Synthesis of [3.3.3]Propellanes by 'Exocyclic' Transannular Cycloaddition of Olefinic Methylenecyclopropanes†

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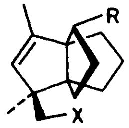
Olefinic methylenecyclopropanes undergo quantitative transannular ring closure under catalysis by Group 10 metals to give [3.3.3]propellanes, through cycloaddition of a trimethylenemethane-like intermediate.

Propellane continues to attract the interest of chemists of various disciplines.[1] Since the discovery of the unique sesquiterpenes modhephene (**1**)[2,3] and 13-acetoxymodhephene (**2**),[4] the [3.3.3] skeleton has been a target of special interest.

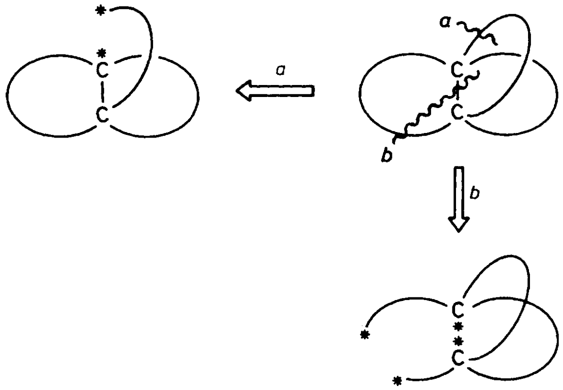


(**1**) R = Me, X = H

(**2**) R = Me, X = OAc

(**3**) R = H, X = OAc

The majority of synthetic approaches to propellanes rely on the formation of a third ring on the framework of a fused bicyclic structure: route *a* in reaction (1). Route *b*, however, in which both the central bond and a peripheral one are formed in a single step by 'exocyclic' transannular cycloaddition, is so far unexplored. In this communication, we report an unusually efficient construction of [3.3.3]propellanes by the latter strategy, involving Group 10 metal-catalysed internal reaction of the olefinic methylenecyclopropanes (**4**).



(1)

Nickel and palladium complexes are known to effect cycloaddition of methylenecyclopropane with an activated olefin, giving methylenecyclopentane through a trimethylenemethane-like intermediate.[5] Although the reaction mechanism remains obscure, intermolecular precedents predict that no conditions would be available for the cyclization of (**4**) to propellane (**5**) [reaction (2)]. Thus, a nickel catalyst would mainly cleave the 2,3-bond of (**4**),[6] to generate an intermediate topologically incapable of cyclization to the propellane skeleton. A palladium catalyst, on the other hand, would cleave the 3,4-bond to form the desired trimethylenemethane-like intermediate (**5**), the regioselectivity of

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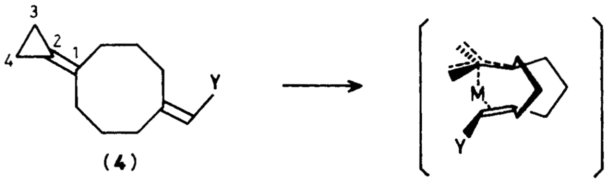
Table 1. Synthesis of propellanes (**6**) by transannular cyclization of methylenecyclopropanes (**4**).[a]

Entry	Substrate/ product	Catalyst (mol %)	Metal : Ph_3P	Temp. (°C)	% Yield
1	(**4a**)/(**6a**)	$Ni(cod)_2/Ph_3P$ (20)	1 : 0.5	110	74[b](94)[c]
2	(**4a**)/(**6a**)	$Ni(cod)_2/Ph_3P$ (20)	1 : 1	110	18[b](78)[c]
3	(**4a**)/(**6d**)	$Ni(acac)_2$/Dibal/Ph_3P (20)	1 : 0.5	90	91[b]
4	(**4a**)/(**6a**)	$PdCl_2(Ph_3P)_2$/Dibal (10)	1 : 2	130	98[d]
5	(**4b**)/(**6b**)	$PdCl_2(Ph_3P)_2$/Dibal (20)	1 : 2	90	74[b]

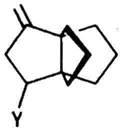
[a] Reaction procedure: to a solution of Pd^{II} or Ni^{II} catalyst in degassed toluene were added Dibal and (**4**) at −72 °C. The vessel was sealed and heated for 6—11 h at the temperature indicated. [b] Determined by capillary g.l.c. [c] Based on conversion. [d] Based on pure isolated material.

