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Tetrahedron Letters
Tetrahedron Letters 48 (2007) 3109–3113

The stereoselective thermal rearrangement of chiral lophine peroxides

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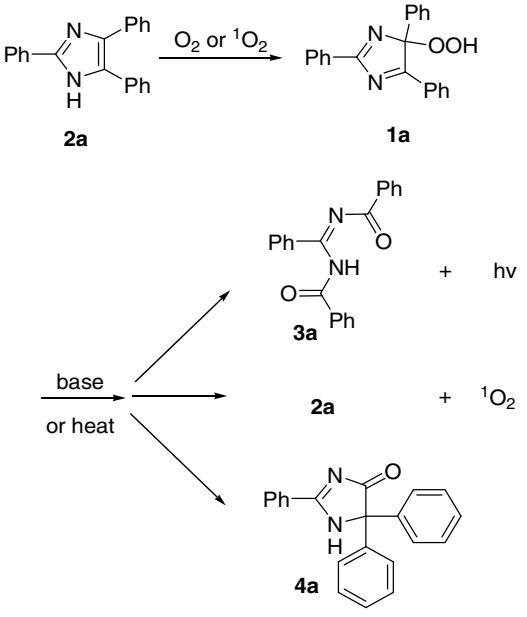
Received 19 January 2007; accepted 26 January 2007
Available online 30 January 2007

Abstract—The thermal reaction of chiral 2-phenyl-4-(*p*-X-phenyl)-5-(*p*-Y-phenyl)-4-*tert*-butyldimethylsilylperoxy-4*H*-isoimidazoles (**5b**: X = CF_3, Y = OMe; **5c**: X = CF_3, Y = F) was carried out in DMSO. The chiral 2-phenyl-5-(*p*-X-phenyl)-5-(*p*-Y-phenyl)-5*H*-imidazol-4-ones (**4b**: X = CF_3, Y = OMe; **4c**: X = CF_3, Y = F) were quantitatively obtained in 50–60% enantiomer excess (ee). The mechanism for the reaction was proved to be stereoselective 1,5-phenyl migration. Although the sigmatropic 1,5-phenyl migration should be thermally allowed according to the Woodward–Hoffmann rule, the migration actually includes a stepwise process.

Since 4-hydroperoxy-2,4,5-triphenyl-4*H*-imidazole (**1a**) was identified as the intermediate of the chemiluminescence (CL) of lophine (**2a**) by Sonnenberg et al.,[1] White et al.,[2] and Kimura et al.,[3] the CL reaction of lophine-peroxides has been gradually revealed. Recently, we reported that lophineperoxide (**1a**) underwent three different but simultaneous reactions upon treatment with base to provide the corresponding amidine (**3a**) accompanied with chemiluminescence, imidazole (**2a**) with singlet oxygen, and a trace of imidazolone (**4a**)[2b] as illustrated in Scheme 1. The peroxides, after protection as silyl peroxide, 2,4,5-tirphenyl-4-*tert*-butyldimethylsilyl-peroxy-4*H*-*iso*-imidazole (**5a**), underwent an exclusive 1,5-phenyl migration in DMSO to give solely imidazolone (**4a**) in excellent yield (Scheme 2).

We became aware of two reports which suggested important meanings of this type rearrangement. It had been demonstrated that tetrahydrobenzimidazoles rearrange, on treatment with base, an alkyl halide and the singlet oxygen, to provide 4-imidazolonespirocyclopentane.[4] Further, Lovely et al.[5] reported that tetrahydrobenzimidazoles, on treatment with dimethyldioxiane (DMDO), rearranged to provide 5-imidazolones exclusively with good to excellent levels of diastereoselectivity. This kind of stereochemistry is a key for the synthesis of natural compounds including imidazolone moieties.[4–6] Further, the sigmatropic migration of an aryl group is known



Scheme 1.

