Notizen / Notes

Synthesis of 1-Phenyl-1,2- and 4-Phenyl-1,5-dihydropentalenes

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An efficient one-pot synthesis of 3-substituted 1-phenyl-1,2-dihydropentalenes from α,β-unsaturated ketones is described. These compounds can be rearranged to their 1,5-dihydro isomers using different methods such as acid catalysis and vacuum-flash thermolysis or by chromatography on alumina.

Dihydropentalenes[1] are versatile starting materials for the synthesis of complex molecules with a polyquinane structure[2]. Serveral methods have been applied to prepare these compounds either in their 1,2-dihydro or 1,5-dihydro form[3]. The well-known Hafner route[4], which uses vinamidinium salts and cyclopentadienylsodium, leads to 6-(2-dialkylaminovinyl)pentafulvenes, which easily rearrange to 1-dialkylamino-1,5-dihydropentalenes in analogy to the electrocyclization of 6-vinylpentafulvene developed by Gajewski[5]. Only two reports describing the direct conversion of α,β-unsaturated carbonyl compounds into 1,2- or 1,5-dihydropentalenes are known. In one case the yields are very poor (<5%)[6], the other one describes special conditions (KF/DMSO) used in the synthesis of hexaphenyl-1,2-dihydropentalene[7].

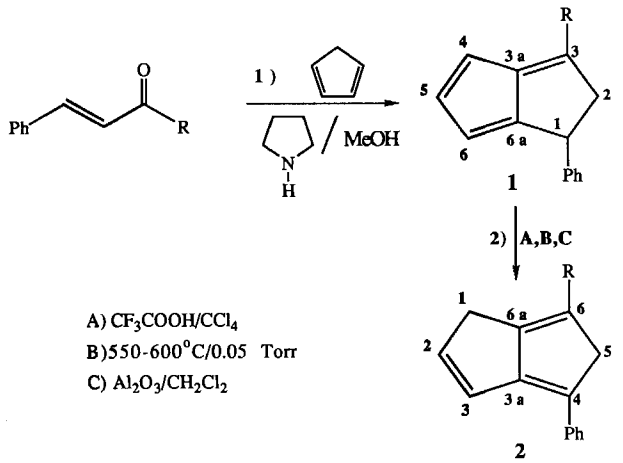

Table 1. Substituents, reaction times and yields for step 1

	R	Reaction time [h]	Yield (%)
a	CH_3	0.5	72
b	CH_2CH_3	1.5	75
c	$CH_2CH_2CH_3$	2.0	63
d	$CH_2CH_2CH=CH_2$	4.0	68
e	$CH(CH_3)_2$	12.0	37
f	Cyclopropyl	24.0	42
g	Phenyl	24.0	32

Our goal was to develop an efficient method for the synthesis of these compounds because of their use in polyquinane[8] and domino

Table 2. ^{1}H-NMR (200 MHz, $CDCl_3$) data of compounds **1**, **2** (δ values, J in Hz)

