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Synthesis of Terminally Substituted 9-Alkylidene-10-methyl Acridans

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Summary. ω-Substituted undecanals **1** and **2** reacted with acridine derivatives **3** and **5** to give the terminally substituted 9-alkylidene-10-methylacridans **6**. The compounds prepared were highly fluorescent and exhibited chemiluminescent activity.

Keywords. Acridans; Chemiluminescence.

Synthese von terminal substituierten 9-Alkyliden-10-methylacridanen

Zusammenfassung. Die ω-substituierten Undecanale **1** und **2** reagierten mit Acridinderivaten **3** und **5** zu den terminal substituierten 9-Alkyliden-10-methylacridanen **6**. Die untersuchten Verbindungen zeigten eine starke Fluoreszenz und waren auch chemilumineszent.

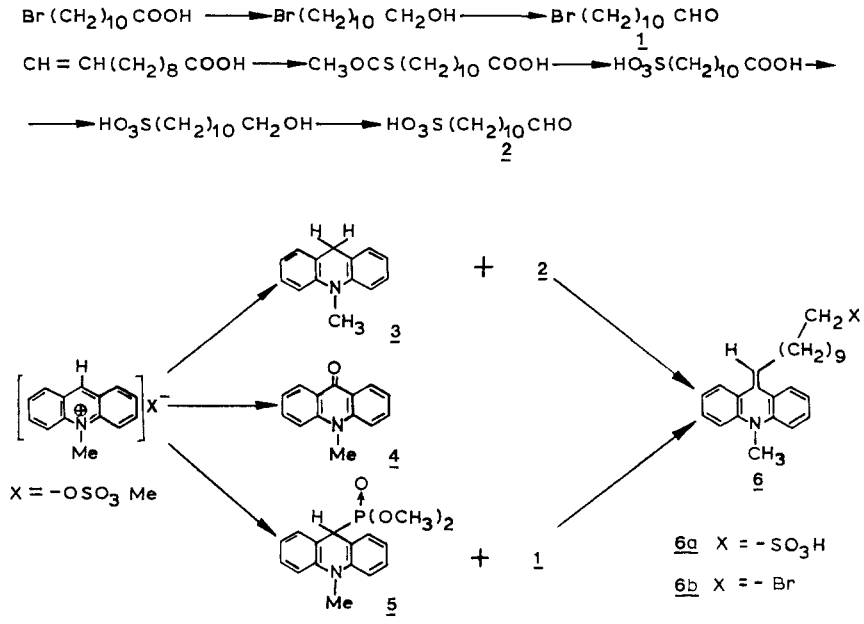
Introduction

Acridine and its derivatives have long been targets for research for both physical organic and synthetic chemists [1]. Taking into consideration that acridones are fluorescent, we considered developing new heterobifunctional alkylidene derivatives for chemiluminescence studies. We reasoned that an introduction of a long unbranched chain with a strongly polar small group such as a salt of sulfonic acid **6 a** might make a convenient micelle, provided that the bulky acridan could be accommodated in the core. We further expected that salts of **6 a** could offer materials reasonably soluble in water and/or in ethanol, i.e. materials suitable for chemiluminescence studies in such media. In this paper we wish to discuss the attempted preparation of compound **6 a** and to report the synthesis of 9-(11-bromoundecalidene)-10-methylacridan **6 b**.

Results and Discussion

The route to the linear aliphatic bifunctional aldehydes **1** and **2** required for the carbonyl olefinization proved to be difficult; similar problems were also encoun-

tered with the ω-bromoaldehyde C_{12} analogue [2]. We started the synthesis of the bifunctional moieties $Y(CH_2)_{10}X$ (where Y = Br, SO_3H and X = CHO) from the 11-bromoundecanoic and undecen-10-oic acids, respectively. Direct reduction of the carboxylic acids to the respective aldehydes, even though attempted [3], failed to produce the expected products. The carboxylic acids were then reduced to give the terminal bromo and sulfonic α-alcohols, while subsequent oxidation gave the corresponding aldehydes **1** and **2**. It was not attempted to purify the aldehydes via the bromo acetals, as in the reported case of C_{12} [2], since spectroscopic analyses on freshly prepared **1** and **2** showed a sufficient degree of purity. The sulfonic acid undecanol was synthesized from its thiol ester by a free radical reaction using α,α-azo-butyronitrile, followed by oxidation with peroxyacetic acid to give 11-sulfonic undecanoic acid. All sulfonic acid derivatives were difficult to analyze because of their marked hygroscopicity.



