Tetrahedron Letters,Vol.30,No.50,pp 6967-6968,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

SYNTHESIS OF IODOCUBANES BY DECARBOXYLATIVE IODINATION

John Tsanaktsidis and Philip E. Eaton*
Department of Chemistry, The University of Chicago,
5735 S. Ellis Avenue, Chicago Illinois 60637.

Summary: An efficient method is described for the preparation of iodocubanes from the corresponding carboxylic acids utilizing thiohydroxamic ester methodology with 2,2,2-trifluoroiodoethane as the iodide source.

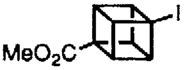
As part of our ongoing studies into the chemistry of cubane and its derivatives,[1] a convenient and efficient synthetic procedure for iodinated cubanes was required. The ready availability of many cubane carboxylic acids[2] made iodinative decarboxylation the method of choice. Iodocubane was first prepared by Abeywickrema and Della,[3] in moderate yield from cubane carboxylic acid by photoreaction with *tert*-butyl hypoiodite. This process proved unsatisfactory for our purposes as it results in partial polyiodination[4] and gives material which can be purified completely only with difficulty. Recently, Moriarty and his coworkers described the synthesis of some iodocubanes using a hypervalent iodine oxidative decarboxylation.[5] We have developed an efficient, alternative approach.

Barton and coworkers have described the decarboxylative iodination of both aliphatic and aromatic acids *via* radical decomposition of the thiohydroxamic esters in the presence of an iodine source.[6] Several different iodine sources were employed (*e.g.* CHI_3), each of which, however, had its own disadvantage. Looking to expand the existing[7] Barton thiohydroxamic ester methodology for bromo- and chlorocubanes to iodocubanes, we searched for a suitable iodinating agent. An ideal reagent would (i) readily donate iodine, (ii) give rise to a stable, localized carbon radical capable of functioning as an effective radical chain carrier, (iii) be easily removable from the final reaction mixture, and (iv) be stable under the prevailing reaction conditions. 2,2,2-Trifluoroiodoethane (bp 50 °C) meets these criteria, and indeed we have obtained clean, high-yield conversions of various cubane carboxylic acids *via* their thiohydroxamic esters to the corresponding iodides using this iodide source (Table 1). This approach should prove efficacious for preparation of other stable iodides.

Typically, a benzene solution of a preformed acid chloride is added with stirring to a boiling, illuminated (tungsten lamp) suspension of the sodium salt of N-hydroxypyridine-2-thione in dry benzene containing excess 2,2,2-trifluoroiodoethane and a catalytic amount of N,N-dimethylaminopyridine to accelerate the initial esterification. The crude iodides are readily purified by chromatography through a short column of silica gel and/or by crystallization or sublimation. When more volatile iodides are formed, *viz.* iodocubane, dichloromethane can be used instead of benzene.

***Example Procedure*:** A mixture of 4-chlorocubane carboxylic acid (1.25g, 6.85 mmol), oxalyl chloride (1.3 ml, 14.9 mmol, 2.5 equiv), N,N-dimethylformamide (1 drop) and dry dichloromethane (10 ml), protected with a $CaCl_2$ guard tube, is stirred at room temperature until homogeneous (1 h), then concentrated *in vacuo* and released to nitrogen. The residue is taken up in dry thiophene-free benzene (10 ml). Separately, a well-stirred suspension of the sodium salt of N-hydroxypyridine-2-thione[10] (1.1 g, 7.4 mmol, 1.1 equiv) in dry benzene (25 ml) containing 2,2,2-trifluoroiodoethane (Aldrich or Fairfield, stored over copper, 1.7 ml, 17.3 mmol, ~2.5 equiv) and a catalytic amount 4-N,N-dimethylaminopyridine is brought to boiling and irradiated with a 300W tungsten lamp. The benzene solution of the acid chloride is added dropwise over 10 min. After a further 30 min at reflux, the solution was cooled, washed successively with portions of water, conc. HCl and water, dried ($MgSO_4$, K_2CO_3) and concentrated under reduced pressure (distillation at atmospheric pressure in the case of iodocubane). The crude product was crystallized from (MeOH/CCl_4) affording pure 4-chloroiodocubane as colourless crystals (1.56 g, 82%): mp 156-156.5 °C; ^{1}H-NMR ($CDCl_3$) δ 4.23-4.32 ppm (6H, symmetrical multiplet).

TABLE 1. Conversion of various cubane carboxylic acids to the corresponding iodides.

Substrate	Product	Isolated Yield (%)	mp (°C)	
			found	reported
		92	32-3	31[3]
		92	124-5	112-4[8]
		82	156-6.5	-----
		87	197-7.5	190-6[5]
		88	227-7.5	226-7[9]

Acknowledgements. This work was supported by the Office of Naval Research and ARDEC (via Geo-Centers, Inc.).

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(10) N-Hydroxypyridine-2-thione, sodium salt was recovered from a 40% aqueous solution (Olin Corporation), crystallized twice from 95% ethanol and dried under high vacuum (~60 °C/1 mTorr) for several hours.

(Received in USA 25 September 1989)