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Condensation of 1,3-Diketones with 1,8-Diaminonaphthalene: Synthesis of *Bis*(2,3-dihydroperimidine-2-spiro)cycloalkanes

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Summary. Cyclic 1,3-diketones like cyclopentane-1,3-dione, cyclohexane-1,3-dione, and 5,5-dimethylcyclohexane-1,3-dione react with 1,8-diaminonaphthalene to afford new condensed heterocyclic spiro systems.

Keywords. 1,3-Diketones; 1,8-Diaminonaphthalene; 2,3-Dihydroperimidine; Spiro compounds.

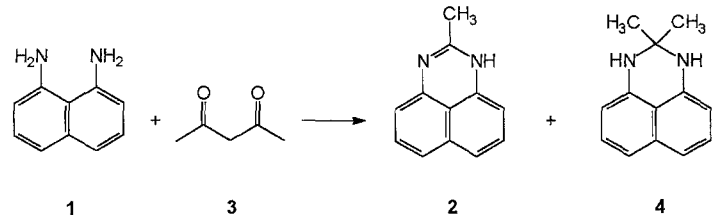
Kondensation von 1,3-Diketonen mit 1,8-Diaminonaphthalin: Synthese von *Bis*(2,3-dihydroperimidin-2-spiro)cycloalkanen

Zusammenfassung. Cyclische 1,3-Diketone wie Cyclopentan-1,3-dion, Cyclohexan-1,3-dion und 5,5-Dimethylcyclohexan-1,3-dion reagieren mit 1,8-Diaminonaphthalin zu neuen kondensierten heterocyclischen Spiranen.

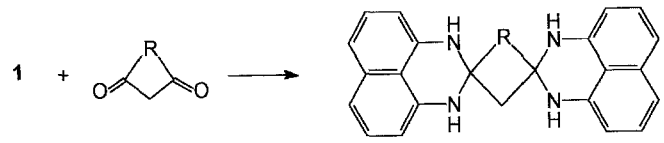
Introduction

The synthesis of perimidine based heterocyclic systems by reaction of 1,8-diaminonaphthalene (**1**) and carbonyl compounds, [1–3] is of considerable importance in view of their utility as dye intermediates and coloring materials for polymers [4]. In addition, they have been reported to possess anti-inflammatory, CNS depressant, anti-bacterial, and anti-fungal activities [5].

Direct heating of **1** and benzyl methyl ketone results in the formation of toluene and 2-methylperimidine (**2**, [6]). This observation suggests that similar formation of perimidine derivatives should occur from 1,3-diketones such as pentane-2,4-dione (**3**). The formation of **2** and 2,2-dimethyl-2,3-dihydroperimidine (**4**) by heating of **1** with **3** prompted us to examine this reaction using cyclic 1,3-diketones such as **5a, 5b**, and **5c**. We report here a one-pot synthesis of the hitherto unknown *bis*(2,3-dihydroperimidine-2-spiro)cycloalkanes **6a**, **6b**, and **6c**.



1 3 2 4



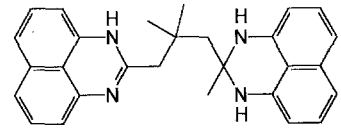
5

5,6	R
a	CH_2CH_2
b	$CH_2CH_2CH_2$
c	$CH_2CMe_2CH_2$

6

Results and Discussion

Cyclopentane-1,3-dione (**5a**) and cyclohexane-1,3-dione (**5b**) undergo a smooth condensation reaction with 1,8-naphthalenediamine at room temperature to yield the symmetrical 1:2 (diketone:diamine) adducts **6a** and **6b**, respectively. However, 5,5-dimethylcyclohexane-1,3-dione (**6c**) afforded, in addition to the expected symmetrical condensation product **6c**, a second 1:2 adduct (**7**) in which the 1,3-dione is incorporated as an acyclic C_6 unit, obviously derived from a *retro-Dieckmann* type ring cleavage of **5c** [7, 8].



7

The structures of compounds **6a–c** and **7** were deduced from their elemental analyses and their IR, ^{1}H NMR, and ^{13}C NMR spectra. The nature of these compounds as 1:2 adducts was apparent from the mass spectra which displayed molecular ion peaks at $m/z = 378$, 392, and 420. The base peak in the mass spectra of compounds **6a–c** and **7** is located at $m/z = 182$ ($C_{12}H_{10}N_2$) and corresponds to the 2-methylperimidine ion. The mass spectra of **6c** and **7** are similar except for the relative intensities of some peaks. Initial fragmentations involve loss of the 2-methylperimidine moiety.

