Synthesis of Tropolone and Tropone Derivatives Condensing Fluorene Moiety

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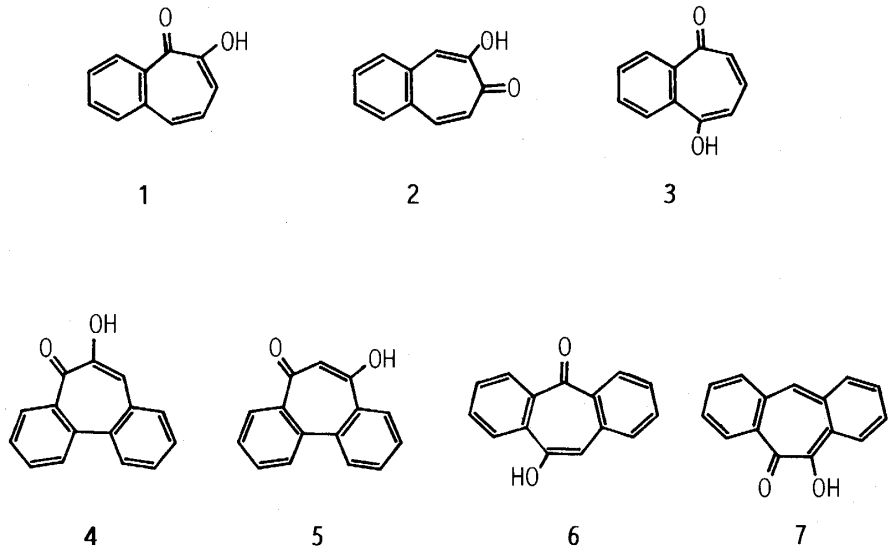
(Received July 15, 1991)

Abstract

A new type of tropolone and tropone derivatives condensing fluorene moiety were prepared from 8,9-dihydro-8-oxo-13b*H*-tribenzo [*a, cd, h*] azulene by oxidation with selenium dioxide and by dehydrogenation with DDQ, respectively.

Introduction

Tropolones, seven-membered ring compounds, are well known as nonbenzenoid aromatic compounds. [1] These derivatives condensed with one or two benzene moieties such as 6-hydroxy-5*H*-benzocyclohepten-5-one (**1**),[2] 6-hydroxy-7*H*-benzocyclohepten-7-one (**2**),[3] 9-hydroxy-5*H*-benzocyclohepten-5-one (**3**),[4] 6-hydroxy-5*H*-dibenzo[*a,c*]-cyclohepten-5-one (**4**),[5] 7-hydroxy-5*H*-dibenzo[*a,c*]cyclohepten-5-one (**5**),[6] 10-hydroxy-



Scheme 1

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5*H*-dibenzo[*a*,*d*]cyclohepten-5-one (**6**),[7] and 11-hydroxy-10*H*-dibenzo[*a*,*d*]cyclohepten-10-one (**7**)[8] have also been well investigated.

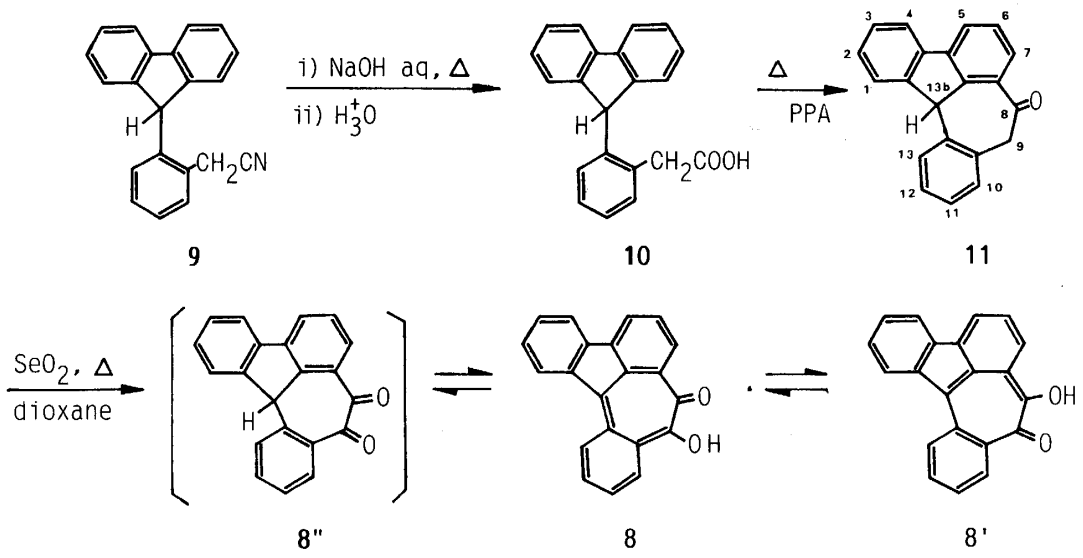
In many cases, these tropolones are known to exist as a mixture of tautomer of hydroxyketones and diketones. Using for an example, we can show the tautomerism as follows.[7]

Scheme 2

During the cause of our investigation on the tropylium ion condensing fluorene moiety,[9] we now find a new type of tropolone and tropone. In this paper, we wish to report on the synthesis of the tropolone and tropone, and their relative compounds.