Keywords: 1,5-Sigmatropic migration; Lophine peroxide; Imidazolone; Imidazol-4-ol; Rearrangement; Stereoselectivity.
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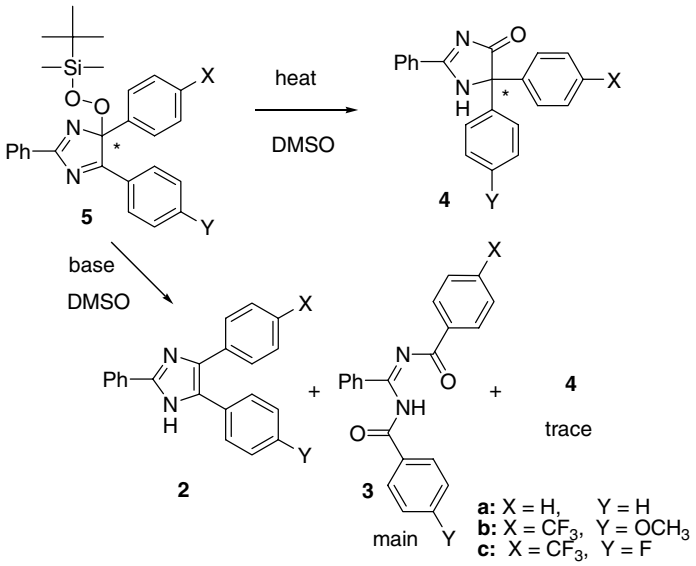
0040-4039/$ - see front matter © 2007 Published by Elsevier Ltd.
doi:10.1016/j.tetlet.2007.01.146



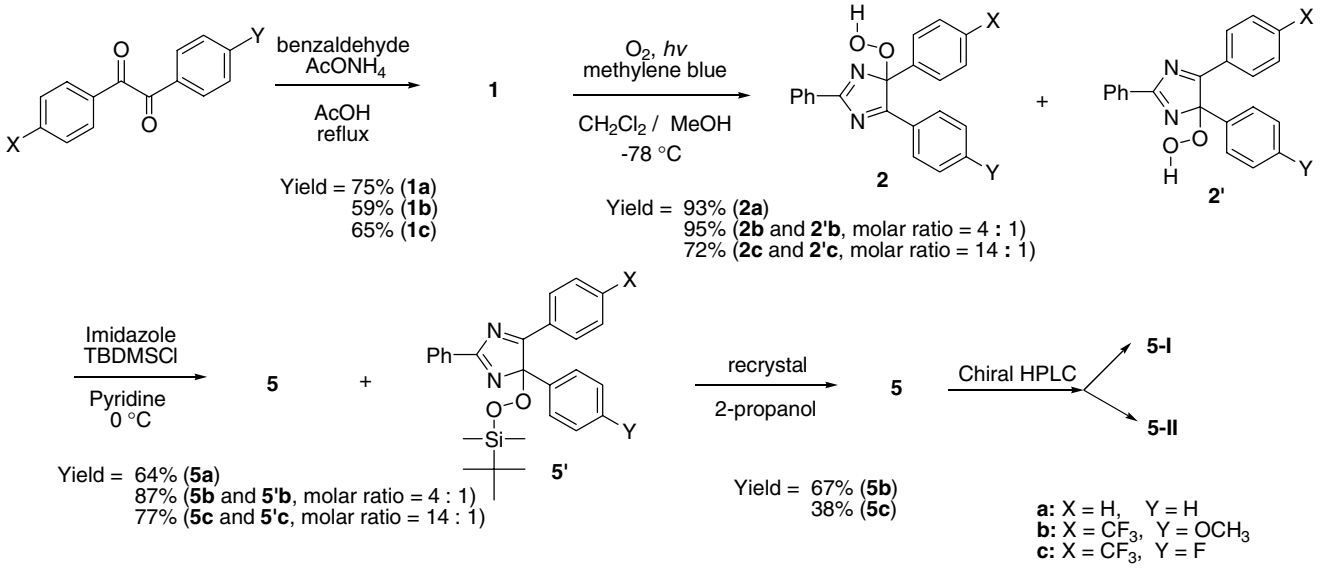
Scheme 2.

for 1,2,3,4,5-pentaphenylcyclopentadienol,[7] which is a π analogue of **5**, but its stereochemistry has not been tested.

We thought that two chiral peroxides **5b** and **c** (Scheme 2) could straightforwardly contribute to elucidate the stereochemistry of the migration. When the chiral peroxides (**5b** and **c**) were subjected to the thermal reaction, the corresponding imidazolones **4b** and **c** were exclusively obtained in 50–60 ee % in DMSO.

The Assignment of the absolute configuration by comparison between the CD spectra and the calculated CD spectra. Chiral peroxides **5-I** (HPLC: the first fraction) and **5-II** (HPLC: the second fraction) were prepared in five steps as shown in Scheme 3.[3,8,9] In order to determine the absolute configuration, the CD spectra were recorded, and the calculation of CD spectra were carried out based on the GAUSSIAN 03w software package,[10] as show in Figure 1. A geometry optimization was performed using the B3LYP functional with 6-31G* basis sets. The absolute configurations of **5-I** and **5-II** were assigned as ***S*-5** and ***R*-5**, respectively, as illustrated in Figure 1. The absolute configurations of products **4-I** (HPLC: the first fraction) and **4-II** (HPLC: the second fraction) were also assigned to ***R*-4** and ***S*-4**, respectively, as illustrated in Figure 2.