	1-H[a]	2-H[b]	4-H[c]	5-H[d]	6-H[e]
1a	4.15	2.88/3.49	6.23	6.79	5.85
	[Ph: 7.18; R: 2.15 (s)]				
1b	4.11	2.90/3.56	6.22	6.82	5.82
	[Ph: 7.12; R: 1.28 (t, 3H, J = 7.3), 2.61 (q, 2H, J = 7.3)]				
1c	4.03	2.95/3.47	6.18	6.72	5.80
	[Ph: 7.09; R: 1.09 (t, 3H, J = 7.3), 1.61 (tq, 2H, J = 7.3, 7.5), 2.41 (t, 2H, J = 7.5)]				
1d	4.14	2.92/3.54	6.26	6.81	5.85
	[Ph: 7.21; R: 2.18 (m, 2H), 2.27 (m, 2H), 4.90 (m, 2H), 5.71 (ddt, 1H)]				
1e	4.08	2.92/3.50	6.22	6.79	5.83
	[Ph: 7.15; R: 1.12 (d, 6H, J = 6.8), 2.91 (sept, 1H, J = 6.8)]				
1f	4.17	2.67/3.47	6.29	6.77	5.78
	[Ph: 7.12; R: 0.94- 1.04 (m, 4H), 2.01 (m, 1H)]				
1g	4.51	2.86/3.61	6.19	6.42	6.09
	[Ph: 7.20- 7.75]				
	1-H[f]	2-H[g]	3-H[g]	5-H[h]	
2a	3.01	6.52	6.80	3.58	
	[Ph: 7.18- 7.40; R: 2.00 (s)]				
2b	2.95	6.54	6.82	3.59	
	[Ph: 7.11- 7.35; R: 1.02 (t, 3H, J = 7.2), 3.60 (q, 2H, J = 7.2)]				
2c	3.09	6.60	6.91	3.62	
	[Ph: 7.05- 7.22; R: 0.72 (t, 3H, J = 7.4), 1.41 tq, 2H, J = 7.0, 7.4), 2.40 (t, 2H, J = 7.0)]				
2d	3.12	6.59	6.89	3.67	
	[Ph: 7.10- 7.25; R: 2.40 (t, 2H, J = 7.9), 2.54 (t, 2H, J = 8.0), 5.08 (m, 2H), 5.93 (ddt, 1H)]				
2e	3.00	6.56	6.88	3.60	
	[Ph: 7.20- 7.36; R: 1.01 (d, 6H, J = 6.6), 2.61 (sept, 1H, J = 6.6)]				
2f	3.09	6.38	6.61	3.51	
	[Ph: 7.19- 7.36; R: 0.82- 0.94 (m, 4H), 1.78 (m, 1H)]				
2g	3.11	6.58	6.93	3.59	
	[Ph: 7.20- 7.64]				

[a] d, $^3J = 6.7 \pm 0.2$. — [b] AB system, $^2J = 18.6 \pm 0.2$. — [c] d, $^3J = 5.1 \pm 0.1$. — [d] m_c. — [e] s. — [f] m_c. — [g] m_c. — [h] s.

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Diels-Alder cycloaddition[9] chemistry. The pyrrolidine-catalyzed addition/condensation reaction of β-phenyl-substituted α,β-unsaturated ketones with cyclopentadiene, which has already been applied to benzalacetone[10], can be optimized for a series of 3-substituted 1-phenyl-1,2-dihydropentalenes **1**. As shown in Table 1, the reaction rate strongly depends on the steric demand of the alkyl substituent. Whereas unbranched enones are completely converted within 1–4 hours, the reaction time for compounds **1e–g** is prolonged, and the product yield decreases to 20–40%.

The 1,2-dihydropentalenes **1a–g** are stable under slightly basic conditions, whereas treatment with catalytic amounts of acid (method **A**) leads to a rapid isomerization to the corresponding 1,5 isomers **2**. A serious problem in this rearrangement step are proton-catalyzed decomposition reactions of the 1,5-dihydropentalenes **2**, which often lead to a pronounced decrease in yield in the second step.

For some compounds (especially the volatile trienes **1a** and **b**) vacuum-flash thermolysis (method **B**) has proved to be a versatile method to convert the 1,2-dihydropentalenes into their 1,5-dihydro isomers. However, the most efficient method for effecting this transformation is chromatography on alumina. In all cases, we have succeeded in isolating the 1,5-dihydropentalenes in yields higher than 92%. An additonal advantage of this method is, that the column can be used several times without regeneration, and therefore compounds **2** can be synthesized in 10-g quantities.

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Table 3. ^{13}C-NMR (50.4 MHz, $CDCl_3$) data of compounds **1**, **2** (δ values)

