99. Cycloaddition of Carbodiimides with a Heteroaromatic Substituent to Allenic Acids

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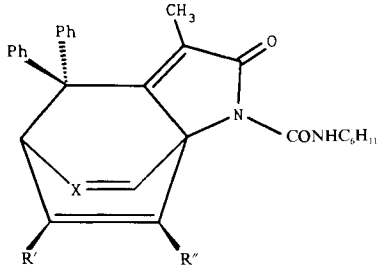
Cycloaddition of the allenic acid **3** with the *N*-cyclohexyl-*N'*-heteroaromatic carbodiimides **2a** and **2b** gave the isomeric pyrido[1,2-*a*]pyrimidinones **4** and **5** and thiazolo[3,2-*a*]pyrimidinones **6** and **7**, respectively, instead of the expected *Diels-Alder* adducts analogous to **1**. The compounds of the latter type, *i.e.* **8** and **9**, were formed from **3** and carbodiimides **2c** and **2d**, respectively, containing an *N'*-(pyrazin-2-yl) or *N'*-(pyrimidin-2-yl) substituent.

1. Introduction. – Several reports on intramolecular *Diels-Alder* reactions of allenic (dienophile) derivatives containing a heteroaromatic ring (diene) appeared during the past decade [1–6]. We recently published the spontaneous cycloaddition at room temperature of allenic derivatives bearing phenyl, naphth-1-yl, and pyrid-3-yl substituents affording the tricyclic compounds **1** [3]. The present investigation deals with some new heterocyclic aromatic compounds which serve as dienes[1]).