Thermal rearrangement of chiral lophine peroxides. The chiral peroxides ***R*-** and ***S*-5b** and ***R*-** and ***S*-5b** (about 0.001 mmol) were dissolved in DMSO (1 ml), and refluxed for 10 min. The reaction mixture was subjected to HPLC analysis using a chiral column. The results are summarized in Tables 1 and 2. Figure 3 shows the



Scheme 3.

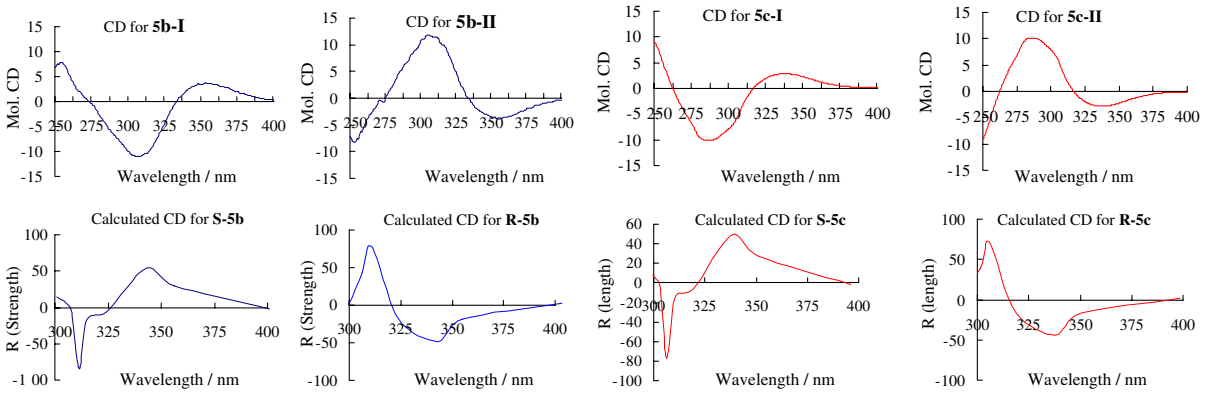


Figure 1. The CD spectra (above) of **5b**,**c** recorded in EtOH and the calculated CD spectra (below) of **5b**,**c** using the TDDFT-B3LYP method. Rotational strengths (R) are given in cgs (10^{-40} erg esu cm/G).

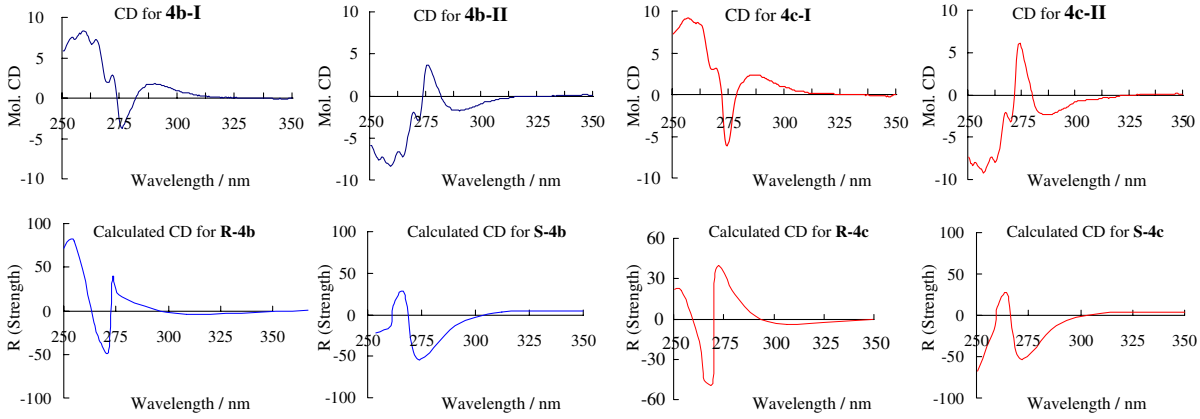
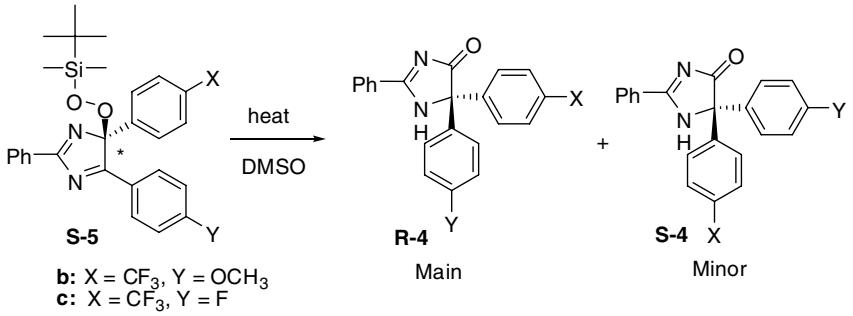


