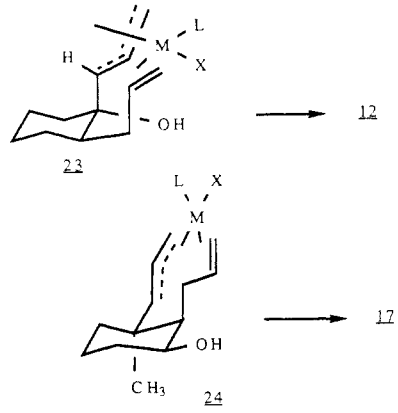
9 illustrate that formation of the *trans*-perhydroindanes preferably to exclusively places the vinyl group at C(8) or C(9) cis to the bridgehead substituent. Folding the proposed syn-π-allylmetal complex in a chairlike array as depicted in **21** and **22** nicely rationalizes the observations. This conformational picture also accommodates the dramatically opposite results in the two *cis*-perhydroindane cases (eq 5 and 8). A chair folding with the syn-π-allylmetal unit in an axial orientation as in **23** places the vinyl substituent on the exo face in the product as in **12**. On the



other hand, a chair folding with the syn-π-allylmetal unit in an equatorial position as in **24** orients the vinyl group on the endo face in the product as in **17**. The 15:1 preference for the contra-steric product in the latter case provides a measure of the conformational bias for a chairlike transition state in the cyclication.

The extraordinary reactivity of the allenes toward this catalyst is underscored by the current requirement that the vinyl group be unsubstituted in order to effectively capture the proposed π-allylmetal intermediate in preference to intermolecular capture by another allene. The facile addition of π-allylnickel complexes to allenes has previously been noted.[15] Nevertheless, the fact that the strain associated with forming the *trans*-perhydroindane even with a bridgehead methyl group does not deter the process demonstrates that strain effects are not as important as steric effects. The failure to effect related cyclizations using a catalyst derived from palladium(0) and a carboxylic acid, presumably a hydridopalladium carboxylate, emphasizes the importance of the nickel–chromium catalyst.[16]

The ability to use allenes as partners in intramolecular carbametalations opens a new dimension to cyclization via isomerization. The excellent chemo- and diasteroselectivity makes the process very useful synthetically. At a minimum, flexibility to generate either 1,2-dimethylenecyclopentanes or 2-vinyl-1-methylenecyclopentanes according to eq 2 from the same enyne now exists. To underscore this point, each of the allenes of eq 3–9 were synthesized in one step from the corresponding acetylene via the novel homologation of Crabbé.[12]

Acknowledgment. We thank the National Science Foundation and the National Institutes of Health for their generous support of our programs. J.M.T. thanks the National Institutes of Health for a postdoctoral fellowship for a portion of his stay in these laboratories. Mass spectra were gratefully provided by the Mass Spectrometry Facility, University of California—San Francisco, supported by the NIH Division of Research Resources.

Supplementary Material Available: Details of the preparation of **11** (2 pages). Ordering information is given on any current masthead page.

(15) Baker, R.; Copeland, A. H. *J. Chem. Soc., Perkin Trans. 1* **1977**, 2560.
(16) Matsuda, K., unpublished work in these laboratories. See: Trost, B. M.; Rise, F. *J. Am. Chem. Soc.* **1987**, *109*, 3161.

A Biomimetic Synthesis of (±)-Petiodial. A Novel Palladium-Catalyzed Enallene Cyclization

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Received April 11, 1988

Extracts of the marine algae of the family Udoteaceae have shown a variety of biological activities which include antimicrobial, cytotoxic, and ichthyotoxic properties.[1] Petiodial (**1**), an unusual cyclopentanoid diterpene which shares a carbon skeleton only with udoteatriol,[2] is one of the biologically active secondary metabolites whose structure, except for stereochemistry, has been suggested on the basis of spectral data.[1,3] We wish to record a synthesis of this compound and, on the basis of this synthesis, suggest a relative stereochemistry. The route involves an unexpected and novel palladium-catalyzed cyclization of an enallene.

