近畿大農紀要 29：53～62 (1996)
Mem. Fac. Agr. Kinki Univ. 29：53～62 (1996)

Steroid-Based SHG Material. I. Preparation and Some Physical Properties of 4-Substituted-Benzylidene Derivatives of Estrone Methyl Ether, Dehydroepiandrosterone, and Androsta-1,4-dine-3,17-dione

Seiji SANO*, Yuuji INOUE**, Ken'ichi ISHIGAKI**, Masahiro TAKATANI**, Makoto KAJI*** and Tadashi OKAMOTO**

Synopsis

As a fundamental study searching for useful nonlinear optical material of secondary harmonic generation (SHG), the efficiency of regulation of parallel molecular arrangement by a steroidal subunit was examined by constructing a molecule having a large steroidal subunit attached with a conjugated π-electron system of substituted benzylidene group which contributes to generation of SHG. Starting from the three steroids shown in the title and 15 substituted benzaldehydes, 45 substituted benzylidenesteroid compounds were prepared and their physical properties were measured. This paper reports the syntheses and some properties such as electronic spectra and melting points of the products.

I. Introduction

Nonlinear optical material is a compound which is crucial for the development of photo-electronic devices in the future.[1] One of the important properties of nonlinear optical effect is the second harmonic generation (SHG) which converts a laser light of high wavelength into a light of low wavelength (1/2 of original) inaccesible or hardly accessible directly. For the purpose of obtaining an efficient SHG material, two important conditions are known : One is the material of large molecular non-linear secondary optical susceptibility, β, and the other is the parallel orientation of these molecules to prevent cancellation of the molecular effect (Fig. 1a). The former is satisfied by a molecule having an electronegative functional group at one end of a long-conjugated π-electron system and an electropositive group at the other end of conjugation (Fig. 2). However, this kind of compound has a large molecular dipole moment at the ground state, and this dipole induces the orientation of molecules in the antiparallel direction as shown in Figure 1b. The positive end of a dipole attracts the negative end of the dipole of the adjacent molecule, cancelling the net polarization and SHG effect of the material.[2] Therefore, the two requirements for large SHG effect described above are not easily satisfied by a planar molecule having a long conjugated π-electron system.

Our strategy toward this target is the construction of a parallel arrangement of molecules, each

* Lab. of Wood Products, Graduate School of Agriculture, Kinki Univ., Nakamachi, Nara 631, Japan (佐野誠二，林産利用学研究室，近畿大学大学院農学研究科農芸化学専攻，奈良市中町)
** Lab. of Natural High-Polym. Chem., Dept. of Agri. Chem., Kinki Univ., Nakamachi, Nara 631, Japan (井上裕二，石垣健一，高谷政弘，岡本忠，天然高分子化学研究室，近畿大学農学部農芸科学科，奈良市中町)
*** Ibaraki Research Lab., Hitachi Chem. Ind. Co. LTD., Higashicho, Hitachi, Ibaraki 317, Japan (鍛治誠，日立化成工業株式会社茨城研究所，日立市東町)

of which has an unsaturated subunit necessary for the generation of SHG (Fig. 3), by introducing a bulky and asymmetric steroid framework in the molecule. This type of material has one drawback, in principle, the dilution of the SHG effect by a bulky steroid group which is used only for the purpose of obtaining parallel orientation of the molecules and acts as a diluent of the SHG

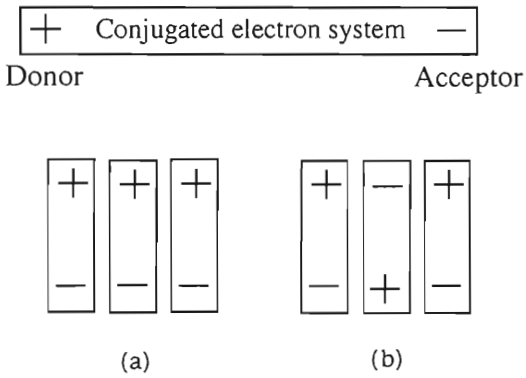


Fig. 1 Molecular arrangement. (a) parallel, (b) antiparallel

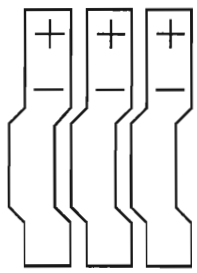


Fig. 2 Supposed parallel arrangement of molecules assisted by steroid rings

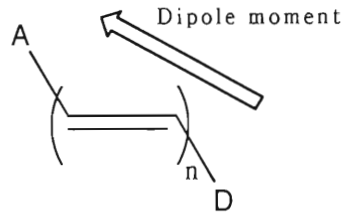
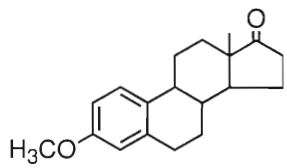
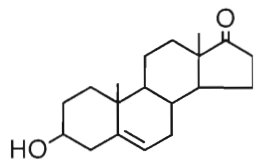


