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A STEREOSPECIFIC SYNTHESIS OF CYCLOPROPANE DERIVATIVES FROM OLEFINS

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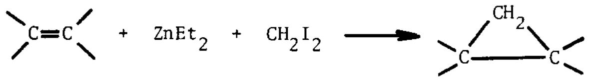
We have reported previously the synthetic route to cyclopropane derivatives from olefins by the reaction with methylene iodide and diethylzinc (1).



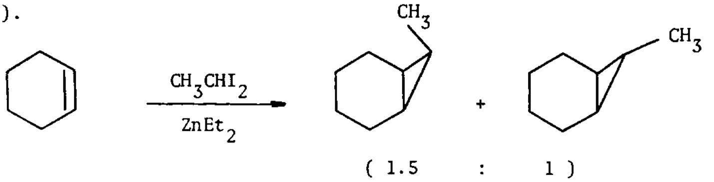
(I)

Although the essential feature of the reaction is similar to that of the Simmons-Smith reaction which involves the treatment of olefins with methylene iodide and zinc-copper couple, this novel route produces cyclopropane derivatives more readily and is particularly useful for vinyl ethers without undesirable polymerization (2). Moreover, the novel route is a homogeneous reaction unlike the procedure of Simmons and Smith, which offers an advantage in studies of the reaction mechanism.

In this paper, we would like to report several extentions of the work to use ethylidene iodide and benzal iodide instead of methylene iodide and to attempt a dissymmetric synthesis of α,β-disubstituted cyclopropane derivatives from olefins. We observed a characteristic behavior of diethylzinc.

In the synthesis of substituted cyclopropane derivatives from olefins by means of substituted carbenes and carbenoids, several kinds of isomers arising from the geometrical modes of reaction, i.e., cis- or trans-addition, front- or rear-attack, and syn- or anti-addition may be obtained. The carbenoid generated from diethylzinc and methylene iodide was found to add stereospecifically to olefins (2). However, as to front- or rear-attack and to syn- or anti-addition, the problem remained unsettled.

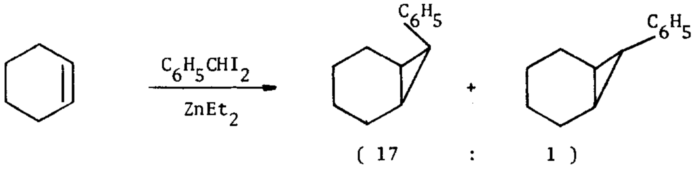
The alkyl and arylcarbenoids from diethylzinc and gem-diiodo compounds were found to react with olefins to give more of the syn isomer than the anti one. For example, from cyclohexene (20.3 ml., 0.2 mole), ethylidene iodide (37.6 ml., 0.4 mole) and diethylzinc (25 ml., 0.25 mole) for 1 hour under refluxing in light petroleum ether (100 ml.) was obtained 14.5 g. (66 % based upon cyclohexene) of 7-methylnorcarane, whose endo/exo isomer ratio was shown to be 1.5 by VPC analysis. The product isomers were separated by fractional distillation through a spinning-band column to give the exo isomer, b.p. 132 — 133°, n_D^{25} 1.4508, and the endo isomer, b.p. 142 — 143°, n_D^{25} 1.4636 (3).



(II)

The above reaction affords predominantly the endo isomer in good yield. This fact is in contrast with the reported result that the combination of ethylidene iodide and zinc-copper couple gives exclusively the exo isomer in poor yield (3). Vinyl isobutyl ether (0.05 mole), ethylidene iodide (0.10 mole) and diethylzinc (0.075 mole) in ether (25 ml.) gave 1-methyl-2-isobutoxycyclopropane in 96 % yield (based upon vinyl ether). Its cis/trans isomer ratio was 2.3. The structures of the isomers were identified by comparing their IR spectra with those of the authentic samples (2). From these results, this alkylcarbenoid is concluded to favor the syn-addition.

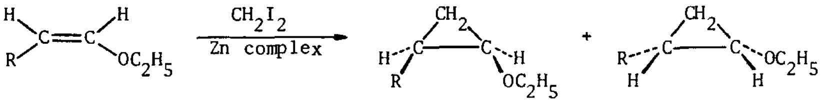
The arylcarbenoid generated from diethylzinc and benzal iodide showed a strong syn-stereoselectivity in its addition to olefins. For example, dropwise addition of diethylzinc (2 ml., 0.02 mole) to cyclohexene (10.2 ml., 0.1 mole) and benzal iodide (3.4 g., 0.01 mole) in 20 ml. of ether at 20° resulted in the formation of 7-phenylnorcarane (64 % based upon the iodide by VPC analysis), b.p. 67 — 80°/0.2 mm.; the endo isomer, n_D^{20} 1.5496 (lit. b.p. 68 — 70°/0.2 mm., n_D^{20} 1.5496 (5)). The endo/exo isomer ratio was 17.



(III)

This strong syn-selectivity has synthetic utility for both the endo and the exo derivatives, because the exo isomer can be obtained easily from the endo isomer by the equilibrium reaction with potassium tert-butoxide in dimethyl sulfoxide (4, 5).

Optically active cyclopropane derivatives were prepared from cis-alkenyl ethyl ethers, methylene iodide and diethylzinc together with L-leucine (6) as an asymmetric cocatalyst.



(IV)

A complex was prepared by the addition of L-leucine to diethylzinc in xylene followed by refluxing at 140° for 10 hours, during which the color of the complex changed from white to grey. This procedure was followed by removal of unchanged diethylzinc and solvent in vacuo. Cis-1-ethoxy-2-ethylethylene (5.0 g., 0.05 mole) was reacted in light petroleum ether (100 ml.) with methylene iodide (8.0 ml., 0.10 mole) and a complex of diethylzinc (20 ml., 0.20 mole) with L-leucine (13.2 g., 0.10 mole) prepared in 100 ml. of xylene at room temperature for 2 days. The yield of cis-1-ethoxy-2-ethylcyclopropane was 56 % based on the olefin, b.p. 114°, n_D^{25} 1.4037, $[\alpha]_D^{25}$ +0.30 (c = 80.6 g./100 ml. in $CHCl_3$). Anal. Calcd. for $C_7H_{14}O$: C, 73.63; H, 12.36. Found: C, 73.48; H, 12.54. Similarly, optically active cis-1-ethoxy-2-isopropylcyclopropane was obtained from cis-1-ethoxy-2-isopropylethylene in 61 % yield based on the olefin; b.p. 125°, n_D^{25} 1.4049, $[\alpha]_D^{25}$ -0.77 (c = 38.2 g./100 ml. in $CHCl_3$). Anal. Calcd. for $C_8H_{16}O$: C, 74.94; H, 12.58. Found: C, 75.08; H, 12.76.

The above findings afford information concerning the stereospecific feature of the reaction (I), i.e., the stereospecific addition and the stereospecific attack of the methylene group controlling the configuration of the resulting cyclopropane derivatives.

Details of the reactions will be reported elswhere in the near future.

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6. $[\alpha]_D^{25}$ = 16.3 at c = 4.480 g./100 ml. in the presence of 6N HCl.