A Facile Synthesis of Homotriptycenes from Anthranol Derivatives

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Abstract: Substituted *trans*-10-benzyl-9-anthranols **5a**,**b** and substituted 10,10-dibenzyl-9-anthranol **8e** undergo intramolecular cyclization in the presence of formic or oxalic acid to give homotriptycenes **9a**,**b**,**e**. Depending on the amount of acid used, a competitive 1,4-dehydration to anthracene derivatives **10a**,**b** was observed for **5a**,**b**. The latter process was the only reaction pathway for anthranols that do not possess electron-donating substituents on benzyl moiety (**5c**,**d** → **10c**,**d**).

Key words: aromatization, condensation, electrophilic substitution, transannular ring closure

Triptycene and its derivatives have attracted great attention because of (1) their rigid aromatic three-dimensional structure and conformational properties,[1] (2) unique electrochemical and photochemical properties,[2] (3) potential pharmaceutical properties,[3] and (4) applications in materials science and supramolecular chemistry.[4] However, only a few examples for the synthesis of homotriptycenes have been reported. Cristol[5] synthesized homotriptycene and its derivatives by ring enlargement of 1-aminoethyltriptycene, but the route was lengthy and required a tedious separation from the concomitant isomers. Szeimies[6] reported an interesting route for the preparation of homotriptycene using a thermal dehydrogenation of annulated dibenzohomobarrelene, but this method has limited applications, because a multi-step synthesis was required for the starting propellane and there was also a limited variation of substituents that could be introduced into the homotriptycene skeleton. Saito[7] also reported an alternative method using the cycloaddition of the strained benzocyclopropene to anthracenes. We now describe a simple route for the preparation of homotriptycenes from 9-anthranols (Scheme 1, Table 1).

9-Anthranol **1**, which is in equilibrium with its tautomer anthrone **1′**, reacted with substituted benzaldehydes **2a**–**d** to give 10-benzylidene-9-anthrones **3a**–**d** in pyridine–piperidine.[8] Catalytic hydrogenation (5% Pd/C) of **3a**–**d** afforded 10-benzyl-9-anthrones **4a**–**d** in 58–90% yield. Subsequent reduction of **4** with $NaBH_4$ then produced 10-benzyl-9,10-dihydro-9-anthranols **5a**–**d** in 87–92% yield. The *trans*-configuration of compounds **5a**–**d** was established by a 2D NOESY NMR study. The proton 9-H shows a cross-peak to the enantiotopic protons of the CH_2 group, but not to the proton 10-H.

Alternatively, 10,10-disubstituted-9-dihydro-9-anthranol **8e** was obtained by bisalkylation of anthrone **1′** with **6e** to generate **7e** (50%). Subsequent reduction of the carbonyl group by $NaBH_4$ then gave **8e** in 94% yield.

Treatment of the mono- or dialkylated anthranol derivatives **5a**–**d** and **8e**, respectively, with formic or oxalic acid led to homotriptycenes **9a**,**b**,**e**[9] and/or to the anthracenes **10a**–**d**. Protonation of the hydroxy group leads to a carbenium ion which then acts as an electrophile to promote the electrophilic aromatic substitution of the benzene ring of the benzyl moiety. This route **5** → **9** represents formally a 1,7-elimination of H_2O, which competes with a 1,4-elimination of H_2O. The latter process furnishes the anthracene derivatives **10**. Whereas the 1,7-elimination pathway is an almost quantitative process for **5a** and **5b**, it does not work for compounds **5c** and **5d**, which do not contain activated electron-donating substituents at the correct positions in the benzene ring. Therefore **5c** and **5d** underwent the 1,4-elimination to give **10c** and **10d**, respectively.

The 10,10-dibenzyl substituted compound **8e**, on the other hand, does not have the possibility of undergoing 1,4-elimination and thus homotriptycene **9e** was the exclusive reaction product upon treatment with acids.

We also observed that the reaction rates were also dependent upon the amount of acid for the 1,4-elimination (Table 2). Table 2 demonstrates that the ratio of **9**:**10** becomes higher with increasing amount of formic acid. Obviously, formic acid is involved in the rate determining step of the 1,7-elimination, whereas this is not the case, or at least to a minor extent (medium effect), for the 1,4-elimination.

