

SYNTHESES AND REGIOSELECTIVE CYCLOADDITION REACTIONS OF CYCLOHEPT-[d]IMIDAZO[1,2-a]IMIDAZOLES (1,3a,9-TRIAZACYCLOPENT[a]AZULENES): FORMATION OF 2,3-DIAZACYCLOHEPTA[ef]CYCL[3.2.2]AZINE SYSTEM¹⁾

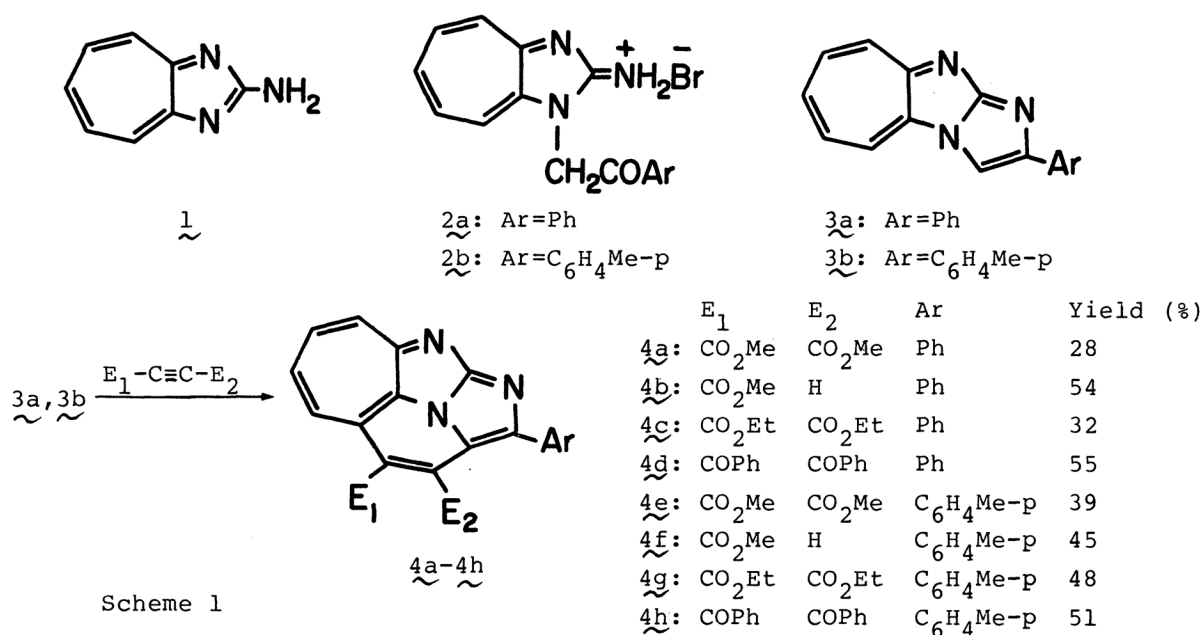
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Cyclohept[d]imidazo[1,2-a]imidazoles (1,3a,9-triazacyclopent[a]-azulenes), being synthesized from 2-aminocycloheptimidazole, was allowed to react with reactive acetylenes to give 2,3-diazacyclohepta[ef]cycl[3.2.2]azines regioselectively.

Recently, the cyclazine systems have attracted attentions for their interesting physical and chemical properties,²⁾ whose efficient synthetic method is the cycloaddition to adequate N-bridged heterocycles [e.g., cycloaddition of indolizines with dimethyl acetylenedicarboxylate (DMAD) leads to cycl[3.2.2]azines^{3,4)}]. In the course of our studies on azaazulenes,⁵⁾ we investigated syntheses of cyclohept[d]-imidazo[1,2-a]imidazoles (1,3a,9-triazacyclopent[a]azulenes) which would provide a convenient synthetic route to 2,3-diazacyclohepta[ef]cycl[3.2.2]azines.

