1-Nitro-1-phenylthiopropene, a New Reagent for 3-Methylfuran Synthesis

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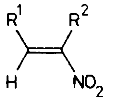
Summary The preparation of 1-nitro-1-phenylthiopropene and its reaction with 1,3-diones leading to 3-methylfurans are described.

ALIPHATIC nitro-olefins, readily available from nitroalkanes and aldehydes, are useful Michael acceptors and have recently been used in simple syntheses of 1,4-diones[1,2] and 3-acylfurans.[2,3]

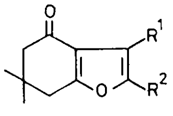
As shown recently,[3] nitro-olefins bearing an α-alkyl substituent, such as 2-nitropropene[1] (**1a**), 2-nitrobut-1-ene[1] (**1b**), and 2-nitrobut-2-ene[1] (**1c**), react with 1,3-dicarbonyl compounds, *e.g.* dimedone (**5a**), in the presence of KF in hot xylene or dimethoxyethane to give 2-alkylfurans (**2a**—**c**) in moderate to good yields. However, the reaction of dimedone with 1-nitropropene† (**1d**) which has no α-alkyl substituent did not give the expected 3-methylfuran (**2d**) under similar conditions.

We have now extended the scope of this type of reaction to provide a convenient synthetic method for 3-alkylfuran derivatives, which can be applied to the synthesis of natural furanoids. Here we report the preparation of 1-nitro-1-phenylthiopropene (**1e**) and its reaction with 1,3-diones leading to 3-methylfurans. The nitro-olefin (**1e**) was conveniently prepared as follows; addition of n-propyl nitrate (3 mol. equiv.) to the dianion[4] of phenylthioacetic acid at 0 °C in tetrahydrofuran, followed by acidification with dilute HCl, gave nitro(phenylthio)methane[5] (**3**; 53%) with evolution of CO_2. Nitro-aldol condensation of (**3**) and acetaldehyde (1·3 mol. equiv.) with 5% methanolic KOH (1 mol. equiv.) at −10 °C for 1 h and then at 0 °C for 7 h, followed by neutralisation with AcOH (1·1 mol. equiv.) gave the nitro-alcohol (**4**; 81%) [b.p. 90—98 °C (bath temp.) at 0·3 mmHg]. Since dehydration of (**4**) by McMurry's method[6] gave low and variable yields (30—48%) of (**1e**) [b.p. 70—75 °C (bath temp.) at 0·1 mmHg], the procedure was modified. Thus, (**4**) was added to a solution of $MeSO_2Cl$ (3 mol. equiv.) and Et_3N (3 mol. equiv.) in CH_2Cl_2 at −78 °C and the mixture was then warmed to 0 °C to give (**1e**) in 80% (reproducible) yield.‡

The reaction of (**1e**) and 1,3-diones was carried out as described previously.[2,3] A suspension of dimedone (**5a**), KF (0·2 mol. equiv.), and (**1e**) (1·2 mol. equiv.) in xylene was heated at 110 °C for 8 h to afford a 1:4 diastereoisomeric mixture of the dihydrofurans (**6a**) and (**6b**) as the major product (71%) in addition to the 2-(phenylthio)furan (**7a**; 10%). This result is different from that in the reaction of (**5a**) and (**1a**) leading to the direct formation of the furan derivative (**2a**).[2,3] After separation, both isomers (**6a**) and (**6b**) were converted into the same furan (**7b**) in high yields. Oxidation of (**6a**) with $NaIO_4$ in aq. MeOH to the corresponding sulphoxide and subsequent elimination of benzenesulphenic acid in refluxing CCl_4 containing pyridine afforded the 3-methylfuran derivative (**7b**; 91% overall yield). The *cis*-isomer (**6b**) was also similarly transformed into (**7b**) (83% overall yield), although active alumina had to be added in the second step to cause epimerisation of the *cis*-sulphoxide to the *trans*-isomer prior to *syn*-elimination of the sulphenic acid.



