MESOIONIC SIX-MEMBERED HETEROCYCLES, XVII[1].
CYCLOADDITION OF BENZYNE TO MESOIONIC PYRIMIDINES

Thomas Kappe[*] and Dietmar Pocivalnik

Institut für Organische Chemie, Karl-Franzens-Universität,

Heinrichstr. 28, A-8010 Graz, Austria

Abstract — Benzyne (1) reacts with mesoionic pyrimidines (2a-e) yielding below 40°C the primary cycloadducts 3a-e. At higher temperatures the iso-quinolin-3-ones 4a-e are formed under the loss of phenyl isocyanate. Further addition of 1 to 4e yields the adduct 5, which is converted at 200°C into the anthracene derivative 6.

Mesoionic six-membered heterocycles of the pyrimidine, 1,3-oxazine and 1,3-thiazine series may be envisaged as 1,4-dipolar systems[2-4]. In such a light they appear to be suitable candidates for 1,4-dipolar cycloadditions. This presumption has been verified in a number of cases: Mesoionic pyrimidines have been shown to react with dimethyl acetylenedicarboxylate to yield 2-pyridones[3,4] via primary 2+4π-cycloadducts[4]. Whereas diethylamino-1-propine[5], N,N-dimethylamino-phenylacetylene, ethyl propiolate as well as dimethyl maleate failed to give defined products[4], maleic anhydride[3], maleic imides[6], arylcyanates[7] and tetracyanoethene[5,6] gave stable 4+2π-cycloadducts. Bicyclic pyrimidine[4], 1,3-oxazine[8] and 1,3-thiazine[9] mesoions add dimethyl acetylenedicarboxylate to produce quinolizin-4-ones which are otherwise difficult to obtain. Recently, cycloaddition reactions of o-quinoid compounds with mesoionic pyrimidines and 1,3-oxazines have been studied by Friedrichsen[10].

We now report the 1,4-dipolar cycloaddition of benzyne (1) to mesoionic pyrimidines (2a-e). When 2a-e were allowed to react with diazotized anthranilic acid[11-13] under conditions which generate benzyne[12] the adducts 3a-e were obtained in 42-62% yields. If heated to higher temperatures (70°-210°C, depending on the nature of the substituents, Method A, see Table 1) the "diazabarrelenc-diones" 3 lose phenyl isocyanate to form isoquinolin-3(2H)-ones (4a-e). It is of interest to note that upon heating above 70°C the N-benzyl-N'-phenyl compound 3d expels preferentially phenyl isocyanate yielding the isoquinolone 4d and traces only of 4e (resulting from the loss of benzyl isocyanate).
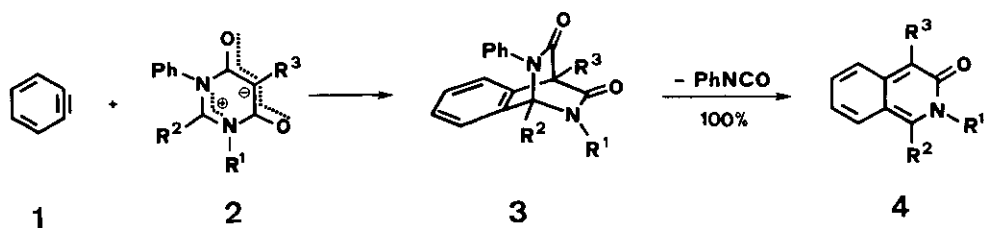
Table 1. R-Key of 2-4 and Yields and M.p.'s of 3 and 4

