

CHARLES W. JEFFORD

JACQUES A. ZUBER

Department of Organic Chemistry,  
University of Geneva

1211 Geneva 4, Switzerland

## NEW REARRANGEMENTS AND STRUCTURES IMPLICATING SMALL RINGS\*

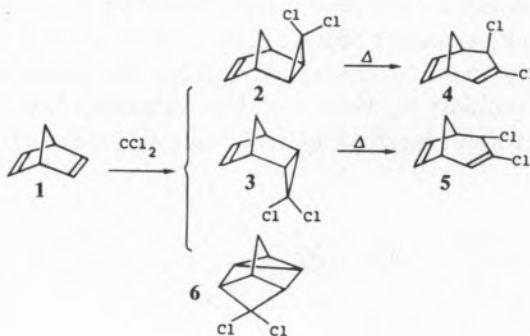
### PROLOGUE

Appropriately substituted cyclopropane and cyclobutane rings are prone to rearrangement. The classic processes, ring opening and contraction exemplified respectively by the cyclopropyl-allyl and cyclobutyl-cyclopropylcarbinyl rearrangements are well understood [1, 2]. However, when small ring systems are constrained within rigid, cage-type molecules, new, unusual transpositions and structures are possible. This review deals in turn with the discovery of an unexpected sigmatropic rearrangement arising from the addition of a carbene to a diene, a short synthesis of halogen derivatives of a fluxional molecule, barbaralane, and lastly a revealing study of the rearrangements of a cage-type cation and its carbene analogue, the latter providing the first example of a carbon ylide. In each instance, small rings play a dominant, yet subtle role. In all cases the seemingly simple reaction of norbornadiene with dichlorocarbene constitutes the experimental basis for these diverse findings.

### INTRODUCTION

The basic reaction is simple enough and has been extensively investigated [3], but has never been properly analyzed until very recently [4]. The state of our knowledge at the start was that dihalocarbenes, here exemplified by dichlorocarbene, essentially undergo 1,2 and homo-1,4 additions to norbornadiene (1).

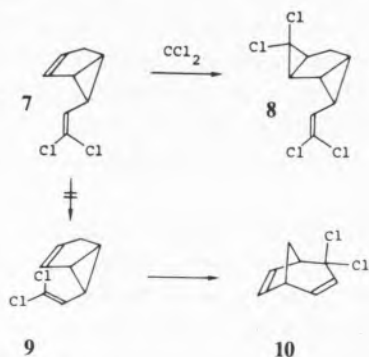
Normally, the exo (2) and endo (3) 1,2 adducts spontaneously rearrange under the experimental conditions to the corresponding exo and endo allylic halides 4 and 5 [5]. The homo-1,4 adduct 6 resists rearrangement. The cyclopropane adducts in themselves are unexceptionable. Everybody knows that singlet carbenes, which the halocarbenes are, in general add to mono-olefins stereospecifically [6]. Consequently, such additions occur in a single step.



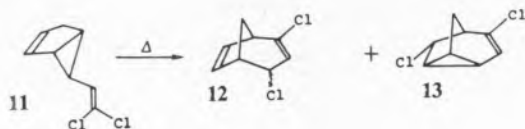
\* The present account is a version of plenary lectures presented by C.W.J. at the 5th Annual Meeting of the Portuguese Chemical Society, Oporto, Portugal, March 29-April 2, 1982, and the 45th Annual Meeting of the Japanese Chemical Society, Tokyo, Japan, April 1-4, 1982.

