SYNTHESIS OF 6-(α-THIENYL)AZULENE FROM 2-BUTOXY-4-(α-THIENYL)-Δ^5-DIHYDROPYRAN

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2,5-Dibutoxy-4-(α-thienyl)-Δ^3-dihydropyran was obtained by bromoalkoxylation at the double bond and dehydrobromination of 2-butoxy-4-(α-thienyl)-Δ^5-dihydropyran. Acid hydrolysis of the product in the presence of N-methylaniline hydrochloride gave a salt of 3-(α-thienyl)glutaconic dialdehyde dianil, treatment of which with cyclopentadienylsodium in alcohol gives the corresponding fulvene, which is thermally cleaved to N-methylaniline and 6-(α-thienyl)azulene.

The most convenient method for the synthesis of azulene hydrocarbons is the widely-known method of synthesis from quaternary pyridinium salts [1], but azulenes with aryl substituents in the seven-membered ring have not been obtained by this method, apparently because of the low accessibility of the corresponding substituted pyridines. While 4-aryl- and 4-heteryl-substituted azulenes (4-phenyl, 4-α-naphthyl, and 4-α-thienyl) are relatively accessible [2], 5-aryl-substituted azulenes are obtained in low yields by expansion of the benzene ring of indane by arylcarbenes formed during the decomposition of aryldiazomethanes and subsequent dehydrogenation [3], and 6-arylazulenes currently remain practically inaccessible compounds. Only 6-phenylazulene, synthesized by an extremely complex and multistep method from cyclopentane-1,2-dicarboxylic acid [4], is known.

We propose a new method for the synthesis of 6-aryl-substituted azulenes on the basis of dihydropyran structures with subsequent conversion of them to salts of aryl-glutaconic dialdehyde dianils and then to fulvenes, which are thermally cyclizable to azulenes by the Ziegler–Hafner method; this helps to avoid the dehydrogenation step, which is basically the chief reason for the extremely low yields. Using this method, on the basis of 2,6-dibutoxy-4-phenyl-Δ^3-dihydropyran [5] we obtained 6-phenylazulene [6], and in the present research we were able to extend this method to the total synthesis of 6-(α-thienyl)azulene.

2-Butoxy-4-(α-thienyl)-Δ^5-dihydropyran (I) was obtained by Diels–Alder condensation of 2-(α-thienyl)acrolein [7] with vinyl butyl ether. Treatment of I with N-bromosuccinimide (NBS) in butyl alcohol gives 2,5-dibutoxy-3-bromo-4-(α-thienyl)tetrahydropyran (II), which splits out hydrogen bromide on prolonged heating with alcoholic alkali to give 2,6-dibutoxy-4-(α-thienyl)-Δ^3-dihydropyran (III), which actually is the cyclic acetal of 3-(α-thienyl)glutaconic dialdehyde.

Acid hydrolysis of 2,6-dibutoxy-4-(α-thienyl)-Δ^3-dihydropyran (III) in the presence of N-methylaniline hydrochloride gave the double salt of 3-(α-thienyl)glutaconic dialdehyde dianil (IV), the structure of which was established on the basis of the results of elementary analysis and the electronic and IR absorption spectra. Treatment of the salt with excess cyclopentadienylsodium in absolute ethanol gives 6-[1-N-phenylmethyl-

