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New routes to condensed polynuclear compounds : Part XVIII—Cyclisations through naphthynes and pyridynes

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Abstract. It has been shown that the KNH_2/NH_3 cyclisation of ortho/meta halogenated Schiff bases, or the corresponding dihydro compounds, succeeds when 1,2-naphthynes and 2,3-pyridynes are involved as intermediates. Using this procedure 3-aza-benzo[j]phenanthridine, 9-azaphenanthridine and 2,11-diazachrysene have been synthesized.

Keywords. 1,2-Naphthynes; 2,3-pyridynes; 3,4-pyridynes; 3-aza-benzo[j] phenanthridine; 9-azaphenanthridine; 2,11-diazachrysene.

1. Introduction

The objective of the present work was to explore the synthetic scope of the recently developed benzyne route (Kessar *et al* 1973) to condensed polynuclear heterocycles. It was of interest to find out if cyclisation can be effected when different arynes or hetrarynes are involved as intermediates. If successful, the investigation could lead to synthesis of some new or otherwise not easily accessible systems.

2. Results and discussion

Condensation of the acid chloride (1) from 3-chloro-2-naphthoic acid (Strohbach 1901) with aniline gave the amide 2 which was reduced with lithium aluminium hydride to get the substrate 3. Its treatment with excess potassium amide in liquid ammonia furnished a mixture from which the known (Klemm and Weisert 1965) benzo[j]phenanthridine (4) was secured in 29% yield. In an alternate procedure to get 4, the amine 3 was oxidised with MnO_2 and the obtained Schiff base 5 reacted with KNH_2/NH_3. A similar reaction of the pyridyl base 6 afforded a cyclisation product (18%), the NMR spectrum of which is consistent with structure 7. As expected on this basis, four singlets can be seen in the spectrum although the one at δ 9·45 is broadened (H-4 meta coupled to H-2) and overlaps with that at δ 9·40. Another feature is a sharp doublet at δ 8·41 (H-1, J=5·5 Hz) which is

very informative since in the alternate structure 8 all the doublets are expected to be broadened by meta coupling. Further, the downfield position of the signals at δ 9·45 (H-4) and δ 9·40 (H-12) is also in accord (Martin *et al* 1966) with structure 7.

To find out if cyclisation involving 2,3–pyridynes are successful, the anilide from 3–bromoisonicotinic acid (Palat *et al* 1967) was converted to imino chloride which was reduced with sodium borohydride. The obtained base 10 was exposed to excess potassium amide in liquid ammonia. The usual work up afforded a mixture (TLC) which was oxidised with MnO_2 in chloroform to get (10% yield) 9-azaphenanthridine (11) (Perkampus and Behjati 1974). To see if 3,4-pyridyne cyclisation with a naphthalene ring is successful, the bromo compound 13 was treated with KNH_2/NH_3 and the product aromatised with MnO_2 in chloroform. This procedure afforded 2,11–diazachrysene (14) in a 65% yield.

It may be concluded that cyclisations involving 1,2-naphthynes and 2,3–pyridynes are successful but the yields are poor as compared to the corresponding 2,3-napthhthynes (Kessar *et al* 1978) and 3,4–pyridynes (Kessar *et al* 1976). Nevertheless because of simplicity, this procedure constitutes a very convenient method for the synthesis of the systems reported in the present work.