The ^{1}H and ^{13}C NMR data for compounds **6a–c** and **7** are shown in Table 1. The ^{1}H and ^{13}C NMR data for perimidine derivatives **2** and **4** are also given for comparison. The ^{1}H and ^{13}C NMR data for 2-methylperimidine are in agreement with time-averaged C_{2v} symmetry which results from a fast 1,3-proton shift [9]. The ^{1}H NMR spectrum of **6a** exhibits signals for methylene protons at 2.11 and

2.16 ppm (each s), along with a fairly broad band for the NH group at $\delta = 3.8$ ppm. The aromatic region of the ^{1}H NMR spectrum of **6a** consists of multiplets at $\delta = 6.64$ and 7.2–7.4 ppm. The intensity ratio of these signals is 1:2, as is expected from the symmetrical structure of this molecule. The ^{13}C NMR spectrum of **6a** shows nine distinct resonances, also in agreement with the symmetrical structure. Partial assignments of these resonances are given in Table 1.

The ^{1}H and ^{13}C NMR spectra of **6b** and **6c** are similar to those of **6a** except for the 1,3-diketone residues which exhibit characteristic signals with appropriate chemical shifts (see Table 1). The ^{1}H and ^{13}C NMR spectra of **7** are more complicated and clearly demonstrate the presence of both perimidine and 2,3-dihydroperimidine moieties, along with an acyclic C_6 unit. Partial assignments of **7** are given in Table 1.

The structural assignments made on the basis of the NMR spectra of compounds **6a–c** and **7** were supported by their IR spectroscopic properties. Compounds **6a–c** exhibit a single band for the N–H group, whereas **7** shows two distinct bands at 3320 and 3475 cm^{-1} for the two different types of N–H groups [10].

Table 1. ^{1}H and ^{13}C NMR data for compounds **2**, **4**, **6** and **7**

	δ (ppm; $CDCl_3$, *TMS*)
2	^{1}H: 2.13 (3H, s, CH_3), 5.1 (1H, br s, NH), 6.48[a] (2H, dd, *J*=5.5 and 2.8 Hz), 7.0–7.3[b](4H, m)
	^{13}C: 21.95 (CH_3), 107.95(C4 and C9), 119.64 (C6 and C7), 121.70 (C9b), 128.27 (C6a), 135.40 (C5 and C8), 140.61 (C3a and C9a), 153.48 (C2)
4	^{1}H: 1.50 (6H, s, $2CH_3$), 4.2 (2H, br s, 2NH), 6.47[a] (2H, *J*=6.1 and 2.0 Hz), 7.0–7.3[b] (4H, m)
	^{13}C: 28.91 ($2CH_3$), 64.54 (C2), 105.91 (C4 and C9), 117.11 (C6 and C7), 113.40 (C9b), 127.01 (C5 and C8), 134.66 (C6a), 140.28 (C3a and C9a)
6a	^{1}H: 2.11 (2H, s, CH_2), 2.16 (4H, s, CH_2CH_2), 3.8 (4H, br s, NH), 6.64[a] (4H, dd, $J = 5.8$ and 3.1 Hz), 7.2–7.4[b] (8H, m)
	^{13}C: 37.83 ($2CH_2$), 51.02 (CH_2), 74.19 (C2), 108.81 (C4 and C9), 115.48 (C9b), 118.74 (C6 and C7), 126.89 (C5 and C8), 134.58 (C6a), 140.16 (C3a and C9a)
6b	^{1}H: 1.7–2.1 (6H, m, $3CH_2$), 2.58 (2H, s, CH_2), 5.5 (4H, br s, NH), 6.52[a] (4H, dd, $J = 5.9$ and 3.0 Hz), 6.9–7.3[b] (8H, m)
	^{13}C 17.6 (C-CH_2-C), 36.94 (CH_2-*C*-CH_2), 43.90 (CH_2), 65.48 (C2), 104.94 (C4 and C9),112.23 (C9b), 114.83 (C6 and C7), 126.80 (C5 and C8), 133.89 (C6a), 140.69 (C3a and C9a)
6c	^{1}H: 1.06 (6H, s, CMe_2), 1.70 (4H, s, $2CH_2$), 2.02 (2H, s, CH_2), 4.5 (4H, br s, NH), 6.61[a] (4H, dd, $J = 5.7$ and 2.9 Hz),7.2–7.4[b] (8H, m)
	^{13}C: 31.64 (*CMe*$_2$), 32.29 ($2CH_2$), 45.77 (*C*Me_2), 48.37 (CH_2), 67.51 (C2), 108.64 (C4 and C9), 113.2 (C9b), 118.49 (C6 and C7), 127.01 (C5 and C8), 134.46 (C6a), 139.30 (C3a and C9a)
7	^{1}H: 1.19 (6H, s, CMe_2), 1.41 (3H, s, CH_3), 1.92 (2H, s, CH_2), 2.59 (2H, s, CH_2), 5.6 (3H, br s, NH) 6.4–6.6[a] (4H, m), 7.2–7.4[b] (8H, m)
	^{13}C[c]: 30.34 (CH_3), 31.11 (*CMe*$_2$), 35.14 (CH_2), 45.36 (*C*Me_2), 48.95 (CH_2), 67.43 (C2′), 104.15 and 104.86 (C4, C9, C4* and C9*), 112.15 (C9b*), 115.81 (C6* and C7*), 119.84 (C6 and C7), 121.57 (C9b), 127.21 and 128.27 (C5, C8, C5* and C8*), 134.78 and 135.27 (C6a and C6a*), 140.61 and 140.93 (C3a, C9a, C3a* and C9*), 155.76 (C2)

