PERKIN 2
COMMUNICATION

A comparison of the Cieplak model and the cation complexation model as applied to selected 2,3-disubstituted norbornan-7-ones[†]

Veejendra K. Yadav* and Rengarajan Balamurugan

Department of Chemistry, Indian Institute of Technology, Kanpur 208 016, India.
E-mail: vijendra@iitk.ac.in; Fax: 91-512-597436

Received (in Cambridge, UK) 1st November 2000, Accepted 14th November 2000
First published as an Advance Article on the web 7th December 2000

Compared with the Cieplak model, which is totally inadequate for predicting the π-selectivities of 1a–1c, the antiperiplanar effects in suitably cation-complexed species predict carbonyl pyramidalizations that lead to the observed selectivities.

Norbornan-7-ones (**1**, Fig. 1) have been the subject of intense experimental studies for their facial selectivities caused by *endo*-substituents at positions 2 and 3. The impetus arose particularly because, unlike cyclohexanones, norbornan-7-ones are rigid and devoid of significant geometrical distortions around the carbonyl function.[1] 2,3-Bis(methoxymethyl)norbornan-7-one, **1a**, and 2,3-divinylnorbornan-7-one, **1b**, show *anti*-preference for addition of nucleophiles. These substituents are electron-withdrawing and thus Cieplak's hyperconjugation model[2] predicts *syn*-addition. Mehta[1] and le Noble[3] have attributed the observed *anti*-selectivities to through space donations from these substituents in rigid conformers such as **2** for the divinyl species. In **2**, the vinyl π bonds are held parallel to the C1–C2 and C3–C4 bonds. Though this geometrical assumption may appear logical,[4] it nevertheless prompted us to employ our cation complexation model[5] to see whether or not the right facial preference is predicted and also to test the merits of the above rigid conformer contribution. In the present paper, we demonstrate that (a) the cation complexation model performs well and predicts only the experimental selectivity; (b) the explanation advanced earlier to explain the *anti*-selectivity of **1a** within the ambit of the Cieplak model is inappropriate; and, most important of all, (c) the Cieplak model is inadequate for explaining the *syn*-selectivity of 2,3-bis(methoxycarbonyl)-norbornan-7-one, **1c**.

The Cieplak model requires a nucleophile to approach the carbonyl carbon from a direction that is antiperiplanar (*app*) to the more electron-donating σ bond at the α-carbon. From the transition structures for LiH additions to a series of 2,3-disubstituted norbornan-7-ones, Houk and co-workers have concluded that the hyperconjugative effects are unimportant and that the electrostatic effects constitute the sole control.[6] Electron-withdrawing substituents induce positive charges at C2 and C3 and *syn*-addition is favored. On the other hand, electron-donating substituents induce negative charges at C2 and C3 and *anti*-addition becomes favorable. If so, why do **1a** and **1b** favor *anti*-addition and **1c** the *syn*-addition when the substituents in all are electron-withdrawing? Houk has considered electrostatic repulsion between a nucleophile and the substituents in **1a** and **1b** and electrostatic attraction in **1c**. This differential treatment of similar substituents may, at best, be considered an anomaly.

In application of the cation complexation model to norbornan-7-ones, we have calculated[7] the torsion angles D1 = O8–C7–C1–C2, D2 = O8–C7–C1–C6, D3 = O8–C7–C4–C3 and D4 = O8–C7–C4–C5, both before and after complexation, to assess the direction of carbonyl pyramidalization. We call the pyramidalization '*anti*' when D1 and D3 are smaller than D2 and D4 and '*syn*' when D1 and D3 are larger than D2 and D4, respectively. The '*anti*-pyramidalization' leads to *anti*-addition and the '*syn*-pyramidalization' leads to *syn*-addition. The directional changes in the torsion angles D5 = H–C1–C7–O8 and D6 = H–C4–C7–O8 can also provide information about the direction of pyramidalization. These geometrical data are collected in Table 1, the relevant *app*-effects in Table 2 and the 3D geometries of **1a**–**1c** in Fig. 2.

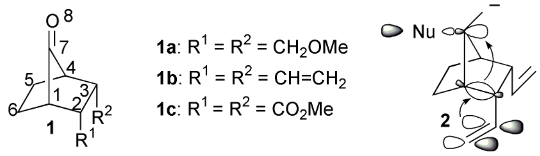

Fig. 1 The structures of species **1** and the proposed rigid conformer of **2**.

