Claisen Rearrangement of 2-Allyloxyindolic Ketoester *via* a Decarboxylative Process†

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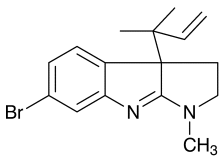
Béatrice Malapel-Andrieu, Simone Piroëlle and Jean-Yves Mérour*

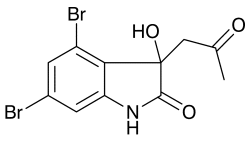
Institut de Chimie Organique et Analytique associé au CNRS, Université d'Orléans, BP 6759, F-45067 Orléans Cedex 2, France

Claisen rearrangement of transient 2-allyloxy-3-hydroxy-1-methylindole generated by decarboxylation of the corresponding ester afforded, at room temperature, (±)-3-allyl-3-hydroxy-1-methylindol-2(3*H*)-one.

The pyrrolo[3,2-*b*]indole framework possessing the 1,1-dimethylallyl group is encountered in the structure of natural products such as flustramine C,[1] which has been obtained from indol-3-one *via* a Claisen rearrangement. Claisen rearrangements have been reported for 3-allyloxyindoles[2] but only at elevated temperatures and giving 2-allylindol-3(2*H*)-one. Sakamoto *et al.*[1] have described an easy rearrangement of 2-allyloxyindole to 3-allylindol-2-one. Convolutamydine A,[3] a metabolite isolated from the marine Bryozoan organism (*Amathia convoluta*) presents an interesting 3-hydroxyindolin-2-one framework; we can envisage the generation of this skeleton from a [3,3]sigmatropic rearrangement of 2-allyloxyindolin-3-one.



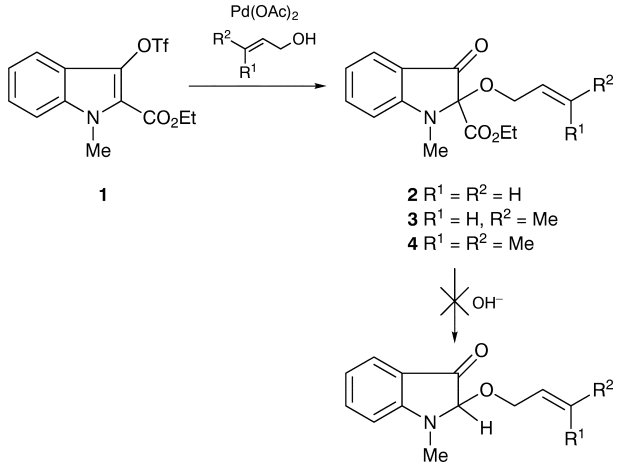
Flustramine C



Convolutamydine A

Recently, we have reported the unexpected synthesis of 2-allyloxydihydroindole derivatives **2–4** from triflate **1** and allyl alcohol in the presence of palladium acetate[4] (Scheme 1). In order to obtain 2-allyloxyindolin-3-ones, which are intermediates in the synthesis of pyrrolo[2,3-*b*]-indole,[1] we considered the decarboxylation of compounds **2–4** by a standard saponification procedure.

Unfortunately, treatment in basic media (ethanolic sodium hydroxide) at room temperature of compounds **2–4** afforded after 3 h the rearranged (±)-oxindoles **5–7**



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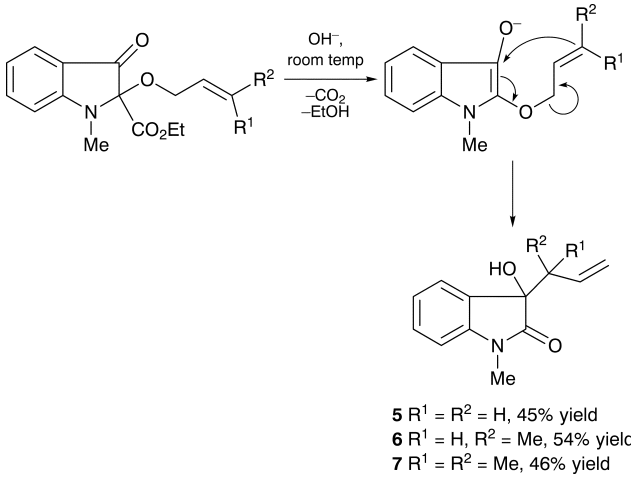
2 $R^1 = R^2 = H$
3 $R^1 = H$, $R^2 = Me$
4 $R^1 = R^2 = Me$