## STEPWISE ADDITION OF DICHLOROCARBENE TO NORBORNADIENE

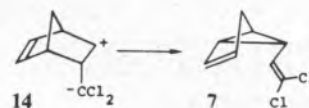
Unfortunately, this neat picture needed to be modified when the reaction mixture was subsequently subjected to careful scrutiny [7]. We then realized that another addition must have occurred, because a second rearrangement product was discovered. Despite the small yield, **7** was isolated and allowed to react further with dichlorocarbene. The structure of the resulting adduct (**8**) was established by single crystal X-ray analysis [8]. The feature of interest is the endo configuration of the vinyl group with respect to the parent cis-fused bicyclo [3.1.0.] hexene fragment. It adopts an extended conformation. It can also be assumed that the mono adduct possesses the same conformation. If the more hindered conformation (**9**) were adopted, then Cope rearrangement to 4,4-dichlorobicyclo[3.2.1]octa-2,6diene (**10**) would be expected to occur spontaneously. In fact, there is ample precedent for this type of rearrangement [9]. In the present case, the bulk of the



chlorine substituents undoubtedly accounts for the preferred conformation of **7**, thereby accounting for its existence [10]. However, on gently warming **7**, isomerization to the exo isomer **11** occurred, which on further heating gave products **12** and **13**. These latter products derive from the presumed intermediate **10**, which must have originated from **11** via a non-concerted, possibly radical, process [11].

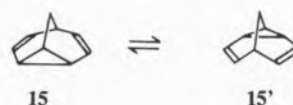


The formation of **7** is one of those rare exceptions [12] encountered in carbene chemistry and thus its origin is of mechanistic interest. Preparation of a pure sample of the exo-cyclopropane adduct **2** revealed that its sole fate on heating was the expected rearrangement to its allylic derivative **4**. No trace of **7** was detected. However, all mixtures obtained from the reaction of dichlorocarbene with norbornadiene at temperatures below  $-10^\circ\text{C}$  always contained the second rearranged product **7**. We therefore believe that 1,2 addition is preceded or accompanied by the formation of a zwitterionic species such as **14** which owes its existence to its electronic stability [13]. The positive charge is homoallylically stabilized and the negative charge enjoys equal stability on the dichloromethylene fragment by virtue of substituent effects. The conformation adopted by the latter group probably prevents collapse to the cyclopropane adduct **3**, which gives the zwitterion a chance to undergo Cope rearrangement (**14**→**7**).



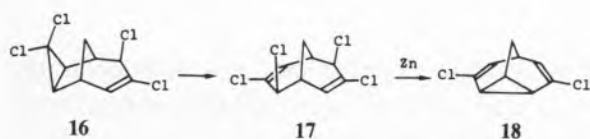
## DIRECT ACCESS TO BARBARALANE DERIVATIVES

Ever since bullvalene was predicted to exist [14], fluxional molecules such as semibullvalene and barbaralane have been of theoretical interest on account of their actual and potentially modifiable valence properties [15]. Although they are beautiful paradigms of dynamic Cope rearrangement, familiar to students of chemistry, they are nonetheless rare

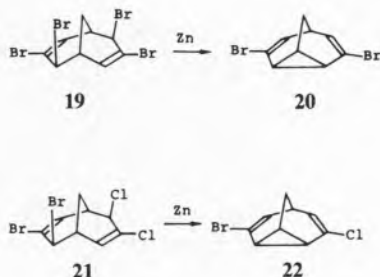


species as they are relatively hard to make in sizable quantities. Barbaralane (**15**  $\rightleftharpoons$  **15'**) and its derivatives constitute such a case as they are only obtained by multistep syntheses, often starting from uncommon precursors [16]. We realized that an appropriate double adduct of dichlorocarbene and norbornadiene contains the barbaralane skeleton. In practice, addition of a single equivalent of dichlorocarbene to the exo-allylic chloride **4**, itself obtained in

30% yield, gave the exo adduct **16** which rearranged uniquely to the double allylic dichloride **17** having  $C_2$  symmetry. A stereochemical consequence of the additions and the subsequent rearrangements is that both the allylic chlorine substituents have the exo configuration [17]. This means that they are nicely arranged for homo-1,4 dechlorination. Indeed, heating **17** with zinc dust in acetone afforded 3,7-dichlorobarbaralane (**18**) in 90% yield. The rearranged diadduct **17** can also be obtained directly by treating norbornadiene with a large excess of dichlorocarbene.



