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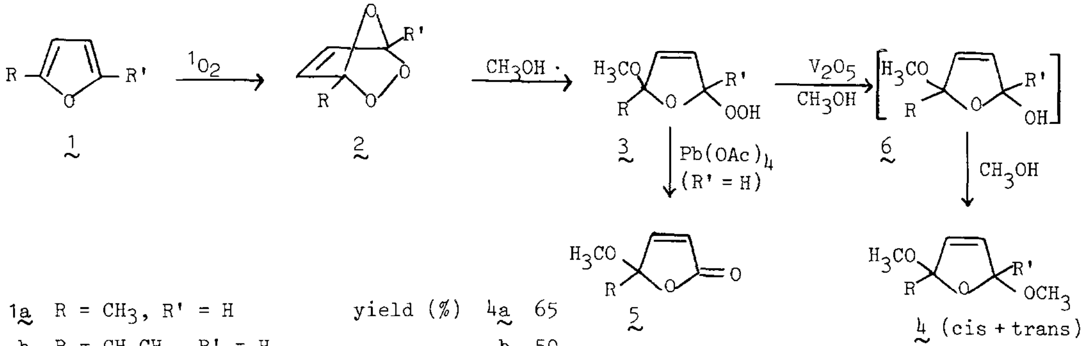
A PHOTO-OXIDATIVE ANALOGUE OF THE CLAUSON-KAAS REACTION

Ben L. Feringa* and Robert J. Butselaar

KONINKLIJKE/SHELL-LABORATORIUM, AMSTERDAM
(Shell Research B.V.), The Netherlands

2,5-Dimethoxy- 2,5-dihydrofurans and spiroketals are obtained upon V_2O_5-catalysed degradation of hydroperoxides formed in furan photo-oxidations.

The oxidation of furans with singlet oxygen is widely applied to provide multifunctional building blocks in natural product syntheses[1]. Upon photo-oxidation of alkyl-furans (1) in nucleophilic solvents such as methanol, hydroperoxides 3 are formed (Scheme 1)[1,2]. We now report a novel conversion of alkyl-furans into dimethoxydihydrofurans (4) via photo-oxidation followed by vanadium pentoxide-catalysed degradation of hydroperoxides 3.



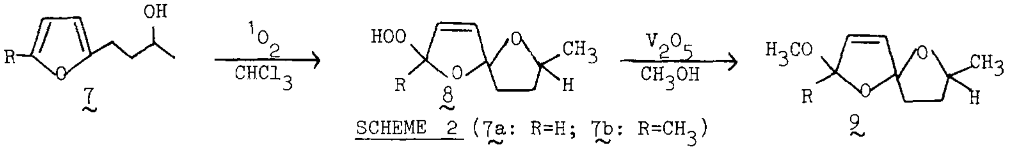
		yield (%)	
1a	$R = CH_3$, R' = H	4a	65
b	$R = CH_2CH_3$, R' = H	b	50
c	$R = R' = CH_3$	c	72
d	$R = CH_2CH_2\underset{\underset{O}{\|}}{C}CH_3$, R' = H	d	30

SCHEME 1

When a methanolic solution of 2-methylfuran (1a) is photo-oxidized using Rose Bengal as a sensitizer and subsequently stirred at room temperature with a catalytic amount (0.5-1 % mol) of V_2O_5 for 20 h, a mixture of dimethoxydihydrofurans (4a; diastereomer ratio 3:2) is formed in 65 % yield. They are easily separated from the only by-product, γ-butyrolactone 5a, by distillation or chromatography[3a]. The results of the combined photo-oxidations and V_2O_5-catalysed reactions of a few other substituted furans are summarized[3b,c] in Scheme 1. Products 4 are presumably formed via V_2O_5-catalysed degradation[5] of hydroperoxide 3 to hemiacetal 6, followed by acid-catalysed acetalization.