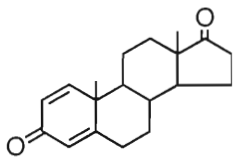
Fig. 3 SHG active molecule. A, electron acceptor group; D, electron donor group



Estrone methyl ether (EME)



Dehydroepiandrosterone (DA)



1,4-Androstadien-3,17-dione (A)

Fig. 4 Steroid substrates examined

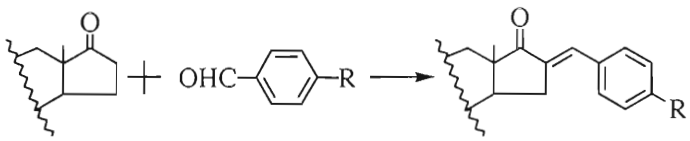


Fig. 5 Synthetic pathway
R=donor group ($N(CH_3)_2$, OCH_3, OC_4H_9, OC_2H_5, CH_3, 3,4-$(OCH_3)_2$, SCH_3, $NHCOCH_3$), H, and acceptor group (C_6H_5, F, Cl, Br, CF_3, CN)

effect. However, if it is considered that even in an effective SHG material such as 2-methyl-4-nitroaniline,[3] the effect of each molecure is not fully utilized in a bulk material because of some antiparallel arrangement involved. Our strategy is more likely to succeed in that the highly regulated parallel orientation of molecules might be attained by steroid groups and covers the decrease of molecular SIIG effect due to dilution effect. To examine this idea, 45 compounds were prepared through condensation reaction of three steroids described in the title (Fig. 4) and 15 substituted benzaldehydes which are shown in Fig. 5. This paper describes the preparation and some physical properties of the condensed products.

II. Results and Discussion

Preparation of the compounds was carried out under alkaline reaction conditions using the three steroids indicated in the title and 15 substituted benzaldehydes. The substituents of the

Table 1. Substituents of benzaldehyde examined and its Hammett σ value

	Donor									Acceptor					
R	NMe_2	MeO	BuO	EtO	Me	$(MeO)_2$	SMe	AcNH	H	Ph	F	Cl	Br	CF_3	CN
σ	-0.60	-0.27	—	—	-0.17	-0.15	-0.05	-0.02	0.00	0.01	0.06	0.23	0.23	0.55	0.63

Table 2. Physical constants of prepared benzylidenesteroids

a. Substituted benzylideneestrone methyl ether

Substituent	NMe_2	MeO	BuO	EtO	Me	$(MeO)_2$	SMe	AcNH	H	Ph	F	Cl	Br	CF_3	CN
mp(℃)	219	173	161	171	208	149	145	250	171	161	150	144	172	148	217
λ max(nm)	382.0	310.2	323.6	323.8	301.0	333.2	340.2	367.2	288.8	321.6	288.8	303.6	298.8	286.2	296.4

b. Substituted benzylidenedehydroepiandrosterone

Substituent	NMe_2	MeO	BuO	EtO	Me	$(MeO)_2$	SMe	AcNH	H	Ph	F	Cl	Br	CF_3	CN
mp(℃)	289	224	116	216	232	151	214	290	192	248	211	219	242	211	280
λ max(nm)	384.6	322.2	324.0	323.8	303.8	334.6	338.4	367.4	293.8	320.6	301.8	296.2	299.2	286.0	298.2

c. Substituted benzylideneandrostadienedione

Substituent	NMe_2	MeO	BuO	EtO	Me	$(MeO)_2$	SMe	AcNH	H	Ph	F	Cl	Br	CF_3	CN
mp(℃)	244	251	206	195	296	176	271	>300	265	175	289	268	254	203	237
λ max(nm)	381.4	323.6	324.6	324.8	304.6	336.8	339.4	322.5	293.0	321.5	299.4	297.4	295.0	285.2	298.8

benzaldehydes are listed in Table 1 with each electron-donating or attracting property by the index of Hammett σ value.[4)]