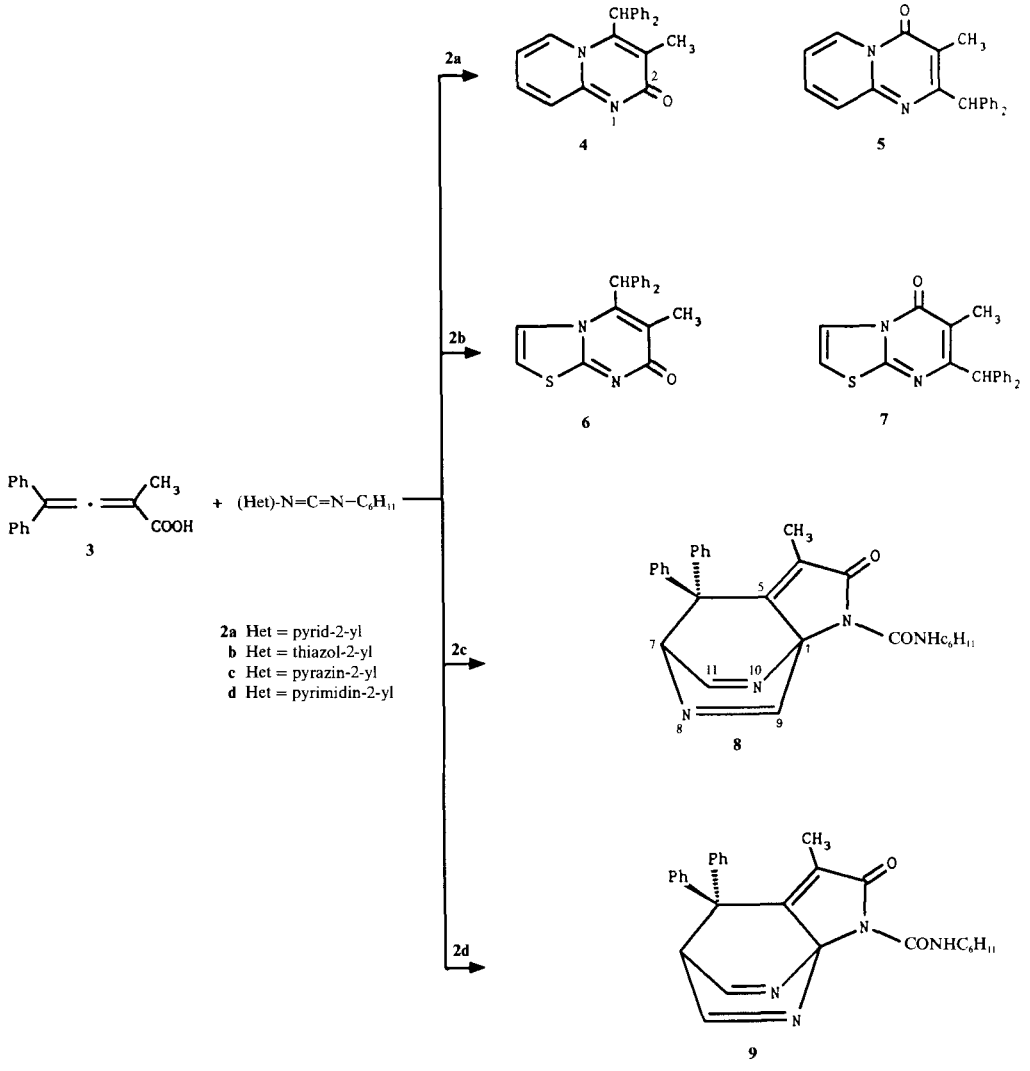


1 X = CH, N, R' = R'' = H or (CH=CH)$_2$

2. Results and Discussion. – The reaction between *N*-cyclohexyl-*N'*-(pyrid-2-yl) carbodiimide (**2a**) and the allenic acid **3** at room temperature gave a mixture of isomeric pyrido[1,2-*a*]pyrimidinones **4** and **5** (*Scheme 1*) instead of the expected *Diels-Alder* adducts analogous to **1**. The distinction between structures **4** and **5** was based on their UV and ^{1}H-NMR spectra, the m.p., and solubilities which are very close to those of the analogous known pyrido[1,2-*a*]pyrimidin-2- and -4-ones [7] [8]. In the case of **2b**, the corresponding thiazolo[3,2-*a*]pyrimidinones **6** and **7** were obtained, albeit in lower yields.

[1]) A preliminary account of some results was given at the '2nd International IUPAC Symposium on Organic Chemistry: Technological Perspectives', Baden-Baden, FRG, 1991.