In considering a synthesis of (±)-petiodial, the development of a strategy patterned after its biosynthesis from a suitable geranyl–geraniol derivative (cf. eq 1) raises the question of specific functionalization of C(19) rather than C(8) during the course of cyclization. An expedient solution to this subtle selectivity question derives from our earlier observations in the complementary behavior observed in the thermal versus Pd^{2+}-catalyzed ene reactions of enyne **2** (eq 2) which we have shown derives from the presence of the terminal double bond, which serves as a remote binding site during the course of the transition-metal-catalyzed process.[4] The intrinsic selectivity of this metal-catalyzed reaction and the existence of a similarly situated double bond in the geranyl–geraniol system suggested a route outlined in Scheme I in which the ring-forming step relies on a chemo- and regiocontrolled Pd^{2+} enyne cyclization (**4** → **5**).[4,5]

As outlined in Scheme I, **4** is readily available from farnesyl bromide.[6,7] Cyclization of **4a** with palladium acetate in warm benzene (65 °C) gives a 2.5–3.3:1 ratio of the silylated and unsilylated cyclized products **10** and **5b** in a sluggish reaction (eq 3). By using benzene-d_6, the reaction may be monitored by ^1H NMR spectroscopy which shows the buildup of an intermediate which we postulate to be an allene, such as **11**, based upon the appearance of an additional vinyl absorption at δ 5.01.

Because palladium-catalyzed enallene cyclization is, to our knowledge, unprecedented, we explored the cyclization of the allene **12** which forms exclusively upon desilylation of the silylacetylene **4a** [$AgNO_3$, ethanol–water, room temperature, 20 min then KCN,[8] room temperature, 20 min, 89%]. Under the cyclization conditions for enyne **4a** in which the enyne reacts sluggishly, enallene **12** cyclizes completely within 1 h to give only **5b** in 82% (eq 3). Addition of *N,N'*-dibenzylideneethylenediamine as a ligand for palladium[9] improves the yield slightly. The extraordinary selectivity for the terminal methylene isomer in contrast to a positional olefinic isomer is to be noted. It is outside the scope of this communication to speculate upon the mechanism of this new enallene cyclization; nevertheless, it is interesting to contrast this reaction to a recently discovered Ni–Cr-catalyzed enallene cyclization which produces a totally different type of product (eq 4).[10] Attempts to cyclize substrates like **12** under the Ni–Cr conditions failed.

(1) Paul, V. J.; Fenical, W. *Tetrahedron* **1984**, *40*, 2913 and earlier references cited therein.
(2) Nakatsu, T.; Ravi, B. N.; Faulkner, D. J. *J. Org. Chem.* **1981**, *46*, 2435. Whitesell, J. K.; Fisher, M.; Jardine, P. D. S. *J. Org. Chem.* **1983**, *48*, 1556.
(3) Fattorusso, E.; Magno, S.; Mayol, L.; Novellino, E. *Experentia* **1983**, *39*, 1275.
(4) Trost, B. M.; Lautens, M. *Tetrahedron Lett.* **1985**, *26*, 4887.
(5) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1985**, *107*, 1781.
(6) VanTamelen, E. E.; Nadeau, R. G. *Bioorg. Chem.* **1982**, *11*, 197.
(7) Enders, D.; Eichenauer, H. *Chem. Ber.* **1979**, *112*, 2933.
(8) Corey, E. J.; Kirst, K. A.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1970**, *92*, 6314.
(9) Trost, B. M.; Jebaratnam, J. *Tetrahedron Lett.* **1987**, *28*, 1611.
(10) Tour, J. M., unpublished work in these laboratories.

