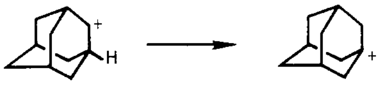
secondary–secondary ion conversion **5** → **6** might have a lower barrier than the tertiary–tertiary ion conversion involved in the model.[13] Taking 3 kcal/mol as a rough estimate of the activation enthalpy of the methyl shift in **5**,[14] we can calculate the energy differences between cations **4a** and **5a** (eq 6a), and between cations **4b** and **5b** (eq 6b) as shown in eq 7a and 7b, respectively. Comparison of

$$\Delta H_7^{(a)} = 14.3 - 3 = 11.3 \text{ kcal/mol} \qquad (7a)$$

$$\Delta H_7^{(b)} = 13.4 - 3 = 10.4 \text{ kcal/mol} \qquad (7b)$$

eq 3 and 7 provides a measure of the excess stability of the 3-methyl-2-norbornyl cations **3** over the acyclic models 3-methyl-2-butyl and 3-methyl-2-pentyl cations: 1.5–2.2 and 0.6–1.3 kcal/mol, respectively. It has to be remembered that the range in each case is determined by the difference in strain between the two stereoisomers of **3**; the lower limits would have to account for any electronic stabilization in the 3-*endo*-methyl-2-norbornyl cation.[15]

The excess stability of the 2-norbornyl cation over "normal" secondary cations has been discussed in terms of structure (bridged or not bridged) for the former.[16] As Arnett pointed out, stabilization over a model cannot by itself prove the existence of bridging, since the latter is a structural characteristic. An abnormal stability of a secondary ion indicates, however, that there should be a structural reason for it.[1,17] Naturally, parameters like the tertiary/secondary ion energy difference are influenced by several structural features, so that a range should be expected, rather than a constant value in all cases.[18] Thus, the value for 2-nonbornyl cations (eq 3) is better considered in the perspective of not only simpler models, like eq 6, but also more complex models, like the recently reported 2-adamantyl/1-adamantyl ion pair (eq 8).[19]



$\Delta H_8 = -4$ kcal/mol (8)

Addendum: In the accompanying paper, Schleyer and Chandrasekhar[13] offer a criticism of the present analysis. I will not comment further upon their selection and treatment of data.[6,14,15] I am somewhat puzzled by the trust which they place in MINDO/3 calculations,[20] as well as by an apparent lack of consistency: if MINDO/3 can be used to determine indirectly the stabilization of the "nonclassical" 2-norbornyl cation,[13] why should we not trust the direct MINDO/3 calculation which predicts the nonbridged 2-norbornyl cation to be the more stable by 2 kcal/mol?[21,22]

I want to emphasize, however, that the actual structure of the 2-norbornyl cation(s) is at best of peripheral interest for this work. Two types of methods have been consistently used to ascertain carbocation structures. The first is the direct structure analysis, basically by spectroscopic means; the second is the energy comparison method by which the actual energy content of an ion is compared with the value predicted for a certain structure of the ion (normally the nonbridged structure). If there is a discrepancy, a different structure is assigned (usually a bridged one). Each such comparison involves four species (e.g., eq 3 and 6a, eq 3 and 6b, eq 3 and 8). For each species the energy content is determined by a number of factors, electronic and steric; the contribution of bridging in one species, if any, is normally less important than the combined variability of all other factors for the four species involved in comparison. In particular, the energy difference for eq 3, which includes a secondary 2-norbornyl cation is very close to the figures for the model eq 6a, and especially 6b, and is larger than the figure for the model eq 8. Therefore, it appears that at the present level the energy comparison method cannot be used reliably to assign carbocation structures; instead, direct structure determinations should be attempted.[23]

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[12] Saunders, M.; Kates, M. R. *J. Am. Chem. Soc.* **1978**, *100*, 7082.

[13] Schleyer, P. v. R.; Chandrasekhar, J. *J. Org. Chem.*, following paper in this issue. Professor P. v. R. Schleyer is acknowledged for sending me a copy of that work prior to its publications.