The results of syntheses and some physical properties of the products are summarized in Table 2. The yields of products were moderate to excellent as shown in Table 2. There was no significant difference between the reactivities of the three steroids, indicating that small structural changes in the A ring of steroid do not have meaningful influence on their reactivities. Electronic spectra of the benzylidenesteroid showed a tendency of gradual change in the wavelength of maximum absorption, λ_{max}, according to the electronic effect of the substituents on the benzylidene conjugation as indicated in the Table. Again, almost no significant difference in the absorption spectra was observed between the three steroid compounds. However, there are some exceptions when the λ_{max} is inspected in detail. The results suggest that there are differences in solvatochromic effect due to solvation, molecular association, hydrogen bonding, and so on, which may be discussed in detail when the results of the experiments, such as SHG efficiency and X ray crystallography of a single crystal of each compound, are available.

The regulation of molecular arrangements which is the end purpose of the present study cannot be discussed before knowing the SHG activities of these compounds. However, the substituent effect on the melting points of these compounds showed a rough tendency in accordance with the electronic effect of the substituent, suggesting rather regular arrangement of these molecules.

III. Experiment

Reagents and Instuments

All reagents and solvents are used as received, unless otherwise stated. Steroids are GR-grade commercial product of Tokyo Kasei Chemical Co. Substituted benzaldehydes (4-methyl, 4-methoxy, 4-chloro, 4-dimethylamino, and 3,4-dimethoxy derivatives) were purchased from Wako Chemical Co. 4-Cyanobenzaldehyde was the product of Aldrich Chemical Co., and 4-fluoro, 4-bromo, 4-methylthio, 4-ethoxy, 4-acetylamino, 4-butoxy, and 4-phenyl derivatives of benzaldehyde were from the Tokyo Chemical Ind. Co., all of which were GR reagents. Benzaldehyde (EP grade reagent of Wako Pure Chemical Ind. Co.) was used after single distillation under a nitrogen atmosphere. All other reagents and solvents are EP-grade reagents.

NMR spectra were measured with a JOEL JNM-EX270 super magnet spectrophotometer. UV spectra were measured on a Shimazu UV-260 autograph. All melting points were measured by Yanagimoto melting point apparatus and the temperatures were uncorrected. Elemental Analyses were carried out by the Analytical Laboratory of Institute for Chemical Research, Kyoto University.

Preparation

1) Synthesis of estrone methyl ether (EME), estrone 8.00 g (29.6 mmol) was dissolved in a 200 ml portion of THF in a 500 ml round bottom flask. The solution was cooled to 5°C and 1.8 g of NaOH (27.6 mmol) and 6.4 g of methyl iodide (45.1 mmol) were added successively under stirring. Then the reaction mixture was allowed to come to room temperature and stirring was continued for 20 hr. After making sure of the consumption of all estrone and the neutrality of the solution, THF was removed from the reaction mixture, and the residue was extracted with ethyl acetate/water. The organic layer was washed with aqueous sodium bicarbonate and water three times each and dried over sodium sulfate overnight. After evaporation of the solvent, estrone methyl ether was obtained in a quantitative yield (8.5 g). Recrystallization from benzene-ethanol produced a colorless rhombohedral prism, m.p. 171-175°C.

2) Synthesis of benzylideneestrone methyl ether (BEME). In a 200 ml round bottom flask EME

(1.00 g, 3.53 mmol), benzaldehyde (470 mg, 4.4 mmol), 4 ml of 2% aqueous NaOH solution, and a 100 ml portion of methanol were combined. The reaction mixture was stirred under reflux at 70° C for 2 h. After confirming the end of the reaction by TLC (eluent; ethyl acetate/hexane=1/2), the reaction mixture was neutralized with 2 N HCl, and concentrated to about 50 ml. The concentrated solution was added to a 250 ml portion of water, saturated aqueous NaCl solution was added, and the mixture was kept at room temperature for crystallization. The crystalline product was then collected through filtration, washed several times with water, and air-dried to obtain 1.08 g (82.2%) of benzylideneestrone methyl ether. After recrystallization from ethanol, it is obtained as colorless needles, yield, 0.56 g, 42.2%; m.p. 171°C.