Scheme 1

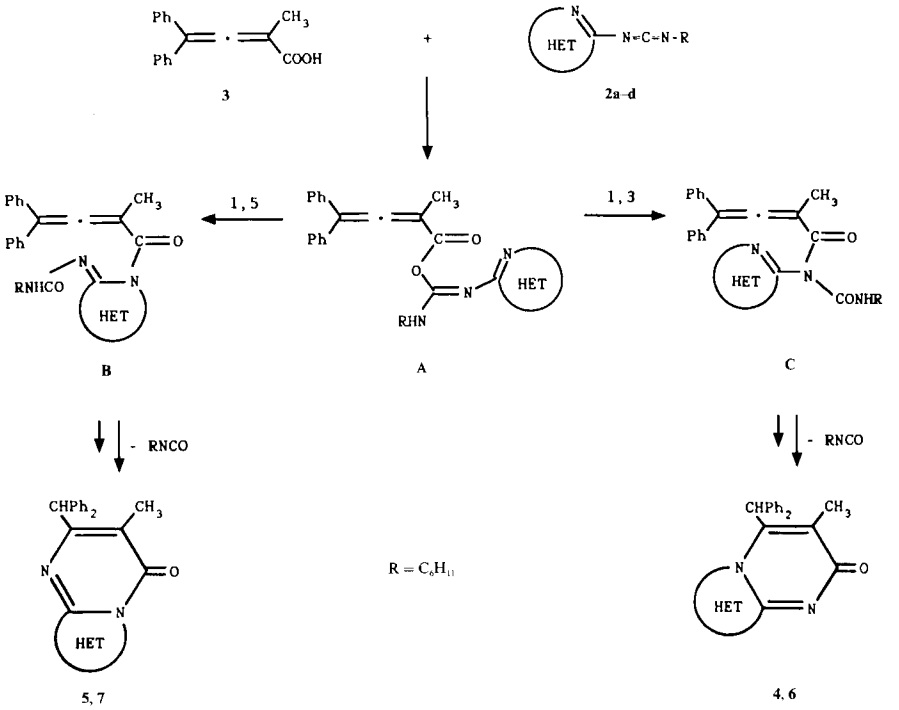


The expected *Diels-Alder* adducts **8** and **9** were obtained (*Scheme 1*), when the *N'*-(pyrazin-2-yl)- and *N'*-(pyrimidin-2-yl)carbodiimides **2c** and **2d** were employed, and no evidence for the reaction course observed in the case of **2a**, **b** was obtained. The main spectral support for structures **8** and **9** was found to be the ^{1}H-NMR signal for H–C(7) (5.18 (*t*, $J = 3.2$ Hz) and 6.28 ppm (*d*, $J = 2.5$ Hz), resp.). The remaining spectral data were similar to the ones reported for the 2,8-diazatricyclic compound [3].

The simultaneous formation of the annelated heterocyclic compounds **4**–**7** can be rationalized as shown in *Scheme 2*: the activated ester **A**, a key intermediate, undergoes a 1,5- or 1,3-acyl migration giving rise to the acylureas **B** and **C**, which subsequently

cyclize to **5** and **7** and to **4** and **6**, respectively. The formation of the pyrimidinone derivatives **4–7** on the one hand, and the *Diels-Alder* adducts **8** and **9** on the other, can be explained with the different nucleophilicities of the imine N-atom in the intermediates **B** and **C** with respect to the sp-C-atom of the allenic moiety (see *Scheme 2*). In the latter case, the pyrazine and pyrimidine rings react as dienophiles and afford the *Diels-Alder* adducts, probably *via* a radical pathway [11].

Scheme 2



Experimental Part

1. *General.* See [3].

2. *Starting Materials.* The *2-methyl-4,4-diphenylbuta-2,3-dienoic acid* (**3**) was obtained as described in [12], and the carbodiimides **2a–d** were prepared in 40–70% yield following the procedure in [13] starting from the corresponding ureas. The carbodiimides were isolated as yellow oils, identified by their IR ($CHCl_3$; 2150–2260*s*) and used directly as crude products.

For N-*Cyclohexyl*-N′-*(pyrid-2-yl)urea*, see [14], for N-*cyclohexyl*-N′-*(thiazol-2-yl)urea*, see [15], and for N-*cyclohexyl*-N′-*(pyrimidin-2-yl)urea*, see [16].

N-*Cyclohexyl*-N′-*(pyrazin-2-yl)urea*: Yellow crystals (52%). M.p. 206–210°. IR ($CHCl_3$): 3390*w*, 3240*w*, 2950*s*, 2875*m*, 1675*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 9.72 (*s*, NHAr); 8.83 (*d*, J = 6.5, NHC_6H_{11}); 8.40 (*s*, H–C(3)); 8.12 (*d*, J = 2.9, H–C(5) or H–C(6)); 8.09 (*d*, J = 2.9, H–C(6) or H–C(5)); 3.95–3.80 (*m*, CH–N); 2.05–1.20 (*m*, 10 H, C_6H_{11}). MS (70 eV): 221 (2), 220 (6, M^+), 139 (3), 122 (4), 95 (100, $[M - C_6H_{11}NCO]^+$), 68 (30).

3. *General Procedure.* A soln. of the carbodiimide **2a–d** (1.2 mmol) and **3** (1.0 mmol) in dry THF (2 ml) was kept at r.t. for 3 days (**2a**), 7 days (**2c**, **2d**), or 3 weeks (**2b**). In the case of **2a**, the crystals were filtered off and washed with THF to give pure **4**. The mother liquor was subjected to column chromatography (alumina, petroleum

ether/Et_2O/AcOEt/acetone 64:12:12:12). The combined fractions containing **5** were evaporated and the residue recrystallized from benzene to afford pure **5**. In the remaining cases, the reaction mixture was subjected to prep. TLC (petroleum ether/AcOEt/acetone 80:12:8 for **2b**, 68:7:25 for **2c**, and 80:9:11 for **2d**). The UV (254 nm)-active zones at R_f 0.60 and 0.00 in the case of **2b** were eluted with $CHCl_3$. The evaporation residues were recrystallized from $(i\text{-}Pr)_2O$ to afford pure **6** and **7**. Analogous workup of the zones at R_f 0.50 and 0.45 in the case of **2c** and **2d**, followed by recrystallization from hexane/Et_2O, gave pure **8** and **9**, resp.

