A Simple Synthesis of 1-*t*-Butyloxycarbonyl-3-formylindole

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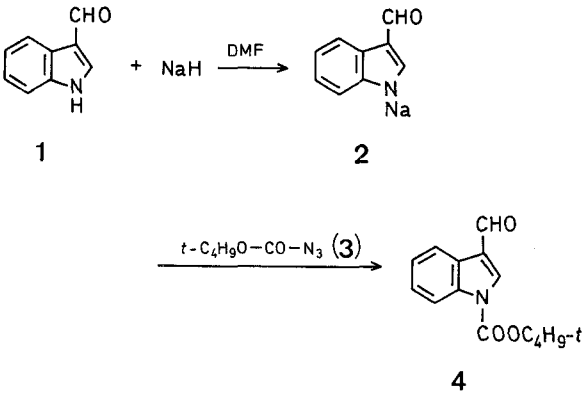
The use of 4CC (four component condensation) in petide fragment coupling has been reported recently[1,2]. The key compound is 1-*t*-butyloxycarbonyl-3-formylindole (**4**) which is obtained by *t*-butyloxylation of 3-formylindole. Compound **4** can be prepared by reacting the 3-formylindole (**1**) with *t*-butyloxycarbonyl chloride at $-30°$ to $-40°$[3,4], or with *t*-butyloxycarbonyl fluoride at 0°[5,6]. We wish to report the synthesis of **4** by reacting the sodium salt of 3-formylindole (**2**) with *t*-butyloxycarbonyl azide (**3**) which is widely used in peptide synthesis[7] (for the preparation of *t*-butyloxycarbonyl amino-acids).



Alkylation and acylation of metaloindole derivatives results in the formation of either **1**, 3- or a mixture of 1- and 3-corresponding alkyl or acyl derivatives depending on the metal, the solvent and the indole derivative used[8]. One would expect alkylation or acylation of 3-formylindole to go exclusively to the 1 position. Indeed reacting the sodium salt of 3-formylindole with *t*-butyloxycarbonyl azide in dimethylformamide at 5° results in the formation of **4** in 92% yield. The product was identical with an authentic sample of **4**[6] (m.p., mixture m.p., I.R., N.M.R., mass spectra).

1-*t*-Butyloxycarbonyl-3-formylindole (4):

To an ice cold solution of 3-formylindole (**1**; 5.8 g, 40 mmol) in dimethylformamide (80 ml) sodium hydride (1.85 g, 50% in mineral oil) was added during 20 min followed by slow addition of *t*-butyloxycarbonyl azide (**3**; 4.3 g, 40 mmol) keeping the temperature below 5°. After one hour excess sodium hydride is decomposed by the addition of a small amount of cold water. The reaction mixture was poured into water (600 ml), left overnight in the refrigerator, filtered, dried and crystallized from ethyl acetate/petrol ether; yield: 10 g (92%); m.p. 121–123°.

$C_{14}H_{15}NO_2$	calc.	C 68.57	H 6.12	N 5.71
(245.3)	found	68.43	6.14	5.52

I.R. (Nujol): $\nu_{max} = 1735, 1680\,cm^{-1}$

^{1}H-N.M.R. ($CDCl_3$): $\delta = 10.06$(s, 1H), 8.18(m, 3H), 7.36(m, 2H), 1.41 ppm (s, 9H).

Mass spectrum: $m/e = 245$ ($M^{\oplus}$), 189, 172, 146, 145, 116, 89, 57.

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