3. Experimental

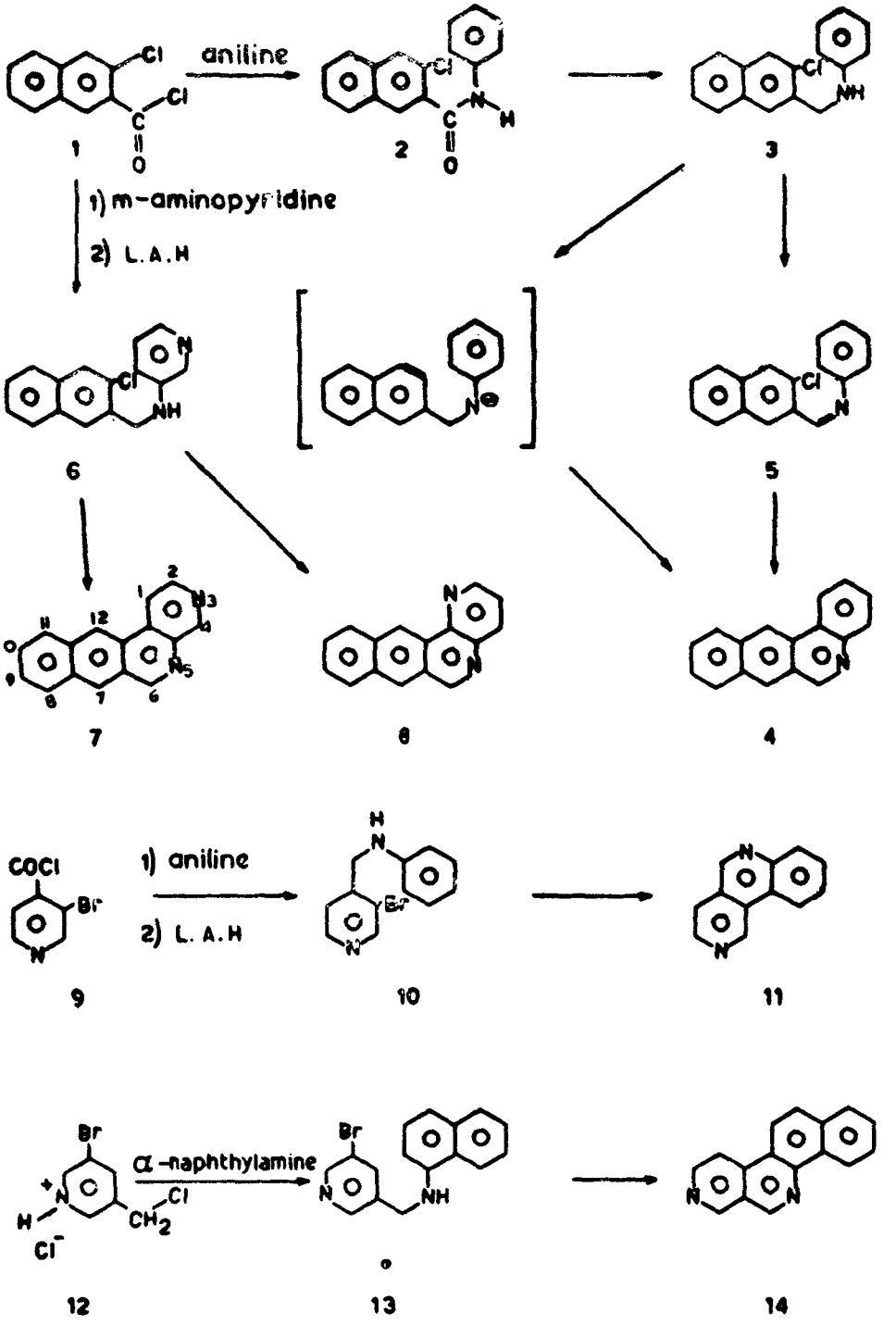
All melting points are uncorrected. IR spectra were run on a Perkin-Elmer 337 apparatus and mass spectra were recorded on a MS-9 spectrometer. NMR spectrum was recorded on Bruker WH 90 spectrometer. Preparative TLC was carried out on silica gel plates. Anhydrous Na_2SO_4 was used for drying organic solutions.

3.1. 3–*Chloro*–2–(*N–phenyl*) *naphthamide* (2)

A solution of aniline (0·45 g) in pyridine (1·8 ml) and ether (15 ml) was added, dropwise with continuous shaking, to a solution of 3-chloro-2-naphthoyl chloride (0·9 g) in ether (40 ml) and the mixture was allowed to stand overnight. After adding water (15 ml), the ether layer was separated. The aqueous layer was extracted with benzene (3 × 20 ml). The combined ether and benzene extract was washed with water, dried and the solvent distilled off. The residue was crystallised from benzene to give the amide 2 (0·43 g, 38%); mp 177–78°; IR (nujol): ν_{max} 1645 cm^{-1} (C=O) (Found : C, 72·63; H, 4·35; N, 4·92. $C_{17}H_{12}ClNO$ requires : C, 72·34; H, 4·25; N, 4·96%).

3.2. *N*-(3-*Chloro-2-naphthylmethyl*) *aniline* (3)

To a stirred suspension of lithium aluminium hydride (0·75 g) in ether (20 ml) was added a solution of anhydrous aluminium chloride (2·67 g) in ether (20 ml) dropwise. After 5 min a solution of the amide 2 (5 g) in ether (30 ml) was added slowly. Stirring was continued for 1½ hr after which the reaction mixture was decomposed by successive addition of water (2 ml) and aqueous sodium hydroxide (10%, 1 ml). The ether layer was separated and the cake extracted with warm benzene. The combined organic layer was washed with water, dried and the


aniline
1) m-aminopyridine
2) L.A.H
1) aniline
2) L. A. H
α-naphthylamine

solvent distilled off. The residue was crystallised from methanol to give the amine 3 (4 g, 84%); mp 115–16° (Found: C, 76·20; H, 5·24; N, 5·33. $C_{17}H_{14}ClN$ requires : C, 76·26; H, 5·23; N, 5·23%).