In similar fashion, two sequential additions of dibromocarbene to norbornadiene afforded the tetrabromo analogue **19** which on treatment with zinc dust gave 3,7-dibromobarbaralane (**20**). Addition of dibromocarbene to **4** gave the rearranged mixed halogenated product **21**, which again on homo-1,4 dehalogenation led to 3-chloro-7-bromobarbaralane (**22**).



All these barbaralanes are fully fluxional molecules at room temperature. Furthermore, they are amenable to further chemical transformation. For example, 3,7-dibromobarbaralane (**20**) was easily converted in 70% yield into its diacetoxo derivative by treatment with cuprous acetate in acetonitrile [18]. In résumé, we would like to emphasize that barbaralanes are now available in high yield by a remarkably simple procedure [19] which could be eventually exploited as a means of preparing homo-aromatic structures [20].

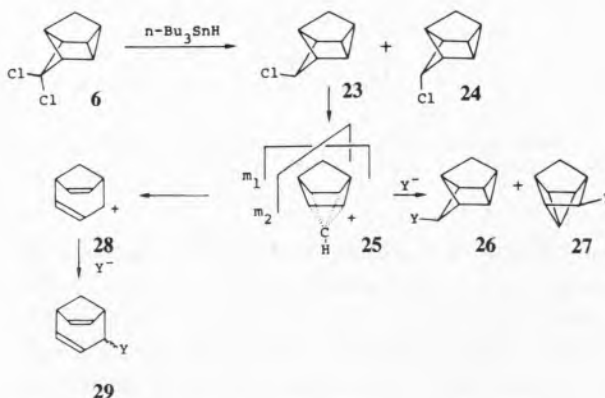
## HOMOQUADRICYCLYL SPECIES

The homo-1,4 adduct **6**, apart from the mechanistic interest attaching to its formation [21], provides an easily accessible, useful substrate for testing hitherto unsuspected rearrangements.

Reductive dechlorination of **6** yielded the exo (**23**) and endo (**24**) monochloro epimers. These, on ionization, as we will see later, lead to two distinct, non-interconvertible, families of carbocations.

It has been reported that solvolyses of derivatives corresponding to the exo series **23** do so with participation of the cyclopropane ring [22]. The result is displacement of the apical carbon atom in the  $C_s$  plane to give the centrosymmetric square pyramidal delocalized cation **25**. This is termed haptotropic rearrangement as four partial bonds are implicated with the formal cationic center, unlike the usual 1,2 sigmatropic rearrangements which involve only two. Conversely, as the product composition revealed, an external nucleophile  $Y^-$  attacks either a basal or the apical position of **25** giving **26** and **27**. Significantly, no other  $C_8H_9$  isomers are formed.

Formation of **26** requires that the apical carbon atom travels back in the mirror plane  $m_1$  to intercept the incoming nucleophile. In other words, the cation **25** remembers from where it came. In principle, the pyramidal ion **25** could displace its apical carbon atom in the second mirror plane ( $m_2$ ), generating the allylic cation **28** which would be eventually captured by solvent to give the substituted derivative **29**.

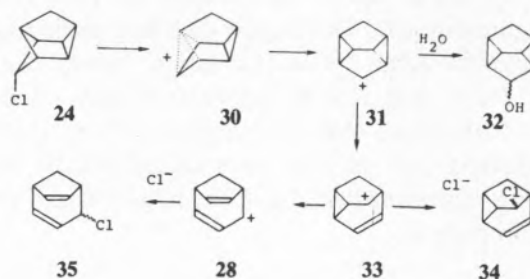


In order to test the likelihood of such a manoeuvre and others as well, we carried out MINDO/3 calculations [23]. From the calculated heats of formation and the reactions paths of minimum energy

lying on the interconnecting potential energy surface, we found that the aforementioned haptotropic rearrangement in the  $m_1$  plane was energetically feasible, whereas rearrangement in the  $m_2$  plane was not (fig.1). In brief, good account was found between our calculations and the known chemistry of the *exo*-23 series.