cycloaddition of which is opposite to that suitable for propellane formation.[7]



(**4**)
a, Y = CO_2Et
b, Y = H

(**5**)



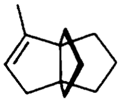
(**2**)

(**6**)
a, Y = CO_2Et
b, Y = H

Despite this prediction, $Ni(cod)_2$ (cod = cyclo-octa-1,5-diene) in the presence of 0.5 equiv. of PPh_3 effected clean cyclization of (**4a**)‡ in the desired manner to give (**6a**)§ in excellent yield (Table 1, entry 1). A Ph_3P : Ni ratio larger than 0.5 : 1 considerably reduced the reaction rate (entry 2). A Ni^0 catalyst generated conveniently from $Ni(acac)_2$ (acac = pentane-2,4-dionato) and di-isobutylaluminium hydride (Dibal) was also effective (entry 3). A palladium catalyst proved much more suitable than a nickel catalyst. The reaction of (**4a**) in the presence of a Pd^0–PPh_3 catalyst afforded (**6a**) in 98% yield of isolated product (entry 4).

The cycloaddition of methylenecyclopropane to simple olefins has been little explored,[8] because of the destruction of the latter under the reaction conditions. The transannular cyclization of the simple methylenecyclo-octane (**4b**),‡ however, proceeded cleanly to give the methylene-[3.3.3]propellane (**6b**) as a volatile solid.

The propellane (**6b**) possesses a highly symmetrical structure, the ^{13}C n.m.r. spectrum of which shows only five methylene carbon signals.§ Treatment with trifluoroacetic acid at room temperature quantitatively produced an endocyclic double-bond isomer (**7**), the ^1H n.m.r. spectrum of which indicated the presence of an isolated $CH_2CH{=}CCH_3$ system.§ The propellane (**6a**) was converted into 13-acetoxy-12-normodhephene (**3**) through several high-yield standard transformations [i, $LiNPr^i_2$/MeI, ii, CF_3CO_2H, iii, $LiAlH_4$, iv, Ac_2O]; the spectra of the product were similar to those of natural 13-acetoxymodhephene.§



(**7**)

In summary, the 'exocyclic' transannular ring closure of an olefinic methylenecyclopropane (the first example of its kind) not only provides a viable route to propellanes, but exhibits unique regioselectivity not observed with its intermolecular counterparts. In addition, the extreme facility of the cyclization suggests that oxidative cleavage of peripheral bonds in propellanes such as (**3**) and (**7**) will serve as an attractive route to functionalized fused bicyclic systems.

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‡ The starting olefinic methylenecyclopropanes were prepared by methylenecyclopropanation (ref. 9), deprotection, and a standard Wittig reaction on a 5-siloxycyclo-octanone, in turn available from *cis*-cyclo-octane-1,5-diol.

§ The structures of the propellanes were determined by i.r., ^1H n.m.r., two-dimensional n.m.r., and mass spectral analyses. For (**6a**) ^{13}C n.m.r. ($CDCl_3$) δ 14.53 (q), 25.09 (t), 25.64 (t), 35.33 (t), 35.80 (t), 39.50 (t), 40.14 (t), 41.81 (t), 50.70 (d), 60.15 (t), 64.12 (s), 64.53 (s), 103.15 (t), and 158.31 (s); for (**6b**) ^1H n.m.r. ($CDCl_3$) δ 1.43 (t, *J* 7.4 Hz, 2H), 1.28—1.72 (m involving br s at 1.47 and 1.48), 2.29 (dt, *J* 1.4 and 7.4 Hz, 2H), and 4.72 (dd, *J* 1.7 and 3.6 Hz, 2H); for (**3**) ^1H n.m.r. ($CDCl_3$) δ 1.05 (s, 3H), 1.11—2.04 (m, 12H), 1.61 (d, *J* 1.7 Hz, 3H), 2.06 (s, 3H), 3.86 (d, *J* 3.6 Hz, 1H), 3.99 (d, *J* 3.6 Hz, 1H), and 5.82 (d, *J* 1.7 Hz, 1H).