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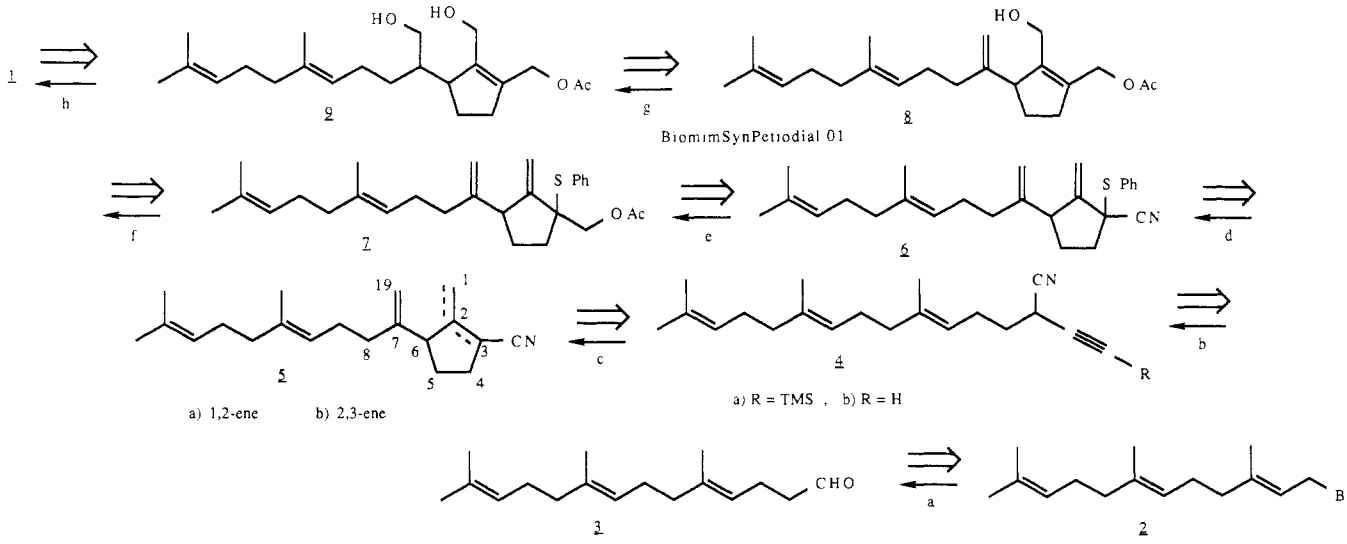
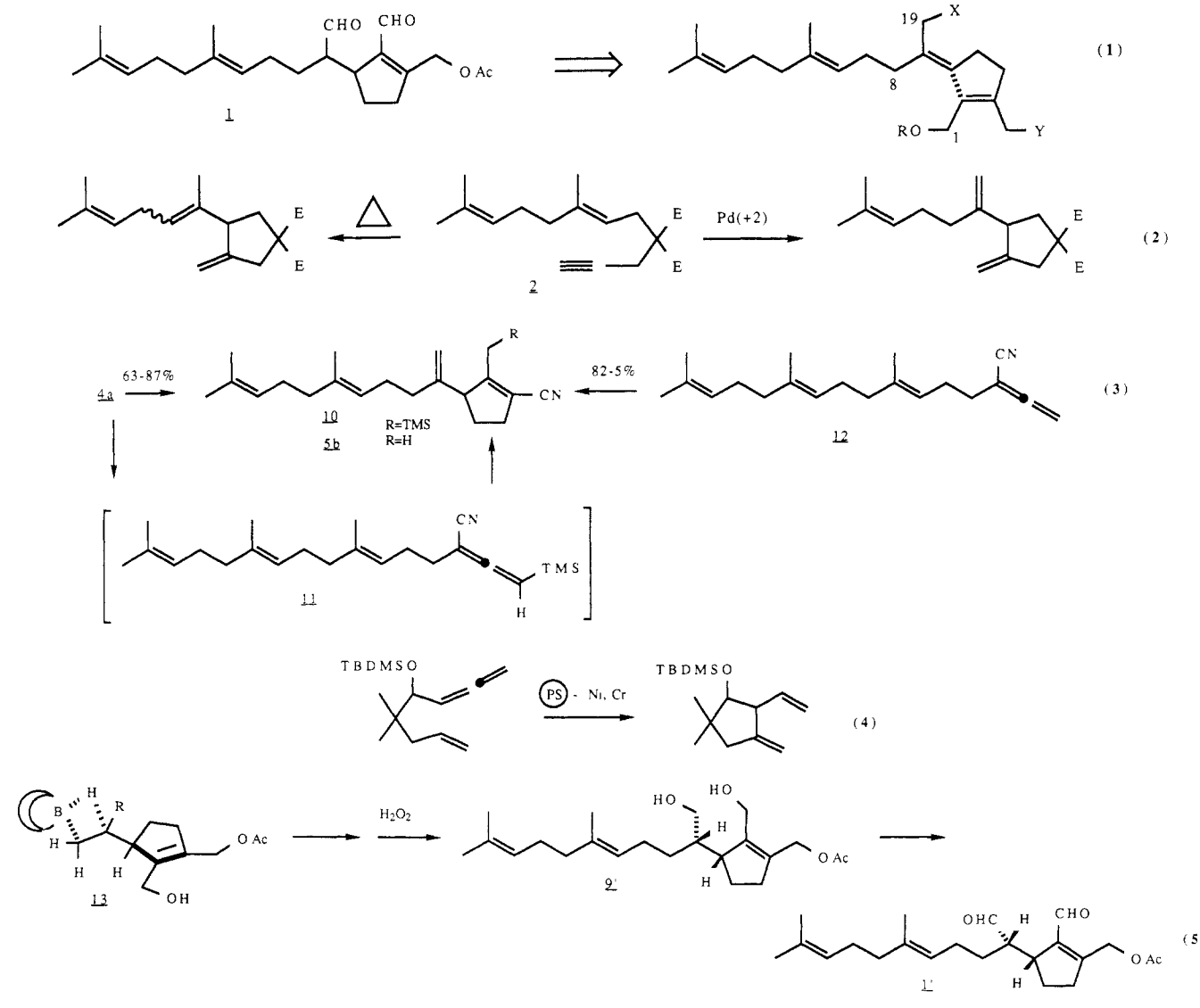
Scheme I. Retrosynthesis and Synthesis of Petiodial[a,b]



