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REDUCTIVE CLEAVAGE OF CYCLOPROPYL KETONES

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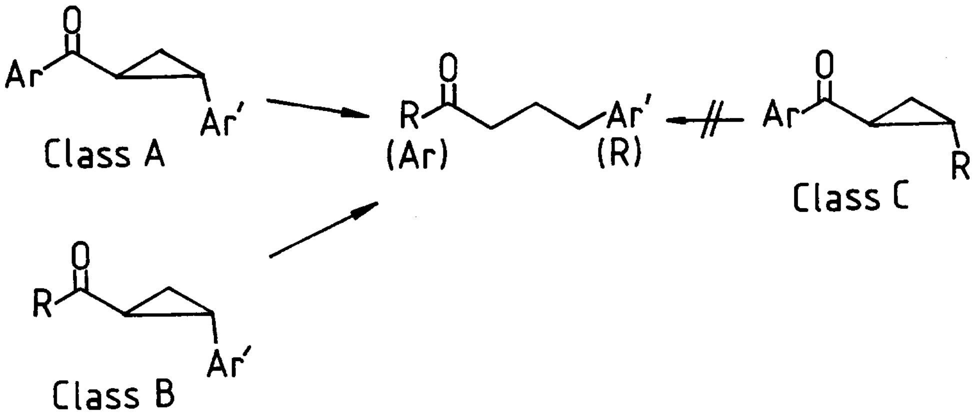
Aryl substituted cyclopropyl ketones are cleaved to acyclic ketones with zinc and zinc chloride or with zinc alone in refluxing alcohol.

Cyclopropanes are important synthetic intermediates due to their exceptional reactivity when functionalised[1], the cyclopropane 'trick'[2], and their ready accessibility.[3] A number of methods have been used for the reductive cleavage of cyclopropyl ketones. Both zinc in hydrochloric acid[4] and zinc with zinc chloride for short periods in refluxing ethanol[5] were successful. However both methods are limited to 1,2-bis-acyl cyclopropanes. For the reductive cleavage of alkyl and aryl cyclopropyl ketones lithium in liquid ammonia has been employed. This method however is frequently complicated by the formation of numerous side products.[1,6]

We now present a new procedure for the reductive cleavage of two of the three classes of cyclopropyl ketones (Scheme 1).



Scheme 1

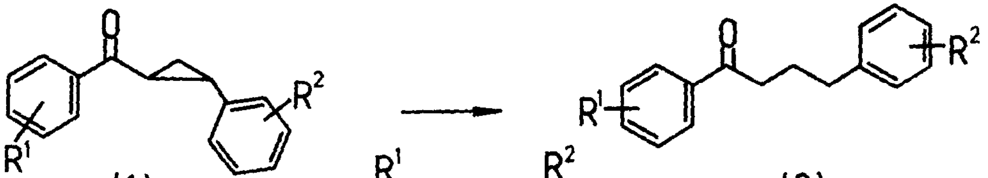
TABLE

Reductive Cleavage of Cyclopropyl Ketones[a]

entry	reactant	method, time	product (yield %)[b]
1	1a	B[c], 30 h	2a (90)
2	1b	A[d], 30 h	2b (90)
3	1b	B[c], 30 h	2b (91)
4	1c	B[c], 30 h	2c (90)
5	1d	B[c], 30 h	2d (89)
6	3	C[e], 12 d	4 (80)
7	5	A[d], 5 d	6 (88)
8	7	D[f], 12 d	8 (80)
9	9	D[f], 11 d	10 (89)
10	11a	A[d], 8 d	-
11	11b	A[d], 8 d	-