[14] In ref 13 the barrier is taken as zero. This implies that in the process **4a** → **7a** the system is effectively at the tranisition state from **5a** to **6a**. Alternatively, **5a** would be an energy maximum. As mentioned in the text, studies on other carbocation rearrangements contradict this assumption and indicate the methyl shift as the rate-determining step (ref 8). Moreover, the relative rates of hydrogen and carbon exchange for the 2-propyl cation in super acid indicate that even the primary 1-propyl cation is not a transition state, but a real intermediate, for which both hydride shift to the secondary ion and cyclization to protonated cyclopropane (equivalent to methyl shift in **5a**) involve energy barriers, the former being actually slightly lower (Saunders, M.; Vogel, P.; Hagen, E. L.; Rosenfeld, J. *Acc. Chem. Res.* **1973**, *6*, 53). The same conclusion was reached for 1-propyl cations generated electrochemically (Laurent, E.; Thomalla, M.; Marquet, B.; Burger, U. *J. Org. Chem.* **1980**, *45*, 4193).

[15] Because only *exo*-**3** and **5a** are discussed in ref 13 the stabilization energy of **3** arrived at in that work is apparently higher.

[16] Brown, H. C. "The Nonclassical Ion Problem" (with comments by P. v. R. Schleyer); Plenum Press: New York, 1977.

[17] Arnett, E. M.; Petro, C.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1979**, *101*, 522.

[18] The equivalent of this parameter in solvolysis reactions, the α-methyl group effect on rates, has been discussed: Fărcaşiu, D. *J. Am. Chem. Soc.* **1976**, *98*, 5301. See also: Brown, H. C.; Ravindranathan, M.; Gundu Rao, C.; Chloupek, F. J.; Rei, Min-Hon *J. Org. Chem.* **1978**, *43*, 3667.

[19] Wesdemiotis, C.; Schilling, M.; Schwarz, H. *Angew. Chem.* **1979**, *91*, 1017. Houriet, R.; Schwarz, H. *Ibid.* **1979**, *91*, 1018.

[20] From the papers cited in ref 13 we find that MINDO/3 (a) predicts *n*-butane to be more stable than isobutane by 6.5 kcal/mol (Bingham, R. C.; Dewar, M. J. S.; Lo, D. H. *J. Am. Chem. Soc.* **1975**, *97*, 1294), (b) predicts the 2-propenyl cation to be more stable than the allyl cation by 8.4 kcal/mol (Köhler, H. J.; Lischka, H. *J. Am. Chem. Soc.* **1979**, *101*, 3479), and (c) predicts the 7-norbornyl cation, "a species legendary in its inertness", to be more stable than the 2-norbornyl cation by 3.1 kcal/mol (Schleyer, P. v. R. In ref 16, p 100; the discussion on that page of the MINDO/3 method is illuminating).

[21] Reference 16, p 97.

[22] This is not a denial of the usefulness of the MINDO/3 method for any case; as any other parametric method, however, it is reliable only inside its range of parameterization; also, one should not reach conclusions based on differences well below the recognized uncertainty of the method.

[23] (a) Reference 13 cites measurements indicating a bridged structure. (b) For a different interpretation of data in super acid solution, see: Kramer, G. M. *Adv. Phys. Org. Chem.*, **1975**, *11*, 177. (c) See also: Beauchamp, J. L. "Abstracts of Papers", 177th National Meeting of the Americal Chemical Society, Honolulu, HI, Apr 1979; American Chemical Society: Washington, D.C., 1979; ORGN-3. (d) For a report on trapping the unsymmetrical 2-norbornyl cation in solvolyses, see: Saito, S.; Moriwake, T.; Takeuchi, K.; Okamoto, K. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 2634.

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Evaluation of the Extra Stability of the Bridged 2-Norbornyl Cation

Summary: The extra stabilization due to bridging in the nonclassical secondary 2-norbornyl cation is evaluated to be 6 ± 1 kcal/mol in stable ion media.