Figure 2. The CD spectra (above) of **4b**,**c** recorded in EtOH and the calculated CD spectra (below) of **4b**,**c** using the TDDFT-B3LYP method. Rotational strengths (R) are given in cgs (10^{-40} erg esu cm/G).

Table 1. The ee % for the rearrangement of ***S*-5** (reaction time = 10 min)

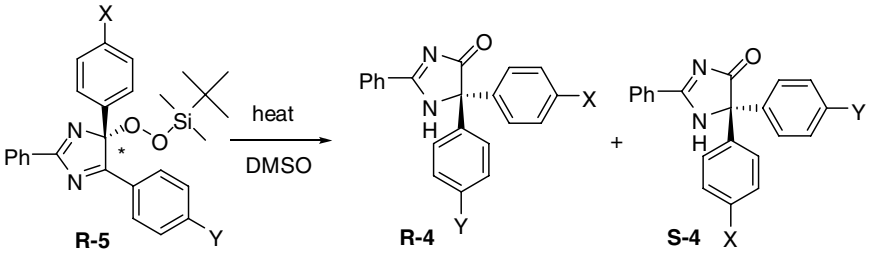


Temperature (°C)	Yield[a,b] (%)					
	***R*-4b**	***S*-4b**	ee (%)	***R*-4c**	***S*-4c**	ee (%)
100	75.5	24.5	51	80	20	60
130	75	25	50	79.5	20.5	59
160	75	25	50	79	21	58
180	74.5	25.5	49	78	26	52
200	74.5	25.5	49	75.5	24.5	51

[a] Yields calculated on the basis of HPLC integral quantity.
[b] The conversion was estimated to be 100% because of no other peak appearing in the ^{1}H NMR spectra.

relation between the ee % and reaction temperature for chiral imidazolones **4b** and **c** as products. In DMSO, the ee % slowly decreased as the temperature increased. It is noteworthy that the ee % was found to be rather low compared to the expected results of thermally allowed 1,5-sigmatropic rearrangement. To find a reason, we

Table 2. The ee % for the rearrangement of ***R*-5** (reaction time = 10 min)



Temperature (°C)	Yield[a,b] (%)					
	***R*-4b**	***S*-4b**	ee (%)	***R*-4c**	***S*-4c**	ee (%)
100	25	75	50	20.5	79.5	59
130	25	75	50	21	79	58
160	25	75	50	21.5	78.5	57
180	26.5	73.5	47	22.5	77.5	55
200	27	73	46	23	75	52

[a] Yields calculated on the basis of HPLC integral quantity.
[b] The conversion was estimated to be 100% because of no other peak appearing in the ^{1}H NMR spectra.

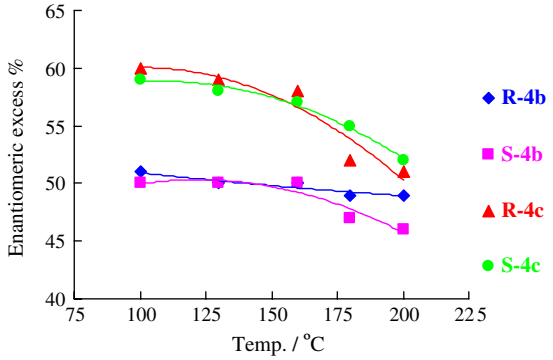
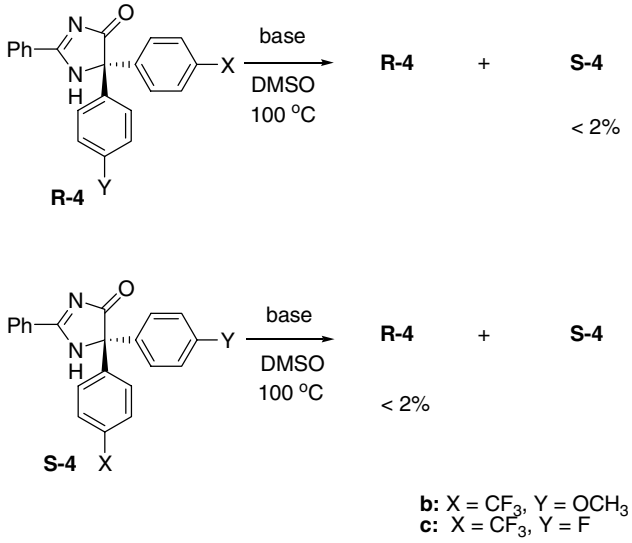