3) Synthesis of 4'-methylbenzylideneestrone methyl ether (Me-BEME). In a 200 ml round bottom flask EME (1.00 g, 3.53 mmol), 4-methylbenzaldehyde (500 mg, 4.2 mmol), 4 ml of 2% agueous NaOH solution, and a 100 ml portion of 2-butanol were combined. The reaction mixture was stirred at 70°C for 2 h. After confirming the end of the reaction by TLC (eluent; ethyl acetate/hexane=1/2), the reaction mixture was neutralized with 2 N HCl, and concentrated to about 50 ml of volume. The concentrated solution was extracted with ethyl acetate/water. The organic layer was washed successively with sodium bicarbonate and water three times each, and dried over sodium sulfate overnight. After evaporation of the solvent, the crude product was 1.03 g (75.2%) of benzylideneestrone methyl ether. Recrystallization of the product from ethanol produced Me-BEME as colorless needles, yield 0.91 g, 66.7%; m.p. 207-209°C.

4) Synthesis of 4'-methoxybenzylideneestrone methyl ether (MeO-BEME). The procedure was the same as 3.2.3 except for the use of 4-methoxybenzaldehyde (694 mg, 5.1 mmol), 2 ml of 10% NaOH, and 90 ml of 2-butanol, and the reaction was continued for 7 h. The yield of crude product was 1.51 g, 106%, and, after recrystallization from ethanol, the product was obtained as colorless needles. Yield was 0.70 g, 48.9%; m.p. 172-173°C.

5) Synthesis of 4'-chlorobenzylideneestrone methyl ether (Cl-BEME). The procedure was the same as above except for the use of 4-chlorobenzaldehyde (5.1 g. 3.6 mmol) and 2 ml of 10% NaOH, and the reaction was continued for 5 h. The yield of crude product was 1.27 g, 88%, and after recrystallization from ethanol, the product was obtained as colorless needles. Yield was 0.75 g 52%; m.p. 144-145°C.

6) Synthesis of 4'-dimethylaminobenzylideneestrone methyl ether (Me_2N-BEME). The procedure was the same as 3.2.3 except for the use of 4 dimethylaminobenzaldehyde (550 mg, 3.7 mmol) and the reaction was continued for 8 h. The yield of crude product was 1.55 g, 106%, and after recrystallization in ethanol, the product was obtained as yellow needles. Yield was 0.81 g, 56%; m.p. 215-223°C.

7) Synthesis of 3',4'-dimethoxybenzylideneestrone methyl ether (DiMeO-BEME). The procedure was the same as described in 3.2.2 except for the use of 3,4-dimethoxybenzaldehyde (636 mg, 3.8 mmol) and 4 ml of 10% NaOH, and the reaction was continued for 20 h. The yield of crude product was 1.73 g, 133%, and after recrystallization from methanol, the product was obtained as colorless needles. M.p. 144-153°C.

8) Synthesis of 4'-cyanobenzylideneestrone methyl ether (CN-BEME). The procedure was the same as 3.2.2 except for the use of 4-cyanobenzaldehyde (480 mg, 3.7 mmol) and 3 ml of 50% NaOH, and the reaction was continued for 21 h. The yield of crude product was 1.48 g, 105%, and after recrystallization from ethyl acetate, the product was obtained as pale yellow needles. Yield was 1.13 g, 81%. m.p. 215-218°C.

9) Synthesis of 4'-trifluoromethylbenzylideneestrone methyl ether (CF_3-BEME). The reaction was started as 3.2.3 except for the use of 4-trifluoromethylbenzaldehyde (1.55 g, 8.8 mmol) and 4 ml of 10% NaOH. The reaction was continued for 46 h with occasional addition of 2-butanol totalling 85 ml. The yield of crude product was 2.33 g, 150%, and after recrystallization from ethyl acetate, the product was obtained as colorless needles. Yield was 0.63 g, 40%; m.p. 147-150°

C.

10) Synthesis of 4'-fluorobenzylideneestrone methyl ether (F-BEME). The procedure was the same as 3.2.2 except for the use of 4-fluorobenzaldehyde (510 mg, 3.6 mmol), 200 ml of methanol, and 4 ml of 10% NaOH, and the reaction was continued for 29 h. The yield of crude product was 1.25 g, 87%, and after recrystallization from ethyl acetate the product was obtained as pale yellow needles. Yield was 0.79 g, 55% ; m.p. 139-163°C.

11) Synthesis of 4'-bromobenzylideneestrone methyl ether (Br-BEME). The procedure was the same as 3.2.2 except for the use of 4-bromobenzaldehyde (660 mg, 3.6 mmol), 200 ml of methanol, and 2 ml of 10% NaOH, and the reaction was continued for 8 h. The yield of crude product was 1.47 g, 92%, and after recrystallization from ethyl acetate, the product was obtained as pale yellow needles. Yield was 1.15 g, 72% ; m.p. 169-175°C.