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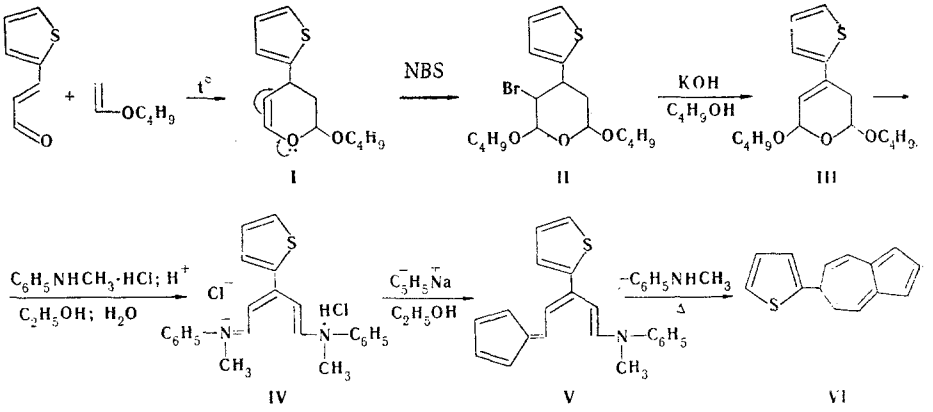
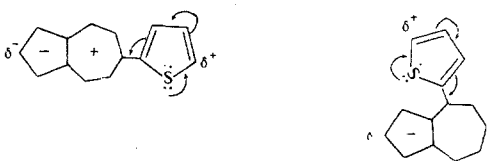
amino-3-(α-thienyl)-1,3-butadien-4-yl]fulvene (V). Compound V was subjected to pyrolytic cleavage by the method proposed for unsubstituted azulene [1]. Instead of benzidine we selected triethanolamine as the solvent and carried out the pyrolysis with superheated steam at 280°C. It is possible that the relatively low yield of 6-(α-thienyl)azulene (8.5%) is due to the hydrophilic character of triethanolamine, as a consequence of which the poor solubility of fulvene V in it prevents the normal course of the intramolecular cyclization and the formation of the final product.



The structure of the 6-(α-thienyl)azulene obtained was proved by the results of elementary analysis and the electronic absorption spectrum. A mass-spectrometric determination of the molecular weight gave 210, which confirmed the composition of azulene VI.

The electronic spectrum of 6-(α-thienyl)azulene has a chief maximum at 600 nm, which corresponds to a bathochromic shift of 20 nm as compared with the absorption spectrum for unsubstituted azulene. The long-wave absorption band of α-thienylazulene VI is shifted bathochromically by 35 nm and is found at 732 nm. These shifts can be explained by the greater delocalization of the electron density of 6-(α-thienyl)azulene; this is due to the capacity for conjugation of the α-thienyl group with the seven-membered ring of the azulene system, which bears a partial positive charge. Conjugation leads to the formation of a chromophore system in which the partial positive charge is on the thiophene ring, while additional negative charge develops on the five-membered ring of azulene; this is manifested visibly also in the case of 4-(α-thienyl)azulene [2] but to a lesser degree (λ_{max} 597 and 716 nm), inasmuch as the geometrical form of the molecule in this case causes a lower value of the electromagnetic oscillator than for the 6-substituted derivative, in which the electron-donor substituent is most remote from the acceptor — the five-membered ring.



Inasmuch as phenyl groups have a weaker electron-donor capacity, their effect on the electronic spectra of the corresponding substituted azulenes is similar to the effect of α-thienyl groups but is manifested considerably more weakly.

EXPERIMENTAL

2-Butoxy-4-(α-thienyl)-Δ^5-dihydropyran (I). A 69-g (0.5 mole) sample of 2-(α-thienyl)acrolein was heated in a glass ampule with 100 g (1 mole) of vinyl butyl ether and 0.5 g of hydroquinone at 200° for 14 h. Distillation of the reaction mixture gave 75.6 g (63.4%) of 2-butoxy-4-(α-thienyl)-Δ^5-dihydropyran (I) as a pale-yellow oil with bp 154-159° (5 mm), n_D^{20} 1.5192, and d_4^{20} 1.09. Found: C 65.5; H 7.4; S 13.3%; MR_D 66.2. $C_{13}H_{18}O_2S$. Calculated: C 65.5; H 7.6; S 13.5%; MR_D 66.9.