Table 1 Selected B3LYP/6-31G* geometrical parameters of **1a**–**1c** and their complexes. D1 = O8–C7–C1–C2; D2 = O8–C7–C1–C6; D3 = O8–C7–C4–C3; D4 = O8–C7–C4–C5; D5 = H9–C1–C7–O8; D6 = H14–C4–C7–O8

Substrate	D1	D2	D3	D4	D5	D6
1	124.56	−124.56	−124.56	124.56	−0.00	−0.00
1a	122.29	−124.50	−121.49	125.08	−0.63	+1.06
1a–H^+	115.56	−132.55	−114.70	132.56	−5.54	+7.12
1a–Li^+	119.50	−127.88	−119.66	127.33	−2.52	+2.93
1b	121.31	−125.33	−121.31	125.33	−1.01	+1.01
1b–H^+	112.13	−135.90	−112.85	135.20	−8.82	+8.08
1b–Li^+	119.16	−128.15	−119.13	128.19	−3.02	+3.03
1b–BH_3	120.48	−126.71	−120.42	126.46	−1.95	+1.84
1c	125.10	−121.76	−122.35	124.79	+2.49	−0.39
1c–H^+	127.39	−120.03	−123.95	123.96	+3.52	−1.32
1c–$2H^+$	133.32	−111.84	−132.66	115.05	+10.2	−8.33
1c–$2Li^+$	127.12	−119.98	−126.78	120.15	+4.64	−4.51

Table 2 The B3LYP/6-31G* *app*-effects from second order perturbation theory analysis of the Fock matrix in NBO basis for **1a**–**1c** and their complexes

	E/kcal mol^{-1}			
Substrate	$\sigma_{C1–C2}$–$\pi^*_{C7–O8}$	$\sigma_{C1–C6}$–$\pi^*_{C7–O8}$	$\sigma_{C3–C4}$–$\pi^*_{C7–O8}$	$\sigma_{C4–C5}$–$\pi^*_{C7–O8}$
1a	3.46	3.41	3.38	3.15
1a–H^+	9.65	5.76	7.95	5.44
1a–Li^+	6.36	4.56	5.61	4.48
1b	3.64	3.08	3.64	3.08
1b–H^+	10.0	4.67	10.1	4.75
1b–Li^+	6.27	4.31	6.28	4.30
1b–BH_3	4.93	3.94	4.81	3.78
1c	3.13	3.44	3.76	3.08
1c–H^+	6.21	7.40	8.02	6.38
1c–$2H^+$	4.60	6.92	5.91	7.57
1c–$2Li^+$	4.37	4.89	4.45	4.82

[†] The Cartesian coordinates of species **1a**–**1c** and their complexes are available as supplementary data. For direct electronic access see http://www.rsc.org/suppdata/p2/b0/b008808k/

DOI: 10.1039/b008808k

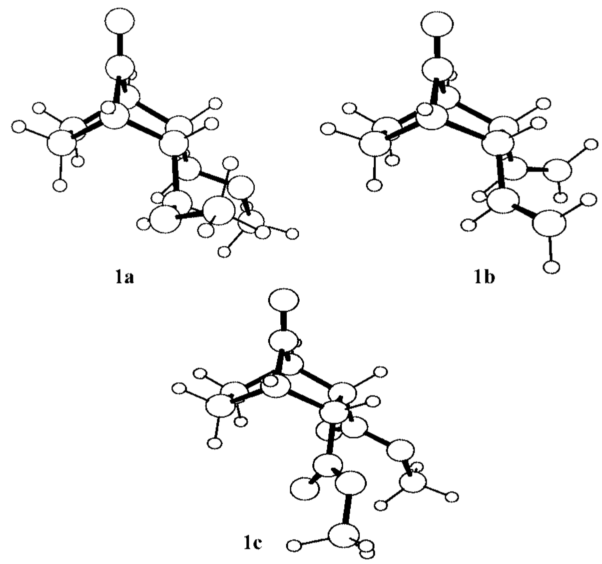

Fig. 2 Computed 3D structures of **1a**–**1c**.

