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Tandem reactions initiated by the oxidative decarboxylation of 1-benzoyl-2(*S*)-*tert*-butyl-6(*S*)-carboxyperhydropyrimidin-4-one

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Abstract—Treatment of the title perhydropyrimidinone with diacetoxyiodobenzene and iodine followed by addition of allyltrimethylsilane and boron trifluoride etherate afforded 1-benzoyl-2(*S*)-*tert*-butyl-2,3-dihydro-4(*H*)-pyrimidin-4-one in 65–71% yield, via an efficient three-step radical decarboxylation-oxidation-β-elimination tandem reaction. In contrast, when addition of allyltrimethylsilane/$BF_3·OEt_2$ was suppressed, a remarkable five-step tandem process led to the formation of vinylic iodide, 1-benzoyl-2(*S*)-*tert*-butyl-5-iodo-2,3-dihydro-4(*H*)-pyrimidin-4-one as the main product. © 2002 Elsevier Science Ltd. All rights reserved.

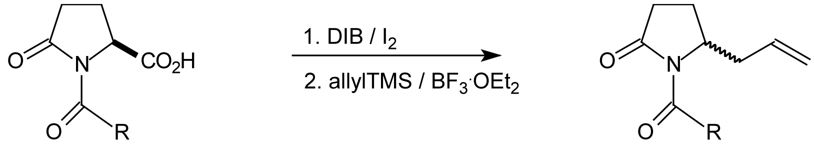
Synthetic applications of diacetoxyiodobenzene have received considerable attention.[1] In a series of relevant papers, Suárez and co-workers[2] have presented diacetoxyiodobenzene/iodine (DIB/I_2) as an effective mixture of reagents for the oxidative decarboxylation of carboxylic acids (Eq. (1)).

$$R–CO_2H \xrightarrow{DIB/I_2} R–CO_2I \xrightarrow{-CO_2} RI \qquad (1)$$

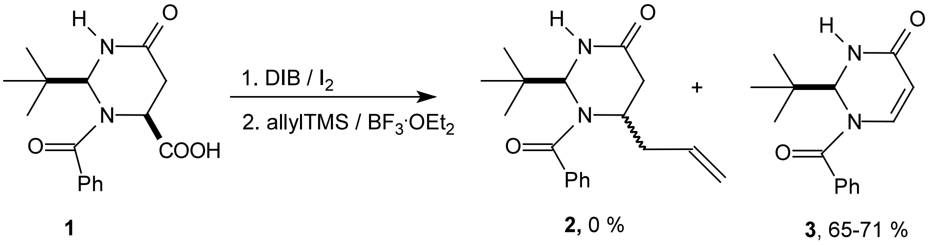
We were particularly interested by a recent application of the Suárez oxidation, where the radical decarboxylation–oxidation of α-amino acids is followed by nucleophilic trapping of the generated iminium ion (Eq. (2)).[3]

In this report, we describe the contrasting reaction course encountered when 1-benzoyl-2(*S*)-*tert*-butyl-6(*S*)-carboxy-2,3-dihydro-4(*H*)-pyrimidin-4-one, **1**, a useful intermediate for the enantioselective synthesis of α-substituted β-amino acids,[4,5] was treated with the DIB/I_2/allyltrimethylsilane/$BF_3·OEt_2$ reagent mixture (Eq. (3)). Although the anticipated allylated derivative **2** was not observed, interesting three- and five-step tandem processes led to the formation of other valuable decarboxylated products.

With the aim to achieve overall substitution of the carboxylic group in pyrimidinone **1** by an allyl moiety (cf. Eq. (3)), the former substrate was treated with DIB (2 equiv.) and iodine (1 equiv.) in CH_2Cl_2, followed by allyltrimethylsilane (allylTMS, 5 equiv.) and $BF_3·OEt_2$ (1 equiv.), under the same conditions employed by Suárez et al.[3] in the corresponding transformation of



(2)



(3)

Keywords: pyrimidinones; decarboxylation; elimination reactions; radicals and radical reactions; allenes.

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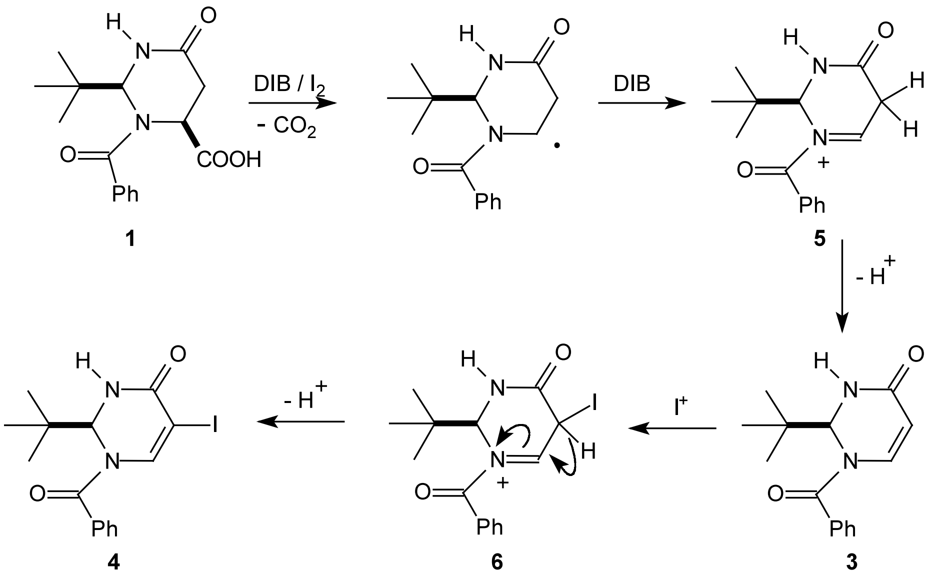