12) Synthesis of 4'-methylthiobenzylideneestrone methyl ether (MeS-BEME). The procedure was the same as 3.2.2 except for the use of 4-methylthiobenzaldehyde (600 mg, 3.9 mmol) and 2 ml of 10% NaOH, and the reaction was continued for 20 h. The yield of crude product was 1.44 g, 97%, and after recrystallization from ethyl acetate, the product was obtained as pale yellow needles. Yield was 10.97 g, 65% ; m.p. 144-145°C.

13) Synthesis of 4'-ethoxybenzylideneestrone methyl ether (EtO-BEME). The procedure was the same as 3.2.12 except for the use of 4-ethoxybenzaldehyde (660 mg, 4.4 mmol) and the reaction was continued for 26 h. After recrystallization of the crude product from ethyl acetate, the product was obtained as pale yellow needles. Yield was 0.65 g, 44% ; m.p. 168-175°C.

14) Synthesis of 4'-acetylaminobenzylideneestrone methyl ether (AcNH-BEME). The procedure was the same as 3.2.12 except for the use of 4-acetylaminobenzaldehyde (590 mg, 3.6 mmol) and the reaction was continued for 18 h. After recrystallization of the crude product (1.23 g, 81%) from chloroform-methanol, the product was obtained as yellow needles. Yield was 0.60 g, 40% ; m.p. 247-253°C.

15) Synthesis of 4'-butoxybenzylideneestrone methyl ether (BuO-BEME). The procedure was the same as 3.2.12 except for the use of 4-butoxybenzaldehyde (657 mg, 3.7 mmol) and 0.5 ml of 50% NaOH, and the reaction was continued for 24 h. After recrystallization of the crude product (1.46 g, 93%) from methanol, the product was obtained as colorless needles. Yield was 0.56 g, 35% ; m.p. 161°C.

16) Synthesis of 4'-phenylbenzylideneestrone methyl ether (Ph-BEME). The procedure was the same as 3.2.12 except for the use of 4-phenylbenzaldehyde (646 mg, 3.6 mmol) and 5 ml of 50% NaOH, and the reaction was continued for 93 h. After recrystallization of the crude product (1.56 g, 99%) from ethyl acetate, the product was obtained as colorless crystals. Yield was 1.36 g, 88% ; m.p. 161°C.

17) Synthesis of benzylidenedehydroepiandrosterone (BDA). In a 200 ml round bottom flask a mixture of dehydroepiandrosterone (DA) 1.00 g (3.47 mmol), benzaldehyde 0.75 g (7.1 mmol), 1 ml of 50% NaOH, and 100 ml of methanol was refluxed at 70°C for 17 h under stirring. After completion of the reaction was ensured by TLC (eluent ; ethyl acetate/hexane=1/2), the reaction mixture was neutralized with 2 N HCl and concentrated to the volume of 80 ml under reduced pressure. The concentrate was added to a flask containing 200 ml of distilled water, brine was added to the mixture, and it was kept at room temperature. The crystalline which appeared was collected by filtration, washed thoroughly with water, and air-dried to obtain the crude product 1.40 g (107%). Recrystallization of the crude product from methanol produced the product as pale colorless fiber. Yield was 0.46 g, 36% ; m.p. 189-194°C.

18) Synthesis of 4'-methylbenzylidenedehydroepiandrosterone (Me-BDA). The procedure was the same as 3.2.17 except for the use of 4-methylbenzaldehyde (857 mg, 7.1 mmol). The yield of crude product was 1.40 g, 103%, and after recrystallization from ethanol, the product was obtained as colorless fiber. Yield was 1.10 g, 82% ; m.p. 229-235°C.

19) Synthesis of 4'-methoxybenzylidenedehydroepiandrosterone (MeO-BDA). The procedure was the same as 3.2.17 except for the use of 4-methoxylbenzaldehyde (763 mg, 5.6 mmol) and 2 ml of 50% NaOH. The yield of crude product was 1.35 g, 96%, and after recrystallization from ethanol, the product was obtained as colorless needles. Yield was 0.99 g, 70% ; m.p. 222-226°C.