The torsion angle changes in **1a** and **1b** on carbonyl protonation suggest *anti*-addition for both. This is in accordance with experimental observations.[1] From reactions with $NaBH_4$ in MeOH and MeLi in Et_2O, 40:60 and 34:66 and 36:64 and 27:73 selectivities in favor of *anti*-addition were observed for **1a** and **1b**, respectively. We sought a rationale for this *anti*-preference in the orientations of the substituents and their *app*-interactions[8] with $\sigma^*_{C1–C2}$ and $\sigma^*_{C3–C4}$. Whereas the CH_2–O bond on C2 is *app* to C2–C3 (O–C–C2–C3 = 170.99–175.00°), the CH_2–O bond on C3 is *app* to C3–C4 (O–C–C3–C4 = 168.97–171.97°). The sums of the $\sigma_{C1–C2}$–$\pi^*_{C=O}$ and $\sigma_{C3–C4}$–$\pi^*_{C=O}$ and of the $\sigma_{C1–C6}$–$\pi^*_{C=O}$ and $\sigma_{C4–C5}$–$\pi^*_{C=O}$ interactions are, respectively, 6.84 and 6.56 kcal mol^{-1} in **1a**, 17.60 and 11.20 kcal mol^{-1} in **1a**–H^+, and 11.97 and 9.04 kcal mol^{-1} in **1a**–Li^+. The better interactions of $\pi^*_{C=O}$ with $\sigma_{C1–C2}$ and $\sigma_{C3–C4}$ in comparison to the interactions with $\sigma_{C1–C6}$ and $\sigma_{C4–C5}$ are set to favor *anti*-pyramidalization and, hence, the observed *anti*-addition. It is interesting to note that one of the two C–H bonds of the methylene on C2 is *app* to C1–C2 (H–C–C2–C1 = 171.07–174.43°) and the $\sigma_{C–H}$–$\sigma^*_{C1–C2}$ interaction energy is 3.61, 4.02 and 3.98 kcal mol^{-1} in **1a**, **1a**–H^+ and **1a**–Li^+, respectively. The most interesting feature is the observation that in contradiction to the hypotheses of Mehta and le Noble neither the $\sigma_{C–O}$ on C2 nor any of the two electron pair orbitals on this oxygen is in interaction with $\sigma^*_{C1–C2}$.

The sums of the $\sigma_{C1–C2}$–$\pi^*_{C=O}$ and $\sigma_{C3–C4}$–$\pi^*_{C=O}$ and of the $\sigma_{C1–C6}$–$\pi^*_{C=O}$ and $\sigma_{C4–C5}$–$\pi^*_{C=O}$ interactions are 7.28 and 6.16, 20.1 and 9.42, 12.55 and 8.61, and 9.74 and 7.72 kcal mol^{-1} in **1b**, **1b**–H^+, **1b**–Li^+ and **1b**–BH_3, respectively. The larger interactions of $\pi^*_{C=O}$ with $\sigma_{C1–C2}$ and $\sigma_{C3–C4}$ in comparison to its interactions with $\sigma_{C1–C6}$ and $\sigma_{C4–C5}$ favor *anti*-pyramidalization. Both the vinyl groups are in an eclipsing orientation with the *exo*-hydrogens on C2 and C3. The $\pi_{C=C}$–$\sigma^*_{C1–C2}$/$\pi_{C=C}$–$\sigma^*_{C3–C4}$ interaction energy is 3.50, 5.20, 4.42, and 3.84 kcal mol^{-1} in **1b**, **1b**–H^+, **1b**–Li^+ and **1b**–BH_3, respectively. These interactions raise the electron densities of the C1–C2 and C3–C4 bonds in support of the earlier speculations.[1,3]

From the absolute values of D1 *vs.* D2 and D3 *vs.* D4 in **1c**, one experiences great difficulty in predicting the facial selection. While D1 is larger than D2 by 3.34°, D3 is smaller than D4 by 2.44°. Since the sum of the $\sigma_{C1–C2}$–$\pi^*_{C=O}$ and $\sigma_{C3–C4}$–$\pi^*_{C=O}$ interactions (6.89 kcal mol^{-1}) is superior by 0.37 kcal mol^{-1} to the sum of $\sigma_{C1–C6}$–$\pi^*_{C=O}$ and $\sigma_{C4–C5}$–$\pi^*_{C=O}$ interactions (6.52 kcal mol^{-1}), one is led to predict *anti*-addition. This, however, is in contrast to the Cieplak model which predicts $\sigma_{C1–C2}$ and $\sigma_{C3–C4}$ to be inferior to $\sigma_{C1–C6}$ and $\sigma_{C4–C5}$ in their electron-donating abilities due to the $-I$ effects of the ester functions. This reversal is due to orientation effects arising from the ester functions that allow $\pi_{C=O}$–$\sigma^*_{C1–C2}$ (1.59 kcal mol^{-1} on C2) and $\sigma_{C–O}$–$\sigma^*_{C3–C4}$ (1.42 kcal mol^{-1} on C3) interactions. These relative electron-donating abilities were reconfirmed in **1c**–H^+ in which the C7-ketone was protonated; the sum of $\sigma_{C1–C2}$–$\pi^*_{C=O}$ and $\sigma_{C3–C4}$–$\pi^*_{C=O}$ interactions (14.23 kcal mol^{-1}) was superior to the sum of the $\sigma_{C1–C6}$–$\pi^*_{C=O}$ and $\sigma_{C4–C5}$–$\pi^*_{C=O}$ interactions (13.78 kcal mol^{-1}). The *app*-effects, therefore, predicted *anti*-addition, which is in clear violation of the experimental selectivities that varied from 77:23 to 90:10 in favor of *syn*-addition in reactions with various nucleophiles.[1a]

