New Ring Conversion of Monocyclic Ketones to Bicycloenone Skeletons

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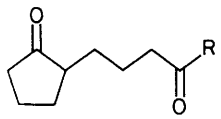
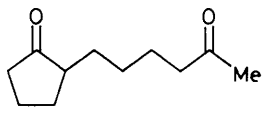
α-Substituted cyclopentanones or cyclohexanones with a carbonyl function at the 4- or 5-position of the side chain were converted to bicycloenones under acetalization conditions (BF_3/ethylene glycol).

Carbonyl groups are often protected as their ethylene acetals, generally by treatment of the carbonyl compounds with ethylene glycol in the presence of a strong acid (*e.g.*, *p*-$MeC_6H_4SO_3H$). The use of $BF_3{\cdot}Et_2O$ instead of a strong acid proceeds faster and with better yields than with *p*-$MeC_6H_4SO_3H$.[1]

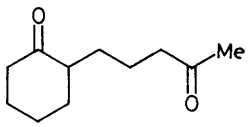
Previously, we have found that cyclopentanones or cyclohexanones with a carbonyl group in a side chain α- or β- to the ring carbonyl group readily undergo ring cleavage under acetalization conditions (BF_3/ethylene glycol).[2] We now report the novel conversion of cyclopentanones or cyclohexanones with a carbonyl function at the 4- or 5-position of an α-side chain to bicycloenones. As shown in Table 1, substrates (**1**), (**2**), and (**3**) afforded the corresponding bicycloenones (**5**), (**6**), and (**7**) under acetalization conditions (BF_3/ethylene glycol/room temp./24 h).† Substrate (**1d**) afforded‡ the ring cleavage product (**4d**) in addition to a small amount of by-product,§ and the bicycloenone was not obtained. However, the isolated (**4d**)‡ could be converted to (**5d**) on re-exposure (30 h) to the acetalization conditions. Compound (**4a**) obtained from (**1a**) by shortening (2 h) the reaction time



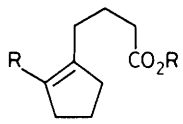
(**1**)



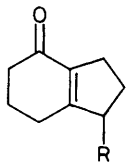
(**2**)



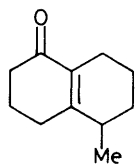
(**3**)



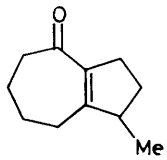
(**4**) R = CH_2CH_2OH
(**8**) R = Me



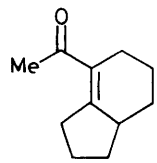
(**5**)



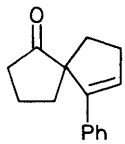
(**6**)



(**7**)



(**9**)

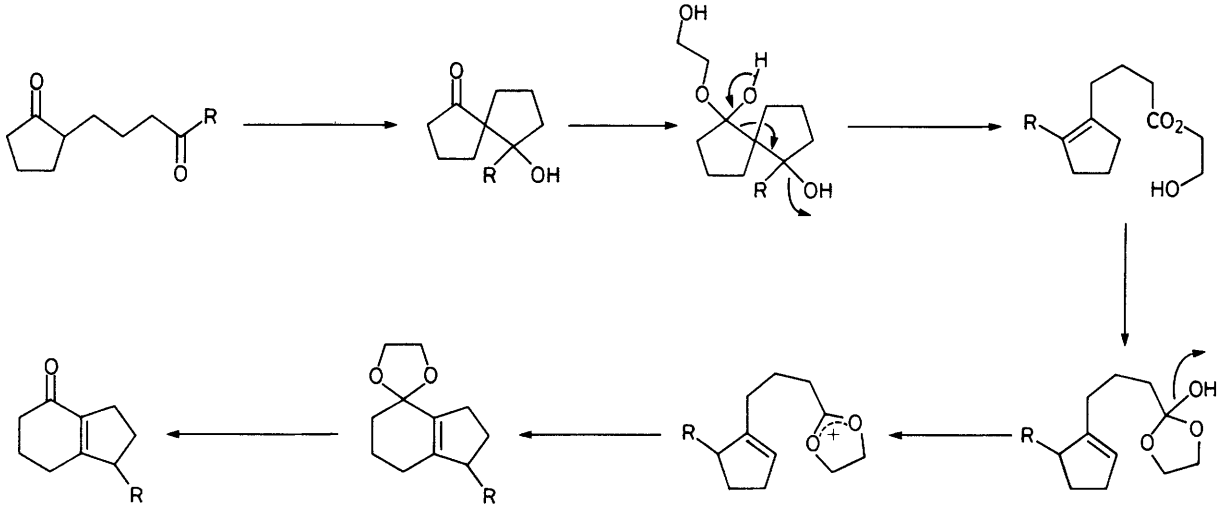


(**10**)

