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Pinacol reduction-cum-rearrangement. A re-examination of the reduction of aryl alkyl ketones by zinc–aluminum chloride

Anya A. Grant, Myron Allukian and Albert J. Fry*

Chemistry Department, Wesleyan University, Middletown, CT 06459, USA

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Abstract—Reduction of alkyl phenyl ketones by zinc and aluminum chloride in acetonitrile results in pinacol condensation followed by rearrangement. The phenyl group migrates in every instance. © 2002 Elsevier Science Ltd. All rights reserved.

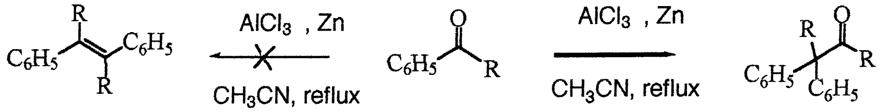
We recently had need for a series of symmetrically substituted dialkylstilbenes (**2**). A report that aryl aldehydes and ketones (**1**) can be condensed to the corresponding alkenes **2** by a mixture of zinc and aluminum chloride in acetonitrile[1] (Eq. (1)) promised to provide a convenient route to the desired substances. However, we report here that in our hands little or no alkene is formed from aryl alkyl ketones (**1**). Rather, the reaction takes a quite different course leading primarily to rearranged dimeric ketones (**3**) (Table 1).

A number of aryl ketones were treated with a mixture of zinc and aluminum chloride in acetonitrile under nitrogen under conditions previously reported to afford substituted stilbenes[1] (ketone:Zn:$AlCl_3$ = 1:2:2; 70°C; 20–24 h). Reaction mixtures were analyzed by GC–MS and ^1H NMR spectroscopy. In every case, the major product was the rearranged ketone **3**, though small amounts of other substances, including **2**, were produced in most reactions (Table 1).

We suggest the mechanistic sequence shown in Scheme 1 to account for these results. Coordination of the ketone to aluminum chloride, followed by zinc reduction and possibly metal exchange, would afford radical **4**. Dimerization of **4** would lead to bridged intermediate **5**; coordination of $AlCl_3$ to **5** would then induce pinacolic rearrangement via cations **6** and **7** to afford ketone **3**. On the other hand, reduction of **4** by zinc,

Table 1. Reduction of phenyl ketones with zinc and aluminum chloride in acetonitrile

Substrate	Rearranged ketone (**3**) (%)	Other products (%)
1a, R = Me	95[3,4]	**2a** (5)
1b, R = Et	82[2]	**2b** (4); 1-phenyl-1-propene (8.5); **11b** (4.5)
1c, R = *i*-Pr	93[3]	**2c** (2); 1-phenyl-2-methylpropene (2); **11c** (3)
1d, R = *n*-Bu	99	1-Phenyl-1-butene (1)
1e, R = *t*-Bu	0.7[5]	**1e** (71.3); **2e** (2); **13** (20); **12** (1); **11e** (2); unk (1); unk (2)
1f, R = C_6H_5	95[6]	**2f** (4); **14** (1); **15** (tr)



2

1a, R = Me
b, R = Et
c, R = n-Pr
d, R = n-Bu
e, R = t-Bu
f, R = C_6H_5

3

(1)

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* Corresponding author. Tel.: (860) 685-2622; fax: (860) 685-2211; e-mail: afry@wesleyan.edu

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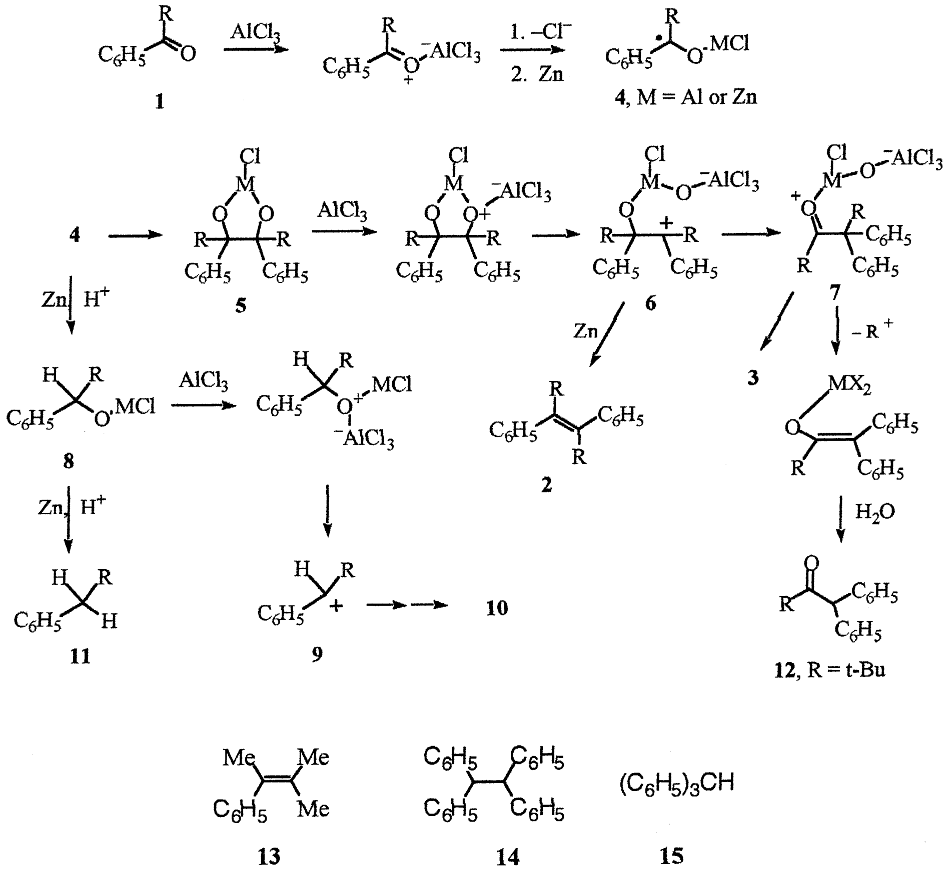