The correctness of our calculational approach was confirmed by predicting the chemistry of the *endo*-24 series which was unknown at the time. Calculations indicated that the *endo* epimer **24** should ionize with participation and weakening of both the distal cyclobutane carbon-carbon bonds to generate a delocalized cyclobutyl cation **30**, which subsequently should undergo a Wagner-Meerwein rearrangement to give the bis-cyclopropylcarbiny cation **31**. In the presence of good nucleophiles, this species will be immediately captured. In reality [24],

periment confirmed these expectations and further showed that these cations exist as discrete, non-degenerate entities [24]. Thermal dissociation of **24** gave a mixture of **34** and **35**.



In view of the expected similarity of behavior towards rearrangement of carbocations and carbenes assumed from their electrophilic character [25], it

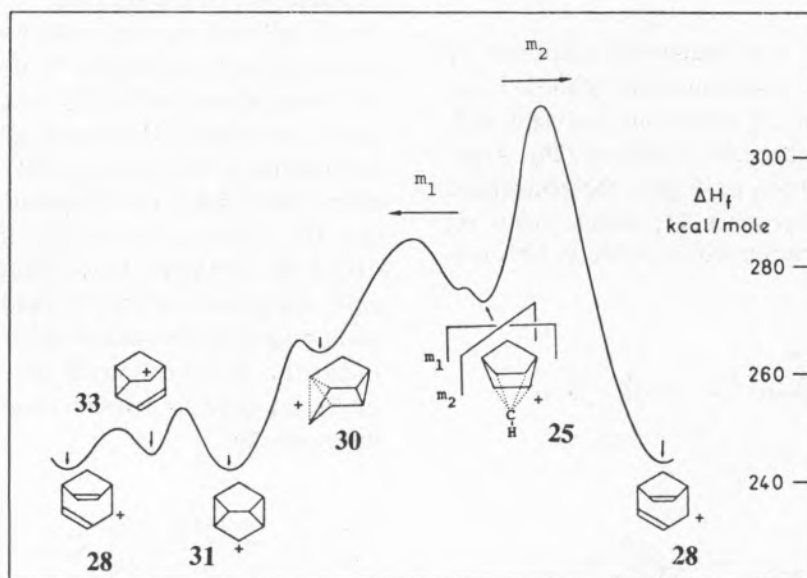


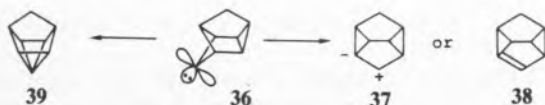
Fig. 1

Heats of formation of some  $C_8H_9$  cations and their interconnecting minimum energy reaction paths as calculated by the MINDO/3 procedure (ref. [23])

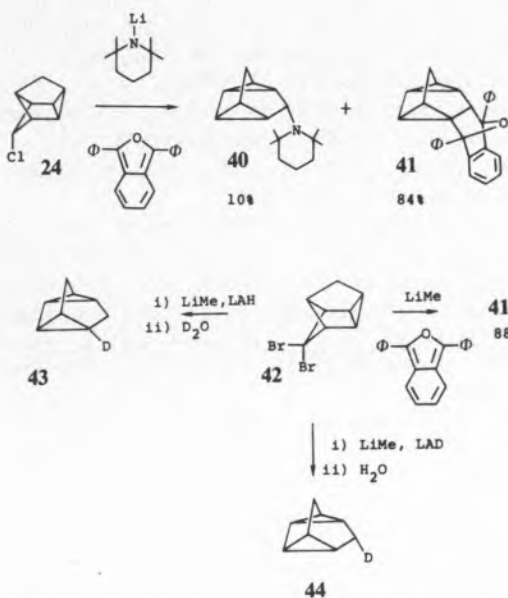
submission of the *endo* epimer **24** in aqueous dioxane (1:2) to an equivalent of silver nitrate in the same solvent gave an instant precipitate of silver chloride and a mixture of the *exo* and *endo* alcohols **32** in 92% yield. Calculations further suggested the stepwise migration of the carbon-carbon bonds giving successively the monocyclopropylcarbiny cation **33** and finally the allylic cation **28**. All these species are predicted to possess similar heats of formation with small intervening barriers (fig. 1). Ex-