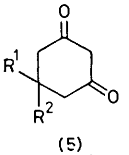
(1)
a; R^1=H, R^2=Me
b; R^1=H, R^2=Et
c; R^1=R^2= Me
d; R^1=Me, R^2= H
e; R^1=Me, R^2= SPh



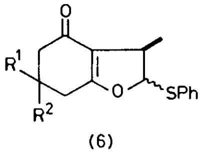
(2)

$PhSCH_2NO_2$
(3)

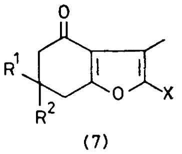
$HOCHMeCH(NO_2)SPh$
(4)



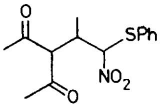
(5)
a; R^1 = R^2= Me
b; R^1 =Me, R^2=H



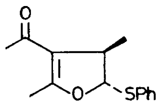
(6)
a; R^1 = R^2= Me, α-SPh
b; R^1 = R^2= Me, β-SPh
c; R^1 = Me, R^2=H, α-SPh
d; R^1 =Me, R^2=H, β-SPh



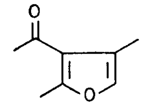
(7)
a; R^1 = R^2=Me, X = SPh
b; R^1= R^2=Me, X = H
c; R^1= Me, R^2= H, X = SPh
d; R^1= Me, R^2=H, X = H



(8)



(9)



(10)

The success of this new furan synthesis was further illustrated by the synthesis of evodone (**7d**),[7] a naturally occurring furano-monoterpene. The KF-catalysed reaction of (**5b**) with (**1e**) produced an 18:82 mixture of (**6c**) and (**6d**) (63%) along with (**7c**) (6%). By the reaction sequence described above, both the stereoisomers (**6c**) and (**6d**) were transformed into (±)-evodone (**7d**) in 74 and 70% yields, respectively.[8]

In contrast to cyclic diones, acetylacetone afforded the normal Michael adduct under standard conditions. When the dione was treated with (**1e**) and KF in refluxing benzene for 8 h, a mixture of two diastereoisomeric nitro-diones (**8**; 88%) was produced, although prolonged reaction at a higher temperature (110 °C, 17 h) in xylene gave a mixture of (**8**) and the dihydrofuran (**9**) (16:9) in low yield (25%).

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† This compound was prepared from 1-nitropropan-2-ol by dehydration using phthalic anhydride (see ref. 1) (58%) with exclusive formation of the *E* isomer. After unsuccessful attempts using the known procedure (P. Staub, *Helv. Chim. Acta*, 1922, **5**, 888), the nitro-alcohol was prepared by a modified procedure in good yield (80%). Details will be published elsewhere.

‡ The *Z* isomer was obtained selectively.

Treatment of (**8**) with *p*-$MeC_6H_4SO_3H$ in refluxing benzene for 4 h afforded (**9**) (44%). Oxidation of (**9**) with $NaIO_4$ followed by refluxing in ether resulted in the formation of (**10**)[9] (86% overall yield). Ready elimination of benzenesulphenic acid allows us to assign the *trans*-stereostructure as shown to the dihydrofuran (**9**).

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[1] M. Miyashita, T. Yanami, and A. Yoshikoshi, *J. Amer. Chem. Soc.*, 1976, **98**, 4679.

[2] T. Yanami, M. Kato, and A. Yoshikoshi, *J.C.S. Chem. Comm.*, 1975, 726.

[3] T. Yanami, A. Ballatore, M. Miyashita, M. Kato, and A. Yoshikoshi, *J.C.S. Perkin I*, in the press.

[4] P. E. Pfeffer and L. S. Silbert, *Tetrahedron Letters*, 1970, 699. Bu^nLi was used to generate the dianion in place of Li di-isopropylamide proposed by the original authors, giving better results.

[5] During this study, an alternative preparation of (**3**) was reported (D. Seebach and F. Lehr, *Angew. Chem.*, 1976, **88**, 540), although detailed results were not given.

[6] J. Melton and J. E. McMurry, *J. Org. Chem.*, 1975, **40**, 2138.

[7] A. J. Birch and R. W. Richards, *Austral. J. Chem.*, 1956, **9**, 241.

[8] For alternative syntheses of evodone, see H. Stetter and R. Lauterbach, *Angew. Chem.*, 1959, **71**, 673; *Chem. Ber.*, 1960, **93**, 603; A. M. Moiseekov, F. A. Lakhvich, and A. A. Akhrem, *Aktval. Probl. Izuch. Efirnomaslich. Rast. Efirn. Masel*, 1970, 159 (*Chem. Abs.*, 1972, **76**, 99847).

[9] This highly volatile furan (**10**) was isolated as its 2,4-dinitrophenylhydrazone, m.p. 174·5—175·5 °C. See also J. W. Batty, P. D. Howes, and C. J. M. Stirling, *Chem. Comm.*, 1971, 534; *J.C.S. Perkin I*, 1973, 65; P. D. Howes and C. J. M. Stirling, *Org.Synth.*, 1973, **53**, 1.