	C-1	C-2	C-3	C-4	C-5	C-6	C-3a	C-6a
1a	42.4	55.5	155.2	110.1	139.9	115.4	153.4	149.2
	[Ph: 126.0 (d), 127.0 (d), 128.3 (d), 144.5 (s); R: 16.4 (q)]							
1b	42.2	53.8	161.5	110.9	139.8	115.2	153.9	148.9
	[Ph: 126.2 (d), 126.9 (d), 128.4 (d), 145.0 (s); R: 12.5 (q), 36.6 (t)]							
1c	45.5	54.1	160.1	111.0	140.1	115.4	153.9	149.1
	[Ph: 126.1 (d), 126.9 (d), 128.1 (d), 144.8 (s); R: 14.3 (q), 21.4 (t), 34.0 (t)]							
1d	42.4	54.1	159.0	111.0	140.4	115.6	154.0	149.0
	[Ph: 126.3 (d), 127.4 (d), 128.7 (d), 145.0 (s); R: 31.4 (t), 32.2 (t), 115.6 (t), 137.6 (d)]							
1e	42.8	55.0	155.6	111.3	139.6	115.7	153.0	150.3
	[Ph: 126.1 (d), 127.0 (d), 128.8 (d), 144.7 (s); R: 18.5 (q), 39.3 (d)]							
1f	42.0	50.9	163.2	109.7	139.2	114.4	153.2	147.0
	[Ph: 126.0 (d), 126.5 (d), 127.9 (d), 145.0 (s); R: 11.2 (t), 14.5 (d)]							
1g	44.1	52.2	166.1	111.4	140.6	115.3	154.2	148.7
	[Ph: 125.2, 126.2, 126.6, 127.3, 127.9, 128.4 (jeweils d), 144.9, 145.5 (jeweils s)]							
2a	30.2	142.9	127.9	129.7	51.3	126.2	150.2	145.0
	[Ph: 125.3 (d), 127.9 (d), 128.5 (d), 137.4 (s); R: 14.1 (q)]							
2b	30.6	142.6	127.5	132.4	49.2	126.3	150.0	145.3
	[Ph: 125.8 (d), 128.0 (d), 128.8 (d), 138.0 (s); R: 7.5 (q), 30.6 (t)]							
2c	30.0	144.2	127.9	132.8	50.1	125.9	150.2	145.6
	[Ph: 124.7 (d), 127.8 (d), 128.9 (d), 137.8 (s); R: 10.1 (q), 17.1 (t), 31.2 (t)]							
2d	30.7	143.0	127.8	133.8	49.6	126.3	150.6	144.9
	[Ph: 125.2 (d), 125.4 (d), 128.6 (d), 137.3 (s); R: 29.0 (t), 33.4 (t), 114.6 (t), 138.6 (d)]							
2e	29.9	143.5	127.6	131.6	50.8	125.8	150.2	144.7
	[Ph: 125.0 (d), 125.8 (d), 128.9 (d), 138.1 (s); R: 15.3 (q), 36.3 (d)]							
2f	30.3	142.6	127.5	130.5	47.0	125.7	150.8	143.5
	[Ph: 124.9 (d), 125.1 (d), 128.4 (d), 138.1 (s); R: 7.6 (t), 11.0 (t)]							
2g	30.6	143.7	128.1	131.4	51.3	127.3	151.1	145.2
	[Ph: 124.4, 124.8, 125.6, 125.8, 127.5, 128.3 (jeweils d), 137.9, 138.5 (jeweils s)]							

Experimental

NMR: Spektrometer AC 200 or WM 400, $CDCl_3$ lock. – M.p.: SMP-20 (Büchi). – Elemental analyses: Institute of Inorganic Chemistry, Univ. of Würzburg.

Starting Materials: The α,β-unsaturated ketones were prepared according to standard procedures[11]. Cyclopentadiene was freshly prepared from dicyclopentadiene[12]. Pyrrolidine was distilled under nitrogen. All reactions were performed under nitrogen using water-free methanol as solvent.

General Procedure for the Synthesis of 3-Substituted 1-Phenyl-1,2-dihydropentalenes **1**: To a solution of 0.1 mol of enone and 0.3 mol of cyclopentadiene in 90 ml of methanol was added dropwise 0.2 mol of pyrrolidine at room temp. for 15 min. After stirring for 30 min to 24 h (see Table 1) at room temp., the mixture was treated with 0.21 mol of acetic acid and extracted with 2 × 200 ml of ether. The ether layer was washed with 2 × 100 ml of water and 150 ml of brine, dried with Na_2SO_4, and distilled at reduced pressure.