occurred to us that the corresponding carbene **36**, once formed, would be confronted with two structurally interesting alternatives. Simple 1,2 rearrangement would give the zwitterion **37** or the anti-Bredt olefin **38**, whereas haptotropic rearrangement would yield the product of insertion into the cyclopropane carbon-carbon bond, a structure containing a tetrasubstituted pyramidal carbon atom **39**. Calculation revealed that the first process is the best option for energetic reasons.





Experimentally the carbene was generated by two different methods. The action of lithium tetramethylpiperide on the endo-chloro epimer **24** in the presence of diphenylisobenzofurane gave the rearranged piperidino derivative **40** (10% yield) and the single Diels-Alder adduct **41** in 84% yield. Repetition of this experiment, but treating instead the dibromocarbene-norbornadiene adduct **42** with lithiummethyl, gave the same Diels-Alder adduct **41** in 88% yield. Clearly a molecule having the anti-Bredt structure **38** has been transiently created in both cases and its provenance was certainly the carbene **36** [26].

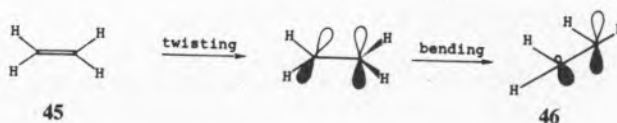


Although four isomers are possible, X-ray analysis of a single crystal of **41** showed the structure to be the result of addition from the least hindered side of **38**, giving the adduct of endo configuration in accordance with the Alder-Stein rule [27].

The question which now arises concerns the nature of the double bond in **37**. It is certainly strained, but where are the electrons? Once again, MINDO/3 calculations provided a ready answer. In short, the double bond is strongly polarized as initially expected. It turns out that the positive charge is not greatly stabilized and is mostly localized on the C3 atom which is at least trigonal. The negative charge

is located on the C2 atom which has the pyramidal configuration. The frontier orbitals are similar to those of the precursive carbene in that the LUMO's and HOMO's are both low lying, thereby indicating potential electrophilic character for the reactive species.

Evidence for these notions was forthcoming from trapping experiments. Submission of the dibromo adduct **42** to lithiummethyl and lithium aluminumhydride in either followed by treatment with deuterated water gave the homoquadricyclane **43** uniquely monodeuterated at the C2 position. The same procedure, but employing lithium aluminum deuteride instead, followed by aqueous work-up, gave the same hydrocarbon, but this time monodeuterated at the C3 position (**44**).



These results represent an experimental realization of the theoretical concept of "sudden polarization" which is supposed to occur to an excited ethylene molecule (**45**) when it is twisted and bent to such a degree that one carbon atom becomes trigonal and the other pyramidal **46** [28]. Not only is homoquadricyclene (**37**) the first example of a carbon ylide, containing as it does such a "frozen", polarized ethylenic fragment, but it also falls well within the impossible category of anti-Bredt molecules ( $S < 5$ ) [29].