Scheme 1 $Tf = CF_3SO_2$

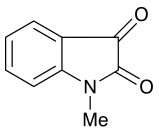


5 $R^1 = R^2 = H$, 45% yield
6 $R^1 = H$, $R^2 = Me$, 54% yield
7 $R^1 = R^2 = Me$, 46% yield

Scheme 2

(45–54% yields). The unexpected formation of these compounds may be explained by an oxy–Claisen rearrangement (Scheme 2). This anionic process may involve enolates of α-allyloxyketones which considerably accelerate the rearrangement and allow it to proceed at room temperature.[5,6] The enolates were generated, after decarboxylation at room temperature, for compounds **2–4**. Compound **6** was obtained as a diastereomeric mixture (50:50) which cannot be separated.

In order to confirm the structure of **5** we have performed a Grignard reaction on *N*-methylisatin **8**; phenylmagnesium bromide,[7] or ethylmagnesium bromide[8] were reported to give the corresponding tertiary alcohols at the 3-position; when allylmagnesium chloride was used (for this reaction), the 2,2-diallyl-1-methylindolin-3-one **9** was obtained in low yield (20%). Such reactivity has been studied by Witkop *et al.*[9] for analogous indolin-3-one compounds.



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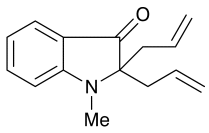

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Thus we considered another way of synthesising 3-allyl-1-methylindolin-2-one by allylation of the 1-methylindolin-2-one **10** with allyl bromide and sodium hydride in toluene; after separation of the monoallyl derivative[10] **11** from the diallyl derivative, the oxidation of the C-3 carbon atom is performed in basic media by air oxidation[11] of the generated anion and afforded the expected compound (±) **5** in 46% yield.

The 3-allyl-3-hydroxyindolin-2-ones may be useful intermediates in the synthesis of natural products and also

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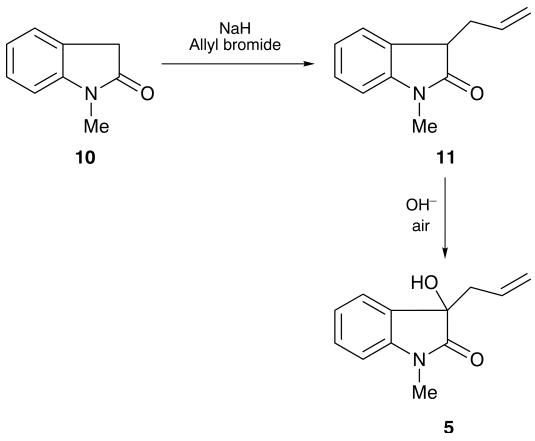
illustrate the easy transformation of indolin-3-one derivatives into indolin-2-one derivatives.



Experimental

Typical Procedure for Claisen Rearrangement: 3-*Allyl*-3-*hydroxy*-1-*methylindolin*-2-*one* **5**.—Compound **2** (150 mg, 0.54 mmol) was dissolved in ethanol (7 ml) and water (two drops) containing KOH in pellets (60 mg, 1.07 mmol). The mixture was stirred for 3 h at room temperature; evaporation left a residue which was dissolved in water (10 ml) and extracted with ethyl acetate (3 × 10 ml). After drying over $MgSO_4$, and evaporation, the residue was chromatographed on a silica gel column (eluent dichloromethane) to give **5** (50 mg; yield 45%); mp 154–156 °C. ν/cm^{-1} (KBr) 3295 (OH), 1697 (CO). δ_H ($CDCl_3$) 2.56–2.78 (m, 2H, CH_2); 3.17 (s, 3H, NCH_3); 3.28 (br s, 1H, OH); 5.06–5.13 (m, 2H, $CH{=}CH_2$); 5.55–5.72 (m, 1H, $CH{=}CH_2$); 6.82 (d, 1H, H_{arom}, *J* 8.2); 7.10 (t, 1H, H_{arom}, *J* 8.2); 7.32 (t, 1H, H_{arom}, *J* 8.2); 7.38 (d, 1H, H_{arom}, *J* 8.2). δ_C ($CDCl_3$) 26.1 (CH_3); 42.8 (CH_2); 75.9 (C-3); 108.4 (CH); 120.3 (=CH_2); 123.0 (CH); 124.1 (CH); 129.6 (CH); 129.8 (C); 130.5 (CH); 143.2 (C); 177.9 (CO). MS (IS): *m*/*z* 204 (M^++1) (Found: C, 70.85; H, 6.57; N, 6.94. $C_{12}H_{13}NO_2$ requires C, 70.92; H, 6.45; N, 6.89%).

