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RADICAL CHEMISTRY OF THIOHYDROXAMIC ACID ESTERS

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Abstract : Thiohydroxamic esters in general decompose smoothly by a radical chain reaction to give carbon radicals which can be quenched in a synthetically useful manner.

We have recently reported[1,2] that the esters of N-hydroxy-2-thiopyridone (1) decompose smoothly at moderate temperatures to give carbon radicals which can be captured by a number of additives to give synthetically useful products. In the absence of additives a chain reaction produces a decarboxylative rearrangement as shown in (2) giving (3).

The thiopyridone (1) is expensive. We are glad to report that the chemistry we have observed is a general reactivity of thiohydroxamic esters and that inexpensive starting materials can be used.

We have studied three thiohydroxamic acids (4), (5) and (6). The compounds (4)[3] and (5)[4] are already known. Compound (6) was prepared easily from chloroacetone by reaction with ethyl xanthate anion to give the ketone (7)[5] (80%). The oxime (8) of this compound, m.p. 59-60°, was prepared in the usual way (85%). On treatment with aqueous potassium hydroxide[6] at 0° in CH_2Cl_2 (vigorous stirring) this oxime gave (6)[7], m.p. 93-94° (79%). Compounds (4), (5) and (6) were converted into their palmitoyl derivatives (9), (10) and (11) in 99, 96 and 94% yield using standard procedures[1]. These derivatives were then examined for their suitability (entries 1-3) for the thermal decarboxylative rearrangement [(2) → (3)]. The ester (11) rearranged readily to give the expected[1] product (17). The esters (9) and (10) rearranged at higher temperatures and gave lower yields of the expected products (12) and (14).

The reduction[1] of the esters (9), (10) and (11) by hydrogen atom transfer from t-butyl thiol was also examined (entries 4-7). The compounds (9) and (11) gave excellent yields of pentadecane (16), but (10) was more difficult to reduce. The expected[1] second product from these reactions is the product of t-butylthiyl radical transfer. In only one case (from (11) was this type of product (20) isolated in good yield. We synthesised the other two disulphides expected (19) and (25) and showed that they were unstable under the conditions of the reaction in the presence of t-butylthiol. Under these conditions the observed sulphur containing products were obtained. It is thus clear that all the reduction reactions follow the precedent[1] already established.

Finally, we examined the three esters (9), (10) and (11) for their capacity (entries 8-11) to give the type of Hunsdiecker products obtained earlier[2] with esters of type (2). Esters (9) and (11) gave excellent yields of Hunsdiecker product but (10) did not react. From ester (11) we isolated in good yield the expected[2] trichloromethyl derivative (23).

The driving force[8,9] for the fragmentation of thiohydroxamic esters is the conversion of thiocarbonyl to carbonyl and, in appropriate cases, the energy of aromatisation in going to product. Reactions of esters of types (2) and (11) are aided by both types of driving force. Esters of type (9) have only the first factor in their favour, those of type (10) have the same factor plus a minor aromatisation driving force.

The facts here reported are in agreement with this analysis and it is clear that compound (6) is an excellent, inexpensive alternative to compound (1) for the generation of radicals in preparatively useful quantities.

Acknowledgments

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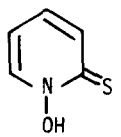

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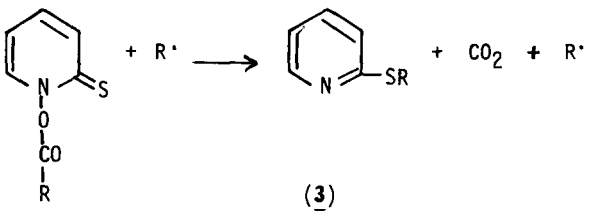

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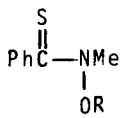

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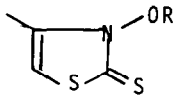
(9) R = $COC_{15}H_{31}$



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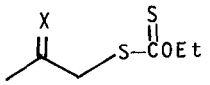
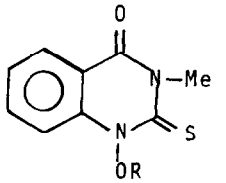
(11) R = $COC_{15}H_{31}$



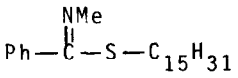
(7) X = O

(8) X = N-OH



(5) R = H

(10) R = $COC_{15}H_{31}$



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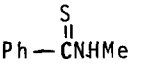

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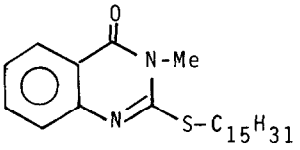

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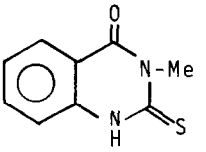

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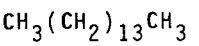

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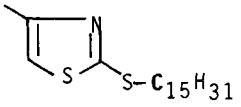

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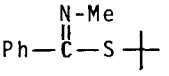

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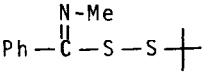

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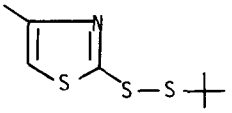

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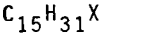
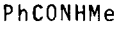


(21) X = Br

(24) X = Cl



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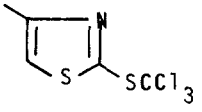

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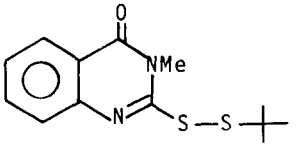

(25)

Table

Entry / Compound	Solvent etc.	Temp. ° /hrs	Products (%)
1 (**9**)	no solvent	170/3	(**12**) (60), (**13**) (21)
2 (**10**)	toluene	110/3	(**10**) recovered (91)
	xylene	140/40	(**14**) (54), (**15**) (23), (**16**) (16)
3 (**11**)	toluene	110/0.75	(**17**) (84)
	benzene	80/1.5	(**17**) (50), (**11**) (46)
4 (**9**)	benzene + t-BuSH	80/0.5	(**16**) (83), (**13**) (82)
5 (**9**)	toluene + t-BuSH	110/1	(**16**) (85), (**13**) (48), [(**18**) + (**19**)] (34)
6 (**10**)	benzene + t-BuSH	80/3	(**10**) recovered (97)
(10)	xylene + t-BuSH	140/48	(**16**) (74), (**15**) (75), (**10**) (9), (**14**) (5)
7 (11)	benzene + t-BuSH	80/2	(**16**) (90), (**20**) (92)
8 (**9**)	toluene + $BrCCl_3$	110/0.75	(**21**) (77), (**22**) (83)
9 (**10**)	toluene + $BrCCl_3$	110/4	no reaction
10 (**11**)[a]	benzene + $BrCCl_3$	80/1	(**21**) (92), (**23**) (93), (**17**) (6)
11 (**11**)[a]	toluene + CCl_4	95/2	(**24**) (82), (**23**) (74), (**17**) (13)

a : In these experiments the ester (**11**) was generated *in situ* in presence of $BrCCl_3$ or CCl_4 as already described[1,2].

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