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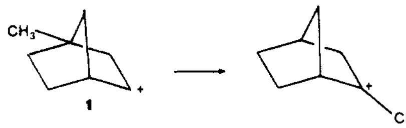
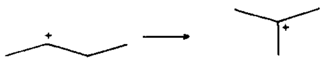
Sir: In the preceding paper, Fărcaşiu[1] evaluates the results of earlier measurements[2] of the heats of isomerization of secondary to tertiary cations in the norbornyl (eq 1) and acyclic (eq 2) series. He emphasizes that the difference in energy between eq 1 and 2, 7.6 kcal/mol, indicating some extra stabilization of the secondary over the tertiary 2-norbornyl cation, should be subjected to further analysis before final conclusions can be drawn. In particular, Fărcaşiu points out that the degrees of chain branching involved in eq 1 and 2 are different. We agree that more appropriate comparisons would involve eq 3 and 4. However, since it is not possible to carry out the required experimental measurements, these last two equations have to be evaluated indirectly. Our analysis differs significantly from that of Fărcaşiu.[1]

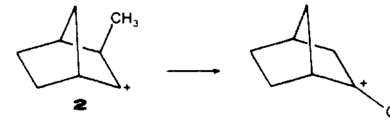


1

$\Delta H = -6.6$ kcal/mol (1)



$\Delta H = -14.2$ kcal/mol (2)



2

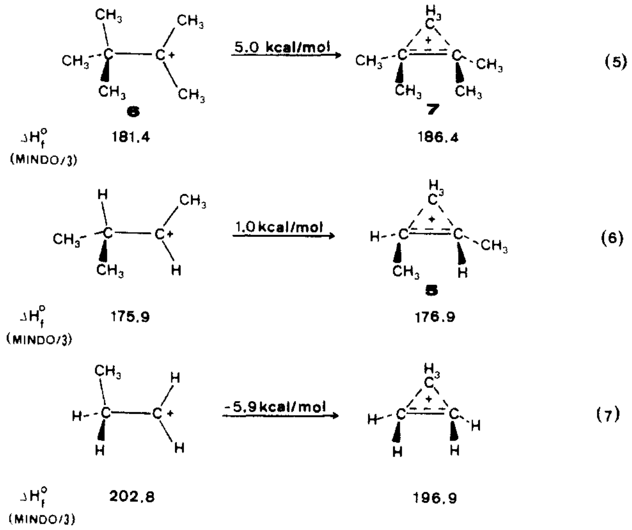
$\Delta H_{est} = -8 \pm 1$ kcal/mol (3)

4 **3**

$\Delta H = -14.3$ kcal/mol (4)

The first step involves estimating the energy difference between the hypothetical classical secondary 2-norbornyl cations, 1 and 2. Molecular mechanics calculations on the parent hydrocarbons indicate a 2.5 kcal/mol (EAS force field)[3] greater stability of 1-methylnorbornane over 2-*exo*-methylnorbornane, the less strained epimer. Fărcaşiu reports force-field calculations on the methyl-substituted norbornyl cations themselves, but the same difference, 2.5 kcal/mol, between 1 and 2 is found. However, Fărcaşiu did not apply the correction for β-alkyl branching, known to be necessary in rigid polycyclic carbocation systems to correct for hyperconjugative and/or inductive effects for which the force-field calculations are not parameterized.[4] For each β-branch, corrections of 3 kcal/mol for secondary cations and 1.5 kcal/mol for tertiary cations have been proposed.[4c] Thus, Fărcaşiu's 2.5 kcal/mol energy difference between 1 and 2 probably is too large and actually may vanish when this β-branching correction is applied. On the other hand, Sorensen[5] has presented several examples where extra methyl groups in *tert*-2-methylnorbornyl cations prefer bridgehead positions thermodynamically, but no quantitative values seem to be available. We conclude that a smaller correction, perhaps −1 ± 1 kcal/mol (instead of −2.5 kcal/mol), shoud be added to the energy of eq 1 in order to evaluate eq 3, if classical cation structures for 1 and 3 be assumed. A more serious disagreement lies in the next step of the analysis.

Scheme I



In evaluating eq 4, Fărcaşiu makes use of the average experimental activation energy for methyl equilibration of 3 ($\Delta H^{\ddagger} = 14.3 \pm 0.5$ kcal/mol).[6] This methyl scrambling can be presumed to involve the secondary cation, 4, and the methyl bridged species 5 (Scheme I) as possible intermediates or transition states.[6] Fărcaşiu assumes that 5 represents a transition state for the overall methyl scrambling process in 3 and further assumes that 4 lies about 3 kcal/mol lower in energy than 5. This value is taken from the experimental activation free energy for methyl scrambling in 6.[7] Since 6 is known to have a classical structure,[7,8] the methyl-bridged species 7 (eq 5) should be a transition state.