2-4	R^1	R^2	R^3	3			4		
				yield	dec.°C	(recryst.)	yield[a]	m.p.°C	(recryst.)
a	Ph	CH_3	CH_2Ph	62%	210°	(xylene)	A 100%	145°	(xylene)
b	Ph	Ph	C_2H_5	44%	100°	(acetone)	A 100% B 57%	208°	(xylene)
c	Ph	Ph	$n-C_4H_9$	46%	120°	(ether)[b]	A 100% B 59%	142°	(cyclohexane)
d	CH_2Ph	Ph	CH_2Ph	42%	70°	(acetone)[c]	A 95%	110°	(cyclohexane)
e	Ph	Ph	CH_2Ph	46%	82°	(ether)[d]	A 100%	185°	(cyclohexane)

[a] A: by thermal decomp. of 3; B: by the reaction of 1 with 2 without isolation and purification of 3. [b] partial decomp. if recryst. from acetone. [c] cryst. with 1/2 molecule of acetone. [d] cryst. with 1/2 molecule of ether according to elemental analysis and ^{1}H-NMR.
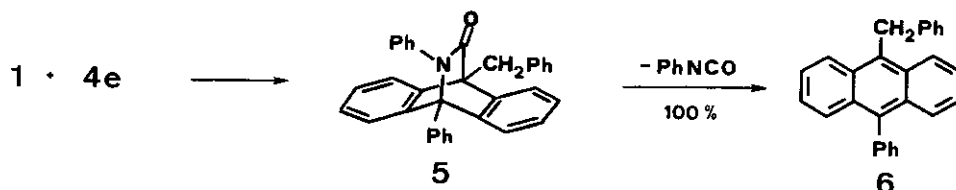
The highly substituted isoquinolones 4 are yellow colored and show a greenish yellow fluorescence under UV-light. They are stable compounds if compared with the unsubstituted [14] or N-methyl-iso-quinolin-3-one[14,15], which are readily oxidized by air, give photo-dimers[14] and Diels-Alder additions[14,15]. However, the latter reaction can lead to complications if the generation of benzyne from 2-diazonium anthranilate in the presence of 2 is conducted at temperatures above 45°C. As shown in the synthesis of 3e at 48°C (see Experimental), the Diels-Alder compound 5, resulting from the addition of benzyne to 4e, is formed in 30% yield (besides 46% of 3e). Since the reaction takes place below the decomposition temperature of crystalline 3e, an equilibrium between 3e on one side and 4e and phenyl isocyanate on the other side can be assumed in solution.

