Novel Formation of 5-Aminocinnolines from 5-Oxo-5,6,7,8-tetrahydrocinnolines—Abnormal Course of Schmidt and Beckmann Rearrangements

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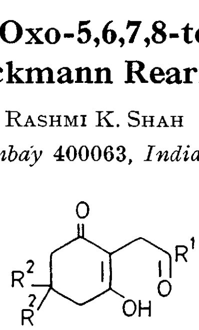
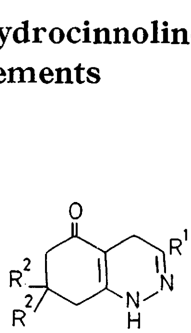
Summary 5-Oxo-5,6,7,8-tetrahydrocinnolines upon treatment with sodium azide and sulphuric acid afford 5-aminocinnolines which are also obtained from the respective 5-oximino-5,6,7,8-tetrahydrocinnolines.

In a previous publication[1] we described the anomalous reactions of *NN*-disubstituted hydrazines with 2-phenacyldimedone (**1**) to form 3-amino-4-oxo-4,5,6,7-tetrahydroindoles. Interaction of (**1**) with hydrazine in alcohol led to the yellow oxo-hexahydrocinnoline (**4**) (80—90%), m.p. 235—238°. Treatment of (**4**) with *p*-toluenesulphonyl chloride in pyridine afforded the oxotetrahydrocinnoline (**7**) (75%)†, m.p. 121—123°, forming oxime (**8**), m.p. 261—262°, which was also directly obtained from (**4**) (95%) by treatment with 2 equivalents of hydroxylamine hydrochloride in pyridine at 100°. Acetonyldimedone (**2**) and 2-phenacylcyclohexane-1,3-dione (**3**) were likewise transformed into oximes (**9**) and (**10**) respectively through (**5**) and (**6**).

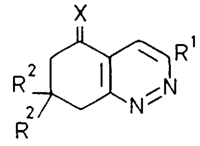
Ketone (**7**) was unaffected by sodium azide in trifluoracetic acid–anhydride solution; but treatment with sodium azide in sulphuric acid during 2 h at room temperature, followed by neutralization afforded the 5-aminocinnoline (**11**) (75%)†, m.p. 209—211°. Compound (**11**) was also obtained from oxime (**8**) by treatment with polyphosphoric acid, sulphuric acid, or phosphorus oxychloride–pyridine (70, 85, 40% respectively). Oximes (**9**) and (**10**) were likewise converted by polyphosphoric acid into 5-aminocinnolines (**12**), m.p. 235—236° and (**13**), m.p. 219—221° (95 and 50% respectively). The u.v. spectrum of (**12**), λ_{max} (1N HCl) 245, 281, 360, 472 nm (log ϵ 4·42, 3·82,



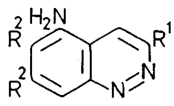
(1) R^1=Ph; R^2=Me
(2) R^1=R^2=Me
(3) R^1=Ph; R^2=H



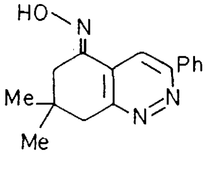
(4) R^1=Ph; R^2=Me
(5) R^1=R^2=Me
(6) R^1=Ph; R^2=H



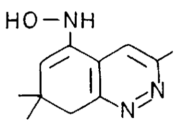
(7) R^1=Ph; R^2=Me; X=O
(8) R^1=Ph; R^2=Me; X=NOH
(9) R^1=R^2=Me; X=NOH
(10) R^1=Ph; R^2=H; X=NOH



(11) R^1=Ph; R^2=Me
(12) R^1=R^2=Me
(13) R^1=Ph; R^2=H



(14) (8)



(15)

Satisfactory mass, n.m.r., and i.r. spectral data were obtained.

3·28, 2·65) has a strong resemblance to that of 5-aminocinnoline.[2] Diazotisation of (**13**) followed by treatment with hypophosphorous acid afforded the known 3-phenylcinnoline.[3] The transformations of ketone (**7**) and oximes (**8**)—(**10**) provide simple synthetic routes to 5-aminocinnolines which are not readily accessible.[2]

The simple conversion of oximes (**8**)—(**10**) into 5-aminocinnolines constitute new examples of the Semmler–Wolff rearrangement.[4] N.m.r. data on ketone (**7**) and oxime (**8**) suggest that the oximino-group of the latter is *anti* to the pyridazine ring as shown in (**14**). The reluctance of the electron-deficient pyridazine ring in (**8**)—(**10**) to migrate under acidic conditions may allow tautomerization into species (**15**), which upon loss of the elements of water (with or without methyl migration as the case may be), will lead to 5-aminocinnolines. The formation of (**11**) from (**7**) under Schmidt reaction conditions must be due to similar reasons and to our knowledge has no precedent in the literature.

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