However, eq 5 represents a tertiary cation–tertiary cation rearrangement and *cannot* properly be used to model processes like the methyl equilibration in 3 (cf. eq 4 and 6) in which interconversions between secondary carbocation centers are involved. It is axiomatic in carbocation chemistry that the relative energy of bridged species (as rearrangement transition states or as intermediates) will decrease relative to their classical counterparts as the degree of substitution is increased.[6,9a,10c] This is shown by the results of MINDO/3 calculations[10] (Scheme I), which compare the differences between classical and bridged forms in the tertiary (eq 5), secondary (eq 6), and primary (eq 7) cation series.

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[1] Fărcaşiu D. *J. Org. Chem.*, preceding paper in this issue.

[2] Arnett, E. M.; Pienta, N.; Petro, C. *J. Am. Chem. Soc.* **1980**, *102*, 398.

[3] Engler, E. M.; Andose, J. D.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1973**, *95*, 8005.

[4] (a) Ōsawa, E.; Engler, E. M.; Godleski, S. A.; Inamoto, Y.; Kent, G. J.; Kausch, M.; Schleyer, P. v. R. *J. Org. Chem.* **1980**, *45*, 984. Engler, E. M.; Fărcaşiu, M.; Sevin, A.; Sense, J. M.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1973**, *95*, 5769. (c) Gund, T. A.; Schleyer, P. v. R.; Unruh, G. D.; Gleicher, G. J. *J. Org. Chem.* **1974**, *39*, 2995.

[5] Sorensen, T. S. *Acc. Chem. Res.* **1976**, *9*, 257.

[6] (a) Saunders, M.; Hagen, E. L. *J. Am. Chem. Soc.* **1968**, *90*, 2436. (b) Brouwer, D. M. *Recl. Trav. Chim. Pays-Bas* **1968**, *87*, 210. (c) Saunders, M.; Vogel, P.; Hagen, E. L.; Rosenfeld, J. *Acc. Chem. Res.* **1973**, *6*, 53. (d) Brouwer, D. M.; Hogeveen, H. *Prog. Phys. Org. Chem.* **1972**, *9*, 179.

[7] Saunders, M; Kates, M. R. *J. Am. Chem. Soc.* **1978**, *100*, 7082.

[8] Schleyer, P. v. R.; Lenoir, D.; Mison, P.; Liang, G.; Surya Prakash, G. K.; Olah, G. A. *J. Am. Chem. Soc.* **1980**, *102*, 683.

[9] Brown, H. C. (with comments by Schleyer, P. v. R.) "The Nonclassical Ion Problem"; Plenum Press: New York, 1977; (a) Chapter 7, p 101; (b) Chapter 6, p 83 ff; (c) p 258–259.

[10] (a) Bingham, R. C.; Dewar, M. J. S.; Lo, D. H. *J. Am. Chem. Soc.* **1975**, *97*, 1285. (b) Bischof, P. K.; Dewar, M. J. S. *Ibid.* **1975**, *97*, 2278. Dewar, M. J. S. *Chem. Brit.* **1975**, *11*, 97; (c) Saunders, M.; Chandrasekhar, J.; Schleyer, P. v. R. In "Rearrangements in Ground and Excited States"; De Mayo, P., Ed.; Academic Press: New York, 1980; Essay 1, p 1.

J. Org. Chem. **1981**, *46*, 227-228

As pointed out by Dewar[10b] and by Lischka and Köhler,[11] MINDO/3 often provides remarkably good results in such comparisons between small classical and nonclassical cations as judged from experimental data or from high-level ab initio calculations.[12,13] Although the MINDO/3 estimate of the energy difference favoring **6** over **7**, 5.0 kcal/mol (eq 5), is in satisfactory agreement with the experimental barrier to methyl scrambling in **6**, 3.5 kcal/mol, the trends in the MINDO/3 results (Scheme I) probably are more significant. Thus, the bridged classical ion energy difference in the secondary case (eq 6) is 4.0 kcal/mol less than that in the tertiary (eq 5). This contradicts the assumption of Fărcaşiu that **5** should lie about 3 kcal/mol *higher* in energy than **4**. We conclude that **4** and **5** probably are comparable in energy in nonnucleophilic media. No correction of the measured activation energy for methyl equilibration in **3** is thus needed, and this value is given in eq 4.