Results and Discussion

Our synthesis of the tropolone contains an intramolecular ring condensation. Sequence of the reactions are shown in Scheme 3.

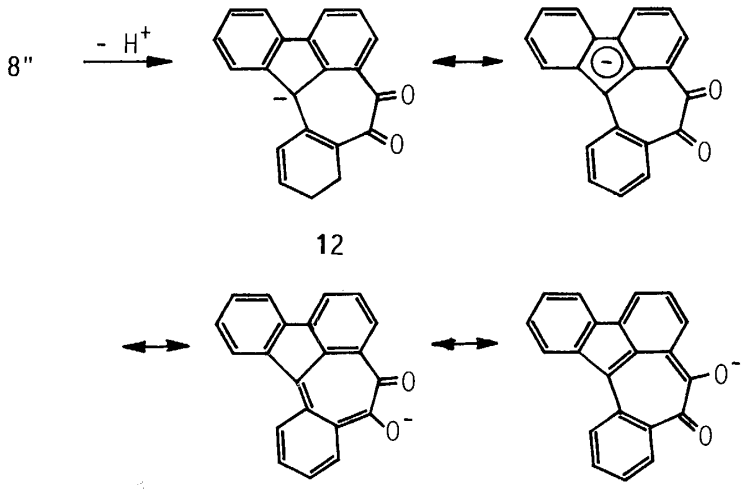


Scheme 3

That is, alkali hydrolysis of 9-(2-cyanomethylphenyl) fluorene (**9**), which was prepar-

ed from 9-(2-methylphenly)-9-fluorenol via several steps,[10] gave *o*-(9-fluorenyl)-phenylacetic acid (**10**). Dehydration of **10** by heating in polyphosphoric acid gave a five-cyclic compound, 8,9-dihydro-8-oxo-13b*H*-tribenzo [*a, cd, h*] azulene (**11**). Oxidation of **11** with selenium dioxide in dioxane afforded a mixture of tropolones, 9-hydroxy-8*H*-tribenzo [*a, cd, h*] azuren-8-one (**8**) and 8-hydroxy-9*H*-tribenzo [*a, cd, h*] azuren-9-one (**8'**). Actually, its IR spectrum showed carbonyl absorption at 1670 and 1690 cm^{-1} (IR intensity; 1670 cm^{-1}>1690 cm)$^{-1}$ and hydroxyl absorption at 3350 cm^{-1}. Mass spectrum of the product showed m/e=268 (M^+-28).[11] Compound **8** and **8'** should be derived from diketone, 8,9-dihydro-8,9-dioxo-13b*H*-tribenzo [*a, cd, h*] azulene (**8"**). Compound **8**, **8'**, and **8"** are tautomeric with each other.

It is very interesting to find that although compound **7** exists only as diketone **7'** oxidation product of **11** exists as tautomer of tropolones **8** and **8'**. We can consider that acidity of hydrogen of 13b*H*-position in **8"** (analogous to **7'**) is larger than that of hydrogen of 5-position in **7'** because stable cyclopentadienide ion (**12**) is readily caused by elimination of the proton from 8" (Scheme 4).



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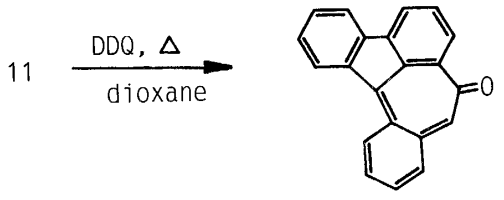
Scheme 4

The dehydrogenation of **11** with DDQ in dioxane under reflux for 24 h gave tropone,



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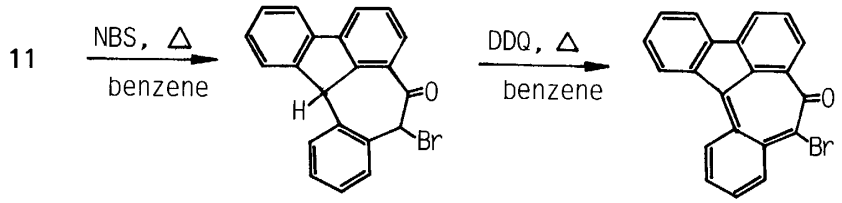
Scheme 5

8*H*-tribenzo[*a, cd, h*]azuren-8-one (**13**), in good yield. The structure of **13** was confirmed by its ^{1}H NMR, IR, and mass spectral data.