Compound **6**: yield 54%: solid; 50:50 mixture of two diastereomers A and B; mp 142–144 °C; ν/cm^{-1} (KBr) 3330 (OH), 1695 (CO). δ_H ($CDCl_3$ + D_2O) 0.75 [d, 3H, CH_3(A), *J* 6.9]; 0.98 [d, 3H, CH_3(B), *J* 6.9]; 2.67–2.85 [m, 1H, CH(A + B)]; 3.15 [s, 3H, NCH_3(A)]; 3.19 [s, 3H, NCH_3(B)]; 5.08–5.28 [m, 2H, =CH_2(A + B)]; 5.60–5.74 [m, 1H, CH=(A)]; 6.00–6.12 [m, 1H, CH=(B)]; 6.78–6.82 [m, 1H, H_{arom}(A + B)]; 7.05–7.11 [m, 1H, H_{arom}(A + B)]; 7.29–7.37 [m, 2H, H_{arom}(A + B)]. δ_C ($CDCl_3$) 12.1 [CH_3(A)]; 13.0 CH_3(B)]; 24.9 [CH(A)]; 25.1 [CH(B)]; 43.8 [CH_3(A)]; 45.9 [CH_3(B)]; 75.5 [C-3(A)]; 75.9 [C-3(B)]; 107.1 [CH=(A)]; 107.2 [CH=(B)]; 117.1 [CH_2(A)]; 117.7 [CH_2(B)]; 121.9 [CH(A + B)]; 123.0 [CH(A + B)]; 128.5 [C(A + B)]; 128.6 [CH(A + B)]; 135.7 [C(A + B)]; 135.7 [CH(A)]; 136.0 [CH(B)]; 176.5 [CO(A + B)]. *NB*: Assignments for diastereomers A or B may be interchanged. MS (IS): *m*/*z* 218 (M^++1) (Found: C, 72.05; H, 7.09; N, 6.34. $C_{13}H_{15}NO_2$ requires C, 71.87; H, 6.96; N, 6.45%).

Compound **7**: yield 46%; oil. ν/cm^{-1} (film) 3417 (OH), 1724 (CO). δ_H ($CDCl_3$) 1.07 (s, 3H, CH_3); 1.15 (s, 3H, CH_3); 2.80 (br s, 1H, OH); 3.14 (s, 3H, NCH_3); 5.12 (dd, 1H, =CH_2, *J* 1, 17); 5.20 (dd, 1H, =CH_2, *J* 1, 10); 6.15 (dd, 1H, CH=, *J* 10, 17.0); 6.78 (d, 1H, H_{arom}, *J* 7.2); 7.04 (t, 1H, H_{arom}, *J* 7.2); 7.28 (t, 1H, H_{arom}, *J* 7.2); 7.38 (d, 1H, H_{arom}, *J* 7.2). δ_C ($CDCl_3$) 21.0 (CH_3); 23.1 (CH_3); 27.1 (CH_3); 44.6 (C); 81.1 (C); 108.9 (CH=); 116.5 (CH_2=); 123.3 (CH); 126.8 (CH); 129.5 (C); 130.6 (CH); 142.9 (CH); 145.3 (C); 178.9 (CO). MS (IS): *m*/*z* 232 (M^++1) (Found: C, 72.45; H, 7.57; N, 6.14. $C_{14}H_{17}NO_2$ requires C, 72.70; H, 7.41; N, 6.06%).

