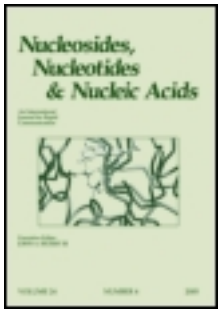

Nucleosides, Nucleotides and Nucleic Acids

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Nucleolipids as Potential Organogelators

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NUCLEOLIPIDS AS POTENTIAL ORGANOGELATORS

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□ *Four different series of nucleolipids or bola-nucleolipids were synthesized or re-synthesized. Most of the compounds were studied with respect to their gelation properties toward either water or aromatic, hetero-aromatic, and aliphatic hydrocarbons. Bola-nucleolipids* ***6*** *and* ***7*** *do not gelate any solvent tested, neither as sole additive nor by adding up to 10 wt% of a 1:1 mixture. The nucleolipid* ***22*** *carrying the antiviral acyclovir as a head group proved to be a potent organogelator for aromatic hydrocarbons such as toluene, but not for hetarenes, aliphatic hydrocarbons or water. The mono-tailed nucleolipid* ***24*** *exhibits excellent organogelator properties for both aromatic and aliphatic hydrocarbons. These were studied as a function of concentration and temperature.*

Keywords Organogelator; nucleolipid; gelation properties

INTRODUCTION

Nucleolipids are hybrid molecules composed from a nucleobase, a nucleoside, a nucleotide or a nucleic acid (either DNA or RNA) and a lipophilic moiety which might be either a single- or double-chained alkyl (or alkenyl) chain or a carbocyclic hydrocarbon such as cholesterol, a vitamin, or a bile acid.

Various nucleoside chemotherapeutics such as 1-ß-D-arabinofuranosyl-cytosine, -adenine, -7-deazaadenine, and -5-fluorouracil have been connected to various lipids by chemical means and are applied as pharmacologically active derivatives with enhanced catabolic stability and activity compared to the parent compounds.[1]