Figure 3. Relation between the ee % of **4b**,**c** and the reaction temperature in DMSO (reaction time = 10 min).

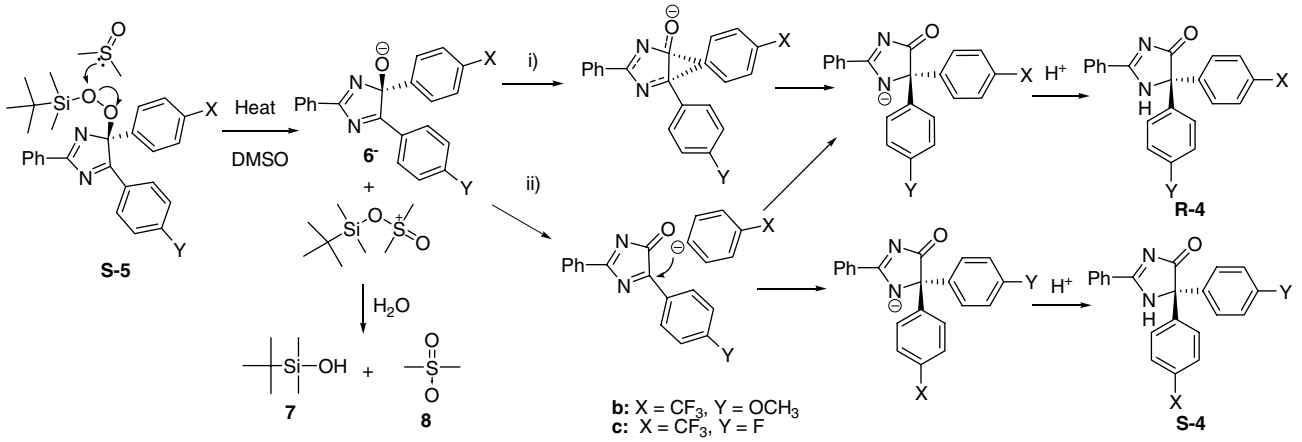


Scheme 4.

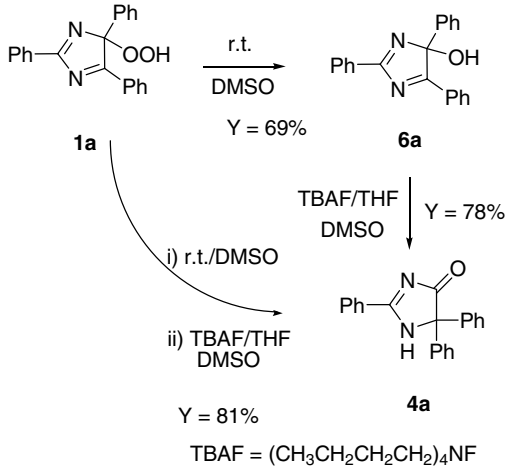
took the isomerization of ***R*-** and ***S*-4** into account. Optically pure chiral compounds **4** were dissolved in DMSO, and an excess of base (tetrabutyl ammonium fluoride in THF, or KOH/methanol) was added. The solution was heated for 10 min at 100 °C (Scheme 4). The HPLC analysis showed the conversions of the isomerization were less than 2%. It was much less than the decreases of ee % in the thermal rearrangement reactions of **5**.

We can draw a mechanism for the stereoselective 1,5-phenyl migration of the chiral peroxides (**4b** and **c**) as shown in Scheme 5. It is reasonable to imagine the formation of alcohol anion $\mathbf{6}^-$ as an intermediate. Fortunately, alcohol **6a** was available from hydroperoxide **1a**. Smooth rearrangement to **4a**, on the treatment of base, was confirmed even at the room temperature, as shown in Scheme 6.

