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Cycloadditions with Hetaryl Dieneamines
A Direct Route to Hetarylazulenes

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Hetaryl dieneamines readily available from fused N-aryl azolium salts with secondary amines were found to undergo cycloadditions. With N-phenylmaleinimide and acetylene dicarboxylic ester, [4 + 2] cycloaddition took place to yield tetrahydroisoindolone (**2**) and phtalic acid (**3**) derivatives, respectively. Reaction with fulvene reagent **4** resulted in a [6 + 4] cycloaddition followed by a spontaneous elimination and allowed a convenient route to hetaryl azulenes (**5**–**7**).

(Keywords: Cycloaddition: Dieneamine; Push-pull system; Azulene synthesis)

Zykloadditionen mit Hetaryldienaminen. Eine direkte Route zu Hetarylazulenen

Die aus kondensierten N-Aryl-azoliumsalzen leicht zugänglichen Hetaryldienamine gehen Zykloadditionen ein. Mit N-Phenylmaleinimid und Acetylendicarbonsäureester traten [4 + 2]-Zykloadditionen ein, wobei Tetrahydroisoindolon- (**2**) und Phtalsäurederivate (**3**) erhalten wurden. Die Reaktion mit Fulvenreagenz **4** führte zu einer [6 + 4]-Zykloaddition und anschließender spontaner Eliminierung; das erwies sich als eine bequeme Route zu Hetarylazulenen (**5**—**7**).

Introduction

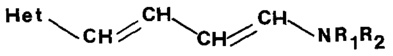
In our earlier publications [1–3] we reported that treatment of bridge head nitrogen containing fused azolium salts with nucleophiles proved to be a suitable tool for preparation of hetaryl dienes (e.g. dieneamines **1 b**–**g**) in good yield. Because of this relatively easy access to hetaryl dienes, the investigation of the reactivity of these push-pull type compounds seemed to be of interest.

Results and Discussion

In one of our preliminary papers [3] we indicated that dieneamine **1 b** when treated with N-phenylmaleinimide gave a crystalline cycloadduct.

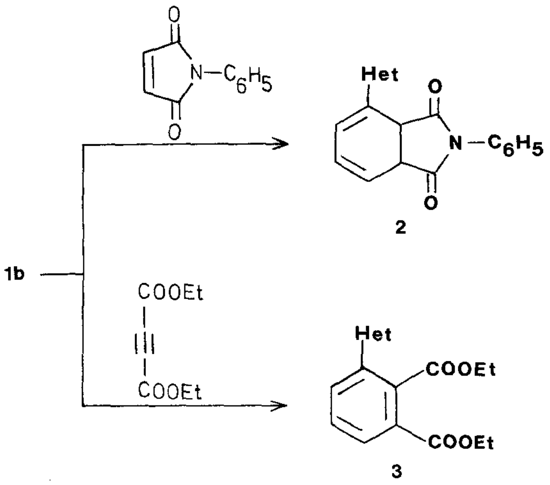
Structure elucidation of this product revealed now that this cycloaddition proceeded as expected in a [4 + 2] manner followed by elimination of morpholine and resulting in 2-phenyl-4-[2-(4-chlorophenyl)tetrazolyl-5]-1,3,3a,7a-tetrahydroisoindole-1,3-dione (**2**).