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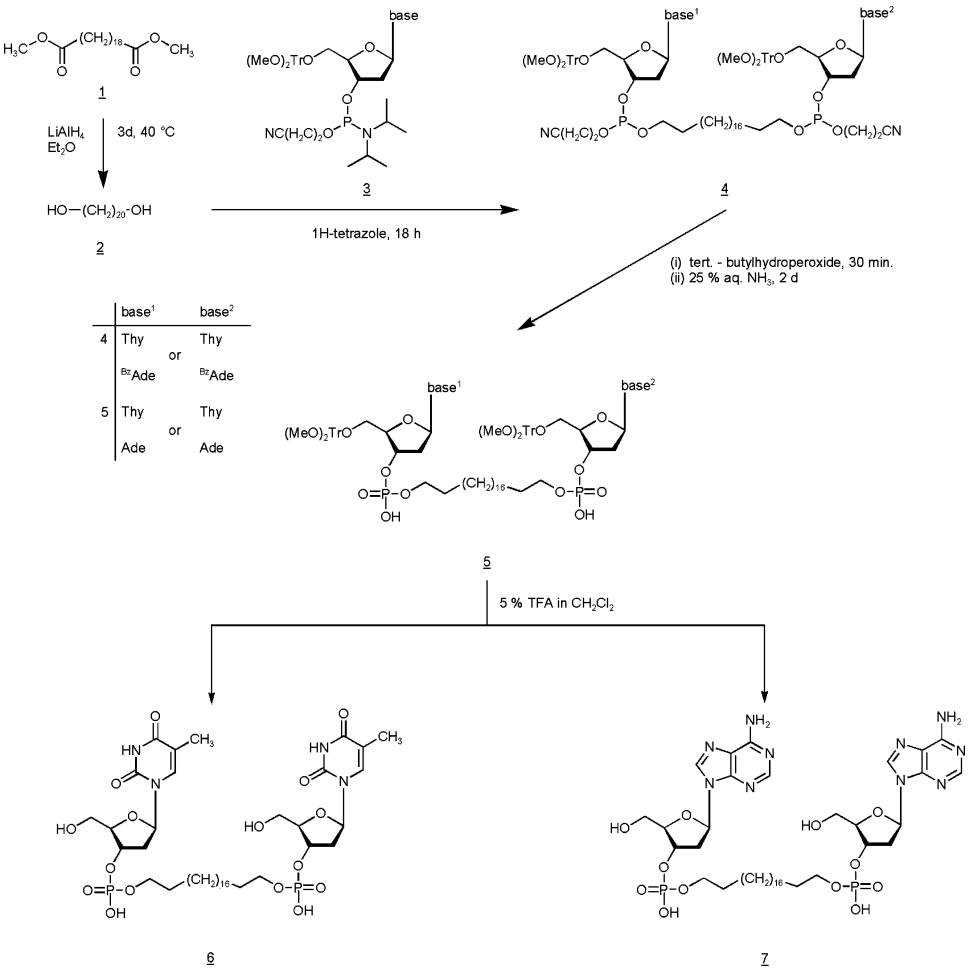
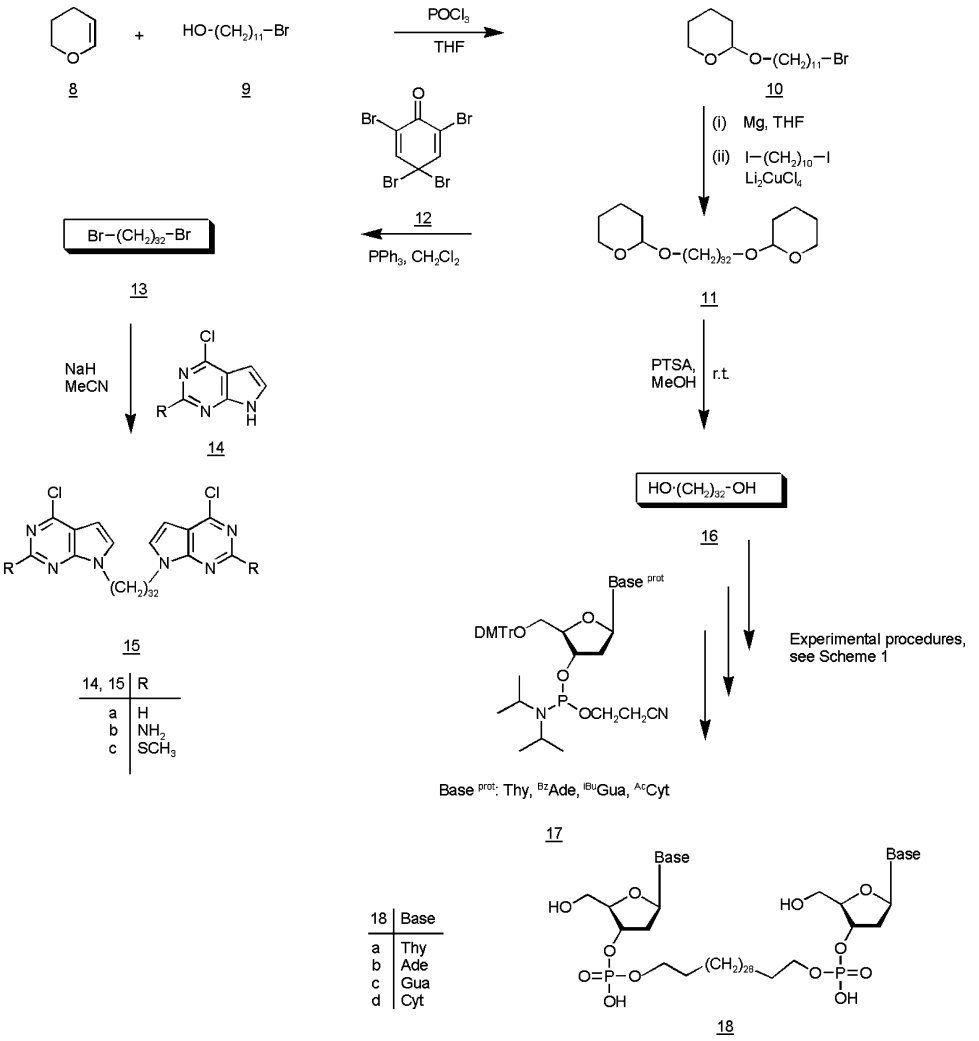


SCHEME 1

RESULTS AND DISCUSSION

In the beginning of our study we have synthesized or resynthesized several bola-nucleolipides (**6**, **7**, **15**, **18**, **22**, **24**) (Schemes 1 and 2) and have studied most of them with respect to their gelation properties toward either water or aromatic, heteroaromatic and aliphatic hydrocarbons.[1,2]

The synthesis of the bisuridylic acid derivative **6**[^{31}P-NMR (D_2O/TRIS-HCl): 9.02 ppm] was carried out according to Iwaura et al.[2] The bisadenylic acid derivative **7**[^{31}P-NMR (D_2O/TRIS-HCl): 9.20 ppm] was prepared analogously starting from the corresponding benzoyl-protected phosphoramidite of 2′-deoxyadenosine. Contrary to the fact that for compound **6** hydrogelation properties were reported,[2] we have demonstrate that



SCHEME 2

neither **6** nor **7** do gelate any solvent tested, neither as sole additive nor by adding up to 10 wt% of an equimolar mixture.

