Tetrahedron Letters, Vol.31, No.14, pp 1965-1968, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

FURTHER STUDIES ON CARBON-CARBON BOND FORMATION BASED ON THE RADICAL REACTIONS OF ACYL DERIVATIVES OF *N*-HYDROXY-2-THIOPYRIDONE

Derek H.R. Barton* and Jadab C. Sarma

Department of Chemistry, Texas A&M University, College Station, Texas 77843, U.S.A.

Abstract - By careful exclusion of oxygen, carbon radicals, generated from the W lamp photolysis of *O*-acyl derivatives of *N*-hydroxy-2-thiopyridone, can be added efficiently to methylvinyl ketone. Extension to the radical from pent-4-enoic acid provides another synthesis of cyclopentane derivatives. Analogous additions with other electrophilic olefins are also reported.

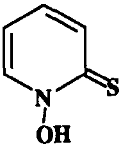
The acyl derivatives of thiohydroxamic acids are an excellent source of carbon radicals.[1,2] In earlier studies[1] we generated the radicals by heating the precursors under reflux in benzene or in toluene. Later we realised[3] that the room temperature photolysis (W light) of the acyl derivatives of the inexpensive *N*-hydroxy-2-thiopyridone **1** is a milder procedure and gives higher yields. This methodology was used in all the peptide chemistry carried out in collaboration with Prof. Potier.[4] Others have also developed the same technique.[5,6,7]

In our original studies[8] on carbon-carbon bond formation we used both photochemical and thermal activation. Amongst the olefinic radical acceptors methylvinyl ketone afforded only 40% of adduct, based on the acyl derivative **2**. Recently we had occasion to look again at addition to methylvinyl ketone. Using the acyl derivative **3** as a standard radical source, we varied systematically the ratio of **3** to methylvinyl ketone. Besides small amounts of the rearrangement product **4**, the dimer **5** was the principal by-product.

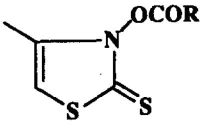
The optimum methylvinyl ketone concentration was close to 5 mmol for 1 mmol of **3**. The yields were much better than those we obtained before. This is due to complete displacement of all oxygen by argon. The previous experiments[8] were done under nitrogen. We did not appreciate how sensitive radicals of type **6** are towards traces of oxygen.

Further results are shown in Table 1. In each case the adduct from methylvinyl ketone was obtained in a satisfactory yield. Entries 3 and 5 deal with the phenoxymethyl and β-acetylethyl radicals respectively. The latter is, of course, from the readily available levulinic acid. We had not used either of these radicals before.

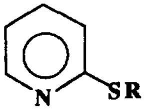
Oxidation of adducts **11** through **15** with *m*-chloroperbenoic acid afforded in the usual way[1] the corresponding sulfoxides, which on refluxing in benzene gave the corresponding unsaturated ketones **16** through **20** in good yield. As usual[1] all the olefins were of *trans*-configuration. Ketone **17**[9] and ketone **20**[10] are known already.



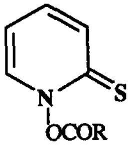
1



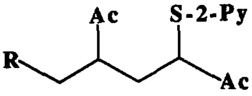
2 R=$CH_3(CH_2)_{14}$



4 R = $CH_3(CH_2)_{14}$

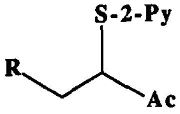


3 R = $CH_3(CH_2)_{14}$
7 R = $PhCH_2CH_2$
8 R = $PhOCH_2$
9 R = 1-Adamantanyl
10 R = $CH_3COCH_2CH_2$
22 R = CH_2=CH-CH_2-CH_2

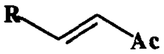


5 R = $CH_3(CH_2)_{14}$

6 R = $CH_3(CH_2)_{14}$



11 R = $CH_3(CH_2)_{14}$
12 R = $PhCH_2CH_2$
13 R = $PhOCH_2$
14 R = 1-Adamantanyl
15 R = $CH_3COCH_2CH_2$



16 R = $CH_3(CH_2)_{14}$
17 R = $PhCH_2CH_2$
18 R = $PhOCH_2$
19 R = 1-Adamantanyl
20 R = $CH_3COCH_2CH_2$

Table 1[a]

Entry	Acyl Derivative[b]	Adduct (%)[c]	Unsaturated ketone (%)
1	**3**	**11** (79)	**16** (85)
2	**7**	**12** (75)	**17** (79)
3	**8**	**13** (81)	**18** (78)
4	**9**	**14** (77)	**19** (69)
5	**10**	**15** (68)	**20** (70)

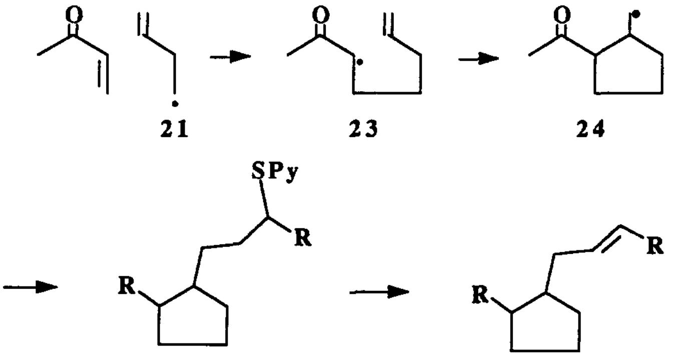
a) Typical Experiment. To 3 (2 mmol) in dry CH_2Cl_2 (10 ml) under argon was added methylvinyl ketone (10 mmol). The solution was irradiated with a 150 watt (W) lamp at 0-5°, monitoring the reaction by T.L.C. In all additions 5 equiv. of methyvinyl ketone were used.

b) Acyl derivatives were prepared from the appropriate acid chloride (3, 7, 8, 9) or from the acid (10) by the D.C.C. method.[1]

c) All compounds gave satisfactory N.M.R., I.R., M.S. and high resolution M.S. spectra.

This work shows that methylvinyl ketone is a good trap for carbon radicals. It could provide a radical alternative to the Mannich-Robinson procedure.

We also examined methylvinyl ketone as an acceptor for the γ-butenyl radical 21 derived from the pent-4-enoic acid derivative **22**. According to precedent[11] addition of **21** will afford the electrophilic radical **23**, which wil readily cyclise to nucleophilic radical **24**. There is then a second addition and the final product is **25** (61%) as a mixture of isomers. We then studied other electrophilic olefins to afford compounds **26** through **29** in yields of 50, 60, 57 and 55% respectively.



21 **23** **24**

25	R = COMe	**30**	R = COMe
26	R = SO_2Ph	**31**	R = SO_2Ph
27	R = CN	**32**	R = CN
28	R = CO_2Me	**33**	R = CO_2Me
29	R = $CO_2Ad(2)$	**34**	R = $CO_2Ad(2)$

As before, oxidation of **25** through **29** afforded the corresponding sulfoxides which on thermal elimination (benzene reflux) gave the olefins **30** through **34** in yields of 77, 80, 81, 88 and 74% respectively. Formulae **29** and **34** refer to derivatives of adamantan-2-ol.

Our work complements the well known method of Stork[12] using methyl trimethylsilylvinyl ketone.

Acknowledgements. We thank the N.I.H. and the Welch Foundation for their support of this work.

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(Received in USA 28 November 1989)