CHEMISTRY LETTERS, pp. 805-806, 1982.

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)

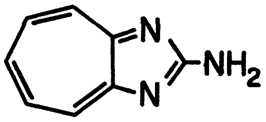
Noritaka ABE,* Tarozaemon NISHIWAKI, and Hideko YAMAMOTO
Department of Chemistry, Faculty of Sciences,
Yamaguchi University, Yamaguchi 753

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.

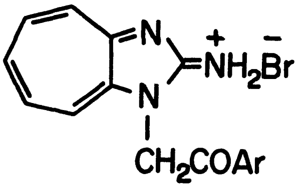
Recently, the cyclazine systems have attracted attentions for their interesting physical and chemical properties,2) whose efficient synthetic method is the cycloaddition to adequate N-bridged heterocycles [e.g., cycloaddition of indolizines with dimethyl acetylenedicarboxylate (DMAD) leads to cycl[3.2.2]azines3,4)]. 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-phenacylcycloheptimidazole 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 ε 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 **3b**7) [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.

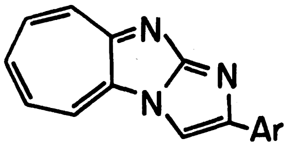
Treatment of **3a** with DMAD in acetonitrile under reflux for 2 h gave dimethyl 1-phenyl-2,3-diazacyclohepta[ef]cycl[3.2.2]azine-8,9-dicarboxylate (**4a**)7) [28% yield, fluorescent yellow needles, mp 215-216°C, m/e 385 (M^+), UV_{max} (EtOH) 237 nm (log ε 4.42), 270^{sh} (4.45), 292 (4.57), 380 (4.39), 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 **4b**7) [54% yield, fluorescent yellow needles, mp 246-248°C, UV_{max} (EtOH) 235 nm (log ε 4.27), 241 (4.26), 263 (4.23), 292 (4.49), 300^{sh} (4.43), 319 (3.93), 333 (3.95),



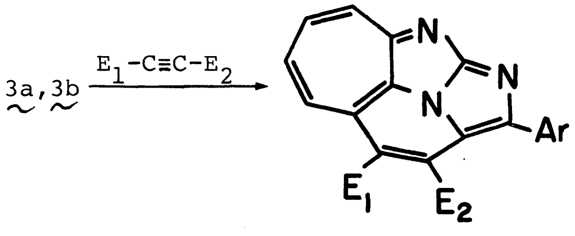
1



2a: Ar=Ph
2b: Ar=C_6H_4Me-p



3a: Ar=Ph
3b: Ar=C_6H_4Me-p



4a-4h

Scheme 1

	E_1	E_2	Ar	Yield (%)
4a:	CO_2Me	CO_2Me	Ph	28
4b:	CO_2Me	H	Ph	54
4c:	CO_2Et	CO_2Et	Ph	32
4d:	COPh	COPh	Ph	55
4e:	CO_2Me	CO_2Me	C_6H_4Me-p	39
4f:	CO_2Me	H	C_6H_4Me-p	45
4g:	CO_2Et	CO_2Et	C_6H_4Me-p	48
4h:	COPh	COPh	C_6H_4Me-p	51

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-4h[7] (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.

This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education (No. 5670021).

References

1) Studies on Heterocyclic Analogs of Azulenes. X. Part IX, under submission.
2) W. Flish and U. Krämer, Adv. Heterocyclic Chem., 22, 321 (1978).
3) J. C. Godfrey, J. Org. Chem., 24, 581 (1959).
4) A. Galbraith, T. Small, and V. Boekelheide, J. Org. Chem., 24, 582 (1959).
5) T. Nishiwaki and N. Abe, Heterocycles, 15, 547 (1981).
6) T. Nozoe, T. Mukai, K. Takase, I. Murata, and K. Matsumoto, Proc. Japan Acad., 29, 452 (1953).
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.

(Received March 20, 1982)