Scheme 1



1

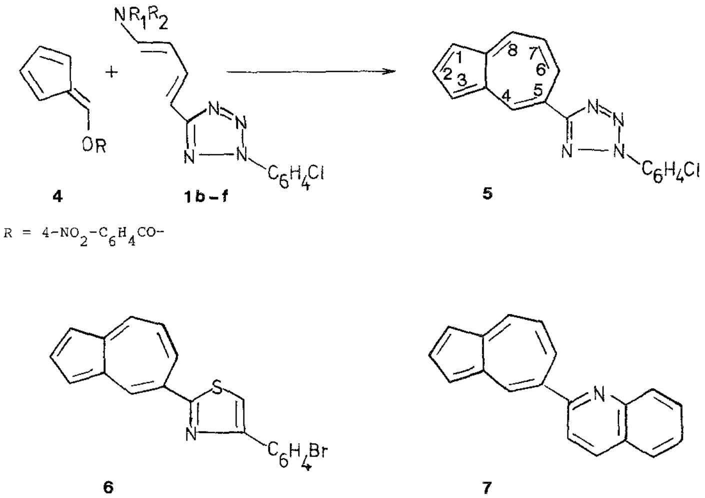
	Het	NR_1R_2
a	H	diethylamino
b	2-/4-chlorophenyl/tetrazolyl-5	morpholino
c	2-/4-chlorophenyl/tetrazolyl-5	piperidino
d	2-/4-chlorophenyl/tetrazolyl-5	pyrrolidino
e	2-/4-chlorophenyl/tetrazolyl-5	dimethylamino
f	2-/4-chlorophenyl/tetrazolyl-5	diethylamino
g	4-/4-bromophenyl/thiazolyl-2	diethylamino
h	2-quinolyl	pyrrolidino
i	2-quinolyl	piperidino



We found that this type of cycloaddition can occur with other dienophiles too. Thus, reaction of **1 b** with diethyl acetylene dicarboxylate yielded diethyl 3-[2-(4-chloro-phenyl)-tetrazolyl-5]-phtalate (**3**).

A recent paper from *Houk* et al. [4] on [6 + 4] cycloaddition of simple dieneamines (e.g. **1 a**) with fulvenes prompted us to investigate the reactivity of hetaryldieneamines with such reagents. These authors reported that dieneamine **1 a** when reacted with *p*-nitrobenzoyloxyfulvene (**4**) (which is the most reactive fulvene derivative for such reactions) azulene was obtained in good yield.

Scheme 2



Reaction of **1 b** with fulvene reagent **4** showed that after few hours the starting diene compound disappeared from the reaction mixture and a new blue spot could be registered on tlc. By use of column chromatography, 5-(2-chlorophenyltetrazolyl-5)azulene (**5**) could be isolated. The ^{1}H-NMR spectrum of **5** showed unambiguosly (H-4 appeared as a singlet) the selective formation of the 5-substituted azulene. This regiospecifity seems to be in good agreement with earlier theoretical considerations and experimental findings [5].

Because of the rather poor yield (14%) of the above experiment, we also made efforts to compare dieneamines with various amine moieties in this cycloaddition reaction. For this purpose, piperidino-, pyrrolidino-, dimethylamino- and diethylamino-tetrazolylbutadienes (**1 c–f**) have also been prepared and reacted with reagent **4**. Table 1 shows that all of these dieneamines gave rise to tetrazolylazulene **5**, however, in different yields: the optimal yield (65%) was found with derivative **1 f**. Although by enhancement of the basicity of the amine component a shorter reaction time was achieved, no essential gain in yield was obtained, probably because of the acceleration of nondesired side reactions (e.g. **1 c** vs. **1 d**)

Table 1. *Characteristics and yields of hetarylazulenes*

Compound	m.p. [°C]	Molecular formula and analysis	Starting diene-amine	Reaction conditions temperature/time [°C]	[h]	Yield [%]
5	144–145	$C_{17}H_{11}ClN_4$				
		Calcd. C 66.56 H 3.61 N 18.25 Cl 11.56	**1 b**	50	6	14
		Found C 66.35 H 3.73 N 18.43 Cl 11.61	**1 c**	50	6	14
			1 d	25	3	33
			1 e	25	7	50
			1 f	25	7	65
6	165–166	$C_{19}H_{12}BrNS$				
		Calcd. C 62.31 H 3.30 N 3.82 S 8.75	**1 g**	50	8	46
		Found C 62.51 H 3.19 N 3.59 S 8.64				
7	94–96	$C_{19}H_{13}N$				
		Calcd. C 89.38 H 5.13 N 5.48	**1 h**	25	8	10
		Found C 89.23 H 5.28 N 5.42	**1 i**	25	10	12

and the decrease of the steric demand of the amine moiety (**1 e**) did not improve the yield either.

