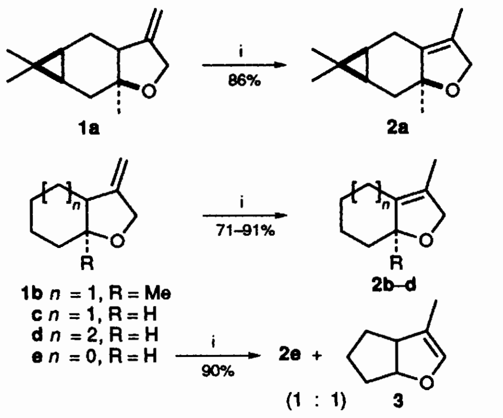
A New Synthetic Route to 2,5-Dihydrofurans

Jean-Pierre Dulcère, Nathalie Baret and Jean Rodriguez

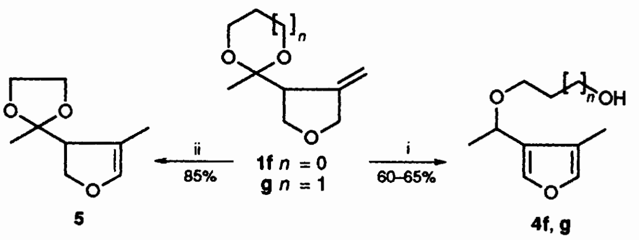
Faculté des Sciences et Techniques de St Jérôme, Laboratorie de Synthèse Organique URA CNRS 1411, av. Esc. Normandie-Niemen, D 12, F-13397 Marseille Cedex 20, France

$\mathrm{Bu^tOK}$–dimethyl sulfoxide-catalysed selective isomerization of 3-methylene tetrahydrofurans **1** provides a new convenient route to 2,5-dihydrofuran **2** precursors of furan-2(3*H*)-ones **8** or furans **4** or **9**.

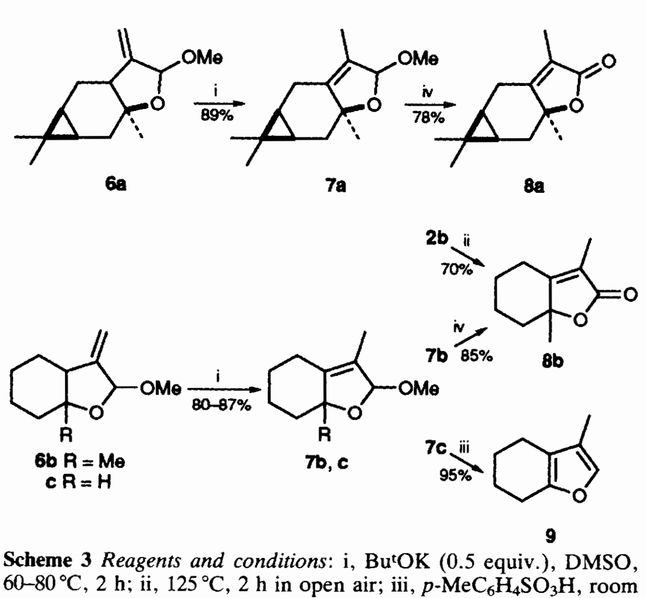
Furans and dihydrofurans are of special interest since they constitute the basic framework of many naturally occuring compounds.[1] Although numerous synthetic routes to 2,5-dihydrofurans are known,[2] the most convenient approaches usually involve the formation of the heterocycle by electrophilic cyclizations of α-allenic derivatives.[3] We report here a simple and versatile preparation of fused bicyclic 3-methyl-2,5-dihydrofurans, using readily available 3-methylene tetrahydrofurans.[4] The selective isomerization of **1a–d**, promoted by $\mathrm{Bu^tOK}$ (0.5 equiv.) in DMSO (60–80 °C) affords 2,5-dihydrofurans **2a–d**[†] in 71–91% yields (Scheme 1). This isomerization proceeds under kinetic control, since conversion of 2,5-dihydrofurans into their thermodynamically more stable 2,3-dihydrofurans was previously achieved upon heating either with $\mathrm{Bu^tOK}$–$\mathrm{Bu^tOH}$ at 185–215 °C,[5] or in the presence of metal catalysts.[6] The reactivity of the bicyclo[3.3.0] derivative **1e**, leading to a mixture of dihydro isomers **2e** and **3** in a 1 : 1 ratio accounts for the instability of the kinetic product **2e** with respect to larger ring size homologues **2a–d**. Interestingly, under the same reaction conditions 4-acyl-3-methylenetetrahydrofuran ketals **1f,g**[7] provide functionalized furans **4f,g**[‡] by ring opening of the ketal moiety (Scheme 2). It is worth noting that the previously reported[7] isomerization of **1f** promoted by Pd/C and H_2 resulted in the formaiton of the 2,3-dihydro thermodynamic isomer **5**.



