Ring Expansion of Succinoin Derivatives. New Synthetic Routes to Cyclopentenones

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Acid-catalysed ring expansion reactions of cyclobutane derivatives bearing a vicinal substituted-diol group give α-aryl and α-vinyl substituted cyclopentenones in good yields.

We report here two of the new methods that we have developed recently for the preparation of α-aryl- and α-vinyl-cyclopentenones. The syntheses start with the high-yield preparation of the cyclobutanone (2) by an aldol-type coupling of acetals with the cyclobutene (1) with $BF_3 \cdot Et_2O$ as catalyst.[1]

The first approach [method (A)] leading to β-alkyl substituted ketones (6) necessitates the transformation of (2) into (3). Amongst the various Wittig conditions tried, the Wittig reagent generated in tetrahydrofuran (THF) from $Ph_3PCH_3^+Br^-$ and KH worked best. The crucial ring enlargement of (3) to the desired (6) was achieved with an excess of trifluoroacetic acid at room temperature (30 min to 12 h). The examples are listed in Table 1. All three stages of the sequence are very clean and purification of (2) and (3) is not mandatory; the overall yield of (**6a**) from the intermediate *trans*-hex-2-enal dimethyl acetal was 75%. Starting from *p*-tolualdehyde acetal this reaction sequence constitutes a short formal synthesis of (±)-cuparene, since (**6c**) has previously been converted into this sesquiterpene.[2]

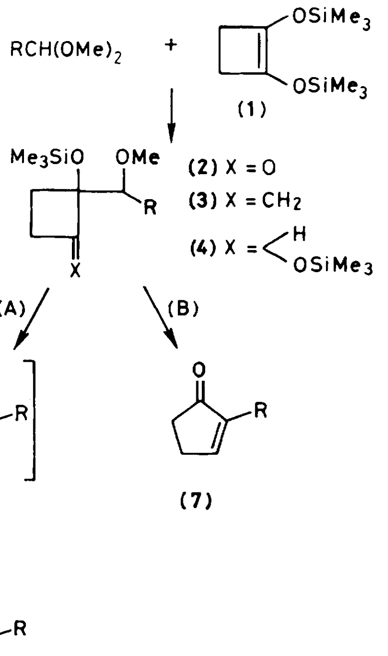
Table 1. Synthesis of cyclopentenones by method (A).

Compound series	Yield, %			$t_{1/2}$ (3)→(6)[e]
	(2)[a]	(3)	(6)	
a	100	90[b]	80	<1 min
b	76	88[b]	97	<2
c	100	83[b]	90	<1
d	91	78[c]	81	2.5
e	87	76[d]	83	7

[a] Catalyst: 1 equiv. of $BF_3 \cdot Et_2O$ in methylene chloride; −70 °C for 10—60 min. [b] $Ph_3PCH_3^+Br^-$, KH in THF, room temp. [c] $Ph_3PCH_3^+BF_4^-$, KH in THF, room temp. [d] $Ph_3PCH_3^+Br^-$, Me_2EtCOK in refluxing toluene. [e] See the text.

The rate of rearrangement of (3), as monitored by ^1H n.m.r. spectroscopy at 35 °C in 40 equiv. of CF_3CO_2H (Table 1) implies the rate-limiting departure of the benzylic or allylic alkoxy-group followed by the rapid migration of the *exo*-methylene group. For (**3e**), ^1H n.m.r. spectroscopy revealed the accumulation (*ca.* 40%) of (**5e**), which gradually isomerized to (**6e**) during several hours. It is notable that the allylic silyl ether on the cyclobutane ring does not ionise; such an ionisation must occur with aliphatic acetals, however, since the present method does not work with aliphatic acetals.

The second route [method (B)] is suitable for the preparation of β-unsubstituted enones, and is complementary to the



a; R = *trans*-CH=CHPr^n
b; R = *trans*-CH=CHPh
c; R = *p*-MeC$_6$H$_4$
d; R = Ph
e; R = *p*-ClC$_6$H$_4$

Scheme 1

first one. It is initiated by LiAlH$_4$ reduction of (**2**) in ether, followed by silylation (Me$_3$SiCl–4-dimethylaminopyridine–Et$_3$N) to obtain (**4**). Treatment of (**4**) with SnCl$_4$ in methylene chloride at 0 °C cleanly gave (**7**). The reaction could be carried out without purifying the intermediates. The overall yield of (**7a**) was 50% from the hexenal acetal.

Although these methods have so far found rather restricted applications in the synthesis of α-aryl and α-vinyl enones, the ready access to these compounds renders the methods attractive as alternatives to existing cyclopentenone syntheses.†

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† Representative spectral properties of the key compounds are as follows: (**3**) i.r. (neat) *ca.* 1660, 885—830 cm^{-1} (C=CH$_2$), ^{1}H n.m.r. (CCl$_4$) 0.1 (s), *ca.* 3.25 (s), and 4.7—5.0 (m); (**6**) i.r.(neat) 1690—1680 cm^{-1}, ^{1}H n.m.r. (CCl$_4$) 5.85 (t, *J* 17 Hz), 6.53 (dt, *J* 6.5 and 17 Hz), and 7.0—7.2 (m).