General Procedure for the Synthesis of 6-Substituted 4-Phenyl-1,5-dihydropentalenes **2**. – A) *Acid-Catalyzed Rearrangement:* A solution of 5.00 mmol of **1** in 40 ml of CCl_4 was treated at 0°C with 100 µl of trifluoroacetic acid. The solution was stirred until no **1** could be detected by TLC. After treatment of the solution with 1 g of K_2CO_3 in 10 ml water and extraction with 2 × 30 ml of CCl_4, the solvent was evaporated; yields: 55–70%.

Table 4. Physical and analytical data of compounds **1**, **2**

	Mol. formula	Mol. mass	Yield (%)	b.p. [°C/Torr] m.p. [°C]		Elemental analysis C	H
1a	$C_{15}H_{14}$	194.3	72	110-112/0.1	Calcd.	92.73	7.26
					Found	92.91	7.38
1b	$C_{16}H_{16}$	208.3	75	125-127/0.1	Calcd.	92.26	7.74
					Found	92.58	7.38
1c	$C_{17}H_{18}$	222.3	63	133-136/0.08	Calcd.	91.89	8.11
					Found	92.13	8.24
1d	$C_{18}H_{18}$	234.3	68	140-142/0.08	Calcd.	92.26	7.74
					Found	92.30	7.71
1e	$C_{17}H_{18}$	222.3	37	120-125/0.1	Calcd.	91.84	8.16
					Found	91.88	8.65
1f	$C_{17}H_{16}$	220.3	42	160-163/0.02	Calcd.	92.68	7.32
					Found	93.02	7.23
1g	$C_{20}H_{16}$	256.3	32	180-183/0.02	Calcd.	93.71	6.29
					Found	94.02	6.44
2a	$C_{15}H_{14}$	194.3	94	74-76	Calcd.	92.73	7.26
					Found	92.66	7.18
2b	$C_{16}H_{16}$	208.3	92	oil	Calcd.	92.26	7.74
					Found	92.75	8.03
2c	$C_{17}H_{18}$	222.3	95	oil	Calcd.	91.89	8.11
					Found	91.62	8.48
2d	$C_{18}H_{18}$	234.3	96	oil	Calcd.	92.26	7.74
					Found	92.20	8.05
2e	$C_{17}H_{18}$	222.3	92	oil	Calcd.	91.84	8.16
					Found	92.11	8.09
2f	$C_{17}H_{16}$	220.3	97	oil	Calcd.	92.68	7.32
					Found	92.61	7.52
2g	$C_{20}H_{16}$	256.3	93	142-144	Calcd.	93.71	6.29
					Found	93.69	6.33

B) *Vacuum-Flash Thermolysis:* 10 mmol of **1** was distilled through a quartz tube heated to 550–600°C at 0.01 Torr. **2** was collected in a dry-ice-cooled trap; yields: 25–80%.

C) *Chromatography on Alumina:* 10 mmol of **1** was chromatographed on 100 g of alumina (ICN alumina N, Akt. I) with CH_2Cl_2 (water-free, pretreated with 10 g of K_2CO_3) as eluent. The resulting solution was dried and the solvent evaporated; yields: 92–97%.

Spectral, physical, and analytical data of compounds **1** and **2** are compiled in Tables 2, 3, and 4.

CAS Registry Numbers

1a: 122902-53-8 / **1b**: 130031-93-5 / **1c**: 130031-94-6 / **1d**: 130031-95-7 / **1e**: 130031-96-8 / **1f**: 130031-97-9 / **1g**: 94579-28-9 / **2a**: 122902-54-9 / **2b**: 130031-98-0 / **2c**: 130031-99-1 / **2d**: 130032-00-7 / **2e**: 130032-01-8 / **2f**: 130032-02-9 / **2g**: 122902-55-0 / 4-phenyl-3-buten-2-one: 122-57-6 / 1-phenyl-1-penten-3-one: 3152-68-9 / 1-phenyl-1-hexen-3-one: 4646-80-4 / 1-phenyl-1,6-hexadien-3-one: 3425-62-5 / 5-methyl-1-phenyl-1-penten-3-one: 3160-32-5 / 1-cyclopropyl-3-phenyl-2-propen-1-one: 54454-40-9 / 1,3-diphenyl-2-propen-1-one: 94-41-7 / cyclopentadiene: 542-92-7

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