The above discrepancy is not without good reason. Why must only the 7-keto oxygen undergo cation complexation when the carbonyl oxygen of the ester function bears a similar or even better charge? The NBO analysis indicated the carbonyl oxygen on C2 to be the most negative of all the oxygen atoms and more negative (0.61 units) than the oxygen of the C7-keto group (0.51 units). This also necessitates cation complexation of the ester oxygen. Both the D1 and D2 and D3 and D4 differences in **1c**–$2H^+$ are now unambiguously in favor of *syn*-addition, supported by the *app*-effects. The sum of the $\sigma_{C1–C2}$–$\pi^*_{C=O}$ and $\sigma_{C3–C4}$–$\pi^*_{C=O}$ interactions (10.51 kcal mol^{-1}) is inferior to the sum of $\sigma_{C1–C6}$–$\pi^*_{C=O}$ and $\sigma_{C4–C5}$–$\pi^*_{C=O}$ interactions (14.49 kcal mol^{-1}). A similar conclusion is drawn from the **1c**–$2Li^+$ variant of **1c**–$2H^+$.

We conclude that while the rigid conformer concept for **1b** is valid in explaining its *anti*-selectivity, it is not so for **1a**. In **1a**, it is rather the electron-donating interaction of one of the two methylene C–H bonds with $\sigma^*_{C1–C2}$ that plays the key role in promoting *anti*-pyramidalization. Further, the Cieplak selectivity of **1c** on account of its ground state structure and the hyperconjugation effects in it meets with failure. However, the geometry resulting from the allowance of a suitable level of cation complexation possesses all the features of the observed *syn*-selectivity.

Acknowledgements

The author thanks the Council of Scientific and Industrial Research, New Delhi for financial support and the Computer Center, IIT Kanpur for generous allocation of computer time on a Silicon Graphics series of minisupercomputers.

References

1 (*a*) G. Mehta and F. A. Khan, *J. Am. Chem. Soc.*, 1990, **112**, 6140; (*b*) G. Mehta and F. A. Khan, *J. Chem. Soc., Chem. Commun.*, 1991, 18.
2 A. S. Cieplak, *J. Am. Chem. Soc.*, 1981, **103**, 4540; A. S. Cieplak, B. D. Tait and C. R. Johnson, *J. Am. Chem. Soc.*, 1989, **111**, 8447.
3 H. Li, G. Mehta, S. Padma and W. J. le Noble, *J. Org. Chem.*, 1991, **56**, 2006.
4 For other examples, see: T. Laube and T.-K. Ha, *J. Am. Chem. Soc.*, 1988, **110**, 3511; D. Kost and H. Egozy, *J. Org. Chem.*, 1989, **54**, 409.
5 D. A. Jeyaraj, A. Yadav and V. K. Yadav, *Tetrahedron Lett.*, 1987, **38**, 4483; D. A. Jeyaraj and V. K. Yadav, *Tetrahedron Lett.*, 1997, **38**, 6095; V. K. Yadav and D. A. Jeyaraj, *J. Org. Chem.*, 1998, **63**, 3474; V. K. Yadav, G. Senthil and D. A. Jeyaraj, *Tetrahedron*, 1999, **55**, 14211; V. K. Yadav, D. A. Jeyaraj and R. Balamurugan, *Tetrahedron*, 2000, **56**, 7581.
6 M. N. Paddon-Row, Y.-D. Wu and K. N. Houk, *J. Am. Chem. Soc.*, 1992, **114**, 10638. For related work, see: S. S. Wong and M. N. Paddon-Row, *J. Chem. Soc., Chem. Commun.*, 1990, 456; S. S. Wong and M. N. Paddon-Row, *J. Chem. Soc., Chem. Commun.*, 1991, 327; Y.-D. Wu, J. A. Tucker and K. N. Houk, *J. Am. Chem. Soc.*, 1991, **113**, 5018.
7 All the geometry optimizations and the calculations of NBO charges were performed at the Becke3LYP/6-31G* level using the program Gaussian 94, Revision C.2, M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. W. Jones, B. G. Johnson, M. A. Robb, J. R. Cheeseman, T. Keith, G. A. Petersson, J. A. Montgomery, K. Raghavachari, M. A. Al-Laham, V. G. Zakrzewski, J. V. Ortiz, J. B. Foresman, J. Cioslowski, B. B. Stefanov, A. Nanayakkara, M. Challacombe, C. Y. Peng, P. Y. Ayala, W. Chen, M. W. Wong, J. L. Andres, E. S. Replogle, R. Gomperts, R. L. Martin, D. J. Fox, J. S. Binkley, D. J. Defrees, J. Baker, J. P. Stewart, M. Head-Gordon, C. Gonzalez and J. A. Pople, Gaussian, Inc., Pittsburgh, PA, 1995.
8 P. Deslongchamps, *Stereoelectronic Effects in Organic Chemistry*, Pergamon Press, New York, 1983.