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β-HYDROXYETHYLTRIALKYLAMMONIUM ION AS A SELECTIVE PHASE-TRANSFER CATALYST FOR DIHALOCYCLOPROPANATION

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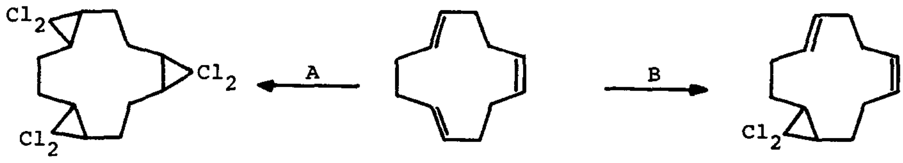
Dichlorocarbene as generated by the phase-transfer technique[1] is remarkably reactive and often provides an effective means of cyclopropanation.[1b,c] By using cetyltrimethylammonium bromide (A) as a catalyst we have now obtained a tetracyclic product I[2,3] in a quantitative yield from 1,5,9-c,t,t-cyclododecatriene (1,5,9-CDT). In contrast, catalysis by means of β-hydroxyethyltrialkylammonium ion results in highly selective dichlorocarbene addition producing II[4] in 72% yield under the same standard condition.[5] A mixture of an olefin, 4 or 5 equiv each (per ethylenic moiety) of chloroform and 50% NaOH aq, and a quaternary ammonium catalyst (0.025 equiv) was stirred at 55° for 3 hr under a nitrogen atmosphere. After usual workup the product was isolated by distillation, and the purity of the product was checked by gas chromatography.

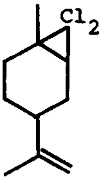
The same catalyst B was effective to yield a mono-carbene adduct III[2,6] (62% yield) from dl-limonene. This is again in sharp contrast to the catalysis of A, in which only a bis-cyclopropanated product is produced.[2a] The selective dichlorocarbene reaction has further been applied to 4-vinylcyclohexene to



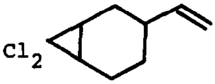
I

II

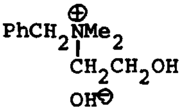
afford IV[7] in 93% yield[8] and to 3-methyl-2,6-heptadien-1-ol whose trisubstituted ethylenic moiety only is subject to the cyclopropanation.[5b,9]



III

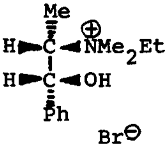


IV



$$PhCH_2\overset{\oplus}{N}Me_2\,CH_2CH_2OH\;\;OH^{\ominus}$$

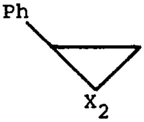
B



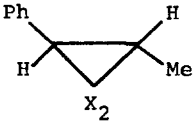
C

In order to clarify the role of β-hydroxyl group we examined asymmetric dichlorocarbene addition to styrene using the salt C.[10] The resulting adduct Va (70% yield) showed $[\alpha]_D^{18}$ +3.18° (*c* 25.9, $CHCl_3$). The asymmetric induction was further observed in the reaction with *trans*-propenylbenzene giving VIa (73% yield), $[\alpha]_D^{28}$ +1.20° (*c* 17.1, $CHCl_3$) which was successively reduced to VIc, $[\alpha]_D^{28}$ -1.04° (*c* 17.9, $CHCl_3$), with sodium in liquid ammonia. Although the degree of the asymmetric induction was calculated to be as low as 0.9%,[11] the asymmetric dihalocarbene addition seems unprecedented. The β-hydroxyethyl unit[13] of the catalyst is responsible to the asymmetric dihalocyclopropanation. This was evidenced by the dichlorocarbene addition to styrene in the presence of (+)trimethyl-α-phenethylammonium bromide[14] resulting in a much lower induction (76% chemical yield, $[\alpha]_D^{26}$ -0.14° (*c* 14.1, $CHCl_3$)).

Furthermore, the β-hydroxyethyl moiety in the catalyst is a prerequisite for dibromocarbene addition to olefins. The catalyst B proved to be effective



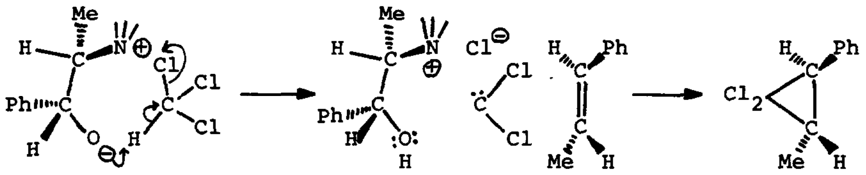
Va X = Cl
b X = Br



VIa X = Cl
b X = Br
c X = H

in the reaction with styrene, cyclohexene, and allyl bromide, giving the corresponding *gem*-dibromocyclopropane in 77, 71, and 51% yield respectively. Under the present reaction condition neither long reaction time nor the presence of ethanol[15] is required. The catalyst C again induced asymmetric induction in dibromocarbene addition to styrene (73% yield, $[\alpha]_D^{24}$ +0.10° (*c* 20.6, $CHCl_3$)) and *trans*-propenylbenzene (60% yield, $[\alpha]_D^{20}$ +0.48°, *c* 20.0, $CHCl_3$, 0.6% ee).[16]