The reaction of **11** with *N*-bromosuccinimide in benzene under reflux for 2h gave 9-bromo-8,9-dihydro-8-oxo-13b*H*-tribenzo[*a, cd, h*]azulene (**14**). Furthermore, dehydrogenation of **14** with DDQ in benzene afforded bromotropone, 9-bromo-8*H*-tribenzo-[*a, cd, h*]azulen-8-one (**15**). These compounds were also confirmed by their spectral data.



14 15

Scheme 6

Besides, in order to examine an aromaticity of **13**, treatment of **13** with hydrazine hydrate was carried out in THF or dioxane under reflux for many hours. However, expected aminotropone derivatives was not obtained. Furthermore, the reactions of **13** with hydroxylamine in pyridine-ethanol or with $LiAlH_4$ in THF gave inseparable mixtures instead of expected oxime or alcohol, respectivery.

Experimental

All the melting points are uncorrected. ^{1}H NMR spectra were recorded on a JEOL-MH-100 spectrometer. The IR spectra were measured on a JASCO IRA-1 spectrometer. Mass spectra (MS) were obtained with JEOL JMS-D100 with direct inlet systems and at an ionization energy of 75 eV.

o-(9-Fluorenyl) phenylacetic Acid (10)

To a solution of 9-(2-cyanomethylphenyl)fluorene (**9**) (yellow oil; 7.0g, 0.025mol) in ethylene glycol (40ml) was added NaOHaq (NaOH: 13.0g, H_2O: 20ml), and the mixture was refluxed in an oil bath kept at 165 ℃ for 30h. After cooling to room temperature, the reaction mixture was poured into water (20ml), and obtained sodium carboxylate was filtered, washed with benzene. The sodium salt was added into an aqueous mixture of HCl and H_2SO_4, and then was extracted with chloroform (20ml x3). The chloroform solution was washed with water, dried over $MgSO_4$ and concentrated in vacuo to give a residue which was washed with petroleum ether affording **10** as colorless needles; yield 6.3g (84%); mp 142-144℃. ^{1}H NMR ($CDCl_3$) δ=2.44, 4.02 (0.8H and 1.2H, two s, 2'-CH_2), 4.99, 5.34 (0.4H and 0.6H, two s, 9-H), 6.40 (0.6H, d, J=8Hz, 6'-H), 6.9-7.8 (11.4H, m, $H_{arom.}$).[12] IR (KBr): 1700cm^{-1} (CO).

8,9-Dihydro-8-oxo-13b*H*-tribenzo[a, cd, h]azurene (11)

To a melted homogenous mixture of commercially available polyphosphoric acid (205g) and P_2O_5 (45g) was added **10** (8.0g, 0.027mol), and the mixture was heated in an oil bath kept at 165℃ for 3.5h. After cooling to room temperature, the reaction mixture was poured into water (100ml), extracted with chloroform (30ml x3). The chloroform solution was washed with dil. NaOHaq and water, and then dried over $MgSO_4$ and concentrated in vacuo to give a residue. The residue was washed with ether and recrystallized from ethanol to give **11** as yellow needles; yield 4.54g (60%); mp 184-186℃. ^{1}H NMR ($CDCl_3$) δ=4.01 (1H, d, J=14Hz, 9-H), 4.61 (1H, d, J=14Hz, 9-H), 5.69 (1H, s, 13b-H), 7.1-8.0 (11H, m, $H_{arom.}$). IR (KBr): 1680cm^{-1} (CO).

Synthesis of Tropolones 8 and 8' by Oxidation of 11 with SeO_2

To a solution of **11** (0.5g, 1.8mmol) in dioxane (25ml) was added SeO_2 (0.6g, 5mmol), and the mixture was refluxed for 2.5h. After a separated Se was filtered, the filtrate was evaporated in vacuo. The crude product was dissolved in chloroform and chromatographed on silica gel to give a mixture of 9-hydroxy-8*H*-tribenzo[*a, cd, h*]-azuren-8-one (**8**) and 8-hydroxy-9*H*-tribenzo[*a, cd, h*]azulen-9-one (**8'**) as yellow crystails; yield 0.15g (29%); mp 235-237℃. ^{1}H NMR (DMSO-d_6) δ=6.80-8.05 (12H, m, $H_{arom.}$ and 9-OH). IR (KBr): 1670, 1690 (CO), 3350cm^{-1} (OH). MS m/e: 268 (M^+-CO).