We found furthermore that this cycloaddition reaction can be extended to different hetaryl derivatives. Thus, thiazolylbutadiene **1 g** reacted in an analogous manner to give thiazolylazulene **6**. Azulene attached to a six membered heterocycle (**7**) could also be obtained by reacting quinolyldieneamines (**1 h, i**) with fulvene reagent **4**. Our attempt to improve the yield of **7** by preparing a quinolyldieneamine bearing a diethylamino substituent (which proved to ensure an optimal yield in the above cases) failed possibly because of its unstability.

These findings reveal that hetaryldieneamines easily undergo cycloadditions of both [4 + 2] and [6 + 4] types. Although few hetarylazulenes have been reported in the literature [7], this route represents a more convenient and direct access to azulenes bearing hetaryl substituent.

Acknowledgments

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Experimental

Nmr spectra were obtained on a Varian XL-100 equipment, the ir spectra on a Specord 75 apparatus. Melting points are uncorrected.

Hetaryl Dieneamines (**1 b–i**)

Solvents for recrystallization, melting points, yields and elementary analyses are shown in Table 2.

Compounds **1 b** and **1 i** were prepared as described earlier [3, 6].

Compounds **1 c–g**: A solution of azolium salt (5.0 mmol) in acetonitrile (15 ml) was treated with the appropriate amine (50 mmol) with stirring at 0 °C. The mixture was allowed to stand overnight at this temperature and was then poured onto ice water. The precipitate was filtered and recrystallized.

Compound **1 h**: A solution of benzo[c]quinolizinium salt (5.0 mmol) in acetonitrile (15 ml) was treated with pyrrolidine (3.0 g, 51 mmol) and the mixture was refluxed for 30 min. A similar workup as above yielded dieneamine **1 h**.

2-Phenyl-4-[2-(4-chlorophenyl)tetrazolyl-5]-1,3,3a,7a-tetrahydroisoindole-1,3-dione (**2**)

A solution of dieneamine **1 b** (0.32 g, 1 mmol) and N-phenylmaleinimide (0.18 g, 1 mmol) in benzene (10 ml) was refluxed for 8 h. The resulting colorless precipitate was filtered and recrystallized from dimethylformamide to give 0.35 (72%) of product, m.p. 203–204°.

Anal. calcd. for $C_{21}H_{14}ClN_5O$ (403.84): C 62.46, H 3.49, N 17.34, Cl 8.78. Found: C 62.78, H 3.71, N 17.52, Cl 9.03. ^{1}H-NMR (*DMSO-d_6*): 8.08–6.25 (12 H, m, H-*Ar*), 2.88 (1 H, d, H-3a), 2.15 (1 H, dd, H-7a) ppm.

Table 2. *Characteristics of novel hetaryldieneamines*

Compound	m.p. [°C]	Solvent of recrystallization	Yield [%]	Molecular formula		Analysis		
						C	H	N
1 c	129–131	Acetonitrile	76	$C_{16}H_{18}ClN_5$	Calcd.	60.85	5.75	22.18
					Found	61.01	6.12	22.43
1 d	141–143	Methanol	80	$C_{15}H_{16}ClN_5$	Calcd.	59.67	5.34	23.21
					Found	59.72	5.67	23.46
1 e	113–115	Acetonitrile	75	$C_{13}H_{14}ClN_5$	Calcd.	56.62	5.12	25.40
					Found	56.87	5.45	25.84
1 f	71–72	Ethanol	70	$C_{15}H_{18}N_5Cl$	Calcd.	59.30	5.97	23.00
					Found	59.40	5.98	23.09
1 g	86–87	Petrol ether	42	$C_{17}H_{19}BrN_2S$	Calcd.	56.36	5.28	7.72
					Found	56.36	5.43	7.77
1 h	128–130	Petrol ether	66	$C_{17}H_{18}N_2$	Calcd.	81.56	7.24	11.28
					Found	81.56	7.07	11.06

