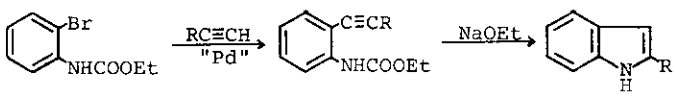
CONDENSED HETEROAROMATIC RING SYSTEMS. X.[1] SYNTHESIS OF BENZINDOLES FROM o-BROMONAPHTHYLAMINES

Takao Sakamoto, Yoshinori Kondo, and Hiroshi Yamanaka*
Pharmaceutical Institute, Tohoku University,
Aobayama, Sendai 980, Japan

Abstract———Benz[f]indole, of which few effective preparative methods are known, was easily synthesized by palladium-catalyzed reaction of ethyl 3-bromo-2-naphthylcarbamate with trimethylsilylacetylene and subsequent cyclization with sodium ethoxide in ethanol. By the same method, benz[g]indole and benz[e]indole were obtained from 2-bromo-1-naphthylcarbamate and 1-bromo-2-naphthylcarbamate, respectively.

Previously, we reported[2] a facile method for the synthesis of indole derivatives (3) from ethyl o-ethynylphenylcarbanilates (2), prepared by the palladium-catalyzed reaction of ethyl o-bromophenylcarbanilate (1), as shown in Scheme 1.



1 2 3

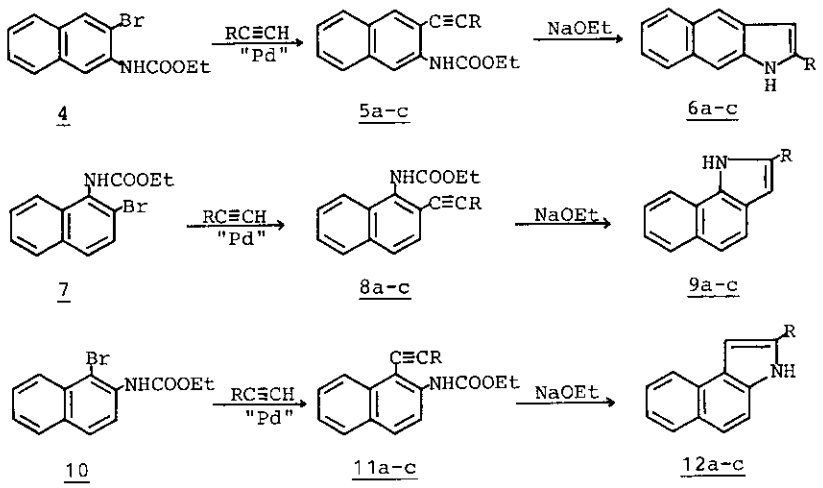
"Pd":$PdCl_2(PPh_3)_2$-CuI-Et_3N

Scheme 1

As an extension of the above method, we now report the synthesis of three kinds of benzindoles (6, 9, and 12), among which few preparative methods are known for benz[f]indoles (6a-c).

Firstly, 3-bromo-2-naphthylamine,[3] 2-bromo-1-naphthylamine,[4] and 1-bromo-2-naphthylamine[5] were converted into the corresponding carbamates (4, mp 110-111°C, 86 %; 7, mp 132-133°C, 82 %; 10, mp 87-89°C, 65 %) by treatment with ethyl chloroformate in pyridine. When the crude ethyl 3-(trimethylsilylethynyl)-2-naphthylcarbamate (5a), prepared by the condensation of 4 with trimethylsilylacetylene in the presence of dichlorobis(triphenylphosphine)palladium, was treated with sodium

ethoxide in ethanol, benz[f]indole (6a), mp 188-190°C,[6] was obtained in 48 % overall yield from 4. Similarly, benz[g]indole (9a), mp 169-170°C,[7] and benz[e]indole (12a), mp 201-203°C (picrate)[8] were synthesized from 7 and 10 in 53 and 54 % yields, respectively. The physical constants and spectral data of all these compounds are in good agreement with the reported values.



"Pd":$PdCl_2(PPh_3)_2$-CuI-Et_3N

a:R=H
b:R=Ph
c:R=Bu

Scheme 2

When 1-hexyne and phenylacetylene were employed instead of trimethylsilylacetylene, the benzindoles possessing a substituent at the 2-position were easily synthesized. The yields and melting points of the 2-substituted benzindoles (6b, 6c, 9b, 9c, 12b, and 12c) are listed in Table I.