[a] (a) $LiCH_2CH{=}NN(CH_3)_2$, THF–HMPA, −78 °C, 1 h, 80% then CH_3I, 5% aqueous HCl, room temperature, 0.5 h, 88%. (b) i. TMS−≡−Li, THF, −78 °C, 2 h, 87%; ii. Ph_3P, CBr_4, THF, room temperature, 15 min, 98%. iii. CuCN, LiBr, DMF, 80 °C, 40%. (c) See text. (d) LICA, THF, $PhSSO_2Ph$, −78 °C to −20 °C, 1 h, 70%. (e) i. DIBAL-H, $PhCH_3$, −78 °C, 10 min then H_3O^+, 60%; ii. LAH, THF, room temperature, 20 min, 71%; iii. Ac_2O, DMAP, C_5H_5N, CH_2Cl_2, room temperature, 0.5 h, 98%. (f) TBA-oxone, CH_2Cl_2, room temperature then $(CH_3O)_3P$, $(CH_3)_2NH_2Cl$, THF–CH_3OH, 60 °C, 43%. (g) 9-BBN (5 equiv), 0 °C, 2 h, then NaOH, H_2O_2, 43%. (h) $(COCl)_2$, DMSO, CH_2Cl_2, −60 °C then $(C_2H_5)_3N$, −60 °C to room temperature, 77%. [b] The depicted structures have been fully characterized by spectral data and elemental composition established by high resolution mass spectroscopy and/or combustion analysis.

Scheme II



With a very efficient synthesis of **5b** via the allene **12** in hand, we have completed the synthesis of the carbon skeleton of petiodial in five steps from farnesyl bromide. Completion of the total synthesis requires adjustment of the oxidation level. Introduction of the oxygen at C(1) of **5** commenced with regioselective α-sulfenylation.[11] Minimization of γ-sulfenylation requires use of lithium *N*-cyclohexylisopropylamide as base and *S*-phenyl benzenethiosulfonate as the sulfenylating agent. Of the two γ-protons in the sulfenylation step, abstraction of the proton on the methyl group occurs selectively in spite of the doubly allylic nature of the ring methine proton. To maintain differentiation of the alcohol functions, the cyano group is transformed to an acetoxymethyl group prior to the proposed sulfoxide rearrangement[12] as outlined in Scheme I.

