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A PRACTICAL ALTERNATIVE TO THE HUNSDIECKER REACTION

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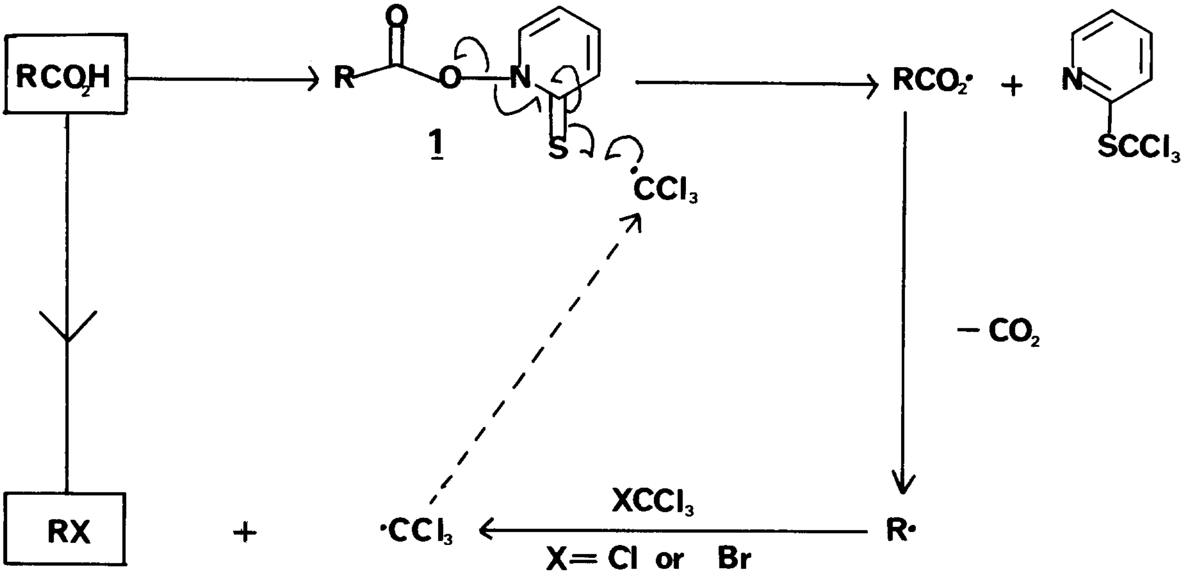
Summary.- Carboxylic acid esters derived from N-hydroxy-pyridine-2-thione react with carbon tetrachloride, bromotrichloromethane or iodoform in a radical chain reaction to give the corresponding noralkyl chlorides, bromides or iodides in high yield.

In a recent Communication[1] we have demonstrated that carboxylic acid esters (1) derived from N-hydroxy-pyridine-2-thione undergo efficient radical chain decarboxylation to the corresponding nor-alkane on heating with either tri-*n*-butyl-stannane or *tert*. butyl mercaptan. Moreover, the esters, *per se*, also suffer smooth decarboxylative rearrangement to noralkyl pyridyl sulphides[1], presumably by an analogous mechanism invoking the 2-pyridylthiyl radical as chain carrier.

Consideration of the propensity for these substrates to participate in radical chain reactions led us to speculate that use of the trichloromethyl radical as chain carrier and halogen atom abstraction by the resultant alkyl radical from carbon tetrachloride or bromotrichloromethane as solvent should therefore provide a useful method for the synthesis of alkyl halides (Scheme). With the exception of tertiary butyl hypoiodite[2], all currently used variations of the original Hunsdiecker reaction[3] use heavy metal salts such as those of mercury[4], thallium[5] and lead.[2,6]



Scheme

The results presented in the Table confirm our idea and show that high yields of primary, secondary and tertiary chlorides and bromides can be obtained in a reaction which tolerates ester and ketonic functionality. The isolation of 2-trichloromethylthiopyridine (2) in a comparable yield to that of the alkyl halide lends support to the proposed mechanistic hypothesis.

TABLE(a)

Acid	Alkyl Chloride (%)		Alkyl Bromide (%)	
(3)	(4)	70	(5)	95
(7)	(8)	72	(9)	90[b]
(11)	(12)	88[b]	(13)	98
(14)	(15)	95	-	-
(16)	-	-	(17)	72
Pivalic	Me_3C-Cl	82	-	-

a) Yields are isolated yields based on the starting carboxylic acid.

b) 2-Trichloromethylthiopyridine was isolated in 90 + 2% yield.

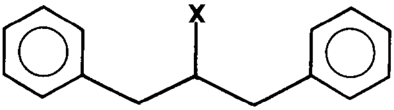
$CH_3(CH_2)_{14}X$

(3) $X=CO_2H$

(4) $X = Cl$

(5) $X = Br$

(6) $X = I$

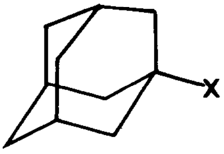


(7) $X = CO_2H$

(8) $X = Cl$

(9) $X = Br$

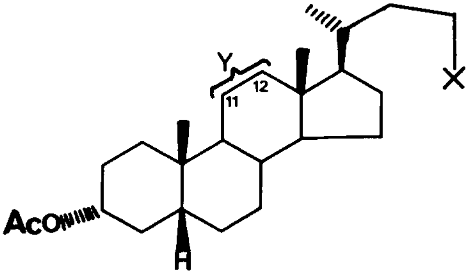
(10) $X = I$



(11) $X=CO_2H$

(12) $X= Cl$

(13) $X =Br$



(14) Y = 12α Acetoxy , $X = CO_2H$

(15) Y = 12α Acetoxy , $X = Cl$

(16) Y= 11 oxo , $X = CO_2H$

(17) Y= 11 oxo , $X = Br$

From the practical standpoint, the experiment is easily performed without isolation of the intermediate ester (**1**) by simple addition of the derived acid chloride to a refluxing suspension of the sodium salt of N-hydroxypyridine-2-thione (10% molar excess) in carbon tetrachloride or bromotrichloromethane as solvent under a nitrogen atmosphere. 4-Dimethylaminopyridine is used as a catalyst.

We than turned our attention to the preparation of the corresponding alkyl iodides. Initial experiments using a slight excess of elemental iodine in refluxing benzene gave only 26% (**6**) from (**3**). Use of iodoform, however, and hence by implication the diiodomethyl radical as chain carrier, gave iodide (**6**) in 74% yield. In a similar fashion (**10**) was obtained from (**7**) in 60% yield.

We consider that these mild neutral conditions for transformation of a carboxylic acid into the derived noralkyl halide should find application in organic synthesis.

Acknowledgement

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References

1. D.H.R. Barton, D. Crich and W.B. Motherwell, J.C.S. Chem. Comm., 000 (1983).
2. D.H.R. Barton, H.P. Faro, E.P. Serebryakov and N.F. Woolsey, J. Chem. Soc., 2438 (1965).
3. For a review see R.G. Johnson and R.K. Ingham, Chem. Rev., **56**, 219 (1956).
4. J.S. Cristol and W.C. Firth, J. Org. Chem., **26**, 280 (1961).
5. A. McKillop, D. Bromley and E.C. Taylor, J. Org. Chem., **34**, 1172 (1969).
6. J.K. Kochi, J. Amer. Chem. Soc., **87**, 2500 (1965).

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