Diethyl 3-[2-(4-Chlorophenyl)tetrazolyl-5]-phtalate (**3**)

A solution of dieneamine **1b** (0.32 g, 1 mmol) and diethyl acetylenedicarboxylate (0.22 g, 1 mmol) in dry ether (20 ml) was allowed to stand at room temperature for 24 h. The separated colorless crystals were suction filtered and recrystallized from dioxane to give 0.20 g (49%) of product, m.p. 265–266°.

Anal. calcd. for $C_{19}H_{17}ClN_4O_4$ (400.83): C 56.93, H 4.28, N 13.98, Cl 8.85. Found: C 57.21, H 4.67, N 14.12, Cl 8.92. ^{1}H-NMR (*DMSO-d*$_6$): 8.01–7.80 (m, 7 H, H-*Ar*), 4.23 (qq, 4 H, —CH_2—), 1.88 and 1.77 (tt, 6 H, CH_3) ppm.

Hetarylazulenes (**5**–**7**)

To a solution of *p*-nitrobenzoyloxyfulvene (**4**) (0.243 g, 1 mmol) in benzene (15 ml), a solution of the appropriate hetaryldieneamine (**1b**–**i**) was added dropwise with stirring in an argon atmosphere. This mixture was stirred at ambient temperature (Table 1) and was monitored by tlc. After disappearance of the spot of fulvene **4** (for reaction times, see Table 1) the solvent was evaporated and the residue was chromatographed over a silica gel column (60 g of silica). Elution with benzene and evaporation of the blue fractions gave hetarylazulenes **5**–**7** of satisfactory purity. Melting points and elementary analyses are shown in Table 1.

Compound **5**: ^{1}H-NMR ($CDCl_3$): 9.41 (s, 1 H, H-4), 8.70 (d, 1 H, H-6), 8.40 (d, 1 H, H-8), 7.97 (t, 1 H, H-2), 7.70 (AA'BB', 4-chlorophenyl), 7.63 (d, 1 H, H-3), 7.50 (d, 1 H, H-1), 7.31 ppm (t, 1 H, H-7). IR (KBr): 1 570, 1 495, 1 410, 1 384, 1 080, 995 cm^{-1}. UV (hexane): λ_{max} (ε): 710 (264), 672 (272), 634 (522), 610 (469), 589 (488), 565 (374), 534 (290).

References

[1] *Gelléri A, Messmer A, Nagy S, Radics L* (1980) Tetrahedron Lett 21: 663

[2] *Hajós Gy, Messmer A* (1984) J Heterocyclic Chem 21: 809

[3] *Gelléri A, Messmer A* (1973) Tetrahedron Lett 14: 4295

[4] (a) *Dunn LC, Yan-Min Chang, Houk KN* (1976) J Am Chem Soc 98: 7095; (b) *Gupta YN, Mani SR, Houk KN* (1982) Tetrahedron Lett 23: 495

[5] (a) *Dunn LC, Houk KN* (1978) Tetrahedron Lett 19: 4311; (b) *Houk KN, George JK, Duke RE Jr* (1974) Tetrahedron 30: 523

[6] *Morler D, Kröhnke F* (1971) Liebigs Ann Chem 744: 65

[7] (a) *Brunken J, Poppe E-J* (1960) Chem Ber 93: 2572; (b) *Hafner K, Bernhard C, Muller R* (1961) Liebigs Ann Chem 650: 35; (c) *Nozoe T, Ito S* (1961) Recent advances in the chemistry of azulenes and natural hydroazulenes. In: *Zechmeister L* (Hrsg) Fortschritte der Chemie Organischer Naturstoffe, vol 19. Springer, Wien, p 101