[a] Aromatic protons in the *ortho*-position relative to the nitrogen atom; [b] remaining aromatic protons; [c] carbon atoms of the 2,3-dihydroperimidine moiety are indicated by an asterisk

The reactions described herein represent a simple entry into the synthesis of *bis*(2,3-dihydroperimidine-2-spiro)cycloalkanes. The presence of a fairly flexible chain in **7** makes a study of its DNA binding properties quite attractive [11].

Experimental

Melting points were measured with an Electrothermal 9100 appartus and are uncorrected. Elemental Analyses for C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer. IR spectra were recorded on a Shimadzu IR-460 spectrometer. ^{1}H and ^{13}C NMR spectra were measured with a JEOL EX-90A spectrometer at 90 and 22.6 MHz, respectively. Mass spectra were recorded on a Finnigan-MAT 8430 mass spectrometer operating at an ionization potential of 35 eV.

General procedure

To a magnetically stirred solution of 1,8-diaminonaphthalene (0.79 g, 5 mmol) in methanol (5 ml), a solution of 1,3-diketone (2.5 mmol) in methanol (3 ml) was added dropwise and stirred for 2 h at room temperature. After 48 h, the colorless solids were collected by filtration, and the filtrate was then refluxed for 10 h. However, except for **5c** which yielded **7**, no additional compounds could be isolated. The separated solids were recrystallized from ethanol/water.

1,3-Bis-(2,3-dihydroperimidine-2-spiro)cyclopentane (**6a**)

M.p.: 86–87°C; yield: 95%; IR (KBr): ν_{max} = 3315 (N–H) cm^{-1}; MS: *m/z* (%) = 378 (M^+, 2), 196 (M^+-$C_{12}H_{10}N_2$, 20) 182 ($C_{12}H_{10}N_2^+$, 100); $C_{25}H_{22}N_4$ (378.47); calcd.: C 79.33, H 5.86, N 14.81; found: C 78.9, H 5.8, N 14.4.

1,3-Bis(2,3-dihydroperimidine-2-spiro)cyclohexane (**6b**)

M.p.: 226–227°C; yield: 35%; IR (KBr): ν_{max} = 3315 (N–H) cm^{-1}; MS: *m/z* (%) = 392 (M^+, 4), 210, (M^+-$C_{12}H_{10}N_2^+$, 40) 182 ($C_{12}H_{10}N_2^+$, 100); $C_{26}H_{24}N_4$ (392.49); calcd.: C 79.56, H 6.16, N 14.28; found: C 79.2, H 6.3, N 14.1.

5,5-Dimethyl-1,3-bis(2,3-dihydroperimidine-2-spiro)cyclohexane (**6c**)

M.p.: 227–228°C; yield: 25%; IR (KBr): ν_{max} = 3316 (N–H) cm^{-1}; MS: *m/z* (%) = 420 (M^+, 8), 238 (M^+-$C_{12}H_{10}N_2$,30), 223 (238-CH_3, 40), 182, ($C_{12}H_{10}N_2^+$, 100); $C_{28}H_{28}N_4$ (420.54); calcd.: C 79.96, H 6.71, N 13.32; found: C 79.7, H 6.6, N 13.1.

1-(2-Methyl-2,3-dihydroperimidine)-2,2-dimethyl-3-(2-perimidine)propane (**7**)

M.p.: 165–166°C; yield: 47; IR (KBr): ν_{max}=3320 (N–H), 3475 (N–H) cm^{-1}; MS: *m/z* (%) = 420 (M^+, 7), 238 (M^+-$C_{12}H_{10}N_2$, 25), 223 (238-CH_3, 30), 182 ($C_{12}H_{10}N_2^+$, 100); $C_{28}H_{28}N_4$ (420.54); calcd.: C 79.96, H 6.71, N 13.32; found: C 79.3, H 6.8, N 13.2.

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