3.3. *Benzo[j]phenanthridine* (4)

To liquid ammonia (350 ml) contained in a 500 ml 3-necked flask, fitted with a sealed mechanical stirrer and a KOH guard tube, small pieces of potassium metal were added till the blue colour persisted for about 10 min. Then, after putting in a small crystal of ferric nitrate to catalyse the conversion of potassium metal to potassium amide, potassium metal (0·44 g) was added. When the metal had reacted completely, as indicated by a colour change from blue to grey, a solution of the amine 3 (0·4 g) in dry ether (30 ml) was added at once. The reaction mixture was stirred for additional 3 hr and quenched with ammonium chloride (3 g). Ammonia was allowed to escape. The residue was diluted with water (50 ml) and extracted with ether (3 × 30 ml). The organic layer was washed with water, dried and the solvent distilled off. The residue was purified by preparative TLC and further crystallised from methanol to give a solid (0·1 g, 29%), mp 141–42°; identical with benzo[j]phenanthridine (Klemm and Weisert 1965) (Found: C, 89·16; H, 4·74; N, 6·15. Calculated for $C_{17}H_{11}N$: C, 89·05; H, 4·84; N, 6·11%).

3.4. *N-(3-chloro-2-naphthylmethylene) aniline* (5)

Manganese dioxide (5 g) was added to a solution of the amine 3 (0·5 g) in dry benzene (30 ml) and the mixture refluxed for 3 hr. Manganese dioxide was filtered off and the solvent was evaporated from the filtrate. The residue was crystallised from methanol to give the Schiff base 5 (0·4 g, 80%) mp 109–10°; IR (nujol): ν_{max} 1650 cm^{-1} (C=N). (Found: C, 76·76; H, 4·49; N, 5·07. $C_{17}H_{12}ClN$ requires: C, 76·83; H, 4·52; N, 5·27%).

3.5. *Benzo[j]phenanthridine* (4)

Reaction of the Schiff base 5 (0·3 g) dissolved in ether (20 ml), with potassium amide (from 0·44 g potassium metal) in liquid ammonia (300 ml) and work up as above, gave a solid (0·075 g, 29%); mp 141–42°, identical with 4.

3.6. *3-Chloro-2-(N-3'-pyridyl) naphthamide*

Reaction of 3-aminopyridine (1·5 g) dissolved in ether (30 ml) and pyridine (4·5 ml) with 3-chloro-2-naphthoyl chloride (3 g) gave 3-chloro-2-(N-3'-pyridyl) naphthamide (1·8 g, 47%); mp 154–55° (benzene); IR (nujol): ν_{max} 1630 cm^{-1} (C=O). (Found: C, 67·76; H, 3·76; N, 9·98. $C_{16}H_{11}ClN_2O$ requires: C, 67·96; H, 3·89; N, 9·91%).

3.7. *N-(3-chloro-2-naphthylmethyl)-3-aminopyridine* (6)

Reduction of the above amide (3 g) with a suspension of lithium aluminium hydride (0·5 g) and aluminium chloride (1·78 g) in dry ether (50 ml) gave the

amine 6 (0·3 g, 10%); mp 154–55° (methanol). (Found: C, 71·89; H, 4·78; N, 10·50. $C_{16}H_{13}ClN_2$ requires: C, 71·51; H, 4·84; N, 10·43%).

3.8. 3-*Aza-benzo*[*j*]*phenanthridine* (7)

The amine 6 (0·41 g) in ether (50 ml) was reacted with potassium amide (from 0·468 g potassium metal) in liquid ammonia (300 ml). The reaction mixture was processed as usual to get a semi-solid. It was purified by preparative TLC, dissolved in chloroform (20 ml) and stirred with active manganese dioxide (1·2 g) for 3 hr. Manganese dioxide was filtered off and the solvent was evaporated from the filtrate. The residue was crystallised from pet. ether to give 7 (0·06 g, 18%); mp 138–39°; mass spectrum: m/e 230 (M^+), 203, 202, 176, 175; NMR ($CDCl_3$): δ 9·45 (broadened *s*, 1H, H-4), 9·40 (*s*, 1H, H-12), 9·03 (*s*, 1H, H-6), 8·80 (broadened d, 1H, J ~ 4·5 Hz, H-2), 8·58 (*s*, 1H, H-7), 8·41 (*d*, 1H, J = 5·5 Hz, H-1), 8·22–7·65 (4H). (Found: N, 12·23. $C_{16}H_{10}N_2$ requires: N, 12·17%).

