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THE USE OF ACYL DERIVATIVES OF N-HYDROXY-2-THIOPYRIDONE IN A SIMPLE SYNTHESIS OF PYRROLIDINES AND TETRAHYDROFURANS

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Summary. Photolysis of the N-hydroxy-2-thiopyridone derivatives of 3-N-acetylallylamino, 3-N,N-diallylamino and 3-allyloxy-propionic acids gave cleanly derivatives of N-acetyl-3-methylpyrrolidine, N-allyl-3-methylpirrolidine and of 3-methyltetrahydrofuran respectively. The corresponding reaction with 3-allylthiopropionic acid afforded a radical which fragmented to ethylene and the allylthio radical without cyclization.

Five membered rings, both carbocyclic and heterocyclic are readily synthesized by radical cyclization of aliphatic precursors[1,2]. Most of this work has involved standard tin hydride generation of carbon radicals. However the Kolbe reaction has recently been used and after cyclization, the radical has been coupled with a radical from a second acid[3].

Recently, pyrrolidine rings have been prepared in an ingenious application of N-hydroxy-2-thiopyridone acylcarbamate derivatives[4]. We would like to report our own studies using simple acyl derivatives of N-hydroxy-2-thiopyridone as a convenient source of carbon radicals[5].

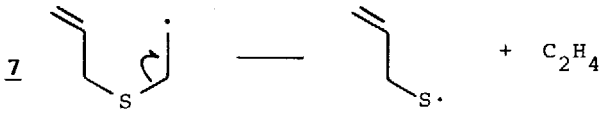
Addition of allylamine to ethyl acrylate (25°C, 2 days) gave 3-allylaminopropionic acid ethyl ester (53%). Acetylation gave the N-acetyl derivative (96%). Hydrolysis and conversion[6] to the deriva-

tive of N-hydroxyl-pyridine-2-thione gave the yellow acyl derivative **1a**. Photolysis at 0°C in methylene dichloride for about 70 min of 6 mmoles of **1a** gave the cyclised product **2a** in 77% yield. Reduction of the latter with nickel boride in the presence of boric acid[7] afforded N-acetyl-methylpyrrolidine **3a** (60-64%).

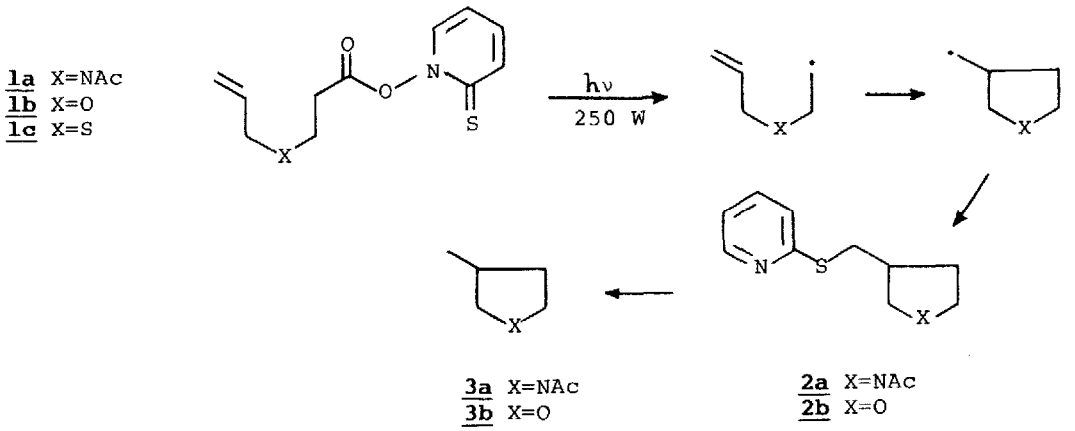
Similarly, the N-hydroxy-2-thiopyridone derivative **1b** of 3-allyloxy-propionic acid[8] was converted to the cyclised product **2b**. Reduction as above afforded 3-methyl-tetrahydrofuran[9] **3b**. In both these cyclizations there was no sign of endo cyclization to give six membered ring compounds[10]. The cyclization process passes through two intermediate radicals and the chain is carried in the usual way[5], so that the products are thiopyridyl derivatives (Scheme 1).

In analogous manner described above for **1a**, 3-N,N-diallylaminopropionic acid was prepared by hydrolisis of corresponding ethyl ester obtained from diallylamine and ethyl acrylate (76%). In our opinion a tandem radical cyclization could take place leading to aza-bicyclooctane derivative **5** as depicted in Scheme 2. Photolysis of **4** (prepared as **1a**) as camphorsulphonate at 0°C in dichloromethane for 60 min gave only the N-allylpyrrolidine derivative **6** (68%). This result is in agreement with data reported by Beckwith and coll.[11] in their attempt to prepare bicyclo [3.2.1.] octanes via radical reactions.