20) Synthesis of 4'-chlorobenzylidenedehydroepiandrosterone (Cl-BDA). The procedure was the same as 3.2.19 except for the use of 4-chlorobenzaldehyde (585 mg, 4.2 mmol) and the reaction was continued for 20 h. The yield of crude product was 1.40 g, 99%, and after recrystallization from ethanol, the product was obtained as colorless needles. Yield was 1.28 g, 90% ; m.p. 217-222°C.

21) Synthesis of 4'-dimethylaminobenzylidenedehydroepiandrosterone (Me_2N-BDA). The procedure was the same as 3.2.19 except for the use of 4-dimethylaminobenzaldehyde (619 mg, 4.2 mmol) and the reaction was continued for 27 h. The yield of crude product was 1.02 g, 70%, and after recrystallization from ethyl acetate the product was obtained as yellow needles. Yield was 0.14 g, 9% ; m.p. 285-292°C.

22) Synthesis of 3',4'-dimethoxybenzylidenedehydroepiandrosterone (DiMeO-BDA). The procedure was the same as 3.2.19 except for the use of 3,4-dimethoxybenzaldehyde (690 mg, 4.2 mmol) and the reaction was continued for 49 h. The yield of crude product was 1.46 g, 94%, and after recrystallization from ethanol, the product was obtained as pale brown-yellow fiber. Yield was 0.47 g, 31% ; m.p. 150-153°C.

23) Synthesis of 4'-cyanobenzylidenedehydroepiandrosterone (CN-BDA). The procedure was the same as 3.2.19 except for the use of 4-cyanobenzaldehyde (460 mg, 3.5 mmol) and the reaction was continued for 22 h. The yield of crude product was 1.28 g, 92%, and after recrystallization from ethyl acetate, the product was obtained as pale yellow crystals. Yield was 0.5 g, 36% ; m.p. 277-282°C.

24) Synthesis of 4'-trifluoromethylbenzylidenedehydroepiandrosterone (CF_3-BDA). The procedure was the same as 3.2.19 except for the use of 4-trifluoromethylbenzaldehyde (766 mg, 4.4 mmol) and 3 ml of 50% NaOH, and the reaction was continued for 15 h. The yield of crude product was 1.57 g, 102%, and after recrystallization from ethanol, the product was obtained as colorless fiber. Yield was 1.15 g, 75% ; m.p. 209-212°C.

25) Synthesis of 4'-fluorobenzylidenedehydroepiandrosterone (F-BDA). The procedure was the same as 3.2.19 except for the use of 4-fluorobenzaldehyde (707 mg, 5.0 mmol) and the reaction was continued for 18 h. The yield of crude product was 1.00 g, 70%, and after recrystallization from ethanol, the product was obtained as colorless fiber. Yield was 0.71 g, 50% ; m.p. 208-214°C.

26) Synthesis of 4'-bromobenzylidenedehydroepiandrosterone (Br-BDA). The procedure was the same as 3.2.19 except for the use of 4-bromobenzaldehyde (650 mg, 3.5 mmol) and reaction was continued for 23 h. The yield of crude product was 1.42 g, 90%, and after recrystallization from ethanol, the product was obtained as colorless fiber. Yield was 1.22 g, 78% ; m.p. 238-246°C.

27) Synthesis of 4'-methylthiobenzylidenedehydroepiandrosterone (MeS-BDA). The procedure was the same as 3.2.19 except for the use of 4-methylthiobenzaldehyde (554 mg, 3.6 mmol) and 6 ml of 50% NaOH, and the reaction was continued for 18 h. The yield of crude product was 1.39 g, 95%, and after recrystallization from ethanol, the product was obtained as colorless needles. Yield was 1.37 g, 94% ; m.p. 212-217°C.

28) Synthesis of 4'-ethoxybenzylidenedehydroepiandrosterone (EtO-BDA). The procedure was the same as 3.2.27 except for the use of 4-ethoxybenzaldehyde (530 mg, 3.5 mmol) and the reaction was continued for 61 h. The yield of crude product was 1.43 g, 98%, and after recrystallization from ethanol, the product was obtained as colorless fiber. Yield was 0.97 g, 67% ; m.p. 214-218°C.

29) Synthesis of 4′-acetylaminobenzylidenedehydroepiandrosterone (AcNH-BDA). The procedure was the same as 3.2.27 except for the use of 4-acetylaminobenzaldehyde (739 mg, 4.5 mmol). The yield of crude product was 1.29 g, 86%, and after recrystallization from ethyl acetate, the product was obtained as yellow needles. Yield was 1.07 g, 71%, m.p. 287-293°C.