## EPILOGUE

The theme which pervades this review is the versatile behavior of carbenes. Firstly, we reported the anomalous addition of dichlorocarbene to norbornadiene. The expected formation of a cyclopropane was foiled, but another was obtained nonetheless by rearrangement of the initially created zwitterion. Secondly, we described the conventional double addition of dihalocarbene to norbornadiene giving a double cyclopropane entity, which on rearrangement to the juxtaposed bis-allylic halides furnished a dynamic bis-vinylcyclopropane structure by dehalogenation. Lastly, we showed how a cyclobutylidene carbene could be induced to rearrange to a

twisted and bent vinylcyclopropane moiety, so producing an all-carbon zwitterion or carbon ylide. We hope to have convinced potential sceptics that suitable exploitation of even simple reactions of carbenes can yield varied and novel results.

## ACKNOWLEDGMENTS

All the present work was conceived and carried out in the Department of Organic Chemistry at the University of Geneva. Most of it is described in the doctoral thesis of J.A.Z. Special thanks are due to J.-C. Rossier, V. de los Heros, J.-C. Perlberger, S. Genevay-Höck, J. Mareda for their important experimental contributions. We are also grateful to U. Burger, F. Kloeti, A. Buchs, G. Bernardinelli, O. Kennard, W.T.C. Cruse for their invaluable help with the structure determinations.

