Pergamon

Tetrahedron Letters, Vol. 35, No. 52, pp. 9749-9750, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)02115-5

A General Route to 3-Unsubstituted 1,5-Diaryl-2,4-pentanediones and -4-Methoxy-2-pentanones

Juha Pulkkinen*, Jouko Vepsäläinen and Reino Laatikainen

Department of Chemistry, University of Kuopio
P.O.Box 1627, FIN-70211 Kuopio, FINLAND

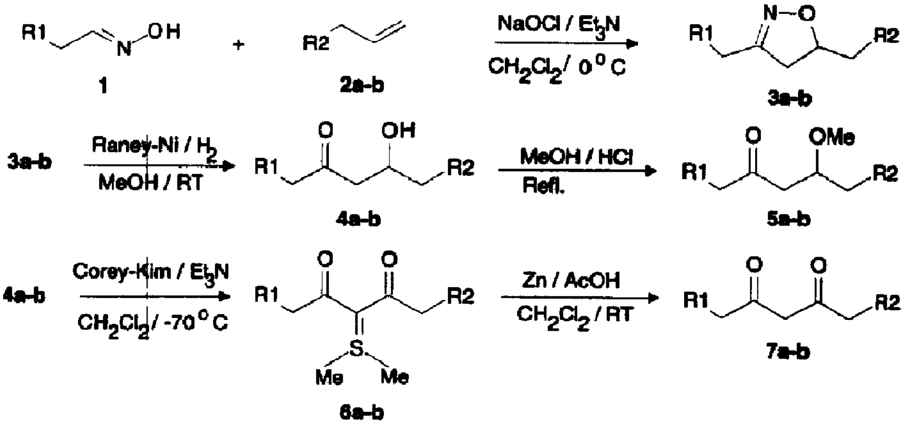
Abstract: 2-Isoxazolines are converted to corresponding 3-hydroxyketones which are used as precusors to produce new 3-unsubstituted 1,5-diaryl-2,4-pentanediones and -4-methoxy-2-pentanones.

3-Unsubstituted 2,4-pentanediones and 4-methoxy-2-pentanones with aromatic groups on 1,5-positions are very flexible structures due to negligible rotational barriers of the skeletal bonds and may thus be used as building units for many novel applications. Having a binding site for a cation they could act, for example, as templates in artificial allosteric systems.

Despite the simplicity of the title structures general routes leading to them have not been reported yet. Only a few papers describe procedures for the diketones **7** with two similar aromatic groups in the same molecule.[1] Methods for the methoxyketones **5** are previously unpublished. To our knowledge this is the first general route to the title structures having different aromatic groups and using the same precursor to produce both the diketones **7** and the methoxyketones **5**.

The traditional way to make β-diketones is an acylation reaction of a methylketone with a carboxylic acid derivative. However, in our case the methylketone would be an arylacetone which tends to undergo acylation to the methylene rather than the methyl group.[2] The synthesis of β-hydroxyketones with an aldol condensation of carbonyl compounds with aldehydes would fail for the same reason.

Several attempts were made to produce the diketones from malonyl chloride and benzyl lithium and from dichloromethane and lithium salts of ethylene dithiolane or ethylene acetal of phenyl acetaldehyde, but in our hands they were unsuccesful. Finally we decided to use a nitrile oxide - olefin [3+2] cycloaddition reaction to build up the five-carbon skeleton of the title structures.[3] An aryl acetaldoxime **1** was reacted with an allylarene **2** in the presence of NaOCl at 0°C to give an 2-isoxazoline **3**, which was then converted to the corresponding 3-hydroxyketone **4** by catalytic hydrogenation with Raney-Ni at room temperature.[4,5] The overall yield was 33- 36 %.



Scheme 1. a: R1 = R2 = C_6H_5; b: R1 = C_6H_5, R2 = C_6F_5.

After trying several oxidizing agents to convert the 3-hydroxyketone **4** to the 1,3-diketone **7** we ended up with the method previously described by Katayama et al.[6] The treatment of **4** with the Corey-Kim reagent (N-chlorosuccinimide-dimethyl sulfide complex)[7] at -70°C gave a dimethylsulfonium diacylmethylide **6** from which **7** was released by Zn catalyzed reduction at room temperature, the yield being 53 - 80 % from two steps.

Surprisingly, the 3-methoxyketone **5** was easily approached by substitution of the hydroxyketone **4** with methanol in the presence of concentrated hydrochloric acid. In mechanistical point of view it seems that chlorine as a nucleofile is necessary, because no reaction occurred with other acids than HCl. The end product **5** is possible to achieve via several routes, but acid catalyzed elimination of water from **4** followed by HCl addition to double bond and substitution of chlorine by methoxy group seems to be the most probable way.

In conclusion we have presented a general route to produce 3-unsubstituted 1,5-diaryl-2,4-pentanediones and -4-methoxy-2-pentanones. All intermediates and products exept **7a**[1] are new compounds.[8]

REFERENCES AND NOTES

1. a) Dashkevich, L. B.; Boksiner, E. I. *Zhur. Obshchei Khim.* **1958**, *28*, 2845. b) Dashkevich, L. B.; Kuzmenkov, L. N. *Zhur. Obshchei Khim.* **1959**, *29*, 2367. c) Bryant, D. R.; Hauser, C. R. *J. Org. Chem.* **1961**, *27*, 694. d) Poss, C. S.; Rychnovsky, S. D.; Schreiber, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 3360.
2. Hauser, C. R.; Swamer, F. W.; Adams, J. T. *Org. React.* **1954**, *8*, 59.
3. Lee, G. A. *Synthesis* **1982**, 508.
4. Ko, S. S.; Confalone, P. N. *Tetrahedron* **1985**, *41*, 3511.
5. Curran, D. P. *J. Am. Chem. Soc.* **1982**, *104*, 4024.
6. Katayama, S.; Fukuda, K.; Watanabe, T.; Yamauchi, M. *Synthesis* **1988**, 178.
7. Corey, E. J.; Kim, C. U. *J. Am. Chem. Soc.* **1972**, *94*, 7586.
8. NMR and mass spectrometric data and additional examples will be reported later.

(*Received in UK* 8 *September* 1994; *revised* 20 *October* 1994; *accepted* 26 *October* 1994)