Scheme 1.

pyroglutamic acid (Eq. (2)). Unexpectedly, the previously reported[4b,i] heterocyclic enone **3** was formed in good yield (Eq. (3)).

Based on reasonable mechanistic considerations,[2,3] the formation of enone **3** can be accounted for in terms of a three-step radical decarboxylation–oxidation–β-elimination tandem reaction as outlined in Scheme 1. It is evident that β-elimination of an acidic proton in iminium ion **5** to give enone **3** is faster than nucleophilic addition to afford allylated product **2** (Eq. (3) and Scheme 1).

Nevertheless, when the allylTMS/BF$_3$·OEt$_2$ reagent mixture was suppressed from the reaction protocol, the main product turned out to be vinylic iodide **4**,[6] accompanied by varying amounts of the enone **3** (Eq. (4)).

It is likely that the iodoenone **4** forms from enone **3** via β-iodination;[7] therefore, the former iodinated enone is apparently generated from a remarkable five-step tandem reaction: (1) radical decarboxylation of pyrimidinone **1**, (2) oxidation to an iminium ion intermediate, (3) β-elimination of a proton to give the enone **3**, (4) β-iodination, and (5) β-elimination of a second proton at C(5) to produce iodoenone **4**[8] (Scheme 1).

Repeated attempts to obtain suitable crystals of iodoenone **4** for crystallographic studies were unsuccessful. Nevertheless satisfactory crystals of 1-benzoyl-2(*S*)-isopropyl-5-iodo-2,3-dihydro-4(*H*)-pyrimidin-4-one, **7**,[9] could be obtained. Fig. 1 shows the crystal structure of iodoenone **7**, an isopropyl analog of **4**.

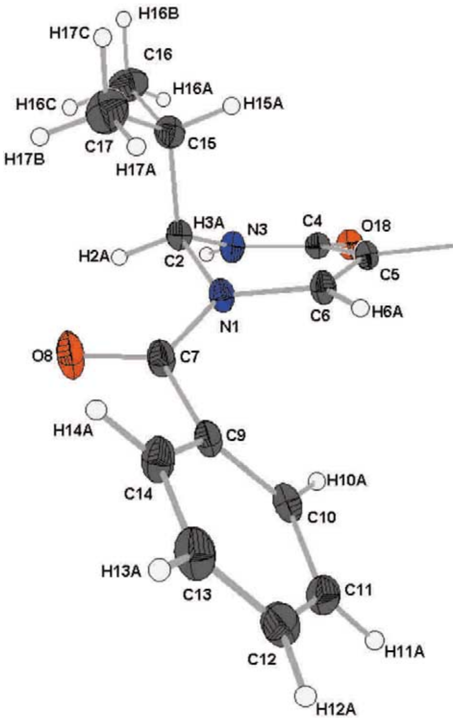
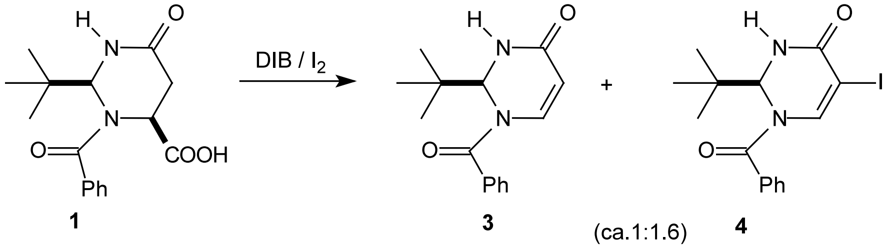
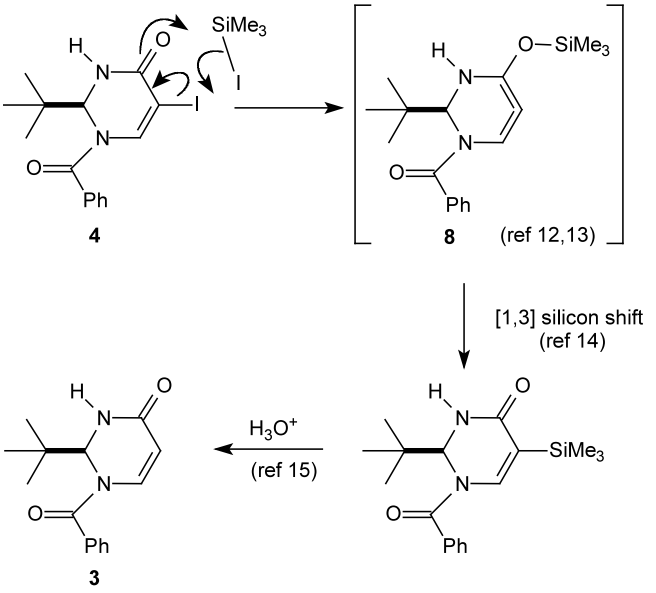


Figure 1. ORTEP drawing of iodoenone **7**, with thermal ellipsoids drawn at 30% probability level.[10]



(4)



Scheme 2.