Treatment of 2-aminocycloheptimidazole (2-amino-1,3-diazaazulene) (1)⁶⁾ with α -bromoacetophenone in abs ethanol under reflux for 7 h gave 2-amino-1-phenacyl-cycloheptimidazole hydrobromide (2a) [colorless prisms, mp 230-231°C] in 80% yield. Cyclization to 2-phenylcyclohept[d]imidazo[1,2-a]imidazole (3a)⁷⁾ was attained by the treatment of the salt with potassium carbonate in hot ethanol for 2 h [76% yield, brown prisms, mp 244-245°C, UV_{max} (EtOH) 232 nm ($\log \epsilon$ 4.50), 245^{sh} (4.22), 334 (4.70), 421 (3.76), 428^{sh} (3.60), 1H NMR⁸⁾ (CF_3CO_2H) δ =7.50-7.90 (5H, m, phenyl), 8.43 (1H, s, H-3), 8.60-9.00 (3H, m, H-6,7,8), 9.20-9.60 (2H, m, H-5,9)]. Similarly, the reaction of 1 with α -bromo-(p-methyl)acetophenone, followed by the treatment with potassium carbonate gave 3b⁷⁾ [64% yield, brown prisms, mp 272-275°C (dec)]. The C-3 position of 3a and 3b is reactive, being deuterated by CF_3CO_2D or brominated by N-bromosuccinimide.

Treatment of 3a with DMAD in acetonitrile under reflux for 2 h gave dimethyl 1-phenyl-2,3-diazacyclohepta[ef]cycl[3.2.2]azine-8,9-dicarboxylate (4a)⁷⁾ [28% yield, fluorescent yellow needles, mp 215-216°C, m/e 385 (M^+), UV_{max} (EtOH) 237 nm ($\log \epsilon$ 4.42), 270^{sh} (4.45), 292 (4.57), 380 (4.39), 418 (4.18), 438 (4.16), IR (Nujol) 1730 and 1705 cm^{-1} (C=O), 1H NMR⁸⁾ ($CDCl_3$) δ =4.03 (3H, s, OMe), 4.05 (3H, s, OMe), 7.45-7.65 (3H, m, phenyl), 7.71 (1H, td, J =9 and 2 Hz, H-5), 7.86 (1H, td, J =9 and 2 Hz, H-6), 8.15-8.35 (2H, m, phenyl), 8.40 (1H, dd, J =9 and 2 Hz, H-4), 9.37 (1H, dd, J =9 and 2 Hz, H-7)]. Likewise, the reaction of 3a with methyl propiolate gave 4b⁷⁾ [54% yield, fluorescent yellow needles, mp 246-248°C, UV_{max} (EtOH) 235 nm ($\log \epsilon$ 4.27), 241 (4.26), 263 (4.23), 292 (4.49), 300^{sh} (4.43), 319 (3.93), 333 (3.95),



373 (4.21), 388 (4.23), 423 (3.97), 446 (4.02), IR (Nujol) 1715 cm⁻¹ (C=O)]. In the ¹H NMR spectrum of 4b,⁸⁾ the H-7 proton was visible at rather lower field [δ 9.53 (dd, J=9 and 2 Hz)] and would be under the deshielding effect of the ester group at C-8. Other seven-membered ring protons were seen at δ 7.77 (td, J=9 and 2 Hz, H-5), 7.88 (td, J=9 and 2 Hz, H-6), and 8.06 (dd, J=9 and 2 Hz). A 1H-singlet at δ 8.03 would be assigned to the H-9 proton. Other protons were seen at δ 4.00 (3H, s, OMe), 7.35-7.60 (3H, m, phenyl), and 8.25-8.55 (2H, m, phenyl). Similarly, 3a and 3b reacted with reactive acetylenes, producing a series of the cyclazines 4c-4h⁷⁾ (Scheme 1).

The reaction of cyclohept[d]imidazo[1,2-a]imidazoles with reactive acetylenes appears to proceed in a regioselective [8 + 2]π cycloaddition type, providing a good route to 2,3-diazacyclohepta[ef]cycl[3.2.2]azines.

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- 7) Satisfactory elemental analyses and spectroscopic data were obtained for all new compounds.
- 8) ¹H NMR spectra were measured at 90 MHz and assignments were confirmed by decoupling techniques.

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