3.9. 3-*Bromoisonicotinanilide*

Thionyl chloride (5 ml) was added to 3-bromoisonicotinic acid (2·02 g) with cooling and then the mixture was heated (60–70°) for 3 hr. Excess thionyl chloride was distilled off under reduced pressure and the resulting acid chloride taken up in ether (25 ml). To this solution was added a solution of aniline (1 g) in pyridine (1·7 g) and ether (25 ml) dropwise and the mixture allowed to stand overnight. After basification with dilute sodium carbonate, the ether layer was separated. The aqueous layer was extracted with ether and combined ether layer was dried. The solvent was distilled off and the residue crystallised from benzene to give 3-bromoisonicotinanilide (1·5 g, 54%), mp 148–49°; IR (nujol): ν_{max} 1635 cm^{-1} (C=O). (Found: C, 52·04; H, 3·15; N, 10·05. $C_{12}H_9BrN_2O$ requires: C, 51·98; H, 3·25; N, 10·10%).

3.10. 3-*Bromo*-4-[(*N-phenyl*) *aminomethyl*] *pyridine* (10)

To a solution of the above amide (2·77 g) in chloroform was added phosphorous pentachloride (2·5 g) and the mixture refluxed for 45 min. Chloroform was evaporated and the resulting brown complex was cooled to 0°. A suspension of sodium borohydride (1·14 g) in ethanol (15 ml) was added to this complex with continuous shaking and the mixture was refluxed. After 45 min the solvent was evaporated and the residue was partitioned between ether and dilute HCl. The acid layer was basified with a solution of sodium carbonate and extracted with ether. Evaporation of the solvent left an oily material (0·45 g, 17%). (Found: C, 54·64; H, 4·22; N, 10·54. $C_{12}H_{11}BrN_2$ requires: C, 54·75; H, 4·18; N, 10·60%).

3.11. 9-*Azaphenanthridine* (11)

Reaction of the amine 10 (0·3 g) with potassium amide (from 0·356 g potassium metal) in liquid ammonia (300 ml) and subsequent treatment of the resulting mixture with MnO_2 in chloroform gave a solid (0·02 g, 10%), mp 163–64° (ether); identical with 9-azaphenanthridine (Perkampus and Behjati 1974) mass spectrum: m/e 180 (M^+), 153, 152, 126, 126, 90. (Found: N, 15·27. $C_{12}H_8N_2$ requires: N, 15·55%).

3.12. 5-*Bromo*-3-(N-1-*naphthyl*) *aminomethyl pyridine* (13)

5-Bromo-3-chloromethylpyridine hydrochloride (1·3 g), prepared according to the method of Kauffmann and Fischer (1973), and α-naphthylamine (2·7 g) were refluxed in ethanol (20 ml) for 2 hr. The solvent was completely removed, the residual oil basified with dil. sodium bicarbonate and extracted with ether. The ether extract was washed with water, dried and the solvent evaporated. The residue, when chromatographed on alumina (with ether: pet. ether, 1: 4), gave the amine 13 (0·95 g, 56·75%), mp 81–82°. (Found: C, 61·45; H, 4·24; N, 8·63. $C_{16}H_{13}BrN_2$ requires: C, 61·34; H, 4·15; N, 8·94%).

3.13. 2,11-*Diazachrysene* (14)

Reaction of the amine 13 (0·313 g) with potassium amide (from 0·39 g potassium metal) in liquid ammonia (300 ml) and subsequent treatment of the solid with MnO_2 in chloroform gave 2,11-diazachrysene (0·15 g, 65%), mp 191–92°; mass spectrum: m/e 230 (M^+), 203, 176. (Found: C, 83·36; H, 4·27; N, 12·64. $C_{16}H_{10}N_2$ requires: C, 83·45; H, 4·38; N, 12·17%).

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References

Kauffmann T and Fischer H 1973 *Chem. Ber.* **106** 220
Kessar S V, Gopal R and Singh M 1973 *Tetrahedron* **29** 167
Kessar S V, Gupta Y P, Pahwa P S and Singh Paramjit 1976 *Tetrahedron Lett.* p. 3207
Kessar S V, Pahwa P S, Pawanjit, Singh Paramjit and Gupta Y P 1978 *Indian J. Chem.* **B16** 92–Part XVI
Kessar S V, Gupta Y P, Singh Paramjit, Jain V and Pahwa P S 1979 *J. Chem. Soc.* (Pakistan) (Communicated)—Part XVII
Klemm L H and Weisert A 1965 *J. Heterocycl. Chem.* **2** 15
Martin R H, Defay F, Geerts-Evrard F and Bogaert-Verhoogen D 1966 *Tetrahedron Suppl.* **8** (Part I) 181
Palat K, Noracek L and Celadnik M 1967 *Collect. Czech. Chem. Commun.* **32** 1191
Perkampus H H and Behjati B 1974 *J. Heterocycl. Chem.* **11** 511
Strohbach E 1901 *Ber dt. Chem, Ges.* **34** 4158