the C_6H_5 substituent (σ_F = 0.16).[9] It should be noted that this model has been shown recently to be best able to rationalize the stereoselectivities of nucleophilic additions to 5-substituted(X)-2-adamantanones as well as electrophilic additions to 5-substituted(X)-2-methyleneadamantanes not mediated by carbocationic intermediates.[11,12]

Full details of this study will be reported in a main paper.

ACKNOWLEDGEMENT

We thank the Australian Research Council for financial assistance.

REFERENCES AND NOTES

1. Bodepudi, V.R.; le Noble, W.J. *J. Org. Chem.* **1991**, 56, 2001 and references cited therein.

2. (a) Cieplak, A.S. *J. Am. Chem. Soc.* **1981**, 103, 4540. (b) Cieplak, A.S.; Tait, B.D.; Johnson, C.R. *J. Am. Chem. Soc.1987,* 109, 5875.

3. Adcock, W.; Iyer, V.S.; Kitching, W.; Young, D. *J. Org. Chem.* **1985**, 50, 3706.

4. (a) The halogen atom abstraction step of Scheme 1 (step 5) is competitive when X or Y is I but not Cl or Br. Such reactions occur readily for alkyliodides. In contrast, halogen atom transfer is much slower for alkylbromides and -chlorides ($(CH_3)_3CX$: X = I, k = 3 x 10^6 $M^{-1}s^{-1}$; X = Br, k ≈ 4.6 x 10^3 $M^{-1}s^{-1}$; X = Cl, k = 6 x 10^2 $M^{-1}s^{-1}$)[4b] (b) Newcomb, M.; Sanchez, R.M.; Kaplan, J. *J. Am. Chem. Soc.* **1987**, 109, 1195.

5. Smith, G.F.; Kuivila, H.G.; Simon, R.; Sultan, L. *J. Am. Chem. Soc.* **1981**, 103, 833.

6. Treatment of a mixture (E/Z = 40/60) of 2-bromo-5-trimethylstannyladamantane (2 and 3; X = $SnMe_3$, Y = Br) with Me_3SnLi (see footnote to Table 1) provides a 50:50 mixture (determined by VPC) of the ditin compounds (2 and 3; X = Y = $SnMe_3$). An attempt to separate these mixtures by HPLC (silica gel/hexane) was not successful.

7. (a) Adcock, W.; Coope, J.; Shiner, V.J., Jr.; Trout, N.A. *J. Org. Chem.* **1990**, 55, 1411. (b) Adcock, W.; Trout, N.A. *J. Org. Chem.* **1991**, 56, 3229.

8. (a) The stereoelectronic requirement for optimization of double hyperconjugation (antiperiplanar relationship of the participant orbitals)[7,8b,c] is met in the E but not the Z isomer of 2,5-disubstituted adamantanes. It should be noted that unlike the 2-adamantyl cation which is pyramidal,[8d] the 2-adamantyl radical is planar.[8e] (b) Krijner, B.; Beverloo, H.B.; Verhoeven, J.W.; Reiss, C.A.; Goubitz, K.; Heijdenrijk, D. *J. Am. Chem. Soc.* **1989**, 111, 4433 and references cited therein. (c) Adcock, W.; Krstic, A.R.; Duggan, P.J.; Shiner, V.J., Jr.; Cooper, J.; Ensinger, M.W. *J. Am. Chem. Soc.* **1990**, 112, 3140. (d) Dutler, R.; Rank, A.; Sorensen, T.S.; Whitworth, S.M. *J. Am. Chem. Soc.* **1989**, 111, 9024. (e) Kira, M.; Akiyama, M.; Ichinose, M.; Sakurai, H. *J. Am. Chem. Soc.* **1989**, 111, 8256.

9. Adcock, W.; Abeywickrema, A.N. *J. Org. Chem.* **1982**, 47, 2957.

10. (a) Adcock, W.; Aldous, G.L.; Kitching, W. *J. Organomet. Chem.* **1980**, 202, 395.. (b) Adcock, W.; Iyer, V.S. *J. Org. Chem.* **1985**, 50, 1538.

11. Adcock, W.; Cotton, J.; Trout, N.A. *J. Org. Chem.* . Submitted for publication.

12. (a) Electrostatic control of Π-facial selectivity of nucleophilic and electrophilic additions has been proposed for other model systems.[12b,c] (b) Paddon-Row, M.N.; Wu, Y.-D.; Houk, K.N. *J. Am. Chem. Soc.* **1992**, 114, 10, 638 and references cited therein. (c) Wu, Y.-D, Na, J.; Houk, K.N. *J. Org. Chem.* **1993**, 58, 4625 and references cited therein.

(*Received in UK* 27 *September* 1993; *revised* 3 *November* 1993; *accepted* 5 *November* 1993)