Synthesis of tropone 13 by Dehydrogenation of 11 with DDQ

To a solution of **11** (1.0g, 3.6mmol) in dioxane (40ml) was added 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) (1.2g, 5.3mmol), and the mixture was refluxed for 24h. After cooling to room temperature, depositing 2,3-dichloro-5,6-dicyanohydroquinone was filtered off and the filtrate was evaporated in vacuo. Obtained residue was washed with benzene and recrystallized from acetone to give 8*H*-tribenzo[*a, cd, h*]azuren-8-one (**13**) as yellow columns; yield 0.87g (88%); mp 302-304℃. ^{1}H NMR (DMSO-d_6) δ=5.2 (1H, s, 9-H), 7.0-8.0 (11H, m, $H_{arom.}$). IR (KBr); 1705cm^{-1} (CO). MS m/e: 280 (M^+).

Bromination of 11 with NBS

To a solution of **11** (0.70g, 2.5mmol) in benzene (30ml) was added *N*-bromosuccinimide (NBS) (0.50g, 2.8mmol), and the mixture was refluxed for 2h. After cooling to room temperature, depositing succinimide was filtrered off and the filtrate was concentrated in vacuo. The residue obtained was dissoloved in benzene and chromatographed on silica gel to give 9-bromo-8, 9-dihydro-8-oxo-13b*H*-tribenzo[*a, cd, h*]azulene (**14**) as yellow columnes; yield 0.34g (38%); mp 173-174℃ (from acetone). ^{1}H NMR ($CDCl_3$) δ=5.75 (1H, s, 13b-H), 6.35 (1H, s, 9-H), 7.0-8.1 (11H, m, $H_{arom.}$). IR (KBr); 1660cm^{-1}(CO). MS m/e; 360 (M^+), 362 (M^++2).

Dehydrogenation of 14 with DDQ

To a solution of **14** (0.30g, 0.83mmol) in benzene (20ml) was added DDQ (0.21g, 0.93mmol), and the mixture was refluxed for 24h. After depositing 2,3-dichloro-5, 6-dicyanohydroqunone was filtered off, the filtrate was concentrated in vacuo to give 9-bromo-8*H*-tribenzo[*a, cd, h*]azuren-8-one (**15**) as yellow crystals; yield 0.1g (34%); mp

200℃ (dec.) (from acetone). ^{1}H NMR (DMSO-d_6) δ=6.9-8.7 (11H, m, $H_{arom.}$). IR (KBr); 1710cm^{-1} (CO). Ms m/e; 358 (M^+), 360 (M^++2).

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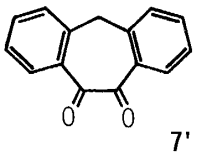
8) This compound exists only as diketone, 5*H*-dibenzo[*a, d*]cgclo-heptene-10, 11-dione (7').
J. Rigaudy and L. Nedelec, *Compt. rend.*, **236**, 1287 (1953); *Bull Soc. Chim. France*, **1959**, 638.



7'

9) S.Kajigaeshi, S. Matsuoka, S. Kuraoka, S. Maruyama, A. Nishida, and S. Fujisaki, *Chem. Express*, **4** , 435 (1989).

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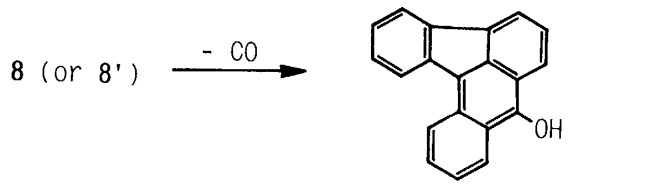
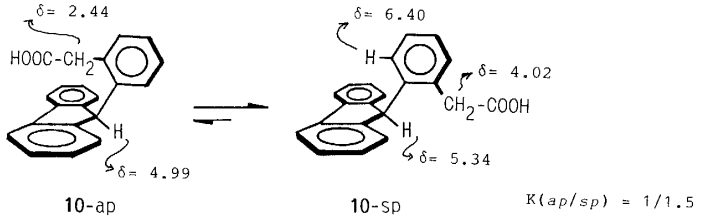
11) Unfortunately, molecular peak (M^+=296) was not confirmed. The value of m/e=268 is maybe a peak for 3-hydroxy-1,2-benzofluoranthene which is fragmentated from **8** or **8'** by the decarbonylation.



12) We can show the conformational equilibrium between *ap*-form and *sp*-form of **10** according to its ^{1}H NMR data as follows;



10-ap 10-sp K(ap/sp) = 1/1.5