Acridine derivatives **3** and **5**, required as starting materials for the syntheses of the substituted 9-alkylidene-10-methylacridans **6**, were easily prepared in high yields. 10-Methylacridinium methyl sulfate was synthesized by the methylation of the corresponding tertiary base. Reduction of the quaternary salt furnished 10-methyl-9,10-dihydroacridine **3**, while its reaction with trimethyl phosphite gave 9-dimethoxyphosphinyl-9*H*-10-methylacridine **5**. 10-Methyl-9-acridone **4** was also prepared from the respective acridinium salt by reaction with potassium ferricyanide. The desired ω-substituted alkylidene-10-methylacridans **6** were accessible by reactions of the appropriate carbonyl compounds with alkali organyls [4].

The dihydro acridine **3** was deprotonated with *Bu*Li at $-70°$ in *THF* and the resulting carbanion reacted with **2** in situ. Neutralization of the crude product **6a** with NaOH or KOH gave the respective Na or K salts. Both the acid and the salts ($-SO_3H$, $-SO_3Na$, $-SO_3K$) could not be purified either by recrystallization and/or thin layer chromatography because of their strong tendency to decompose.

9-(11-Bromoundecalidene)-N-methylacridan **6b** was prepared from the phosphonated **5** acridine and the ω-bromoaldehyde **1**.

Sulfonation of an available long chain halide, namely the nonyl bromide, was successful by prolonged heating with Ag_2SO_3 in acetonitrile, ^{13}C NMR analysis indicating the presence of the C—S peak at 59.73 ppm. This method, when applied to **6b**, failed to produce **6a** and the same was true for all usual sulfonation methods [5].

The sodium and potassium salts of **6a** were screened for chemiluminescence with $^1O_2$ ($NaOCl + H_2O_2$). The crude product was strongly fluorescent as well as chemiluminescent on reaction with either $^1O_2$ or atmospheric oxygen, the chemiluminescence spectrum being identical to that of 10-methyl-9-acridone **4**. The chemiluminescence efficiency of both salts diminished with proceeding purification indicating that the expected product had been obtained but was unstable under the experimental conditions. The fact that the reaction with $^1O_2$ was chemiluminescent (the emission being that of excited 10-methyl-9-acridone) indicates that the expected products were partially produced. The chemiluminescence efficiency, however, could not be measured due to the uncertainty regarding the purity.

Derivative **6b** was also chemiluminescent during its reaction with singlet oxygen with a quantum yield equal to $1.1 \cdot 10^{-5}$ based on material employed.

The chemiluminescence spectra were in all cases similar to that of the 10-methyl-9-acridone **4** fluorescence; the fluorescence of the spent reaction mixtures was also that of **4**. Apparently, the light reaction gives rise to excited 10-methyl-9-acridone probably via a 1,2-dioxetane mechanism.

Experimental

Melting points were determined on an Electrothermal apparatus and are uncorrected. Infrared spectra (KBr, unless noted otherwise) were measured on a Perkin-Elmer 397 spectrophotometer. The NMR spectra were recorded on a Varian FT 80 A spectrometer and the chemical shifts are expressed in ppm (δ), downfield from the internal *TMS* standard.

Chemiluminescence Measurements

Chemiluminescence measurements were carried out in an Aminco "Chem-Glow" photometer with the timer cirquity disconnected, on addition of NaOH (30 μl, 1 *N*), H_2O_2 (30 μl, 3%) and NaOCl (50 μl, 1.7%) to 250 μl ethanolic solutions of the compound under study; for pure compounds, the concentrations was 10^{-4} *M*. Quantum yields, whenever possible, were calculated by comparison with the luminol standard [6], under the same geometry. Correction for self-absorption and for the response of the photomultiplier were unnecessary. Excitation and fluorescence spectra were run on an Aminco-Bowman spectrophotometer. Chemiluminescence spectra were run on the same instrument with the excitation source off, employing very fast scanning.

11-Bromoundecanal (**1**)

11-Bromoundecanol was prepared from the respective acid as described for selective reductions [7] with freshly made diborane (1.9 *M* solution in *THF*) [8]. Yield: 67%, m.p. 43–44°C from *n*-hexane; lit. m.p. 46–46.5°C [9]. IR: 3400 (OH), 2920, 2850 (CH_2) cm^{-1}.

1 was furnished by oxidation [10] of 11-bromoundecanol, the mmolar ratio of CrO_3 : *py* : *alc* being 70 : 140 : 10. Yield: 91%, oil; lit. oil [11]. IR: 2920, 2860 (CH_2), 1750 (CHO) cm^{-1}. ^1H NMR ($CDCl_3$): 1.22 [m, 16 H, —$(CH_2)_8$—], 2.34 (t, 2 H, —CH_2CHO), 3.32 (t, 2 H, —CH_2Br), 9.67 (s, 1 H, —CHO).