2,2-*Diallyl*-1-*methylindolin*-3-*one* **9**.—1-Methylisatin (300 mg, 1.86 mmol) was added portionwise to a solution of allylmagnesium chloride (2 M in THF, 2 ml, 4 mmol) in diethyl ether (10 ml); after refluxing for 3 h, water (10 ml) was added and the mixture extracted with ethyl acetate (2 × 10 ml). Drying over $MgSO_4$ and evaporation left a residue which has chromatographed on a silica gel column (CH_2Cl_2 light petroleum 8:2) to give **9**; oil; 86 mg; yield 20%. ν/cm^{-1} (film) 1691 (CO). δ_H ($CDCl_3$) 2.43 (dd, 2H, CH_2, *J* 7.5, 14); 2.57 (dd, 2H, CH_2, *J* 6.5, 14); 2.98 (s, 3H, NCH_3); 4.90 (br d, 2H, CH_2=); 5.05 (br d, 2H, CH_2=); 5.26–5.45 (m, 2H, CH=); 6.63–6.70 (m, 2H, H_{arom}); 7.42 (td, 1H, H_{arom}, *J* 1.3, 8.0); 7.52 (d, 1H, H_{arom}, *J* 8.0). δ_C ($CDCl_3$) 29.2 (NCH_3); 41.5 (2 × CH_2); 74.5 (C-2); 109.3 (CH); 118.1 (CH); 120.4 (2 =CH_2); 121.8 (C); 126.1 (CH); 127.6 (CH); 139.4 (2 =CH); 162.4 (C); 204.4 (CO). MS (IS): *m*/*z* 228 (M^++1) (Found: C, 79.43; H, 7.69; N, 6.10. $C_{15}H_{17}NO$ requires C, 79.26; H, 7.54; N, 6.16%).

3-*Allyl*-3-*hydroxy*-1-*methylindolin*-2-*one* **5**.—3-Allyl-1-methylindolin-2-one[10] **11** (200 mg, 1.06 mmol) was dissolved in methanol–water (5 ml/0.5 ml) in the presence of 40% sodium hydroxide (0.5 ml); the mixture was stirred at room temperature for 18 h; evaporation of the solvent left a residue which was treated with ethyl acetate (10 ml) and water (10 ml). Extraction with ethyl acetate (2 × 10 ml), drying over $MgSO_4$ and evaporation gave a residue which was chromatographed on a silica gel column using ethyl acetate–light petroleum (2:8) as eluent. All physical data for the solid obtained are identical to those for compound **5**; 100 mg; yield 46%.

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References

1 T. Kawasaki, R. Terashima, K. Sakaguchi, H. Sekiguchi and M. Sakamoto, *Tetrahedron Lett*., 1996, **42**, 7525 and references therein.
2 T. Kawasaki, K. Masuda, Y. Baba, K. Takada and M. Sakamoto, *Chem. Pharm. Bull*., 1994, **42**, 1974; H. Pleininger, H. Sirowej and D. Rau, *Chem. Ber*., 1971, **104**, 1863; T. Kawasaki, K. Masuda, Y. Baba, R. Terashima, K. Takada and M. Sakamoto, *J. Chem. Soc., Perkin Trans. 1*, 1996, 729.
3 S. J. Garden, J. C. Torres, A. A. Ferreira, R. B. Silva and A. C. Pinto, *Tetrahedron Lett*., 1997, **38**, 1501.
4 B. Malapel-Andrieu and J.-Y. Mérour, *Tetrahedron Lett*., 1998, **39**, 39.
5 M. Koreeda and J. I. Luengo, *J. Am. Chem. Soc*., 1985, **107**, 5572.
6 K. Wimalasena and M. P. D. Mahindaratne, *J. Org. Chem*., 1994, **59**, 3427.
7 M. Ogata, H. Matsumoto and K. Tawara, *Eur. J. Med. Chem*., 1981, **16**, 373.
8 W. Balk-Bindseil, E. Helmke, H. Weyland and H. Laatsch, *Leibigs Ann. Org. Bioorg. Chem*., 1995, 1291.
9 B. Witkop and A. Ek, *J. Am. Chem. Soc*., 1951, **73**, 5664.
10 R. W. Daisley and J. Walker, *J. Chem. Soc. C*, 1971, 1375.
11 R. M. DeMarinis, G. Gallagher, R. F. Hall, R. G. Franz, C. Webster, W. H. Huffman, M. S. Schwartz, C. Kaiser, S. T. Ross, J. W. Wilson and P. Hieble, *J. Med. Chem*., 1986, **29**, 939.