Although more experimental results are required for detailed understanding of the catalysis, we may explain the selective carbene addition and the asymmetric cyclopropanation in terms of the scheme below. The catalyst is first converted to a zwitter ion as described earlier.[10] Proton abstraction from haloform and successive liberation of chloride ion produce dihalocarbene which is loosely associated with the hydroxyl group of the catalyst in its close vicinity. Thus slightly modified, electrophilic carbene attacks the C=C bond with reduced vigour and enhanced selectivity under the influence of the neighbouring catalyst.[17]



References and Footnotes

(1) (a) E. H. Cordes and R. B. Dunlap, *Accounts Chem. Res.*, **2**, 329 (1969).
  (b) J. Dockx, *Synthesis*, 441 (1973).
  (c) E. V. Dehmlow, *Angew. Chem.*, **86**, 187 (1974).

(2) The compound gave a satisfactory elemental analysis.

(3) A viscous nondistillable oil. No olefinic absorption was observed in both ir and nmr. Glc (SE 30, 5% on Chromosorb, 75 cm, 182°) revealed the adduct was an inseparable mixture of three stereoisomers. Cf. M. Mühlstädt and J. Graefe, *Chem. Ber.*, **99**, 1192 (1966).

(4) H. Nozaki, S. Kato, and R. Noyori, *Can. J. Chem.*, **44**, 1021 (1966).

(5) (a) G. C. Joshi, N. Singh, and L. M. Pande, *Tetrahedron Lett.*, 1461 (1972). (b) T. Hiyama, M. Tsukanaka, and H. Nozaki, *J. Amer. Chem. Soc.*, **96**, 3713 (1974).

(6) Bp 93-94°/4 mm. Ir (neat): 3300, 1646, 888 (exo methylene), 821, 764 cm^{-1}; nmr (CCl_4) δ 0.8-2.4 (m + s (δ 1.40) + br s (δ 1.67), 14H), 4.50 (br s, 2H).

(7) D. Seyferth, J. M. Burlitch, R. J. Minasz, J. Y.-P. Mui, H. D. Simmons, Jr., A. J. H. Treiber, and S. R. Dowd, *J. Amer. Chem. Soc.*, **87**, 4259 (1965).

(8) When cetyltrimethylammonium bromide was used, the mono-adduct IV (61% yield) was accompanied by bis-adduct (35%).

(9) The observed selectivity is in accordance with that previously recorded, i.e., dihalocarbene prefers more substituted olefins: W. Kirmse, "Carbene Chemistry," 2nd ed., Academic Press, New York, 1971, p 296; R. A. Moss, "Selective Organic Transformations," ed. by B. S. Thyagarajan, Vol 1, Wiley-Interscience, New York, 1970, p 35. It should be noted, however, the selectivity is much improved in the phase-transfer system.

(10) T. Hiyama, T. Mishima, H. Sawada, and H. Nozaki, *J. Amer. Chem. Soc.*, **97**, 1626 (1975).

(11) The sample of 51.3% purity has been recorded to have $[\alpha]_D^{16}$ -57.7°. Thus the optical rotation of the pure sample was estimated to be -112°. T. Sugita and Y. Inouye, *Bull. Chem. Soc. Japan*, **39**, 1075 (1966).

(12) Enantioselective cyclopropanation *via* the asymmetric catalytic decomposition of diazo compounds has been recorded by several authors: H. Nozaki, H. Takaya, S. Moriuti, and R. Noyori, *Tetrahedron*, **24**, 3655 (1968); W. R. Moser, *J. Amer. Chem. Soc.*, **91**, 1135 (1969); Y. Tatsuno, A. Konishi, A. Nakamura, and S. Otsuka, *J. Chem. Soc. Chem. Commun.*, 588 (1974).

(13) The β-hydroxyethylammonium ion has previously been shown to increase the rate of alkaline hydrolysis of *p*-nitrophenyl carboxylates more than cetyltrimethylammonium ion. G. Meyer, *C. R. Acad. Sci.*, *Ser C*, **276**, 1599 (1973); V. Gani, C. Lapinte, and P. Viout, *Tetrahedron Lett.*, 4435 (1973); K. Martinek, A. V. Levashov, and I. V. Berezin, *ibid.*, 1275 (1975).

(14) $[\alpha]_D^{26}$ +9.7° (*c* 2.0, water).

(15) M. Makosza and M. Fedoryński, *Synth. Commun.*, 305 (1973); L. Skatteb∅l, G. A. Abskharoun, and T. Greibrokk, *Tetrahedron Lett.*, 1367 (1973).

(16) The adduct was reduced (Na/liq NH_3) to VIc, $[\alpha]_D^{21}$ -0.66° (*c* 10.6, $CHCl_3$).

(17) The authors are indebted to Prof. I. Tabushi for helpful discussions and to the Ministry of Education, Japanese Government, for partial financial aid (Grant No 911506).