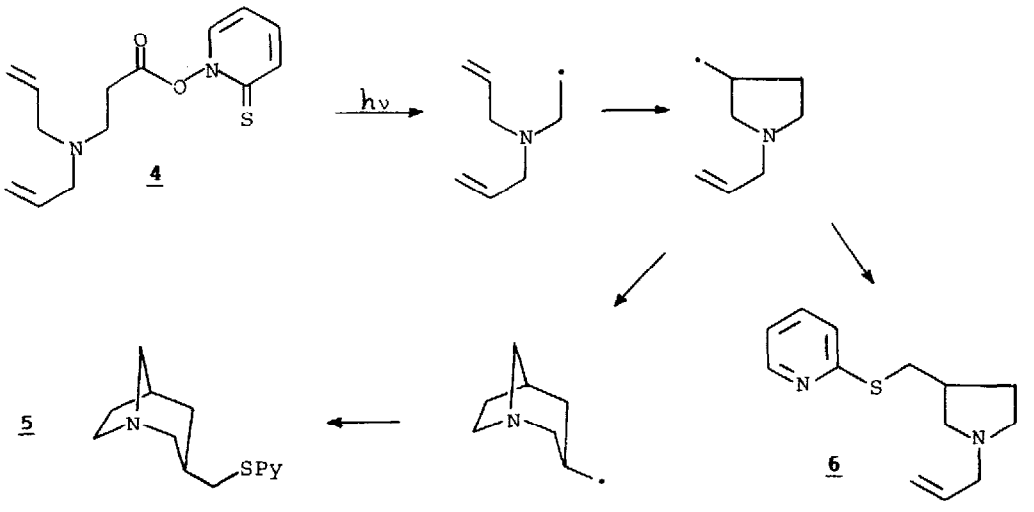
An attempt to prepare thiophane derivatives did not lead to cyclization. Thus, 3-allylthiopropionic acid[12] was converted to its N-hydroxy2-thiopyridone derivative **1c** without difficulty. Photolysis in the usual way gave no cyclic product. 2,2'-Dipyridyldisulphide (18%) and 2-pyridyl-S-allyldisulphide (33%) could be characterized. Clearly, the intermediate radical **7** had fragmented to ethylene and the allylsulphide radical faster than it had cyclized. In fact, this reaction should give sulphide radicals in a very controlled way and without the need of an oxidant. Of course, β-elimination of sulphide radicals is a wellknown reaction[13].



Scheme 1



Scheme 2



REFERENCES

1. A.J.L.Beckwith, Tetrahedron, 37, 3073 (1981); D.P.Curran and S.C.Kuo, J.Am.Chem.Soc., 108, 1106 (1986); G.Stork and N.H. Baine, Tetrahedron Lett., 26, 5927 (1985).
2. Y.Ueno, K.Chino, M.Watamabe, O.Moriya and M.Oxawara, J.Am.Chem. Soc., 104, 5564 (1982); G.Stork and M.Kahn, ibid., 107, 500 (1985); D.J.Hart and J.M.Tsai, ibid., 106, 8209 (1984); J.K. Choi and D.J.Hart, Tetrahedron, 41, 3959 (1985); A.Padwa, H.Nimmesgern and G.S.K.Wong, J.Org.Chem., 50, 5620 (1985)
3. L.Becking and H.J.Shäfer, Tetrahedron Lett., 29, 2797, 2801 (1988); M.Huhtasaari, H.J.Shäfer and L.Becking, Angew.Chem. Int.Ed.Engl., 23, 980 (1984).
4. M.Newcomb and T.M.Deeb, J.Am.Chem.Soc., 109, 3163 (1987).
5. D.H.R.Barton, D.Crich and W.B.Motherwell, Tetrahedron, 41, 3901 (1985); idem, J.Chem.Soc., Chem.Commun., 939 (1983); D.H.R.Barton, S.Z.Zard, E.Castagnino, S.Corsano, Tetrahedron Lett., 27, 6337 (1986); S.Corsano, G.Strappaghetti, D.H.R. Barton and E.Castagnino, J.Chem.Res., 219 (1988).
6. As in the preparation of peptide analogues, see D.H.R.Barton, Y.Hervé, P.Potier and J.Thierry, Tetrahedron, 43, 4297 (1987); ibid., 44 5479 (1988).
7. R.B.Boar, D.W.Hawkins, J.F.Mc Ghie and D.H.R.Barton, J.Chem. Soc., Perkin I, 654 (1973).
8. K.Nakamura, S.Masuda and N.Takaishi, Chem.Abs., 106, 4529j (1987)
9. References to 3-methyltetrahydrofuran.
10. J.E.Baldwin, J.Chem.Soc.,Chem.Commun., 734 (1976); A.L.J. Beckwith, C.J.Easton and A.K.Sevelis, ibid., 482 (1980).
11. A.L.J.Beckwith and G.Moad, J.Chem.Soc., Perkin II, 1726 (1975).
12. J.Bowie, Austr.J.Chem., 22, 1207 (1969).
13. T.E.Boothe, J.L.Green Jr. and P.B.Shevlin, J.Org.Chem., 45, 794 (1988); P.J.Wagner, J.H.Sedom and M.J.Lindstrom, J.Am.Chem.Soc., 100, 2579 (1978); C.Wallings and W.Helmreich, ibid., 81, 1144 (1959); R.A.Jackson, K.U.Ingold, D.Griller and A.S.Nazran, ibid., 107, 208 (1985) and references there cited.

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