Equations 3 and 4 can now be compared in order to provide a corrected estimate, 6 ± 1 kcal/mol, for the extra stabilization associated with the secondary 2-norbornyl cation in stable ion media. This value is in good agreement with other differently based estimates under such conditions[9c] and with the energy expected from solution solvolysis data (compare the Goering–Schwene diagram[9b] and the finding of Arnett, Petro, and Schleyer[14] that nearly 90% of the total ionization energy of a carbocation in stable ion media is reflected in the corresponding solvolysis transition state). This extra stabilization, in principle, might be due to effects other than bridging. However, if the structure of the norbornyl cation is established to be nonclassical by other methods, it is reasonable to attribute the 6 ± 1 kcal/mol stabilization to the energy gained on bridging.

The experimental evidence favoring the bridged structure of the 2-norbornyl cation in nonnucleophilic media, where direct spectroscopic observations can be made, is now overwhelming. The ESCA spectrum has been determined a third time, with the same results as before.[15] Theoretically calculated ESCA spectra for the classical and nonclassical species firmly support the nonclassical assignment.[16] Detailed analysis of the ^{13}C NMR chemical shifts of the 2-norbornyl cation, in comparison with numerous other carbocations, demonstrates its bridged nature.[8] Finally, Saunders' isotopic perturbation probe[10c] shows the structure of the 2-norbornyl cation to be bridged.[17] The time has come to ask the question, "Are remaining doubts concerning the bridged structure of the 2-norbornyl cation resonable or unreasonable?"

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[11] Köhler, H.-J.; Lischka, H. *J. Am. Chem. Soc.* **1979**, *101*, 3479; **1978**, *100*, 5297.

[12] Krishnan, R.; Pople, J. A.; Schleyer, P. v. R., to be published.

[13] Whatever the deficiencies of MINDO/3 in other contexts may be, comparisons within limited reaction series such as eq 5–7 reduce or eliminate possible errors by cancellation. Ab initio results show the same trends, also, for the related energy differences reflecting 1,2-hydride (instead of methide) shifts along the cation series, ethyl, 2-butyl, and 2,3-dimethyl-2-butyl.[10-12] In stable ion media, the experimental hydride shift barrier in the classical 2,3-dimethyl-2-butyl cation is 3.1 kcal/mol,[7] but the latest evidence shows the 2-butyl cation to be hydrogen-bridged (Saunders, M.; Hehre, W. J., private communications). The indicated secondary–secondary vs. tertiary–tertiary energy difference is thus >3.1 but <3.1 ± 2.4[7] = 5.5 kcal/mol, in reasonable agreement with MINDO/3 results[10c] and the related 4.0 kcal/mol difference between eq 5 and 6.

[14] Arnett, E. M.; Petro, C.; Schleyer, P. v. R., *J. Am. Chem. Soc.* **1979**, *101*, 522.

[15] Olah, G. A. Paper presented at the Annual Chemical Congress, Chemical Society, London, Durham, England, Apr 1980.

[16] Clark, D. T.; Chromarty, B. J.; Colling, L. *J. Am. Chem. Soc.* **1977**, *99*, 8120.

[17] Saunders, M.; Kates, M. R. *J. Am. Chem. Soc.* **1980**, *102*, 6867.

A Brief Total Synthesis of *N*-Benzoyl-D,L-daunosamine

Summary: A brief regioselective total synthesis of *N*-benzoyl-D,L-daunosamine [(±)-**7a**] from chlorosulfonyl isocyanate (**2**) and (*E*)-1,3-pentadiene (**1**) is described.

Sir: $[{}_{2}\pi_{s} + {}_{2}\pi_{a}]$ cycloadditions of chlorosulfonyl isocyanate to alkenes have been widely employed to synthesize β-lactam antibiotics and structurally related systems.[1,2] We have extended the preparative utility of this reaction to the biologically important 2,3,6-trideoxy-3-aminohexoses and have accomplished short regioselective syntheses of the *N*-benzoyl derivative [(±)-**7a**] of D,L-daunosamine [2,3,6-trideoxy-3-amino-D,L-*lyxo*-hexose, (±)-**7b**] and the corresponding derivative of the D,L-*xylo*-isomer (±)-**8a**.