General Procedure for the Preparation of Benzindoles

A mixture of an o-bromonaphthylcarbamate (4 mmol), an acetylene (6 mmol), $PdCl_2(PPh_3)_2$ (100 mg), CuI (50 mg), and Et_3N (1 ml) was heated in a sealed tube at 80°C for 2 h. The mixture was diluted with water and extracted with ether. The ethereal extract was purified by SiO_2 column chromatography using C_6H_6 as an eluent. The product obtained from the C_6H_6 eluate, was added to an EtONa-EtOH solution [prepared from Na (460 mg, 20 mmol) and dry EtOH (30 ml)], and the mixture was refluxed for 4 h. The ethanol was removed under reduced pressure, and the residue was diluted with water. The mixture was extracted with $CHCl_3$, and the $CHCl_3$ extract was purified by SiO_2 column chromatography using hexane-C_6H_6 (2:1) as an eluent to give the product.

Table I. Benzindoles from o-Bromonaphthylcarbamates

No.	Yield(%)	mp (°C)	Lit. mp (°C)	^{1}H-NMR ($CDCl_3$) δ(ppm)
6a	48	188-190	192[6]	6.5-6.8(1H,m),7.1-8.2(8H,m)
6b	45	253-255	260[7]	7.0-7.7(6H,m),7.8-8.3(7H,m)[a]
6c	33	viscous oil[b]		0.9-1.2(3H,m),1.3-1.9(4H,m) 2.3-2.7(2H,m),6.6-6.8(1H,m) 7.1-8.1(7H,m)
9a	53	169-170	170-171[8]	6.5-6.7(1H,m),7.1-8.3(8H,m)
9b	42	165-167	165-167[9]	7.0-8.4(13H,m)
9c	30	viscous oil[c]		0.8-1.2(3H,m),1.3-1.8(4H,m) 2.3-2.8(2H,m),6.6-6.8(1H,m) 7.0-8.2(7H,m)
12a	54	viscous oil[d]		6.6-6.8(1H,m),7.1-8.2(8H,m)
12b	38	180-182	175[7]	7.1-8.6(13H,m)
12c	26	viscous oil[e]		0.9-1.3(3H,m),1.3-1.9(4H,m) 2.3-2.8(2H,m),6.6-6.8(1H,m) 7.1-8.0(7H,m)

a) In DMSO-d_6. b) Picrate (red needles): mp 235-240°C (dec.).[10] c) Picrate (brown needles): mp 217-223°C (dec.).[10] d) Picrate (red needles): mp 201-203°C (dec.); lit.[8] mp 205°C (dec.). e) Picrate (brown needles): mp 236-238°C (dec.).[10]

REFERENCES

1. Part IX: T. Sakamoto, N. Miura, Y. Kondo, and H. Yamanaka, Chem. Pharm. Bull., in press.
2. T. Sakamoto, Y. Kondo, and H. Yamanaka, Heterocycles, 1986, **24**, 31
3. H. H. Hodgson and D. E. Hathway, J. Chem. Soc., **1945**, 841.
4. H. H. Hodgson and D. E. Hathway, J. Chem. Soc., **1944**, 538.
5. A. Senier and P. C. Austin, J. Chem. Soc., **1908**, 63.
6. O. Süs, M. Glos, K. Möller, and H.-D. Eberhardt, Liebigs Ann. Chem., 1953, **583**, 150.
7. P. Bigot, G. Saint-Ruf, and N. P. Buu-Hoi, J. Chem. Soc., Perkin Trans. 1, **1972**, 2573.
8. F. C. Pennington, M. Jellinek, and R. D. Thurm, J. Org. Chem., 1959, **24**, 565.
9. H. P. Patel and J. M. Tedder, J. Chem. Soc., **1963**, 4593.
10. 6c: Anal. Calcd for $C_{22}H_{20}N_4O_7$ (picrate): C, 58.41; H, 4.46; N, 12.38. Found: C, 58.23; H, 4.53; N, 12.16. 9c: Anal. Calcd for $C_{22}H_{20}N_4O_7$ (picrate): C, 58.41; H, 4.46; N, 12.38. Found: C, 58.36; H, 4.60; N, 12.22. 12c: Anal. Calcd for $C_{22}H_{20}N_4O_7$ (picrate): C, 58.41; H, 4.46; N, 12.38. Found: C, 58.19; H, 4.37; N, 12.35.

Received, 22nd April, 1986