Most interestingly, a control experiment confirmed that allylTMS reacts with iodine to give iodotrimethylsilane (ITMS). This observation is relevant in view of the ability of ITMS to hydrodehalogenate α-haloketones.[11] In the system at hand, treatment of iodoenone **4** with 1.2 equiv. of ITMS in CH_2Cl_2 resulted in essentially quantitative hydrodeiodination to give the enone **3**. A plausible mechanism is presented in Scheme 2.[12–15]

Most salient is the apparent intermediacy of cyclic allene **8**. Although experimental and theoretical support of the existence of (bent) 1,2-cyclohexadiene derivatives has been reported,[12] six-membered nitrogen-containing allene **8** seems to be the first example of its kind.[13]

In summary, the special structural characteristics of the perhydropyrimidinone substrate **1** lead to distinctive reactivity upon treatment with the Suárez DIB/I_2 decarboxylation protocol. Remarkable three- and five-step tandem reactions afforded then useful enone derivatives **3** and **4**.

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6. *Synthetic procedure and spectroscopic data*: A mixture of the pyrimidinone **1** (304 mg, 1 mmol), DIB (644 mg, 2 mmol) and iodine (253 mg, 1 mmol) was stirred in CH_2Cl_2 (20 ml) until TLC showed disappearance of the starting material (3–4 h). After addition of CH_2Cl_2 (20 ml), the reaction mixture was washed with 5% aqueous $Na_2S_2O_3$ (4×10 ml), 3% aqueous $NaHCO_3$ (2×10 ml), and brine (1×10 ml), dried (Na_2SO_4) and evaporated to a pale yellow syrup which solidifies on standing and was crushed and washed with hexane to afford 219 mg of a 1/1.6 mixture of the enone **3** and the iodoenone **4** (determined by NMR). Repeated crystallization from EtOAc/hexane and CH_2Cl_2/hexane afforded 138 mg (36%) of the pure iodoenone **4**. Mp 258–260°C (descomp.). $[\alpha]^{25}_{\mathrm{D}}=428.4$ ($c=1.0$, $CHCl_3$). ^1H NMR (400 MHz, DMSO-d_6, 120°C) δ (ppm) 0.94 (s, 9H); 5.62 (d, $J=3.3$ Hz, 1H); 7.56–7.52 (m, 6H); 8.25 (broad, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, 120°C) δ (ppm) 168.3, 159.4, 143, 133.8, 131.7, 129.3, 128.2, 76.9, 71, 40.5, 26.2. MS (20 eV) 384 (M^+), 327 (M^+–57), 300, 222, 172, 105, 77. HRMS (FAB), observed 385.0145 (M^++1); estimated for $C_{15}H_{18}N_2O_2I$, 385.0143.
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8. Support for the mechanism advanced in Scheme 1 was gained when in a separate experiment, exposure of the enone **3** to DIB/I_2 in the same conditions described in

Ref. 6, resulted in a clean (61–65% yield) conversion to iodoenone **4**.

9. Exposure of 1-benzoyl-2(*S*)-isopropyl-6(*S*)-carboxyperhydropyrimidin-4-one to DIB/I_2 afforded similar results to those described for pyrimidinone **1** in Ref. 6. The isolated yield of 1-benzoyl-2(*S*)-isopropyl-5-iodo-2,3-dihydro-4(*H*)-pyrimidin-4-one **7** was 37%. Mp 218–220°C. $[\alpha]_D^{25} = 389.27$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR (400 MHz, DMSO-d_6, 120°C) δ (ppm) 0.88 (d, $J = 6.6$ Hz, 3H); 0.95 (d, $J = 6.6$ Hz, 3H); 2.16 (m, 1H); 5.44 (d, $J = 7.3$ Hz, 1H); 7.46–7.60 (m, 6H). ^{13}C NMR (100 MHz, DMSO-d_6, 120°C) δ (ppm) 167.7, 159.4, 142.6, 133.6, 131.8, 129.2, 128.3, 120.7, 75.6, 69.7, 33.5, 18.7, 18.0. MS (20 eV) 370 (M^+), 327 (M^+–43), 300, 222, 172, 105, 77. HRMS (FAB), observed 371.0252 (M^++1); estimated for $C_{14}H_{16}IN_2O_2$, 371.0257.
10. Crystallographic data for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 183998. Copies of the data can be obtained free of charge on application to CCDC. 12 Union Road, Cambridge CB21EZ, UK (Fax: (+44) 1223-336-036. Email: deposit@ccdc.cam.ac.uk).
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