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LIGHT INDUCED HALOGENATIVE DECARBOXYLATION OF THIOHYDROXAMIC ESTERS

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Abstract: The generality of light initiated halogenative decarboxylation of thiohydroxamic esters was studied. This method gave high yields of alkyl chlorides, bromides and iodides derived from primary, secondary and tertiairy substituted carboxylic acids.

The thermal decomposition of thiohydroxamic esters (mixed anhydrides) proceeds via a radical mechanism. The synthetic utility of this system using various radical traps has been elegantly exploited to yield a variety of functional groups.[1] Specifically, the thermolysis of a thiohydroxamic ester, derived from a carboxylic acid chloride and N-hydroxypyridine-2-thione, in CCl_4, $BrCCl_3$, or in the presence of CHI_3 gives the respective alkyl chloride, bromide or iodide. This thermal halogenative decarboxylation, developed by Barton[2] and co-workers, has proven to be useful and quite general. In our laboratories we were interested in this process for a natural product synthesis, but we wanted a technique requiring milder reaction conditions (lower temperatures).

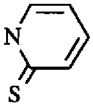
The light initiated decomposition of thiohydroxamic esters proceeds by radical fragmentation and loss of CO_2 under mild conditions.[3] The light process can be done conveniently at room temperature or at a variety of other temperatures, and this process, as shown for other reactions, proceeds in better yields than the thermal process.[4] In the literature there are examples of brominative decarboxylation of several primary acids of suitably protected amino acids/peptides and of citronellic acid using light initiation, but no extensive study exists.[5] We have, therefore, studied the generalization of the light initiated halogenative decarboxylation of thiohydroxamic esters.

The thiohydroxamic esters were prepared in good yield as previously described.[3-5] In a typical experiment, 0.1 g of ester (**1**, **7**, **11**, **15**, **17**) was dissolved (0.03 M) under N_2 in CCl_4 for chlorides, with 5.0 equivalents of $BrCCl_3$ in CCl_4 for bromides, and with 1.2 equivalents of CHI_3 in CCl_4 for iodides. The reaction mixture was irradiated at 20 °C with the appropriate light source (see Table). The reaction mixture was purified on silica gel.

Entry	Ester	hv source	product (%)
1	**1**	350 nm	**2** (96)
2	**1**	tungsten	**3** (98)
3	**1**	tungsten	**4** (94)
4	**7**	sun	**8** (81)
5	**7**	tungsten	**9** (75)
6	**7**	tungsten	**10** (56)
7	**11**	sun	**12** (86)
8	**11**	sun	**13** (75)
9	**11**	sun	**14** (85)
10	**15**	tungsten	**16** (87)
11	**17**	tungsten	**18** (88)
12	**1**	sun	**6** (67) **5** (31)

TABLE

$C_{15}H_{31}X$

1) X=CO_2 

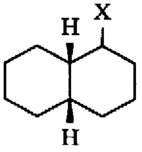
2) X= Cl

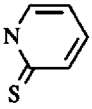
3) X= Br

4) X= I

5) X= S-Pyr

6) X= $C_{15}H_{31}$

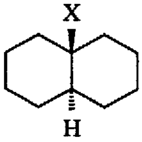


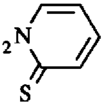
7) X= CO_2 

8) X=Cl

9) X= Br

10) X= I

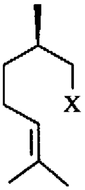


11) X= CO_2 

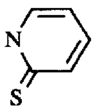
12) X= Cl

13) X= Br

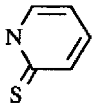
14) X= I



$CH_3(CH_2)_7CH{=}CH(CH_2)_7X$

15) X=CO$_2$ 

16) X= Br

17) X= CO$_2$ 

18) X=Cl

The UV spectrum of **1** in CCl_4 has two major bands which have maxima at 301 nm (ϵ 18,800) and 374 nm (ϵ 7,100). Thus, the wavelengths of highest utility fall in this general range. A variety of light sources (300 nm lamps in a Rayonet reactor, 350 nm lamps in a Rayonet reactor with a uranium glass filter, 250 watt tungsten reflector lamp, and the sun) were tried on **1**, and all gave the same product distribution. The reaction vessel (borosilicate test tube, quartz tube, or Pyrex flask) also had no effect on the product distribution produced from **1**. Therefore, the wavelength of light was concluded not to be important as long as it was being absorbed by ester **1** (275 nm to 430 nm). The time required for typical runs was 15-40 s in the sun, 2 min in the Rayonet reactor with 10 bulbs operating, and 5 min using the tungsten lamp.

The reaction worked well for primary (entries 1-3, 10-12), secondary (entries 4-6), and tertiary (entries 7-9) esters producing chlorides, bromides or iodides (see Table). In entries 10 and 11 the respective double bonds were unaffected. The ester of *cis-cis*-decahydro-1-naphthoic acid (**7**) gave a preponderance of the *trans-cis* over the *cis-cis* halogen containing decalins in a ratio of **8** (8/1), **9** (6/1), and **10** (3/1). The *trans*-decalin ester (**11**) gave the all *trans*-decalins (**12-14**).

The major competing side reaction was R• attacking another ester molecule instead of a $XCCl_3$ molecule (see Mechanism). The extent to which this occurred was 2-7 % for chlorides and 0-2 % for bromides.

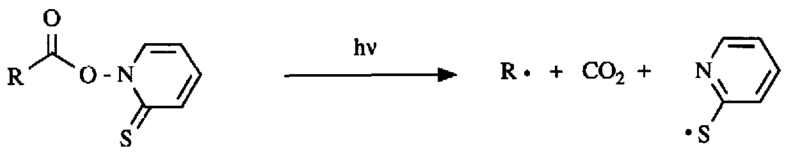
In all of the reactions producing chlorides and bromides, $C_5H_4NSCCl_3$ was isolated in 70-90 %. When the unreactive methylene choride was used as the solvent (entry 12), no chloride was formed but dimer (**6**) and thio ether (**5**) were produced. These findings are good evidence in support of the proposed mechanism.

The iodide reactions (entries 3, 6, 9) were more complex than the chloride or bromide reactions because of iodine formation during the reaction. The chain carrier could not be isolated due to its decomposition or complexation with iodine.

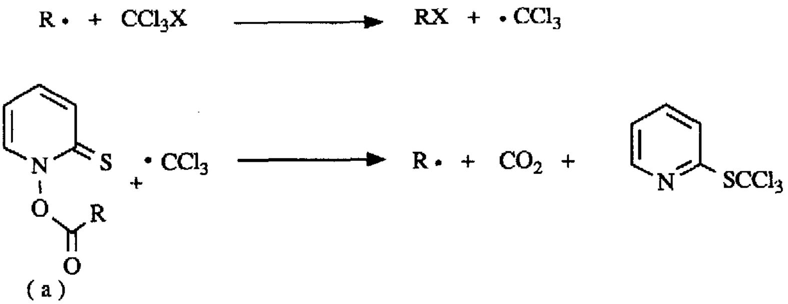
We consider the application of light to decompose thiohydroxamic esters in the presence of CCl_4, $BrCCl_3$, and CHI_3 to be a simple alternative to the thermal technique previously used. It was of note that simple sun light was an excellent source of light to initiate the reaction.

MECHANISM

Initiation



Propagation



Side Reaction

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