Scheme 1 *Reagents and conditions*: i, $\mathrm{Bu^tOK}$ (0.5 equiv.), DMSO, 60–80 °C, 2 h



Scheme 2 *Reagents and conditions*: i, $\mathrm{Bu^tOK}$ (0.5 equiv.), DMSO, 60–80 °C, 2 h; ii, Pd/C, H_2, EtOH, 2 h



Scheme 3 *Reagents and conditions*: i, $\mathrm{Bu^tOK}$ (0.5 equiv.), DMSO, 60–80 °C, 2 h; ii, 125 °C, 2 h in open air; iii, p-$\mathrm{MeC_6H_4SO_3H}$, room temp., 15 min; iv, Jones reagent

2,5-Dihydrofuran derivatives are known to undergo autoxidation to the corresponding furan-2(3*H*)-ones ($\Delta^{\alpha,\beta}$-butenolides),[8] a structural unit encountered frequently in a large number of natural products and associated with biological activity.[9] According to this procedure, the furanone **8b** was prepared in 70% yield, but reproducible results could not be achieved; on the other hand autoxidation of **2a** led to degradation of the starting material.

To perform a more efficient preparation of furan-2(3*H*)-ones, the $\mathrm{Bu^tOK}$–DMSO-catalysed isomerizations were performed on 2-methoxy-3-methylene tetrahydrofurans **6a–c**[7] to afford 2-methoxy-2,5-dihydrofurans **7a–c** (80–89% yields, Scheme 3). The acetal moiety in **7** should provide the lactone unit by oxidation. Although **7c** was aromatized directly into the 2,3-fused bicyclic furan **9** on acid catalysis, Jones oxidation of analogues **7a,b** substituted at the ring junction afforded the expected furanones **8a,b**[§] in 78–85% yields (Scheme 3).

In conclusion, the $\mathrm{Bu^tOK}$–DMSO-promoted isomerization of 3-methylene tetrahydrofurans provides a new and efficient route to fused 2,5-dihydrofurans; depending on the substitution pattern of starting materials, this procedure also constitutes a convenient entry into the preparation of 3-methyl furans and furan-2(3*H*)-ones.

Received, 28th September 1993; Com. 3/05816F

Footnotes

[†] **2b**, IR ν/cm^{-1} 2920, 2850, 1450, 1050; NMR (200 MHz, $CDCl_3$): ^{1}H, δ 4.49 (m, 1 H), 4.37 (d, 1 H, *J* 6 Hz), 2.33–2.43 (m, 1 H), 1.85–1.60 (m, 5 H), 153 (d, 3 H, *J* 1.2 Hz), 1.32–1.45 (m, 2 H), 1.20 (s, 3 H); ^{13}C, δ 136.5, 122.4, 88.7, 76.4, 40.6, 27.1, 23.9, 23.8, 22.9, 9.6.

[‡] Satisfactory analytical and spectral data were obtained for all compounds.

[§] **8b** IR ν/cm^{-1} 2980, 2960, 2760, 1750, 1690; NMR (200 MHz, $CDCl_3$): ^{1}H, δ 2.75 (m, 1 H), 2.68 (m, 1 H), 2.21–1.94 (m, 6 H), 1.75 (d, 3 H, *J* 1.2 Hz), 1.38 (s, 3 H); ^{13}C δ 173.8, 166.3, 118.9, 84.8, 39.9, 27.2, 25.3, 22.9, 22.2, 8.2.