Further the byproducts *tert*-butyldimethylsilanol (**7**) and dimethyl sulfone ($DMSO_2$, **8**) were confirmed by ^{1}H NMR spectroscopy. The ^{1}H NMR spectra of these byproducts were identified by comparison with those of authentic samples. Silanol **7** was further isolated by sublimation of the reaction mixture, and the IR, ^{1}H NMR and ^{13}C NMR were identical with those of the product prepared from the hydrolysis of *tert*-butyldimethylsilyl chloride. In DMSO, the thermal reaction of peroxides (**5**) solely provided imidazolones (**4**) in excellent yield. The mechanism for the reaction was proved to be substantially stereoselective 1,5-phenyl migration by use of chiral peroxides **5**. It is noteworthy that although the sigmatropic 1,5-phenyl migration should be thermally allowed according to the Woodward–Hoffmann rule, the migration actually includes a stepwise process.



Scheme 5.



Scheme 6.

Acknowledgements

We thank Professor M. Kojima for CD measurement and the staff of the SC-NMR Laboratory of Okayama University for measuring NMR spectra. This work was supported by the Ministry of Education, Science, Sports, and Culture of the Japanese Government (17029042).

References and notes

1. Sonnenberg, J.; White, D. W. *J. Am. Chem. Soc.* **1964**, *86*, 5685–5686.
2. (a) White, H. E.; Harding, J. C. *J. Am. Chem. Soc.* **1964**, *86*, 5686; (b) White, H. E.; Harding, J. C. *Photochem. Photobiol.* **1965**, *4*, 1129–1155.
3. Kimura, M.; Nishikawa, N.; Kura, H.; Lim, H.; White, E. H. *Chem. Lett.* **1993**, 505–508.
4. Bernhart, C. A.; Perreaut, P. M.; Ferrari, B. P.; Muneaux, Y. A.; Assens, J. L. A.; Clement, J.; Haudricourt, F.; Muneaux, C. F.; Taillades, J. E.; Vignal, M.-A.; Gougat, J.; Guiraudou, P. R.; Lacour, C. A.; Roccon, A.; Cazaubon, C. F.; Breliere, J.-C.; Le Fur, G.; Nisato, D. *J. Med. Chem.* **1993**, *36*, 3371–3380.
5. Lovely, C. J.; Du, H. W.; He, Y.; Dias, R. H. V. *Org. Lett.* **2004**, *6*, 737–738.
6. (a) Reichard, G. A.; Stengone, C.; Paliwal, S.; Mergelsberg, I.; Majmundar, S.; Wang, C.; Tiberi, R.; McPhail, A. T.; Piwinski, J. J.; Shih, N. Y. *Org. Lett.* **2003**, *5*, 4249–4251; (b) Lee, S. H.; Yoshida, K.; Matsushita, H.; Clapham, B.; Koch, G.; Zimmermann, J.; Janda, K. D. *J. Org. Chem.* **2004**, *69*, 8829–8835; (c) Anthony, P.; Adam, D.; Luc, V. H. *J. Org. Chem.* **2006**, *71*, 5303–5311.
7. (a) Allen, C. F. H.; VanAllan, J. A. *J. Am. Chem. Soc.* **1943**, *65*, 1384–1389; (b) Breslow, R.; Chang, H. W. *J. Am. Chem. Soc.* **1961**, *83*, 3727–3728; (c) Youssef, A. F.; Ogliaruso, M. *J. Org. Chem.* **1972**, *37*, 2601–2604.
8. (a) Davidson, D.; Weiss, M.; Jelling, M. *J. Org. Chem.* **1937**, *2*, 319–327; (b) Coraor, G. R.; Cescon, L. A.; Dessauer, R.; Silversmith, E. F.; Urban, E. J. *J. Org. Chem.* **1971**, *36*, 2262–2267; (c) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190–6191; (d) Clark, G. R.; Nikaido, M. M.; Fair, C. K.; Lin, J. *J. Org. Chem.* **1985**, *50*, 1994–1996.
9. Experimental data (synthesis, reactions, spectral data for new compounds) are available from the author.
10. Frisch, M. J.; Trucks; G. W.; 9. Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A.. Jr., Vreven, T.; Kudin, K. N.; Burant, J .C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. GAUSSIAN 03, Revision B.01; Gaussian, Pittsburgh PA, 2003.