The structural identities of compounds **5**, **8**, **9** and **10** were established by one- and two-dimensional ^1H NMR and ^{13}C NMR spectroscopy. The characteristic data were summarized in Table 3 and Table 4.

Since the starting materials **5** or **8** are easily accessible, this reported facile preparation of homotriptycenes **9** is a more convenient route than other reported procedures. The final ring closure described here is related to a reaction that was found in an addition product between anthranol with lignin model quinone methides.[10]

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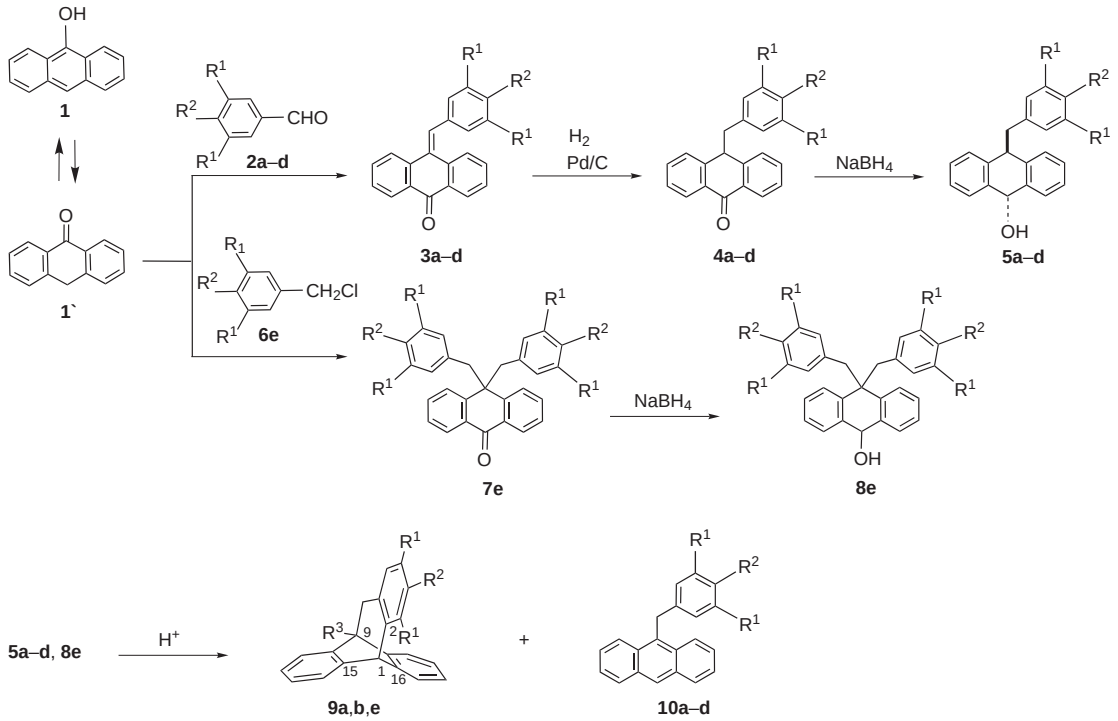

Scheme 1

Table 1 Preparation of Homotriptycenes from 9-Anthranols

	R^1	R^2	R^3	Yield of **9** (%)[a]	Mp (°C)	Yield of **10** (%)[a]	Mp (°C)
a	OMe	H	H	96	165	4	133
b	OMe	OMe	H	96	174	4	107
c	H	OMe	H	–		100	140
d	H	H	H	–		100	133
e	Benzyloxy	H	3,5-Dibenzyloxybenzyl	100	198	–	

Table 2 Product Distribution of the Acid-Catalyzed Dehydration of **5a** in CH_2Cl_2 at Room Temperature

Entry	Molar ratio of **5a**:HCOOH	Time (h)	Conversion (%)	Ratio of **9a**:**10a**[a]
1	1:0.67	2	100	64:36
2	1:2	2	100	67:33
3	1:12	0.5	100	92:8
4	1:56	0.5	100	96:4

[a] Determined by ^{1}H NMR spectroscopy.