References

1 R. L. Danheiser, E. J. Stoner, H. Koyama, D. S. Yamashita and C. A. Klade, *J. Am. Chem. Soc.*, 1989, **111**, 4407; A. W. Burgstahler and G. N. Widiger, *J. Org. Chem.*, 1973, **38**, 3652; F. Bohlmann and Ch. Zdero, *Chem. Ber.*, 1973, **106**, 845; M. D. Grove, D. Weisleder and M. E. Daxenbichler, *Tetrahedron*, 1973, **29**, 2715; D. M. X. Donnelly and M. J. Meegan, in *Comprehensive Heterocyclic Chemistry*, ed. A. R. Katritzky and C. W. Rees, Pergamon, New York, 1984; vol. 3, p. 705.

2 *Rodd's Chemistry of Carbon Compounds*, 2nd edn., ed. S. Coffey, Elsevier, Amsterdam, 1973, p. 125; P. Bravo and C. Ticozzi, *J. Chem. Soc., Chem. Commun.*, 1979, 438; Z. T. Fomum, P. F. Asobo, S. R. Landor and P. D. Landor, *J. Chem. Soc., Chem. Commun.*, 1983, 1455; M. R. Iesce, M. L. Graziano, F. Cermola and R. Scarpati, *J. Chem. Soc., Chem. Commun.*, 1991, 1061; M. Cheng, G. Yang, J. Chow, G. Lee, S. Peng and R. Liu, *J. Chem. Soc., Chem. Commun.*, 1992, 934.

3 A. R. Katritzky, J. Li and M. F. Gordeev, *J. Org. Chem.*, 1993, **58**, 3038; J. A. Marshall and X. Wang, *J. Org. Chem.*, 1990, **55**, 2995; S. Hormuth and H. U. Reissig, *Synlett*, 1991, 179; I. Kuwajima, S. Sugahara and J. Enda, *Tetrahedron Lett.*, 1983, **24**, 1061; A. J. Bridges and R. D. Thomas, *J. Chem. Soc., Chem. Commun.*, 1984, 694; P. Magnus and P. Albaugh-Robertson, *J. Chem. Soc., Chem. Commun.*, 1984, 804; R. Gelin, S. Gelin and M. Albrand, *Bull. Soc. Chim. Fr.*, 1972, 1946; L. Olsson and A. Claesson, *Synthesis*, 1979, 743; P. L., Beaulieu, V. M. Morisset and D. G. Garratt, *Tetrahedron Lett.*, 1980, **21**, 129; J. A. Marshall and E. D. Robinson, *J. Org. Chem.*, 1990, **55**, 3450.

4 M. Okabe, M. Abe and M. Tada, *J. Org. Chem.*, 1982, **47**, 1775; S. Torii, T. Inokuchi and T. Yukawa, *J. Org. Chem.*, 1985, **50**, 5875; K. Nozaki, K. Oshima and K. Utimoto, *J. Am. Chem. Soc.*, 1987, **109**, 2547.

5 R. Paul, M. Fluchaire and G. Collardeau, *Bull. Soc. Chim. Fr.*, 1950, 668.

6 W. Hoffmann and H. Pasedach, *Ger. Pat.*, 1,248,669, 1967, (*Chem. Abstr.*, 1968, **68**, 29574e).

7 J. P. Dulcère, M. N. Mihoubi and J. Rodriguez, *J. Chem. Soc., Chem. Commun.*, 1988, 237; J. P. Dulcère, M. N. Mihoubi and J. Rodriguez, *Nat. Prod. Lett.*, 1992, **1**, 209; J. P. Dulcère, M. N. Mihoubi and J. Rodriguez, *J. Org. Chem.*, 1993, **58**, 5709.

8 T. Sato, G. Izumi and T. Imamura, *Tetrahedron Lett.*, 1975, 2191; J. M. Frincke, D. E. McIntyre and D. J. Faulkner, *Tetrahedron Lett.*, 1980, **21**, 735; S. R. Desai, V. K. Gore and S. V. Bhat, *J. Org. Chem.*, 1992, **57**, 2467.

9 Y. S. Rao, *Chem. Rev.*, 1976, **76**, 625; T. Kametami, M. Kigawa, M. Tsubuki and T. Honda, *J. Chem. Soc., Perkin Trans. 1*, 1988, 1503; G. L. Larson, J. A. Prieto and P. Gonzalez, *Synth. Commun.*, 1989, **19**, 2779; Y. Nagao, W. M. Dai, M. Ochiai and M. Shiro, *J. Org. Chem.*, 1989, **54**, 5211, and references cited therein.