4-(Diphenylmethyl)-3-methylpyrido[1,2-a]pyrimidin-2-one (**4**): Colourless crystals (53%). M.p. 288–293° (dec.). UV (MeCN): 225 (30000), 235 (sh, 29000), 245 (sh, 23100), 257 (sh, 1700). IR ($CHCl_3$): 2980*m*, 1645*m*, 1615*s*, 1595*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.81 (*d*, J = 7.3, H–C(6)); 7.45–7.30 (*m*, 8 H); 7.20–7.10 (*m*, 4 H); 6.45–6.35 (*m*, 1 H); 6.34 (*s*, C*H*Ph_2); 2.27 (*s*, Me). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 151.8, 144.1, 136.5, 126.8 (4*s*, arom. C, C(2), C(3), C(4), C(9a)); 134.4, 130.2, 125.2, 111.4 (4*d*, C(6), C(7), C(8), C(9)); 129.1, 128.2, 127.7 (3*d*, arom. CH); 50.6 (*d*, *C*HPh$_2$); 13.7 (*q*, Me). MS (70 eV): 327 (22), 326 (100, M^+), 298 (8), 297 (11), 287 (18), 221 (26), 191 (30), 78 (41).

2-(Diphenylmethyl)-3-methylpyrido[1,2-a]pyrimidin-4-one (**5**): Colourless prisms (25%). M.p. 164–167°. UV (MeCN): 240 (sh, 13000), 256 (sh, 7050), 342 (8550), 351 (sh, 8300). IR ($CHCl_3$): 3050*w*, 2990*m*, 2930*w*, 1655*s*, 1630*s*, 1595*w*. ^{1}H-NMR (250 MHz, $CDCl_3$): 8.96 (*d*, J = 7.2, H–C(6)); 7.60–7.45 (*m*, H–C(8), H–C(9)); 7.30–7.15 (*m*, 10 arom. H); 7.03 (*td*, J = 7.2, 1.9, H–C(7)); 5.75 (*s*, C*H*Ph_2); 2.36 (*s*, Me). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 164.2, 158.9 (2*s*, 2 arom. C); 148.1 (*s*, arom. C); 141.7 (*s*, arom. C); 133.8, 129.5, 128.2, 126.8, 126.5, 114.6 (6*d*, arom. CH, C(6), C(7), C(8), C(9)); 55.0 (*d*, *C*HPh$_2$); 11.9 (*q*, Me). MS (70 eV): 326 (50, M^+), 297 (27), 165 (28), 159 (9), 129 (15), 78 (100).

5-(Diphenylmethyl)-6-methylthiazolo[3,2-a]pyrimidin-7-one (**6**): Colourless crystals (24%). M.p. 134–135°. IR ($CHCl_3$): 3000*m*, 1650*s*, 1640*s*, 1590*w*, 1550*s*, 1485*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.92 (*d*, J = 4.9, H–C(3)); 7.35–7.20 (*m*, 10 arom. H); 6.90 (*d*, J = 4.9, H–C(2)); 5.66 (*s*, C*H*Ph_2); 2.28 (*s*, Me). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 163.0, 159.7, 158.7 (3*s*, C(5), C(7), C(8a)); 141.3 (*s*, arom. C); 129.4, 128.3, 126.7 (3*d*, arom. CH); 121.6, 111.2 (2*d*, C(2), C(3)); 112.9 (*s*, C(6)); 54.5 (*d*, *C*HPh$_2$); 11.1 (*q*, Me). MS (70 eV): 333 (25), 332 (100, M^+), 331 (54), 317 (4), 303 (8), 224 (17), 207 (15), 165 (17, $[M - CHPh_2]^+$), 149 (30), 99 (20).