There has been intense synthetic *N*-benzoyl-D,L-daunosamine in daunosamine (L_S-**7b**) because it is the glycosidic residue of a number of anthracycline anticancer antibiotics[3] and contributes significantly to their biological activity. Elegant chiral preparations of both the natural L_S[4] and unnatural D_R[5] isomers have been reported. Several shorter total syntheses of (±)-**7b** have also been reported.[6]

Our short total synthesis of *N*-benzoyl-D,L-daunosamine

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[1] For a recent example, see: Johnston, D. B. R.; Schmitt, S. M.; Bouffard, F. A.; Christensen, B. G. *J. Am. Chem. Soc.* **1978**, *100*, 313.

[2] For a recent review on β-lactam synthesis see: Isaacs, N. S. *Chem. Soc. Rev.* **1976**, *5*, 181 and references therein.

[3] (a) Daunorubicin: Arcamone, F.; Franceschi, G.; Orezzi, P.; Cassinelli, G.; Barbieri, W.; Mondelli, R. *J. Am. Chem. Soc.* **1964**, *86*, 5334; Arcamone, F.; Cassinelli, G.; Franceschi, G.; Mondelli, R.; Orezzi, P.; Penco, S. *Gazz. Chim. Ital.* **1970**, *100*, 949. (b) Adriamycin: Arcamone, F.; Franceschi, G.; Penco, S.; Selva, A. *Tetrahedron Lett.* **1969**, 1007; DiMarco, A.; Arcamone, F.; Zunio, F. *Antibiotics* **1975**, *3*, 101–128. (c) Carminomycin: Brazhnikova, M. G.; Zbarsky, V. B.; Potapova, V. L. *J. Antibiot.* **1974**, *27*, 254; Gause, G. F.; Brazhnikova, M. G.; Shorin, V. B. *Cancer Chemother. Rep.* **1974**, *58*, 255; Wani, M. C.; Taylor, H. L.; McPhail, A. T.; Onan, K. D. *J. Am. Chem. Soc.* **1975**, *97*, 5955. (d) 11-Deoxydaunorubicin, 11-deoxydoxorubicin (11-deoxyadriamycin): Arcamone, F.; Cassinelli, G.; DiMatteo, F.; Forenza, S.; Ripamonti, C. M.; Rivola, G.; Vigevani, A.; Clardy, J.; McCabe, T. *Ibid.* **1980**, *102*, 1462. (e) Nogalamycin: Wiley, P. F.; Kelly, R. B.; Caron, E. L.; Wiley, V. H.; Johnson, J. H.; Mackellar, F. A.; Mizsak, S. A. *Ibid.* **1977**, *99*, 542.

[4] Marsh, J. P.; Mosher, C. W.; Acton, E. M.; Goodman, L. *Chem. Commun.* **1967**, 973. Horton, D.; Weckerle, W. *Carbohydr. Res.* **1975**, *44*, 227. Yamaguchi, T.; Kojima, M. *Ibid.* **1977**, *59*, 343. Fronza, G.; Fuganti, C.; Grasselli, P. *J. Chem. Soc., Chem. Commun.* **1980**, 442.

[5] Richardson, A. C. *Chem. Commun.* **1965**, 627. Richardson, A. C. *Carbohydr. Res.* **1967**, *4*, 422. Baer, H. H.; Capek, K.; Cook, M. C. *Can. J. Chem.* **1969**, *47*, 89.

[6] Wong, C. M.; Ho, T. L.; Niemczura, W. P. *Can. J. Chem.* **1975**, *53*, 3144. Dyong, I., Wiemann, R. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 682. Iwataki, I.; Nakamura, Y.; Takahashi, K.; Matsumoto, T. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 2731. Uskokovic, M. R.; Wovkulick, P. Twenty-sixth National Organic Chemistry Symposium of the American Chemical Society, Tuscon, AZ, June 1979; p 41.

0022-3263/81/1946-0227$01.00/0