11-Sulfonic Acid Undecanal (**2**)

Undecen-10-oic acid (1.7 g, 9.2 mmol), thiolacetic acid (1.8 g, 24 mmol) and α-α-azo-butyronitrile (~ 100 mg) in *n*-hexane (18 ml) were heated under reflux for about 24 h. Upon solvent removal under reduced pressure the 11-thiolacetate undecanoic acid was obtained. Yield: 1.5 g (63%) from ethyl acetate: *n*-hexane (1 : 1), m.p. 52–53°C; lit. m.p. 52–54°C [12]. IR: 3 000–2 500 (COOH), 2 920, 2 860 (CH_2), 1 700 (SCO*Et*) cm^{-1}. ^1H NMR ($CDCl_3$): 1.25 [s, broad, 16 H, —$(CH_2)_8$—], 2.24 (s, 3 H, —$COCH_3$), 2.28 (t, 2 H, —CH_2COOH), 2.80 (t, 2 H, —CH_2SCO—).

11-Thiolacetate undecanoic acid (2.6 g, 10 mmol) was added to freshly prepared peroxyacetic acid [13] (from 90 ml Ac_2O, 19 ml 30% H_2O_2, 100 mg H_2SO_4) and the mixture was heated with stirring for 60 h. After lyophilization the hygroscopic 11-sulfonic undecanoic acid was obtained. Yield: 1.7 g (65%) from *n*-hexane, m.p. 70–78°C; lit. m.p. 67.5–80°C [12]. IR: 3 000–2 500 (COOH), 2 920, 2 850 (CH_2), 1 300–1 250, 1 085 (SO_3) cm^{-1}. ^{13}C NMR (CD_3COCD_3): 55.30 (C—S).

11-Sulfonic acid undecanol was synthesized from the above undecanoic acid as described for 11-bromoundecanol, the hygroscopic material obtained was not subjected to further purification. Yield: 89%, oil. IR (CCl_4): 3 200 (OH), 2 900, 2 750 (CH_2), 1 380, 1 080 (SO_3) cm^{-1}. ^1H NMR ($CDCl_3$): 1.48 [s, broad, 18 H, —$(CH_2)_9$—], 3.08 (t, 2 H, —CH_2SO_3H), 3.55 (t, 2 H, —CH_2OH).

2 was synthesized in a reverse manner to that described for the respective bromo analogue; the product was taken from the reaction mixture by repeated extractions using both *THF* and toluene and was subjected to solvent removal under reduced pressure. Yield: 87%, oil. IR (CCl_4): 2 900, 2 870 (CH_2), 1 720 (CHO) cm^{-1}. ^1H NMR ($CDCl_3$): 1.47 [s, broad, 16 H, —$(CH_2)_8$—], 2.49 (t, 2 H, —CH_2CHO), 3.12 (t, 2 H, —CH_2SO_3H), 9.92 (s, 1 H, —CHO).

10-Methyl-9,10-dihydroacridine (**3**)

10-Methylacridinium methyl sulfate was synthesized from dimethyl sulphate and acridine [14]. Yield: 53%, m.p. 206–207°C; the salt was washed with ethyl ether; lit. m.p. 207–208°C [15].

3 was prepared from the sodium borohydride reduction of the above quaternary acridinium salt in ethanol [16]. Yield: 79%, m.p. 98–99°C from *n*-hexane; lit. m.p. 99°C [17].

10-Methyl-9-acridone (**4**)

This was prepared as the pyridinium analog [18]. Yield 72%, m.p. 209–210°C from ethanol; lit. m.p. 210–211°C [17].

9-Dimethoxyphosphinyl-9H-10-methylacridine (**5**)

5 was synthesized from 10-methylacridinium methyl sulphate and trimethyl phosphite as described [15]. Yield: 83% from ethyl acetate—petroleum ether (1 : 1.5), m.p. 103–105°C; lit. m.p. 98–99°C [15].

9-(11-Bromundecalidene)-10-methylacridan (**6b**)

This was synthesized from **5** and **1** in a Wittig-Horner reaction [15]. The crude product obtained was left for several days at ~ − 5° with traces of *n*-hexane to precipitate any unreacted **5** (~ 10%) and was further purified by an oiling out technique from ethyl acetate—methanol (1 : 1.5). Yield: 37%, semi-crystalline product. Anal. $C_{25}H_{32}NBr$; calc. C 70.41, H 7.56, N 3.28%; found C 70.38, H 7.49, N 3.22%. ^1H NMR ($CDCl_3$): 1.30 [m, 16 H, —$(CH_2)_8$—], 1.85 (t, 2 H, >C=CH—CH_2), 2.44 (t, 2 H, —CH_2Br), 3.43 (s, 3 H, N—CH_3), 5.68 (t, 1 H, olefinic), 7.18 (m, 8 H, aromatics).

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