

Structural Investigation and Preparation of 14-alkyl-14H-dibenzo[a,j]xanthenes revised

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Structural Investigation and Preparation of 14-alkyl-14H-dibenzo[a,j]xanthenes revised

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요약. 높은 순도의 14-알킬-14H-다이벤조[a,j]잔텐의 합성법과 AM1 SCF MO 계산을 보고하였다.

주제어: 잔텐, 2-나프탈렌올, 알칸알, AM1 계산

ABSTRACT. Preparation of the title compounds at 0-5 °C is reported along with their AM1 SCF MO calculations. The advantage of this procedure is the high purity of the products.

Keywords: Xanthene, AM1 calculations, 2-naphthalenol, Ethanal, Propanal, Butanal, Ethanediol

INTRODUCTION

Xanthene derivatives are intermediates in organic synthesis and have many applications in laser technology because of their interesting spectroscopic properties.¹ According to a recent report dibenzoxanthene derivatives are candidates as sensitizers in photodynamic therapy (PDT).² PDT is a method of treating tumors by combined use of a photosensitizer and light. In this method, normally non-harmful level of the specific wavelength light excites the preadministered photosensitizer drug for localized tumor control.^{3,4}

RESULTS AND DISCUSSION

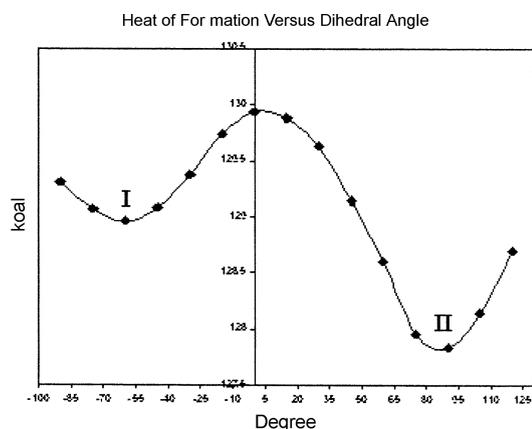
14-Substituted 14H-dibenzoxanthenes may be divided into 14-aryl and 14-alkyl derivatives. 14-Aryldibenzoxanthenes are prepared through their

corresponding arylmethanebisnaphthol intermediates **1** (Scheme 1).⁵⁻⁹

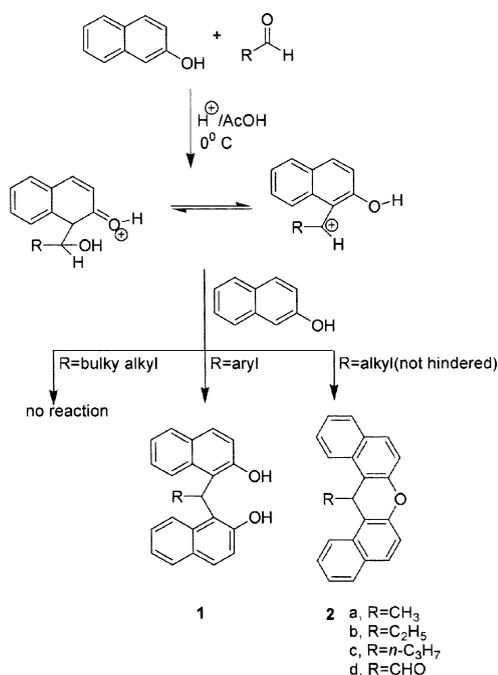
Arylmethanebisnaphthols are in turn synthesized by reacting benzaldehydes and 2-naphthol in glacial acetic acid at low temperatures in the presence of hydrochloric acid, or as described in a recent report, through high-pressure condensation of reactants in the presence of TsOH.⁶⁻¹¹

Alkyldibenzoxanthenes **2** have been synthesized without intermediacy of arylmethanebisnaphthols, by heating corresponding aldehydes and 2-naphthol in acetic acid or formic acid in the presence of hydrochloric acid.²⁻¹⁸ The disadvantage of all these methods is that the product is contaminated with a red color impurity and the necessity, therefore, for further purification. It should be mentioned that other condensation products of 2-naphthol and acetaldehyde have also been documented.¹⁸⁻¹⁹

These facts prompted us to consider the possibil-



Pol 1. H_f versus dihedral angle $\text{CH}_3\text{-CH}_2\text{-CH-C}^{*a}$) for 14-ethyl-14*H*-dibenzo[*a,j*]xanthene (a) C^* is one of the two aromatic carbon atoms attached to the CH group.



Scheme 1

ity of obtaining alkyl derivatives of methanebiphenyls by reacting aliphatic aldehydes and 2-naphthol in acetic acid in the presence of HCl or H_3PO_4 at low temperatures. However, we found that xanthene derivatives have been produced instead. Further investigations showed that unhin-

dered aliphatic aldehydes react with 2-naphthol to give xanthene derivatives. In the case of isobutyraldehyde (2-methylpropanal) no reaction was observed with 2-naphthol. Preparation of alkyl or aryl derivatives of xanthene at relatively high temperatures shows that these are thermodynamically stable compounds. The main question, which remains, is that why at low temperatures the reaction with aromatic aldehydes stops at methanebiphenyl derivatives and hindered aliphatic aldehydes does not proceed at all. Probably, stability of the carbocation and the bulkiness of the aldehydes are two key factors governing the reaction fate. In the case of aromatic aldehydes the carbocation is very stable and has the opportunity to react with another molecule of 2-naphthol, but its R group is too bulky to permit the dehydration step to proceed. The carbocation formed from an aldehyde such as 2-methylpropanal suffers from both its much less stability and the bulkiness of R.