30) Synthesis of 4′-butoxybenzylidenedehydroepiandrosterone (BuO-BDA). The procedure was the same as 3.2.27 except for the use of 4-butoxybenzaldehyde (632 mg, 3.6 mmol) and 2.5 ml of 25% NaOH, and the reaction was continued for 24 h. The yield of crude product was 1.47 g, 95%, and after recrystallization from ethanol, the product was obtained as colorless fiber. Yield was 1.21 g, 78% ; m.p. 110-122°C.

31) Synthesis of 4′-phenylbenzylidenedehydroepiandrosterone (Ph-BDA). The procedure was the same as 3.2.27 except for the use of 4-phenylbenzaldehyde (637 mg, 3.5 mmol) and the reaction was continued for 95 h. The yield of crude product was 1.53 g, 98%, and after recrystallization from ethanol, the product was obtained as colorless fiber. Yield was 0.99 g, 63% ; m.p. 246-250°C.

32) Synthesis of benzylideneandrostadienedione (BA). The procedure was the same as 3.2.17 except for the use of androsta-1,4-diene-3,17-dione (A) 1.00 g (3.52 mmol) and 1 ml of 25% NaOH, and the reaction was continued for 14 h. The yield of crude product was 1.24 g, 95%, and after recrystallization from methanol, the product was obtained as colorless plates. Yield, 1.16 g, 88% ; m.p. 265°C.

33) Synthesis of 4′-methylbenzylideneandrostadienedione (Me-BA). The procedure was the same as 3.2.32 except for the use of 4-methylbenzaldehyde (505 mg, 4.2 mmol) and the reaction was continued for 7 h. The yield of crude product was 1.07 g, 79%, and after recrystallization from methanol, the product was obtained as colorless plates. Yield was 0.78 g, 57% ; m.p. 295-297°C.

34) Synthesis of 4′-methoxybenzylideneandrostadienedione (MeO-BA). The procedure was the same as 3.2.32 except for the use of 4-methoxybenzaldehyde (500 mg, 3.7 mmol) and the reaction was continued for 8 h. The yield of crude product was 1.46 g, 103%, and after recrystallization from methanol, the product was obtained as colorless plates. Yield was 0.44 g, 31% ; m.p. 250-252°C.

35) Synthesis of 4′-chlorobenzylideneandrostadienedione (Cl-BA). The procedure was the same as 3.2.32 except for the use of 4-chlorobenzaldehyde (555 mg, 4.0 mmol) and the reaction was continued for 14 h. The yield of crude product was 1.35 g, 94%, and after recrystallization from methanol, the product was obtained as colorless prisms. Yield was 1.27 g,89% ; m.p. 226-270°C.

36) Synthesis of 4′-dimethylaminobenzylideneandrostadienedione (Me_2N-BA). The procedure was the same as 3.2.32 except for the use of 4-dimethylaminobenzaldehyde (549 mg, 3.7 mmol) and the reaction was continued for 45 h. The yield of crude product was 0.92 g, 63%. Because suitable solvent for recrystallization of this product was not found, it was washed repeatedly with water. M.p.244°C.

37) Synthesis of 3′,4′-dimethoxybenzylideneandrostadienedione (DiMeO-BA). The procedure was the same as 3.2.32 except for the use of 3′,4′-dimethoxybenzaldehyde (619 mg, 3.7 mmol) and 2 ml of 25% NaOH, and the reaction was continued for 45 h. The yield of crude product was 1.36 g, 90%, and after recrystallization from methanol, the product was obtained as colorless plates. Yield was 1.24 g, 82% ; m.p. 175-176°C.

38) Synthesis of 4′-cyanobenzylideneandrostadienedione (CN-BA). The procedure was the same as 3.2.37 except for the use of 4-cyanobenzaldehyde (499 mg, 3.8 mmol) and the reaction was continued for 23 h. The yield of crude product was 1.30 g, 93%. Again, no suitable solvent for recrystallization was found for this product. M.p. 237°C.

39) Synthesis of 4′-trifluoromethylbenzylideneandrostadienedione (CF_3-BA). The procedure was the same as 3.2.32 except for the use of 4-trifluoromethylbenzaldehyde (559 mg, 3.2 mmol)

and the reaction was continued for 23 h. The yield of crude product was 1.27 g, 103%, and after recrystallization from ethanol, the product was obtained as colorless needles. Yield was 0.33 g, 27%; m.p. 203-204°C.