Use of MCPBA leads to olefin epoxidation accompanying sulfur oxidation. On the other hand, clean sulfur oxidation to the sulfoxide occurs by using the newly developed TBA-oxone.[13] The crude sulfoxide is immediately subjected to [2,3]sigmatropic rearrangement[14] to produce the desired hydroxyacetate **8**. Introduction of the final oxygen requires chemoselective hydroboration-oxidation of a 1,1-disubstituted double bond in the presence of three other double bonds. 9-BBN-H (5-fold excess) succeeds and provides a single diastereomer. To minimize steric hindrance in the approach of this bulky hydroborating agent,[15] we propose the transition state depicted in **13** which generates the relative configuration depicted in **9'**.[16] Swern-Moffatt oxidation[17] completes the synthesis. ^{1}H and ^{13}C NMR data correspond very well to the published data. Assuming no epimerization α to the aldehyde leads us to suggest the relative stereochemistry depicted in **1'** for the natural product. Since treatment of **1** with a tertiary amine leads to no change, we can only assume either that no epimerization occurs under these conditions or that any equilibrium lies heavily in favor of one diastereomer. The lack of any obvious chemical reason for the latter leads us to favor the former.

This sequence demonstrates the utility and uniqueness of the palladium-catalyzed cyclizations. The placement of the double bond in **5b** between C(7) and C(19) rather than C(7) and C(8), which does not happen in thermal Alder ene reactions, proceeds more selectively than our model system. Since we showed in the case of substrate **2** that the regioselectivity derives from the presence of the remote double bond as a binding site, the presence of two remote double bonds that might play the role of binding sites in **12** may account for the absence of any alternative isomer. The novel intervention of the allene in this cyclization demonstrates a potential for broader applicability of these metal-catalyzed cyclizations via isomerizations.

Acknowledgment. We thank the National Institutes of Health, General Medical Sciences Institute, for their generous support of our programs. Dr. Yoshiji Fujita of the Kuraray Co., Ltd., generously supplied all *trans*-farnesol. Mass spectra were gratefully provided by the Mass Spectrometry Facility, University of California - San Francisco, supported by the NIH Division of Research Resources.

Supplementary Material Available: Spectral data for **12**, **5b**, **8**, and **9** and a table for comparison of spectral data for natural and synthetic petiodial (2 pages). Ordering information is given on any current masthead page.

(11) Trost, B. M.; Salzmann, T. N.; Hiroi, K. *J. Am. Chem. Soc.* **1976**, *98*, 4887. Trost, B. M.; Massiot, G. S. *J. Am. Chem. Soc.* **1977**, *99*, 4405. Seebach, D.; Teschner, M. *Chem. Ber.* **1976**, *109*, 1601.

(12) Evans, D. A.; Andrews, G. C. *Acc. Chem. Res.* **1974**, *7*, 147. Block, E. *Reactions of Organosulfur Compounds*; Academic Press: New York, 1978; pp 216-266.

(13) Trost, B. M.; Braslau, R. L. *J. Org. Chem.* **1988**, *29*, 1231.

(14) Ishibashi, H.; Nakatani, H.; Sakashita, H.; Ikeda, M. *Chem. Commun.* **1987**, 338.

(15) Cf. carbonyl reductions: Midland, M.; Kwon, Y. C. *J. Am. Chem. Soc.* **1983**, *105*, 3725.

(16) For a closely related case, see: Oppolzer, W.; Jacobsen, E. J. *Tetrahedron Lett.* **1986**, *27*, 1141.

(17) Cf. Razmilic, I.; Lopez, J.; Sierra, J.; Cortes, M. *Synth. Commun.* **1987**, *17*, 95.