CALCULATIONS

To have some idea of molecular shapes, we reverted to semi-empirical calculations. Molecular orbital calculations were performed by MMX-force field implemented in PCMODEL, and AMI calculations were run using MOPAC6.0 program.²⁰⁻²¹ The input files for the AMI calculations were the optimized geometry of MMX force field. The barrier to the interconversion of conformers by AMI was searched by SADDLE keyword. The search for local minima shows two conformers for each 14-alkyl derivative, except for the methyl one. In the first conformer, including its mirror image, the alkyl group is folded over the two naphthalene wings and in the second conformer, the orientation of the alkyl group is nearly opposite to that of the first one. In this context, heats of formations, free energies of activation for the interconversion of the conformers, and the angle between the two naphthalene rings of several 14-substituted-14*H*-dibenzo[*a,j*]xanthene were calculated. Free energy of activation for the interconversion of these two conformers is 1.0 to 1.7 kcal/mol. Wing angle, approximated as

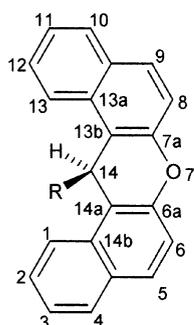


Fig. 1. Numbering system of 14-substituted 14*H*-dibenzo[*a,j*]xanthene.

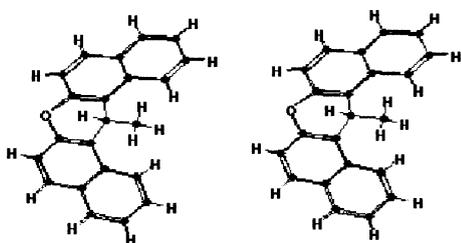


Fig. 2. Stereoview of one conformer of 14*H*-dibenzo[*a,j*]xanthene wing angle=141.09°.

sum of the absolute value of the two imaginary dihedral angles $H_{14}-C_{14}-O_7-C_{7a}$ and $H_{14}-C_{14}-O_7-C_{6a}$ (Fig. 1), is between 139 and 164° (see Figs. 2-4). For methyl derivative, this angle is surprisingly somewhat greater than that of the propyl derivative. This may be due to the special size of methyl group that can insert between the two wings and hence, widen its angle (see the stereoview, Fig. 2).

In addition to the above calculations, we have also plotted the variation of heat of formation of the ethyl derivative with respect to the variation of the dihedral angle between $CH_3-CH_2-CH-C^*$ (see plot and Fig. 3). In conformer **I**, the ethyl group is folded over the naphthalene rings and in conformer **II** its direction is nearly opposite to that of the first conformer.

From this plot we may conclude that the second conformer is more stable than the first one.

CONCLUSION

Unhindered aliphatic aldehydes react with 2-naphthol to give corresponding xanthene deriva-

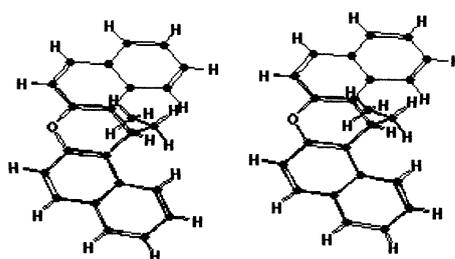


Fig. 3. Stereoview of one conformer of 14-ethyl-14*H*-dibenzo[*a,j*]xanthene wing angle=160.15°.

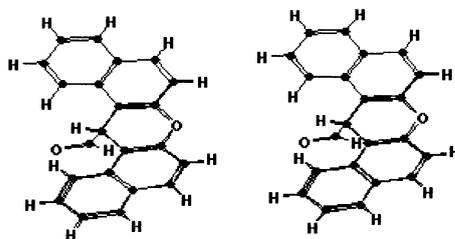


Fig. 4. Stereoview of one conformer of 14-formyl-14*H*-dibenzo[*a,j*]xanthene wing angle=164.27°.

tives at low temperatures in excellent yields. As minimized geometries show, all xanthene derivatives, with the exception of methyl derivative, have the shape of a flying butterfly, the angle between its two wings being 139-160°. The interconversion of all conformers, mirror images included, is fast (with the activation energy 1.0-1.7 kcal/mol).

EXPERIMENTAL

General procedure

2-Naphthol (2.88 g, 0.0200 mole) is dissolved in acetic acid, followed by the addition of 0.0100 mole of the corresponding aldehyde (ethanal, propanal, butanal and ethanedial) at 0 °C. To this mixture, at 0 °C, 0.400 mL H_3PO_4 or $HClO_4$ is added dropwise. The reaction vessel is left for 3-5 days in refrigerator, after which the product crystals are filtered, washed with 60-70% acetic acid and dried in the air.

Melting points and spectral data of **2a-2c** are consistent with the reported ones, i.e. their CH_3 protons appear at relatively high field (near 0.6 ppm) due to anisotropic effect.¹ **2d** melts at about 245 °C.

^1H NMR (TMS/ CDCl_3): δ 5.47(1H, d, $J=5.76\text{Hz}$); δ 7.00-8.25(13H, m); ^{13}C NMR (TMS/ CDCl_3): δ 49.55; δ 112.28; δ 114.98; δ 118.66; δ 123.68; δ 123.37; δ 126.96; δ 129.31; δ 130.30; δ 130.48; δ 130.74; δ 156.54. (The stereoview of **2d** (Fig. 4) will make it clear why the aldehyde carbon appears at δ 156.54 in ^{13}C NMR. The carbonyl hydrogen, which splits its adjacent hydrogen, is also hidden under aromatic hydrogens in ^1H NMR spectrum the integration of which shows 13 hydrogens).

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