Scheme 1.

followed by protonation of the resulting intermediate (probably by adventitious water) would afford intermediate **8**, which could afford monomeric alkenes (**10**) by $AlCl_3$-induced elimination to cation **9**, followed by rearrangement in favorable cases and in any event by final loss of a proton. Alternatively, reduction of **8** by zinc would lead to alkanes (**11**). Pivalophenone (**1e**) constituted an exception to the trends exhibited by the other ketones examined; it reacted slowly under our standard conditions; unreacted **1e** constituted the primary constituent of the reaction mixture after 20 h. The major product at this point was 2-methyl-3-phenyl-2-butene (**13**), accompanied by **2e**, small amounts of two unidentified isomers of **13**, and neopentylbenzene (**11e**). Very likely, dimerization of **4** is slowed sterically in this case, leading to a preponderance of products (**13** and its isomers and **11e**) arising from reduction of **4** by zinc. **1e** also produced a very small amount of dealkylated ketone **12**; this might have arisen by loss of *t*-butyl cation from intermediate **7** to form a metallo enol, which would be converted to **12** during the hydrolytic workup. Benzophenone (**1f**) afforded small amounts of tetraphenylethylene (**2f**), tetraphenylethane (**14**), and triphenylmethane (**15**) in addition to the major product, benzpinacolone (**3f**). The quality of the aluminum chloride employed turned out to have a pronounced influence on the course of these reactions. The most efficient conversion of **1** to **3** took place using a freshly opened bottle of aluminum chloride. Aged samples of $AlCl_3$ afforded large amounts of unreacted starting material and (only) in the case of benzophenone, an increased amount (25% yield) of alkene **2f**. Although we have not observed formation of substituted stilbenes as the predominant products under any conditions, it is possible that the previous literature report[3] involved a different grade of $AlCl_3$ or a sample with a different storage history.

Summary

Aryl alkyl ketones undergo pinacol-type condensation and in situ rearrangement to the corresponding rearranged ketones (**3**) with exclusive migration of the phenyl group when heated with a mixture of zinc and aluminum chloride in acetonitrile.[7,8] This observation is in fact consistent with an earlier report that substituted benzophenones undergo transformation to **3** by the action of zinc and aluminum chloride under ultrasonic irradiation.[6] Similar tandem coupling/rearrangement sequences have been observed with aryl ketones and NbC13(DME).[4]

Acknowledgements

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7. Ketones **3** are all known compounds,[4–8] except for **3d**, mass spectrum m/z (intensity): 307 (m-1, <0.1), 223 (100), 180 (18), 166 (72), 119 (29) and 91 (70); ^{1}H NMR spectrum (300 MHz, $CDCl_3$): δ 7.2–7.6 (m, 10H), 2.3 (t, 2H), 0.9–1.4 (m, 10H), 0.9 (t, 3H), 0.8 (t, 3H).
8. **Reductive coupling of 1a (representative experiment)**. Anhydrous $AlCl_3$ (2.67 g, 20 mmol) and Zn (1.30 g, 20 mmol) were stirred under N_2. Acetonitrile (60 ml) was added. The mixture was allowed to cool, then acetophenone (**1a**) (1.20 g, 10 mmol) was added and the mixture was heated to 70°C and refluxed for 20 h. It was then cooled, diluted with cold water and extracted with dichloromethane. After drying and evaporation, analysis by GC–MS revealed a mixture consisting of ketone **3a** (95%) and 2,3-diphenyl-2-butene (**2a**) (5%).