Table 2. Spectroscopic Data of Compounds $\underline{3}$ and $\underline{4}$

	IR (KBr) cm^{-1}	^{1}H-NMR (CDCl$_3$), δ in ppm	MS (70eV), m/e (%)
$\underline{3a}$	1730s, 1695sh, 1690s, 1610m	1.37(s, CH$_3$), 3.92(s, CH$_2$), 6.5-7.65(m, 19 aromat. H)	444(M$^+$, 4%), 325(M-PhNCO, 100), 297 (325-CO, 36), 220(325-PhCO, 27)
$\underline{3b}$	1740-1720s, 1690s 1605m	1.52(t, J=7Hz, CH$_3$), 2.53(q, J=7Hz, CH$_2$), 6.6-7.9(m, 19 aromat. H)	325(M$^+$-PhNCO, 95%), 297(325-CO, 30), 283(39), 282(100), 204(17), 178(10), 119(PhNCO, 29), 91(16)
$\underline{3c}$	1735s, 1695s, 1605m	1.00(t, J=7Hz, CH$_3$), 1.20-2.65(m, 6 aliph. H), 6.5-7.75(m, 19 aromat. H)	353(M$^+$-PhNCO, 100), 311(60), 310 (61), 282(41), 119(5), 91(5)
$\underline{3d}$	1725s, 1680s, 1595m	2.22(s, 3H of 1/2 acetone), 4.00(s, CH$_2$), 4.32(s, NCH$_2$), 6.4-7.7(m, 24 H)	401(M$^+$-PhNCO, 20%), 310(40), 119 (18), 91(100), 77(20)
$\underline{3e}$	1730s, 1690s, 1600m	1.16(t, J=7Hz, 3H of 1/2 ether), 3.45 (q, J=7Hz, 2H of ether), 3.97(s, CH$_2$), 6.7-7.9(m, 24 aromat. H)	387(M$^+$-PhNCO, 84%), 360(48), 359(96), 283(50), 282(100), 119(11), 70(40)
$\underline{4a}$	1650s, 1630sh, 1615m	2.37(s, CH$_3$), 4.25(s, CH$_2$), 6.6-7.7 (m, 14 aromat. H)	325(M$^+$, 76%), 297(61), 220(100), 204 (15), 162(14), 123(15), 119(5), 115 (13), 91(25), 77(46)
$\underline{4b}$	1640sh, 1625s, 1610sh, 1600sh	1.27(t, J=7Hz, CH$_3$), 3.04(q, J=7Hz, CH$_2$), 6.5-7.45(m, 13 aromat. H), 7.62 (dd, J=9 + 1Hz, H-8)	---
$\underline{4c}$	1650sh, 1630s 1610sh	0.8-1.9(m, 7 aliph. H), 2.7-3.2(m, CH$_2$), 6.5-7.5 (m, 13 arom. H), 7.62 (dd, J=9 + 1Hz, H-8)	353(M$^+$, 100%), 324(16), 311(71), 310 (70), 203(14), 119(14), 105(10), 91 (10), 77(30)
$\underline{4d}$	1650sh, 1630s, 1600sh	4.20(s, CH$_2$), 4.30(s, CH$_2$), 6.5-7.7 (m, 19 aromat. H)	---
$\underline{4e}$	1650sh, 1640sh 1630s, 1600sh	4.32(s, CH$_2$), 6.5-7.7(m, 19 aromat. H)	---

EXPERIMENTAL

General procedure for the preparation of 3a-e: Solid benzenediazonium-2-carboxylate[13] (prepared from 2.74 g anthranilic acid, 0.04 ml CF_3CO_2H and 5 ml isoamyl nitrite in 50 ml tetrahydrofuran according to the literature[11]) was added to a solution of 2 (10 mmole) in 50-60 ml chlorobenzene. The stirred reaction mixture was kept 12 hours at 40°C, filtered, the filtrate taken to dryness in vacuo and the residue crystallized from the appropriate solvent, see Table 1.

4a-e; Method A: Compounds 3 were heated without solvent in vacuo to their decomposition temperature (see table 1), yields are 100%.

4b,c; Method B: The crude products 3b,c (obtained by the general procedure and already contaminated with 4b,c) are heated in xylene for 4 hours.

Isolation of 5 and 3e: The general procedure for the preparation of 3 was followed with the exception that the temperature was 48°C and the reaction time 6 hours. Recrystallization from acetone gave a 30% yield of 5. The mother liquor was evaporated and digested with petroleum ether. Crystallization with ether afforded a 46% yield of 3e.

5: Decomposition at about 180°C. - IR (KBr): 1705s, 1600m, 1495m, 1450m cm^{-1}. - ^{1}H-NMR (CDCl$_3$): δ= 4.27 (s, CH$_2$), 6.9-7.5 (m, 23 aromat. H). - MS: m/e = 344(M$^+$-PhNCO, 100%), 268(25), 267(48), 266(28), 265(53), 252(43), 199(22), 178(25), 177(35), 149(32), 119(49), 115(25), 91(43).

6: Compound 5 is heated 5-6 min. at 180-200°C; yield 100%, prisms from acetic acid, m.p. 156°C, (lit. m.p. 151°C[16], 155°C[17]). - IR (KBr): 1600m, 1490m, 1440m, 1380m cm^{-1}. - ^{1}H-NMR (CDCl$_3$): δ= 5.02 (s, CH$_2$), 7.0-7.8 (m, 18 H), 8.05-8.35 (m, 2 H).

Satisfactory analytical results have been obtained for all new compounds[18].

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