† All compounds gave satisfactory spectroscopic data. Selected spectroscopic data for representative products: (**5b**): i.r. (neat) 1665, 1625 cm^{-1}; ^1H n.m.r. ($CDCl_3$) δ 0.91 (3H, t, *J* 7.3 Hz); ^{13}C n.m.r. ($CDCl_3$) δ 11.4 (q), 23.6 (t), 25.2 (t), 25.6 (t), 27.7 (t), 27.9 (t), 37.9 (t), 50.8 (d), 137.4 (s), 167.8 (s), 198.1 (s); *m/z* 164 (M^+), 136, 135, 108. For (**6**): i.r. (neat) 1660, 1620 cm^{-1}; ^1H n.m.r. ($CDCl_3$) δ 1.11 (3H, d, *J* 6.8 Hz); ^{13}C n.m.r. ($CDCl_3$) δ 19.1 (q), 19.4 (t), 22.7 (2 × t), 29.6 (t), 30.7 (t), 35.2 (d), 38.0 (t), 132.1 (s), 160.6 (s), 199.6 (s); *m/z* 164 (M^+), 149, 136. For (**4d**): i.r. (neat) 3420, 1730, 755 cm^{-1}; ^1H n.m.r. ($CDCl_3$) δ 3.70—3.80 (2H, m), 7.12—7.42 (ArH); *m/z* 274 (M^+), 212, 170.

‡ Friedel–Crafts reaction of the ring cleavage product (**4d**) to give (**5d**) requires a rearrangement of the double bond conjugated to the aromatic ring to the deconjugated form. This rearrangement seems to be caused by treatment with fresh acetalization reagents (BF_3/$HOCH_2CH_2OH$), because (**1a**—**c**) afforded (**5a**—**c**) in a one-pot reaction, and the isolated (**4d**) was converted to (**5d**) on addition of fresh reagents. Compound (**2**) afforded a small amount of (**9**), in addition to (**6**) as the main product (71%).

§ Based on spectroscopic data, the by-product was (**10**).



Scheme 2. Proposed mechanism.

Table 1. Cyclization of the ketones (**1**)—(**3**).[a]

Substrate	R	Product (% yield)
(**1a**)	Me	(**5a**) (82)
(**1b**)	Et	(**5b**) (80), (**4b**) (7)
(**1c**)	Pr^i	(**5c**) (52)
(**1d**)	Ph	(**4d**) (63), (**10**)[b]
(**2**)		(**6**) (71), (**9**) (3)
(**3**)		(**7**) (13)

[a] Conditions: mixture of substrate (0.6 mmol), $BF_3{\cdot}Et_2O$ (7 equiv.), and $HOCH_2CH_2OH$ (5 equiv.) in CH_2Cl_2 (3 ml), stirred at room temp. for 24 h. [b] By-product, small quantity.

was similarly converted to (**5a**) under the acetalization conditions (Scheme 1). However, the methyl ester (**8**) derived by treatment of (**4a**) with K_2CO_3/MeOH was unchanged even after prolonged exposure to the acetalization conditions (30 h). The above findings allow us to propose the mechanism in Scheme 2 involving the aldol condensation, acetalization,

$$(\mathbf{4a}) \xrightarrow{i} (\mathbf{5a})\ (45\%)$$

$$(\mathbf{4d}) \xrightarrow{ii} (\mathbf{5d})\ (73\%)$$

Scheme 1. *Conditions*: i, as in Table 1; ii, as in Table 1, for 30 h.

Grob fragmentation, migration of the double bond, and the formation of a 1,3-dioxolenium ion followed by intramolecular Friedel–Crafts reaction. Thus, this simple, novel ring conversion is useful for the synthesis of 7-alkylbicyclo-[4.3.0]non-1(6)-en-2-ones and 7-alkylbicyclo[4.4.0]dec-1(6)-en-2-ones.

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References

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