2,6-Dibutoxy-4-(α-thienyl)-Δ^3-dihydropyran (III). A 48-g (0.2 mole) sample of dihydropyran I was dissolved in 200 ml of butanol, and 35.6 g (0.2 mole) dry pulverized NBS was added in portions with stirring while maintaining the temperature at +5 to +12°. The reaction mixture was stirred at 20° for 1 h after the addition of the NBS, and the resulting succinimide was removed by filtration. Inasmuch as we were unable to isolate the extremely unstable (on heating) 2,5-dibutoxy-3-bromo-4-(α-thienyl)tetrahydropyran (II), the filtrate was poured into a solution of 50 g of KOH in 0.5 liter of butanol, and the mixture was refluxed for 10 h. The reaction mixture was cooled, water was added, and the mixture was extracted with benzene. The benzene extract was dried with Na_2SO_4, and the solvent was removed by distillation. Distillation of the residue gave 22.3 g (36%) of dihydropyran III as a yellowish oil with bp 170-180° (3 mm), n_D^{20} 1.5167, and d_4^{20} 1.064. Found: C 65.8; H 8.4; S 10.7%; MR_D 85.1. $C_{17}H_{26}O_3S$. Calculated: C 65.7; H 8.4; S 10.3%; MR_D 88.8.

Double Chloride of 3-(α-Thienyl)glutaconic Dialdehyde Dianil (IV). A 14.7-g (0.047 mole) sample of III was dissolved in 20 ml of ethanol, and the solution was stirred with a solution of 15 g (0.1 mole) of N-methylaniline hydrochloride in 30 ml of water containing 3 ml of HCl. The solution became dark-red. The solution was heated to the boiling point and was then allowed to stand at room temperature for 24 h. The solvent was then removed by vacuum distillation while maintaining the temperature at no higher than 90°. The viscous dark-red mass was triturated with absolute ether and vacuum dried at 20° to give 17.6 g (81.9%) of double salt IV. For further purification, a portion of the product was chromatographed with a column filled with silica gel in acetone–alcohol (2:1); λ_{max} 478 nm (in alcohol), and R_f 0.31 in acetone–alcohol (2:1) on a Silufol plate. The unusual doubly charged ion of this salt is evidently stable only owing to the electron-donor effect of the α-thienyl group. Found: Cl 17.2; N 6.3%. $C_{23}H_{23}ClN_2 \cdot HCl$. Calculated: Cl 16.5; N 6.5%.

6-[1-Phenylmethylamino-3-(α-thienyl)-1,3-butadien-4-yl]fulvene (V). An 8.6-g (0.02 mole) sample of double salt IV was dissolved in 15 ml of absolute alcohol, and the solution was mixed with a solution of cyclopentadienylsodium obtained by treatment of 35 g of cyclopentadiene with sodium ethoxide in absolute alcohol. The dark-brown precipitate of fulvene V was washed with water and alcohol and vacuum dried to give 3.13 g (49.6%) of fulvene as a brown powder with R_f 0.44 in acetone–hexane (2:5) on a Silufol plate and λ_{max} 457 nm (in benzene). The compound decomposed without melting when it was heated with the liberation of N-methylaniline and an azulene derivative. Found: N 4.4; S 9.9%. $C_{21}H_{19}NS$. Calculated: N 4.4; S 10.0%.

6-(α-Thienyl)azulene (VI). Fulvene V was subjected to pyrolysis by the method in [2] in triethanolamine at 280° with superheated steam. The green distillate was extracted with hexane, washed with 5% hydrochloric acid, and chromatographed with a column filled with aluminum oxide. A 1.58-g sample of fulvene yielded 0.089 g (8.5%) of azulene VI as dark-blue plates with mp 153-154° (from CH_3OH), R_f 0.61 in acetone–hexane (2:5) on Silufol, and λ_{max} 598, 732 nm (in benzene), log ε, respectively, 2.49, 1.79. Found: C 79.6; H 4.6; S 15.0%. $C_{14}H_{10}S$. Calculated: C 80.0; H 4.8; S 15.2%.

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