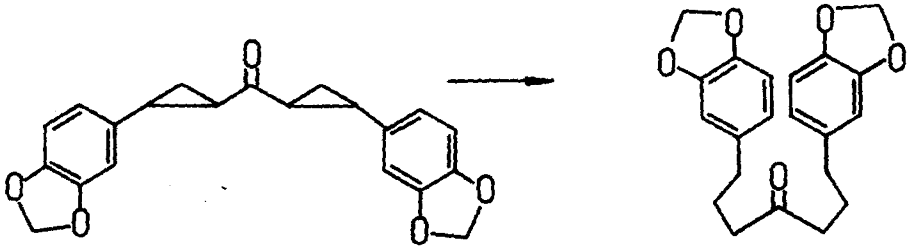
[a] All reactions carried out under N_2. A 0.05 M solution of reactant treated with reagent and heated under reflux. [b] Isolated yields of pure product. [c] Method B:Zn (3 equiv), refluxing ethanol. [d] Method A:Zn (3 equiv) + $ZnCl_2$ (3 equiv), refluxing ethanol. [e] Method C:Zn (5 equiv), refluxing ethanol. [f] Method D:Zn (5 equiv) + $ZnCl_2$ (5 equiv), refluxing n-butanol.

Class A Ketones. Application of Dekker's procedure[5] (zinc, zinc chloride, refluxing ethanol, 10 min) to ketone (1b) effected no reaction. However, when the reaction time was extended to 30 h the exclusive product was the corresponding ketone (2b) (90%) (entry 2, Table). Subsequent investigation showed that zinc chloride was unnecessary (entry 3, Table). The reaction was equally successful with substrates otherwise substituted in the aryl rings (1a, 1c, 1d) (entries 1, 4 and 5, Table). The synthetic potential of the reaction was underlined by the cleavage of ketones (3) and (5) (entries 6 and 7, Table).

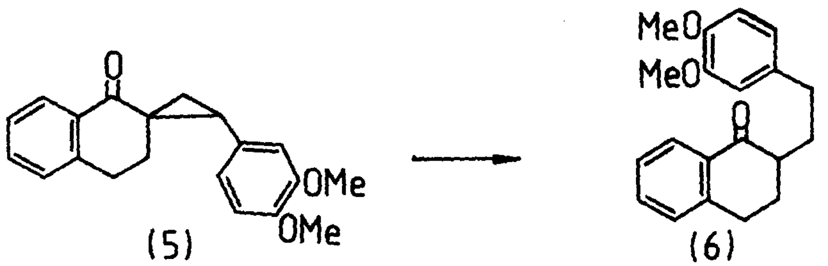


(1) (2)

	R^1	R^2
(a)	H	H
(b)	4-OMe	3-OMe
(c)	3-OMe	4-OMe
(d)	3,4-$(OMe)_2$	3,4-$(OMe)_2$



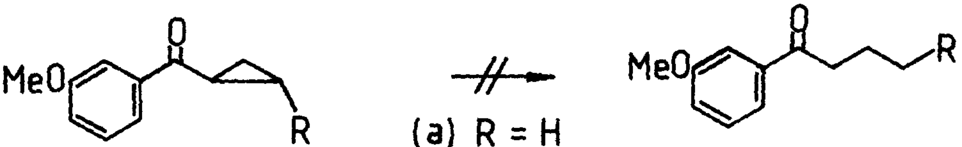
(3) (4)



(5) (6)

(7) (8)

(9) (10)



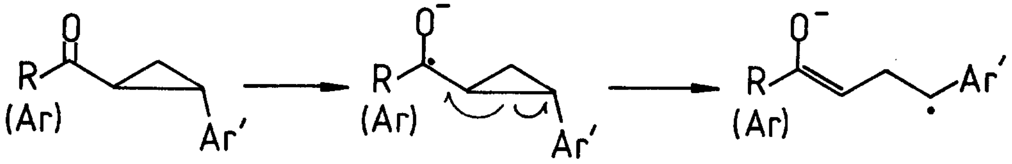
(11) (12)

(a) R = H
(b) R = t-Bu

Class B Ketones. These ketones were much less reactive. Under standard conditions, ketone (7) finally underwent cleavage (70%) following 18 days. This difficulty was in part circumvented by employing n-butanol as solvent (entry 8, Table). By this means also, ketone (9) was converted to (10) (89%) (entry 9, Table).

Class C Ketones. The ketones (11a) and (11b) were recovered unchanged following 8 days reflux (entries 10 and 11, Table).

Comparison of the relative rates of reaction of the three ketone classes suggests the initial formation of a ketyl followed by homolytic cleavage of the cyclopropane ring (Scheme 2).



Scheme 2

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