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THE SYNTHESIS OF LARGE-RING METHYLENECYCLOALKANES BY THE CYCLIZATION OF ALLYLIC DIBROMIDES WITH NICKEL CARBONYL

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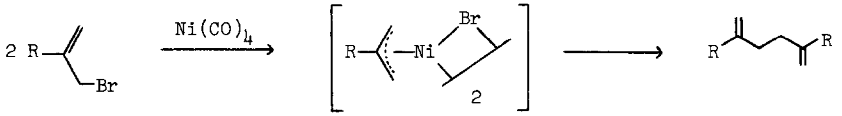
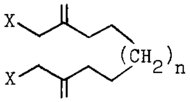
The reaction of allylic halides with nickel carbonyl is a very useful method for the formation of carbon-carbon bonds (e.g. equation 1).[1,2] This reaction has been applied to the intramolecular coupling, or cyclization, of various allylic dihalides.[3,4] Herein we describe a further extension of this work which permits the synthesis of large-ring methylenecycloalkanes.



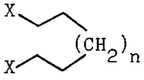
(1)

The allylic dibromides Ia-d were synthesized from the corresponding diols II by the use of phosphorus tribromide.[3,4] The allylic diols II were obtained by reaction of the dihalides III with diethyl sodiomalonate followed by treatment of the resulting tetracarboethoxy compounds IV with sodium hydride and lithium aluminum hydride according to the procedure of Marshall.[5]



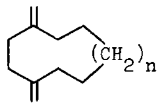
I, X = Br

II, X = OH



III, X = Br or I

IV, X = $CH(CO_2Et)_2$



V

a, n = 4
b, n = 6
c, n = 8
d, n = 12

The reaction of the dibromides Ia-d with an excess of nickel carbonyl was performed in N, N-dimethylformamide (DMF) under the conditions outlined in the table. The cyclization was successful in producing the products of structure V and ring size 14-20 but, interestingly, failed completely for twelve-membered ring formation.

Table

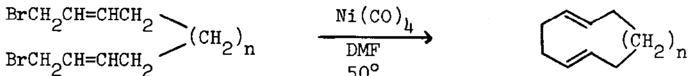
Dibromide	$\left[\frac{\text{Substrate}}{\text{Solvent}}\right]^a$	Addition Time (hr)[b]	Temp. (°C)	Product	Yield (%)[c]
Ia[d]	0.0095	6	50 - 65	--	0
Ib[d]	0.0103	7	50 - 58	Vb	2
Ib[d]	0.0075	21	54	Vb	5
Ib	0.0075	24	55 - 69	Vb	15
Ib	0.0037	32	57 - 67	Vb	37 (20)
Ic	0.0070	32	55 - 65	Vc	64 (45)
Ic	0.0056	56	60 - 70	Vc	81 (59)
Id	0.0061	51	60 - 64	Vc	40 (33)

Footnotes to Table

[a] Mmol of dibromide divided by the total amount of solvent (ml) used for both reagents. [b] The dibromide was added as a dilute solution to a dilute solution of nickel carbonyl. The reaction mixtures were stirred at the stated reaction temperature for an additional 10-13 hr. [c] Yields after bulb-to-bulb distillation of the crude product. The yields after further purification by chromatography on silica gel are given in parentheses. [d] Reaction performed under argon. All other cyclization reactions were performed under carbon monoxide.

A typical procedure is given. 1,4-Dimethylenecyclohexadecane (Vc). To a solution of nickel carbonyl (0.95 ml, 7.3 mmol) and DMF (100 ml) at 60-70° under carbon monoxide was added a solution of Ic (0.300 g, 0.735 mmol) and DMF (100 ml) over a 56-hr period with a syringe drive. After stirring at 65° for an additional 10 hr, the resulting green solution was cooled to 25°, stirred under aspirator pressure to remove excess nickel carbonyl, and poured into a mixture of pentane and water. The organic layer was washed with water, dried over anhydrous magnesium sulfate, and concentrated at reduced pressure. The residue was subjected to bulb-to-bulb distillation at 220° (0.002 Torr), yielding 0.147 g (81%) of clear, colorless oil. Further purification by preparative layer chromatography (silica gel) afforded 0.107 g (59%) of Vc as a clear, colorless oil: nmr ($CDCl_3$) 1.33 (m, 20 H), 2.09 (triplet, J = 7 Hz, overlapping a singlet at 2.17, 8 H), and 4.78 (broad singlet, 4 H); ir (neat) 1640 (w) and 885 (s) cm^{-1}; molecular ion at m/e 248.2507 (calcd. 248.2504); homogeneous by tlc and glpc.

Of interest is the comparison of these results with those obtained earlier[3] in the cases indicated by equation (2). The cyclization of these substrates, performed at substantially higher concentration than employed in the present work, is clearly more favorable than the corresponding ring closure of Ia-Id.

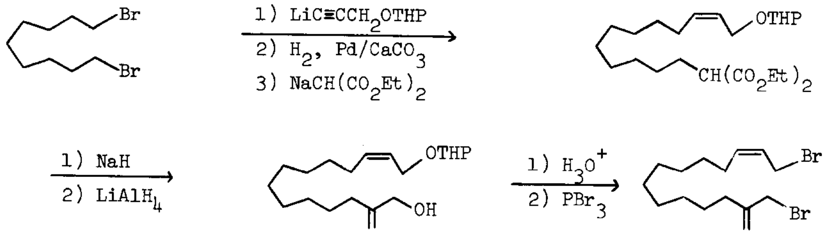


(2)

n = 4, 59%
n = 6, 70-74%
n = 10, 76-84%

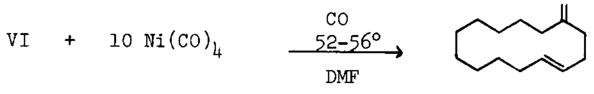
The allylic dibromide VI, which possesses structural features of both I and the linear allylic dihalides studied earlier, was synthesized as shown in the scheme. When VI is treated

Scheme



VI

with nickel carbonyl in the usual manner (conc. 0.0064 M, addition time 32 hr), VII is formed in 60% yield after distillation and 43% yield after chromatography (equation 3). This result is

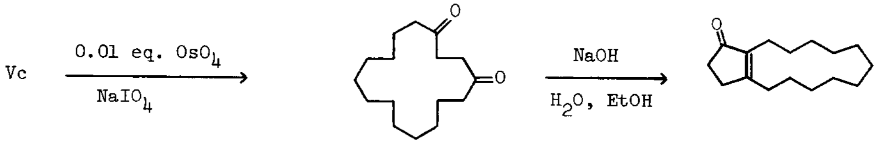


(3)

VII

intermediate between the yields of the 14-membered ring compounds obtained from Ib (15-37%) and the earlier work (70-74%).[3]

The 1,4-dimethylenecycloalkanes are precursors of 1,4-diketones and therefore fused-ring cyclopentenones, as demonstrated by the following result:



60%

100%

The results outlined above provide further data on the scope and utility of the reaction of allylic dihalides as a method of formation of large-sized rings.[7]

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6. Satisfactory infrared, proton magnetic resonance, and high resolution mass spectral data were obtained for each of the cyclization products reported herein.
7. This work was assisted financially by the National Science Foundation.