7-(Diphenylmethyl)-6-methylthiazolo[3,2-a]pyrimidin-5-one (**7**): Colourless crystals (3%). M.p. 211–213°. IR (KBr): 3437*w*, 3057*w*, 1616*s*, 1560*m*, 1498*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.45–7.35 (*m*, 6 arom. H); 7.15–7.10 (*m*, 4 arom. H); 7.05 (*d*, J = 5.0, H–C(3)); 6.52 (*d*, J = 5.0, H–C(2)); 6.12 (*s*, C*H*Ph_2); 2.15 (*s*, Me). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 168.0, 165.0, 144.3 (3*s*, C(5), C(7), C(8a)); 137.2 (*s*, arom. C); 129.5, 128.5, 128.0 (3*d*, arom. CH); 123.4, 121.1 (2*d*, C(2), C(3)); 107.9 (*s*, C(6)); 51.2 (*d*, *C*HPh$_2$); 12.5 (*q*, Me). MS-DCI: 333 (100, $[M + 1]^+$).

(1RS,7RS)-2-(N-Cyclohexylcarbamoyl)-4-methyl-6,6-diphenyl-2,8,10-triazatricyclo[5.2.2.0^{1,5}]undeca-4,8,10-trien-3-one (**8**): Colourless crystals (1.2%). M.p. 175–182° (dec.). IR (KBr): 3320*m*, 2927*m*, 2852*m*, 1720*s*, 1693*m*, 1626*m*. ^{1}H-NMR (250 MHz, $CDCl_3$): 8.27 (*d*, J = 7.1, NH); 8.05 (*d*, J = 3.2, H–C(9), H–C(11)); 7.75–7.10 (*m*, 10 arom. H); 5.18 (*t*, J = 3.2, H–C(7)); 4.05–3.90 (*m*, CH–N); 2.10–1.10 (*m*, 10 H, C_6H_{11}); 1.65 (*s*, Me). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 172.7 (*s*, C(3)); 162.0 (*d*, C(9), C(11)); 150.2 (*s*, NCON); 149.9 (*s*, C(5)); 140.5 (*s*, arom. C); 133.7, 132.2, 131.9, 128.9, 128.5, 128.2 (6*d*, arom. CH); 102.6 (*s*, C(1)); 58.7 (*d*, C(7)); 54.8 (*s*, C(6)); 48.5 (*d*, CHN); 33.0, 25.8, 24.6 (3*t*, C_6H_{11}); 10.7 (*q*, Me). MS-DCI: 330 (25), 328 (20, $[M + 1 - C_6H_{11}NCO]^+$).

2-(N-Cyclohexylcarbamoyl)-4-methyl-6,6-diphenyl-2,9,10-triazatricyclo[5.2.2.0^{1,5}]undeca-4,8,10-trien-3-one (**9**): Colourless crystals (31%). M.p. 200.5–203.5°. IR ($CHCl_3$): 3315*m*, 3010*s*, 2930*m*, 2845*m*, 1710*s*, 1665*m*, 1580*m*. ^{1}H-NMR (250 MHz, $CDCl_3$): 8.49 (*s*, H–C(8)); 8.28 (*d*, J = 8.0 NH); 7.98 (*d*, J = 2.5, H–C(11)); 7.40–7.20 (*m*, 8 arom. H); 7.00–6.95 (*m*, 2 arom. H); 6.28 (*d*, J = 2.5, H–C(7)); 2.05–1.20 (*m*, 10 H, C_6H_{11}); 1.76 (*s*, Me). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 172.7 (*s*, C(3)); 165.1 (*d*, C(8)); 162.9 (*d*, C(11)); 150.3 (*s*, NCON); 148.5 (*s*, C(5)); 141.1, 139,7, (2*s*, arom. C); 129.2, 128.7, 128.3, 128.2, 127.6, 127.5 (6*d*, arom. CH); 87.1 (*s*, C(1)); 73.1 (*d*, C(7)); 57.1 (*s*, C(6)); 48.6 (*d*, CHN); 32.9, 25.5, 24.5 (3*t*, C_6H_{11}); 10.8 (*q*, Me). MS (70 eV): 453 (2), 452 (6, M^+), 424 (2), 327 (100, $[M - C_6H_{11}NCO]^+$), 300 (57), 205 (9).

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