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Table 3 Selected ^{1}H NMR and ^{13}C NMR Data of Compounds **5a–d** and **8e** in $CDCl_3$[a]

Compd	9-H	10-H	α-CH_2	OH	C-9	C-10	α-CH_2
5a–d	4.90 ± 0.13 ^3J = 10.8 Hz	4.25 ± 0.03 ^3J = 6.3 Hz	2.91 ± 0.03 ^3J = 6.3 Hz	1.99 ± 0.04 ^3J = 10.8 Hz	66.8 ± 0.1	48.2 ± 0.3	45.5 ± 0.7
8e	5.01 ^3J = 11.6 Hz		3.61, 3.40	0.32 ^3J = 11.6 Hz	67.5	49.0	52.4, 48.5

[a] TMS as internal standard.

Table 4 Selected ^{1}H NMR and ^{13}C NMR Data of Homotriptycenes **9a**,**b**,**e** in $CDCl_3$[a]

Compd	1-H	9-H	α-CH_2	OCH_3 or OCH_2	C-1	C-9	α-CH_2	OCH_3 or OCH_2
9a	5.69	4.19[b]	3.21[b]	3.63, 3.89	41.9	45.6	37.4	55.1, 56.1
9b	5.55	4.21[c]	3.21[c]	3.67, 3.81, 4.02	43.4	45.6	36.9	55.8, 60.8, 61.8
9e	5.84	–	3.03, 3.90	4.65, 4.83, 5.11	44.7	46.9	40.1, 42.6	69.8, 70.0, 70.7

[a] TMS as internal standard.
[b] ^3J = 2.6 Hz.
[c] ^3J = 3.9 Hz.

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(9) As experimental example, the synthesis of 3,5-dimethoxypentacyclo [7.6.6.$0^{2,7}$.$0^{10,15}$.$0^{16,17}$] heneicosa-2,4,6,10,12,14,16,18,20-nonaene (**9a**) is described here. Compound **3a** (342 mg, 1.00 mmol) was hydrogenated overnight at ambient temperature in 18 mL EtOAc and 6 mL MeOH in the presence of 5% Pd/C (380 mg). The mixture was filtered through silica gel and the volatile parts removed in vacuo. The residue was dissolved in 4 mL diglyme and treated for 30 min with $NaBH_4$ (120 mg, 3.17 mmol), before 2 mL MeOH were added dropwise. After further 10 min stirring, 60 mg (1.59 mmol) $NaBH_4$ was added and the reaction mixture stirred at r.t. overnight. All these procedures after the reaction with H_2 were performed in a N_2 atmosphere. Dropwise addition of oxalic acid led to pH 2. After 1 h stirring H_2O was slowly added. A solid precipitated which was purified by column chromatography [30 × 3 cm SiO_2, PE (bp 40–70 °C)–EtOAc, 30:1]. Colorless crystals of **9a** (222 mg, 68% total yield related to **3a**) were obtained which melted at 165 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.21 (d, ^3J = 2.6 Hz, 2 H, 8-H), 3.63 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 4.19 (t, ^3J = 2.6 Hz, 1 H, 9-H), 5.69 (s, 1 H, 1-H), 6.00 (d, ^4J = 1.8 Hz, 1 H, 4-H), 6.22 (d, ^4J = 1.8 Hz, 1 H, 6-H), 7.09–7.14 (m, 4 H, aromat. H), 7.31–7.35 (m, 4 H, aromat. H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 37.4, 41.9, 45.6, 55.1, 56.1, 96.6, 107.5, 125.1, 125.6, 126.2, 126.2, 141.1, 144.7, 123.0, 136.7, 156.4, 158.5. FD-MS: *m*/*z* (%) = 328 (100) [M^+]. Anal. Calcd for $C_{23}H_{20}O_2$ (328.4): C, 84.12; H, 6.14. Found: C, 84.15; H, 6.17. Structure of **9a** could be additionally established by a crystal structure analysis, which shall be published later.

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