Following the route presented on Scheme 2 bola-nucleolipids such as **15** and **18** carrying a dotriacontane spacer were prepared via compounds **13** and **16**.[3,4] Studies on their gelation properties are under way.

The nucleolipid **22** (Scheme 3), carrying the antiviral acyclovir as head group,[1] proved to be a potent organogelator for aromatic hydrocarbons such as toluene, but not for hetarenes, aliphatic hydrocarbons or water. Such nucleolipids with other pharmacologically active head groups might be useful, e.g. for the topical treatment of skin deseases bringing about their own pharmaceutical formulation (*ger.*: Galenik).

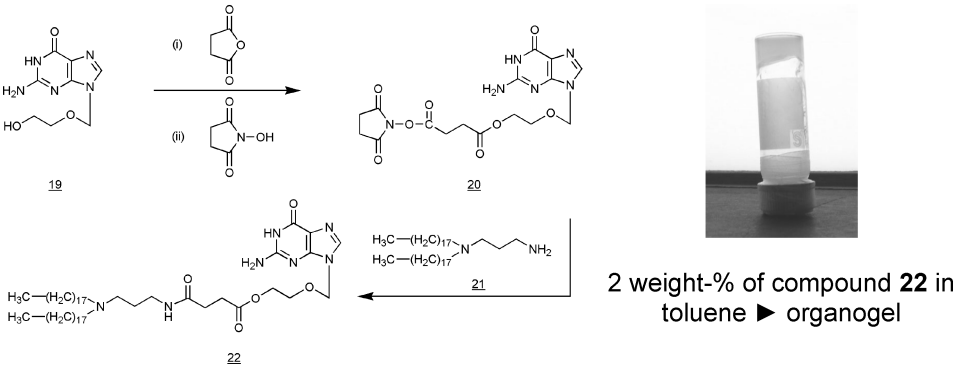
TABLE 1 Gelator properties of **24** in various solvents as a function of concentration

Conc. of 24 (w-%)	Benzene	Decane	Hexane	Toluene
5	G	**G**	**G**	G
2	G/V	**G**	**G**	V
1	L	V	L	L

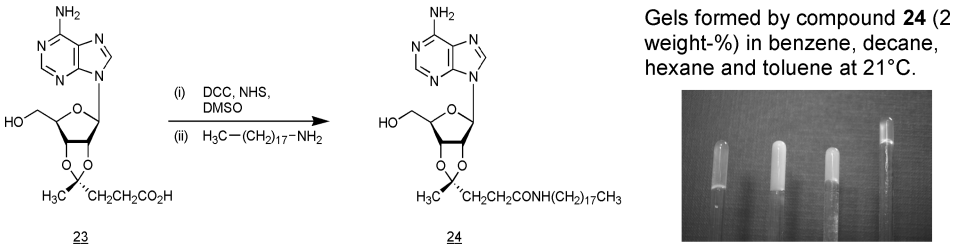
G: gel; V: viscous; L: soluble.

TABLE 2 Gelation properties of **24** in various solvents as a function of temperature

Temp. [°C]	Benzene	Decane	Hexane	Toluene
10	G	G	G	G
r.t.	G	G	G	G
30	G	G	G	V
40	G	G	V	L
50	V	G	L	L



SCHEME 3



SCHEME 4

The mono-tailed nucleolipid **24** (Scheme 4) exhibits excellent organogelator properties for both, aromatic as well as aliphatic hydrocarbons[1] Tables 1 and 2 summarize these properties as a function of concentration and temperature.

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3. **13**: H-NMR ($CDCl_3$): $\delta = 3.38$ (t, CH_2Br); 1.86 (t, $C\underline{H}_2$-CH_2Br); 1.43 (m, $C\underline{H}_2$-CH_2-CH_2Br); ~1.25 (m, CH_2). ^{13}C-NMR ($CDCl_3$): $\delta = 134.1$ (CH_2Br); 32.8 ($\underline{C}H_2$-CH_2Br); ~29 (multiple C); ~28 (multiple C). **16**: ^{1}H-NMR ($CDCl_3$): $\delta = 3.44$ (t, $C\underline{H}_2OH$); 1.32 (t, $C\underline{H}_2$-CH_2OH); 1.31 (m, CH_2). ^{13}C-NMR ($CDCl_3$): $\delta = 63.2$ ($\underline{C}H_2OH$); 32.8 ($\underline{C}H_2$-CH_2OH); 29.6 ($\underline{C}H_2$); 29.4 ($\underline{C}H_2$-CH_2-CH_2OH); 25.7 (CH_2).
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