Evidence for Extreme Activation of C-H Bonds in $[(PhCH_2)_2NNa]_n$: Resultant C-H Bond Cleavage To Give $\{[PhC(H)NC(H)Ph]Na\cdot PMDETA\}_n$

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Received March 11, 1988

In organolithium chemistry evidence is accumulating that lithium atoms situated in abnormally low coordination environments then proceed to interact with nearby CH units of the ligands. For example, the crystal structure of $[(PhCH_2)_2NLi]_3$ revealed a planar $(NLi)_3$ ring whose formally just two-coordinate metal atoms form close contacts with $CH_2\alpha CoCH$ portions of the benzyl groups.[1] Elsewhere, the position of second lithiation of an aromatic such as naphthalene was shown, by MO calculations on model species and by ^{6}Li-^{1}H HOESY NMR experiments, to be directed by Li···HC interactions within the monolithium species.[2] In the light of such findings we decided to explore the occurrence of like interactions in organo*sodium* derivatives: given Na's greater ionicity (so generally higher transmitted reactivity in compounds) compared to Li, one might expect any such metal···hydrocarbon interactions to be even more emphatic.

Our first target was dibenzylamidosodium, $[(PhCH_2)_2NNa]_n$, **1**, the Na analogue of the lithium amide cited above. Red crystals of compound **1** were obtained in high yield (78%) from an equimolar reaction of $(PhCH_2)_2NH$ with a suspension of Bu^{n}Na in hexane. Satisfactory elemental analyses apart, **1** was characterized through its ^{1}H NMR spectrum which showed the expected Ph and CH_2 resonances, but no resonance due to (N)*H*;[3] also relevant is that the IR spectrum of **1** clearly revealed the presence of benzyl CH_2 units [$\nu(CH_2)$, 2705-2610 cm^{-1}]. Given **1**'s low mp and reasonable solubility in hydrocarbons (e.g., 35 mg/mL in toluene) it probably has an oligomeric, rather than a polymeric, structure, e.g., a ring, akin to that found for $[(PhCH_2)_2NLi]_3$, though possibly, in view of the structure found for $(PhCH_2Na\cdot TMEDA)_4$,[4] a larger $(NNa)_n$ ring may be preferred; either way, the crux is that, in the absence of a Lewis base, a ring sodium atom in **1** would be only two-coordinate and so extremely coordinatively unsaturated.

Remarkably, treatment of **1** with the Lewis base PMDETA [$(Me_2NCH_2CH_2)_2$·NMe], or of $(PhCH_2)_2NH$ with Bu^{n}Na in the presence of PMDETA, affords needles of $\{[PhC(H)NC(H)Ph]$-$Na\cdot PMDETA\}_n$, **2**, a dichroic material seen as green by reflected light but deep red by transmitted light. These crystals,[5] obtained in good yield (59%, first crop), are low melting, soluble in hydrocarbons (e.g., 75 mg/mL in toluene), extremely oxygen- and moisture-sensitive, and, over a longer period, light-sensitive also. Evidence for the formulation of **2**, aside from good elemental analyses, was gathered as follows. The key feature of its ^{1}H NMR spectrum, apart from the expected PMDETA and Ph resonances,

(1) (a) Barr, D.; Clegg, W.; Mulvey, R. E.; Snaith, R. *J. Chem. Soc., Chem. Commun.* **1984**, 285, 287. (b) Armstrong, D. R.; Mulvey, R. E.; Walker, G. T.; Barr, D.; Snaith, R.; Clegg, W.; Reed, D. *J. Chem. Soc., Dalton Trans.* **1988**, 617.

(2) (a) Neugebauer, W.; Kos, A. J.; Schleyer, P. v. R. *J. Organomet. Chem.* **1982**, *228*, 107. (b) Neugebauer, W.; Clark, T.; Schleyer, P. v. R. *Chem. Ber.* **1983**, *116*, 3283. (c) Bauer, W.; Clark, T.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1987**, *109*, 970.

(3) Compound **1** $[(PhCH_2)_2NNa]_n$: mp 98-101 °C; Anal. ($C_{14}H_{14}NNa$) C, H, N, Na; ^{1}H NMR spectrum (recorded at 360 MHz in benzene-d_6 solution) Ph (10 H, m, centered at δ 7.16 ppm) and CH_2 (4 H, br s, δ 3.73 ppm).

(4) Schade, C.; Schleyer, P. v. R.; Dietrich, H.; Mahdi, W. *J. Am. Chem. Soc.* **1986**, *108*, 2484.

0002-7863/88/1510-5235$01.50/0