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THE REACTION OF [I,I-BIS(TRIFLUOROACETOXY)IODO]BENZENE WITH N-(BENZYLOXYCARBONYL)-1-AMINOCYCLOPROPANE-1-CARBOXAMIDE

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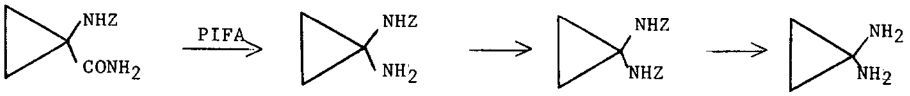
Summary: The treatment of N-(benzyloxycarbonyl)-1-aminocyclopropane-1-carboxamide with [I,I-bis(trifluoroacetyl)iodo]benzene caused cleavage of the cyclopropane ring with the formation of a β-alaninamide derivative.

In a continuation of our studies[1] involving cyclopropylamino acids and their derivatives, we recently attempted to prepare the novel 1,1-diaminocyclopropane (4) by the route outlined in Scheme 1. It was our intention to convert N-(benzyloxycarbonyl)-1-aminocyclopropane-1-carboxamide[2] (1) to the corresponding amine (2) using [I,I-bis(trifluoroacetoxy)iodo]benzene (PIFA). The utility of PIFA for the rearrangement of amides derived from peptides and acylamino acids is well established, and geminal amido-amines using this reagent have been prepared.[3]

Scheme 1



1 2 3 4

$ZNHCH_2CH_2CONHZ$ $Z = PhCH_2OCO-$

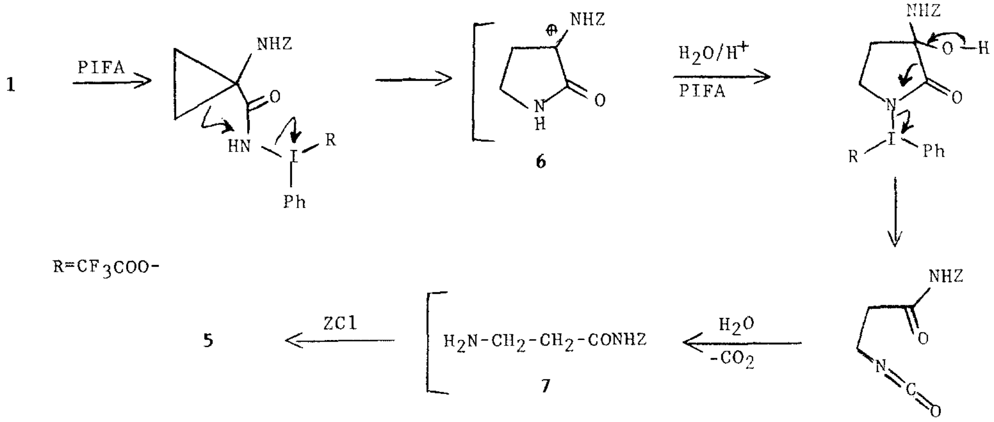
5

Treatment of (1) with 1.5 equivalents of PIFA followed by reaction of the resulting crude ninhydrin positive product with benzyloxycarbonyl chloride did not yield the derived dicarbamate (3), but rather an acyclic material identified as the β-alanine derivative (5) on the basis of spectroscopic and microanalytical data.[4] Further evidence for the identity of (5) was obtained by the formation of β-alanine amide,[5] upon deblocking (H_2/Pd).

A possible mechanism (Scheme 2) for this unexpected rearrangement requires two equivalents of PIFA for the complete conversion of 1 to 5. Indeed, when 1 was treated with 2.4

equivalents of PIFA the β-alanine derivative (5) was obtained in quantitative yield. Although to our knowledge cyclopropylamines have not previously been prepared using PIFA, the usual amide to amine rearrangement caused by PIFA bears at least a formal resemblance to the classical Hoffmann rearrangement,[6] as well as to the amide rearrangement mediated by lead tetraacetate[7]. Both of these reactions have been used to convert cyclopropyl carboxamides to the corresponding cyclopropylamines or their derivatives, apparently without skeletal rearrangement.[8] Since the PIFA catalyzed rearrangement occurred in an acidic medium, the formation of a cationic intermediate such as 6 is possible, and perhaps allowed the reaction to take the anomalous path described here. The unusual β-amino-imide structure (7) formed in high yield in this reaction would be difficult to prepare by direct methods, indicating a possible use for this rearrangement in synthesis.

Scheme 2



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4. Compound 5 had m.p. 127-128°; IR: KBr/Max 1750 (benzyloxycarbonyl C=O), 1680 (amide I) and 1790 cm^{-1} (imide); NMR ($CDCl_3$): δ 2.94-3.01 (m, 2H, $-CH_2-$), 3.47-3.52 (m, 2H, $-CH_2-$), 5.06 (s, 2H, $-CH_2-C_6H_5$), 5.15 (s, 2H, $-CH_2C_6H_5$), 5.26 (br s, 1H, NH), 7.25 (s, 5H, C_6H_5), 7.32 (s, 5H, C_5H_5), 7.57 (br s, 1H, NH). Anal. Calcd. for $C_{19}H_{20}N_2O_5$: C, 64.03; H, 5.66; N, 7.86. Found: C, 64.08; H, 5.70; N, 7.85.

5. An authentic sample of β-alanine amide, prepared by hydrogenolysis of N-Z-β-alanine amide prepared as in ref. 2, had m.p. 150-152°; Ir: KBr/Max 1660 cm^{-1} (amide I); NMR (CD_3COOD): δ 2.73-2.94 (m, 2H, $-CH_2-$), 3.20-3.46 (m, 2H, $-CH_2-$). Anal. Calcd. for $C_3H_9N_2OCl$: C, 28.92; H, 7.28; N, 22.49. Found: C, 29.03; H, 7.31; N, 22.43.

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