## BIBLIOGRAPHY

- [1] U. SCHÖLLKOPF, *Angew. Chem.*, **80**, 603 (1968); V. BUSS, P.v.R. SCHLEYER, L. C. ALLIN, *Top. Stereochem.*, **7**, 253 (1972).
- [2] H. C. BROWN, P.v.R. SCHLEYER, "The Nonclassical Ion Problem", Plenum Press, New York & London, 1977, Chap. 5.
- [3] R.C. DE SELMS, C.M. COMBS, *J. Org. Chem.* **28**, 2206 (1963); E.V. DEHMLOW *Tetrahedron*, **28**, 175 (1972); P.L. KWANTES, G.M. KLUMPP, *Tetrahedron Lett.*, 707 (1976); C.W. JEFFORD, V. de los HEROS, U. BURGER, *Tetrahedron Lett.* 703 (1976).
- [4] J.A. ZUBER, Doctoral Dissertation, University of Geneva, May 1982.
- [5] C.W. JEFFORD, J. MAREDA, J.C.E. GEHRET, nT. KABENGELE, W.D. GRAHAM, U. BURGER, *J. Am. Chem. Soc.* **98**, 2585 (1976).
- [6] W. KIRMSE, "Carbene Chemistry", 2nd Ed., Academic Press, New York, 1971.
- [7] C.W. JEFFORD, G. BERNARDINELLI, J.C. ROSSIER, J.A. ZUBER, *Helv. Chim. Acta*, [Added in proof **65**, 1467 (1982)].
- [8] R. Gerdil, J.A. ZUBER, G. BERNARDINELLI, *Acta Cryst.*, [Added in proof **C39**, 487 (1983)].
- [9] J. MEINWALD, S.S. LABANA, M.S. CHADHA, *J. Am. Chem. Soc.* **85**, 582 (1963); C. CUPAS, W. WATTS, P.v.R. SCHLEYER, *Tetrahedron Lett.* 2503 (1964).
- [10] J.M. BROWN, *J. Chem. Soc., Chem. Commun.* 638 (1967); W. ADAM, O. DE LUCCHI, D. SCHEUTZOW, *J. Org. Chem.* **46**, 4130 (1981).
- [11] J.E. BALDWIN, K.E. GILBERT, *J. Am. Chem. Soc.* **98**, 8283 (1976).
- [12] *Reactive Intermediates*, Vol. II, Ed. M. JONES JR., R.A. MOSS, J. Wiley & Sons, New York, 1981, pp. 92-96.
- [13] J.M. SONNEY, P. VOGEL, U. BURGER, *Tetrahedron Lett.* 825 (1978); U. BURGER, J.M. SONNEY, P. VOGEL, *Helv. Chim. Acta* **63**, 1006 (1980); J. HINE, "Divalent Carbon", Ronald Press Co., New York, 1964, Chap. 3.
- [14] W. VON E. DOERING, W.R. ROTH, *Tetrahedron* **19**, 715 (1963); G. SCHRÖDER, *Angew. Chem.* **75**, 772 (1963); W. VON E. DOERING, K.M. FERRIER, E.T. FOSSEL, J.H. HARTENSTEIN, M. JONES JR., G. KLUMPP, R.M. RUBIN, M. SAUNDERS, *Tetrahedron* **23**, 3943 (1967).
- [15] Y. KOBAYASHI, A. ANDO, K. KAWADA, I. KUMADAKI, *J. Am. Chem. Soc.* **103**, 3958 (1981); L.S. MILLER, K. GROHMANN, J.J. DANNENBERG, L. TODARO, *ibid.* **103**, 6249 (1981).
- [16] H. QUAST, Y. GÖRLACH, J. STAWITZ, *Angew. Chem. Int. Ed. Engl.* **20**, 93 (1981); J.M. MELLOR, B.S. PONS, J.H.A. STIBBARD, *Chem. Comm.* 759, 761 (1979); D. BOSSE, A. DE MEIJERE, *Tetrahedron Lett.* 965 (1978); H. OLSEN, *Acta Chem. Scand.* **B31**, 635 (1977); J.F.M. OTH, H. KWEE, U. PRANGE, G. SCRÖDER, *Tetrahedron Lett.* 1565 (1976); A. BUSCH, H.M.R. HOFFMANN, *ibid.* 2379 (1976).
- [17] C.W. JEFFORD, *Chimia* **24**, 357 (1970).
- [18] G.W. KLUMPP, H. BOSS, M. SCHAKEL, R.F. SCHMITZ, J.J. VRIELINK, *Tetrahedron Lett.* 3429 (1975).
- [19] C.W. JEFFORD, J.C. ROSSIER, J.A. ZUBER, *Angew. Chem.*, [Added in proof **94**, 542 (1982)].
- [20] H. KESSLER, W. OTT, *J. Am. Chem. Soc.* **98**, 5014 (1976); R. HOFFMANN, W.-D. STOHRER, *ibid.* **93**, 6941 (1971); M.J.S. DEWAR, D.H. LO, *ibid.* **93**, 7201 (1971); M.J.S. DEWAR, Z. NAHLOVSKA, B.D. NAHLOVSKY, *Chem. Comm.* 1377 (1971).
- [21] C. W. JEFFORD, PHAN THAN HUY, *Tetrahedron Lett.*, **23**, 391 (1982).
- [22] R.M. COATES, K. YANO, *Tetrahedron Lett.* 2289 (1972); A.V. KEMP JONES, N. NAKAMURA, S. MASAMUNE, *J. Chem. Soc., Chem. Commun.* 109 (1974).
- [23] C.W. JEFFORD, J. MAREDA, J.C. PERLBERGER, U. BURGER, *J. Am. Chem. Soc.* **101**, 1370 (1979).
- [24] C.W. JEFFORD, S. GENEVAY-HÖCK, A. DELAY, J. MAREDA, U. BURGER, *Tetrahedron Lett.* 2549 (1979).
- [25] W. SCHOELLER, *J. Am. Chem. Soc.* **101**, 4811 (1979).
- [26] C.W. JEFFORD, J.C. ROSSIER, J.A. ZUBER, W.T.C. CRUSE, O. KENNARD, [Added in proof *Tetrahedron Lett.*, 181 (1983)].
- [27] K. ALDER, G. STEIN, *Angew. Chem.* **50**, 510 (1937).
- [28] B.R. BROOKS, H.F. SCHAEFER, *J. Am. Chem. Soc.* **101**, 307 (1979).
- [29] G. KÖBRICH, *Angew. Chem. Int. Ed.* **12**, 464 (1973); K.J. SHEA, *Tetrahedron* **36**, 1683 (1980).