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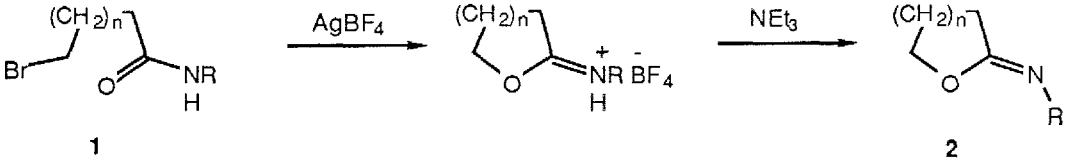
FACILE PREPARATION OF 2-IMINO TETRAHYDROFURANS, PYRANS AND OXEPANS

Alex I. D. Alanine, Colin W.G. Fishwick*, and Csaba Szantay Jr.[1]
School of Chemistry, The University of Leeds, Leeds LS2 9JT.

Summary: a simple and convenient route to 2-imino tetrahydrofurans, pyrans and oxepans which utilizes a silver-assisted intramolecular O-alkylation has been developed and produces these novel imidates in good yields and with high stereoselectivity.

In connection with our studies on the chemistry of azomethine imidate methylides[2] we required access to cyclic imidates of general type **2** (scheme). Inspection of the literature however, revealed the absence of satisfactory routes to these systems.[3] We describe below a simple, convenient, and high-yielding route to these imidates based on a silver-assisted intramolecular O-alkylation from readily available precursors **1** (scheme). In the following paper, we describe the application of these systems to the generation and cycloadditions of novel azomethine imidate methylides.



1 **2**

Scheme

As a general procedure, silver tetrafluoroborate (6mmol) is added to a stirred solution of the amide **1**[4] (6mmol) in anhydrous acetone (30ml) under argon and this mixture is then stirred in the dark for the times indicated in the table. Triethylamine (7.2mmol, 1ml) is then added and after stirring for 5min., ether (20ml) is added and the solution is filtered and washed rapidly with distilled water (2 x 10ml), followed by brine (2 x 10ml). After drying (Na_2SO_4), rapid filtration, and evaporation, the pure imidates were obtained after Kugelrhor distillation. The results of a number of experiments are summarized in the table.

As indicated in the table, cyclizations involving N-alkyl amides (entries 1,3,4,5,7,8,9,10 and 11) are stereospecific and yield the Z-imidates exclusively.[5] Formation of the N-phenyl imidates is less selective but also favours the Z-isomers (entries 2 and 6).

This represents a simple and straightforward method for the preparation of a range of novel imidate systems.

Table. Cyclization of ω-bromo alkylamides **1**.

entry	precursor **1**[a]	time (hr)	product **2**[a,b]	bpt(°C/mmHg)	yield(%)
1	n = 1, R = CH_2Ph	2	n = 1, R = CH_2Ph	106-7/0.02	90
2	n = 1, R = Ph	2	n = 1, R = Ph	104-5/0.02	80[c]
3	n = 1, R = $(CH_2)_3CH_3$	1	n = 1, R = $(CH_2)_3CH_3$	60-1/0.15	81
4	n = 1, R = CH_2SiMe_3	1	n = 1, R = CH_2SiMe_3	60/1.0	88
5	n = 2, R = CH_2Ph	16	n = 2, R = CH_2Ph	126-8/0.02	95
6	n = 2, R = Ph	16	n = 2, R = Ph	115-7/0.02	58[d]
7	n = 2, R = $(CH_2)_3CH_3$	4	n = 2, R = $(CH_2)_3CH_3$	81/0.05	86
8	n = 2, R = CH_2SiMe_3	4	n = 2, R = CH_2SiMe_3	78-9/1.0	95
9	n = 3, R = CH_2Ph	96	n = 2, R = CH_2Ph	127/0.02	83
10	n = 3, R = $(CH_2)_3CH_3$	24	n = 3, R = $(CH_2)_3CH_3$	68/0.01	79
11	n = 3, R = CH_2SiMe_3	24	n = 3, R = CH_2SiMe_3	85/0.02	93

[a] All new compounds gave satisfactory IR, NMR and mass spectral data consistent with the proposed structures. [b] Imidates **2** have the Z stereochemistry exclusively unless otherwise stated. [c] Obtained as a 3:1 mixture of Z and E isomers respectively. [d] Obtained as a 4:1 mixture of Z and E isomers respectively.

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References and notes

1. On leave from the NMR laboratory of the Institute for General and Analytical Chemistry, Technical University, H-1521 Budapest, Hungary.
2. Alanine, A. I. D.; Fishwick, C. W. G. *Tetrahedron Lett.*, **1989**, *30*, 4443.
3. Sterling, C. B. M. *J. Chem. Soc.*, **1960**, 255.
4. Prepared in quantitative yields by stirring a solution of the commercially available acid chlorides and amines (1 equiv.) with triethylamine (1 equiv.) in anhydrous ether for 20 min. For 4-bromobutyroyl amides **1**, n = 1, slow addition of the amines is essential to avoid the formation of substantial amounts of cyclopropyl amides.
5. For the N-phenyl tetrahydrofuranoyl imidate **2**, n = 1, R = Ph, NMR investigations of the E-isomer revealed a distinct NOE connection (steady-state experiment, non-degassed sample) between the phenyl o-protons and the ring α-CH_2's which was totally absent for the Z isomer. For the N-alkyl imidates, the NOE experiments revealed no NOE contact between the NCH_2 and the ring α-CH_2 protons. This result is consistent with the preference of the Z isomer, which is in keeping with earlier observations on simpler imidate systems - see Moriarty, R. M.; Yeh, C.-L.; Ramey, K. C.; Whitehurst, P. W. *J. Am. Chem. Soc.*, **1970**, *92*, 6360.

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