The novel conversion of substituted furans (1) into dimethoxydihydrofurans (4), which are generally used as protected 1,4-dicarbonylsynthons, represents a photo-oxidative analogue of the Clauson-Kaas reaction[4]. The photo-oxidative route has the advantage that it can be effected under mild oxidizing conditions without requiring large quantities of bromine.

In keeping with the preferred addition of methanol to the most hindered site of 2, the photo-oxidation product of 4-(2-furyl)-2-butanol (7a) undergoes an intramolecular attack by the hydroxyl group to give the spirohydroperoxide 8a in quantitative yield. Treatment of 8a with V_2O_5 (1 % mol) in CH_3OH gives the acetal-spiroketal compound 9a (72 %; isolated via distillation[6], b.p. 35-50 °C, 0.05 torr) as a mixture of diastereomers with approximately 1 : 1.2 : 1.7 : 1.8 ratio[7].



SCHEME 2 (7a: R=H; 7b: R=CH_3)

Analogously we obtained the spiroketal-ketal-functionalized compound 9b (diastereomer ratio approximately 1 : 1.5 : 2.4 : 2.5) in > 90 % yield from 7b. Spiroketal functionalities as present in 9a,b are common structural units of many natural products, especially ionophoric antibiotics.

NOTES AND REFERENCES

1. G. Ohloff, Pure Appl. Chem. 43, 481 (1975); H.H. Wasserman and J.L. Ives, Tetrahedron, 37, 1825 (1981).

2. B.L. Feringa, Tetrahedron Lett. 1981, 1443; B.L. Feringa and R.J. Butselaar, ibid., 1981, 1447.

3a. γ-Butyrolactone 5a is obtained as the main product by treatment of 3a with stoichiometric amounts of $Pb(OAc)_4$ in acetic acid or with stoichiometric amounts of V_2O_5 in methanol[1].

3b. 4d: ^{1}H-NMR(CD_3OD); δ = 2.03 (t, J = 7Hz, 2H), 2.15 (s, 3H), 2.55 (t, J = 7Hz. 2H) 3.11, 3.18 (2xs, 3H), 3.46, 3.50 (2xs, 3H), 5.49, 5.79 (2xt, J ≈ 1Hz, 1H) 6.04 (AB quartet, J = 6Hz, J ≈ 1Hz, 2H); ^{13}C-NMR($CDCl_3$) δ = 29.8, 30.0, 32.7, 33.1, 37.9, 38.2, 49.7, 50.4, 55.6, 56.2, 107.1, 108.3, 113.4, 114.8, 131.1, 131.2, 133.3, 133.4, 208.3. MS: (CI)(NH_3) $[M+1]^+$ at m/e 201.

3c. Products 4a-c were independently prepared by existing procedures[4].

4. For a review, see: N.L. Weinberg and H.R. Weinberg, Chem. Rev., 68, 459 (1968).

5. R.A. Sheldon and J.K. Kochi, Oxidation and Combustion Revs., 5 (1973) 135.

6. The only by-product is a spiroketal-γ-butyrolactone, which can also be obtained as the major product using $Pb(OAc)_4$: H. Fukado, M. Takeda, Y. Sato and O. Mitsunobu, Synthesis, 79, 368 (1979).

7. 9a: ^{1}H-NMR($CDCl_3$): δ = 1.13 (d, J = 6Hz), 1.25 (d, J = 6Hz) (together 3H), 2.0 (m, 4H), 3.25, 3.27 (2xs, 3H), 4.25 (m, 1H), 5.54, 5.75 (2xs, 1H) 5.93 (broad s, 2H); ^{13}C-NMR: δ = 21.1, 21.3, 22.0, 22.5; 31.9, 32.2, 32.6; 35.8, 36.7, 37.5, 38.4; 52.5, 53.3, 54.1, 54.3; 75.70, 75.73, 77.2, 77.3; 106.0, 106.3, 107.3, 107.6; 116.5, 116.8, 118.3; 129.6, 130.1, 130.2, 130.3; 134.2, 134.5, 134.6, 134.7.

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