40) Synthesis of 4'-fluorobenzylideneandrostadienedione (F-BA). The procedure was the same as 3.2.32 except for the use of 4-fluorobenzaldehyde (460 mg, 3.2 mmol) and 1 ml of 25% NaOH, and the reaction was continued for 17 h. The yield of crude product was 1.20 g, 105%, and after recrystallization from ethanol, the product was obtained as colorless prisms. Yield was 1.08 g, 94%; m.p. 286-292°C.

41) Synthesis of 4'-bromobenzylideneandrostadienedione (Br-BA). The procedure was the same as 3.2.40 except for the use of 4-bromobenzaldehyde (555 mg, 3.0 mmol). The yield of crude product was 0.81 g, 64%, and after recrystallization from ethyl acetate, the product was obtained as colorless plates. Yield was 0.64 g, 51%; m.p. 253-255°C.

42) Synthesis of 4'-methylthiobenzylideneandrostadienedione (MeS-BA). The procedure was the same as 3.2.40 except for the use of 4-methylthiobenzaldehyde (560 mg, 3.7 mmol) and the reaction was continued for 19 h. The yield of crude product was 1.12 g, 95%, and after recrystallization from methanol, the product was obtained as pale yellow plates. Yield was 0.83 g, 70%; m.p. 268-273°C.

43) Synthesis of 4'-ethoxybenzylideneandrostadienedione (EtO-BA). The procedure was the same as 3.2.40 except for the use of 4-ethoxybenzaldehyde (440 mg, 2.9 mmol) and the reaction was continued for 19 h. The yield of crude product was 1.43 g, 99%, and after recrystallization from methanol, the product was obtained as colorless plates. Yield was 0.72 g, 62%; m.p. 194-196°C.

44) Synthesis of 4'-acetylaminobenzylideneandrostadienedione (AcNH-BA). The procedure was the same as 3.2.40 except for the use of 4-acetylaminobenzaldehyde (599 mg, 3.7 mmol) and the reaction was continued for 48 h. The yield of crude product was 1.22 g, 81%; m.p. 300°C.

45) Synthesis of 4'-butoxybenzylideneandrostadienedione (BuO-BA). The procedure was the same as 3.2.32 except for the use of 4-butoxybenzaldehyde (637 mg, 3.8 mmol) and 2.5 ml of 25% NaOH, and the reaction was continued for 48 h. The yield of crude product was 1.47 g, 94%, and after recrystallization from ethanol, the product was obtained as colorless plates. Yield was 1.09 g, 70%; m.p. 206°C.

46) Synthesis of 4'-phenylbenzylideneandrostadienedione (Ph-BA). The procedure was the same as 3.2.32 except for the use of 800 mg (2.81 mmol) of steroid, 530 mg (2.9 mmol) of 4-phenylbenzaldehyde and the reaction was continued for 48 h. The yield of crude product was 1.25 g, 99%; m.p. 175°C.

References

1) D. Pugh and J.N. Shewood, *Chemistry in Britain*, **24**, 544-548 (1988).
2) R.B. Grubbs, S.R. Marder, and J.W. Perry, *Chemistry of Materials*, **3**, 3-4 (1991).
3) B.F. Levine, C.G. Bethea, C.D. Thurmond, R.T. Lunch, and J.L. Bernstein, *J. Appl. Phys.*, **50**, 2523-2527 (1979).
4) N.B. Chapman and J. Shorter, in "Advan. Linear Free Energy Relationship", 28-32, Plenum Press, London, (1972).

ステロイドを原料とするSHG物質（I），エストロンメチルエーテル，デヒドロエピアンドロステロン，アンドロスタジエンジオンの4-置換ベンジリデン誘導体の合成とその性質

佐野誠二・井上裕二・石垣健一・
髙谷政弘・鍛治誠・岡本忠

要　約

近年急速に発展した光エレクトロニクスの分野では，レーザー波長を自由に変換できる素子として非線形光学材料が注目を集め，中でもレーザー波長を1/2に変換する第2高調波発生（SHG）に期待がよせられている。大きなSHGを持つ材料は，大きな2次非線形分子分極率（β）を持つ分子が同一方向に並ぶ時得られる。本研究は，ステロイド系天然物のもつ非対称構造を分子配列の制御に利用するSHG材料開発の可能性について，表題の三種のステロイドと15種のベンズアルデヒドとから45種の置換ベンジリデンステロイドを合成して検討を行なった。本報告は合成と物性の一部を報告する。