ACYLATION OF 2,4-DIARYL-4H-CHROMENES BY THE ACTION OF ACETIC ANHYDRIDE AND PERCHLORIC ACID

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4H-Chromenes were found to be acylated at the 3-position by the action of acetic anhydride and perchloric acid. The structure was determined of other reaction products – the indenobenzopyrylium and 2,4-diaryl-1-benzopyrylium salts.

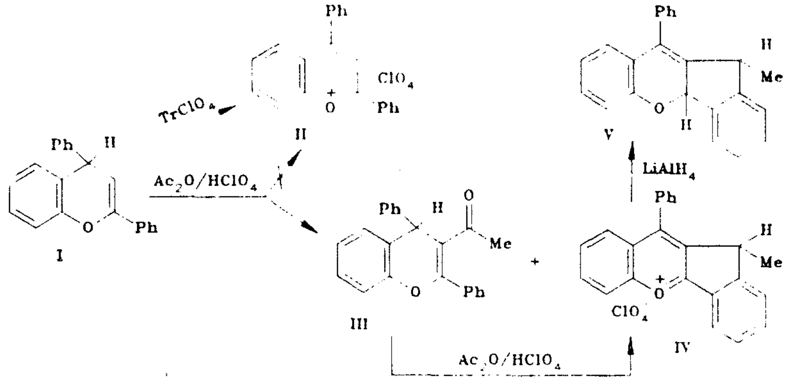
Oxidative dehydrogenation of 4H-pyrans by a mixture of acetic anhydride and perchloric acid is a widely used method for the preparation of pyrylium salts [1, p. 14].

4H-Chromenes contain a pyran ring and at the same time are cyclic vinyl ethers and, therefore, offer two possibilities for the reactions with electrophiles – the oxidative dehydrogenation to 1-benzopyrylium salts and attack by the electrophilic particle at the 3-position of the heterocyclic ring.

We found that 2,4-diaryl-4H-chromenes are acylated by the action of an Ac_2O–$HClO_4$ mixture at the 3-position of the pyran ring, while the expected 2,4-diaryl-1-benzopyrylium salts are not always formed.

The aim of the present work was to study this reaction, since examples of an electrophilic substitution into the pyran ring of 4H-chromenes were previously not known.

The action of perchloric acid in an excess of acetic anhydride on 2,4-diphenyl-4H-chromene (I) leads to formation of 2,4-diphenyl-3-acetyl-4H-chromene (III) and 10-methyl-10H-11-phenylbenzo[b]indeno[2,1-e]pyrylium perchlorate (IV) instead of the expected 2,4-diphenyl-1-benzopyrylium perchlorate (II). The oxidative dehydrogenation of chromene I was not observed in this case.



The acylation of chromene I is promoted by the high nucleophilicity of its double bond. It is known that 2H-chromenes, which are not vinyl ethers like their 4H-isomers, are acylated and formylated in the benzene ring annelated with the pyran ring [2, 3].

Salt IV is a product of further transformations of acetylchromene III under the reaction conditions, as has been confirmed by the action of the Ac_2O–$HClO_4$ mixture on compound III. The suggested reaction scheme includes the protonation of the carbonyl oxygen atom, an electrophilic attack on the benzene ring, and a 1,3-hydride shift

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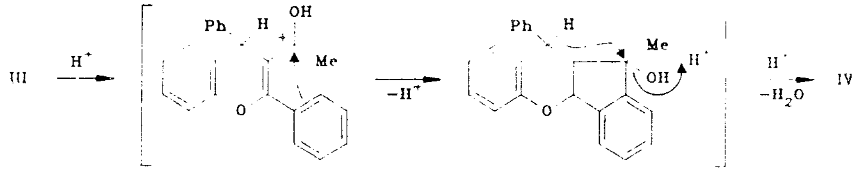
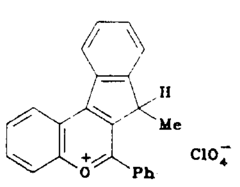


A similar cyclization with the formation of an indene fragment takes place during the protonation of 2-methylene-1,5-diketones [4].

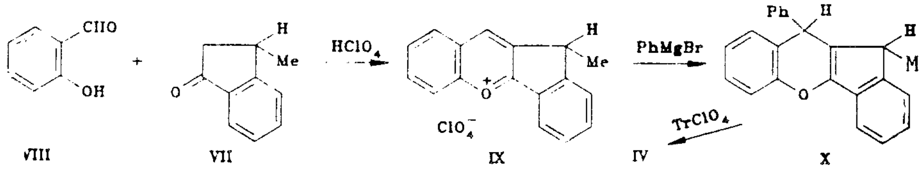
Thus, the acylation of chromene I under the above conditions takes place more rapidly than its oxidative dehydrogenation. Under conditions unfavorable for acylation, and, in particular, by the action of trityl perchlorate on chromene I, salt II was obtained in a 97% yield, the characteristics of which coincide with those described in [5].

The structure of products III and IV were confirmed by PMR and IR spectroscopy. The appearance of a band at 1615 cm^{-1} in the IR spectrum of salt IV confirmed the presence of a pyrylium cation in the molecule. In the PMR spectrum, the doublet of the methyl group at 0.7 ppm and a quadruplet of the tertiary proton at 4.2 ppm with an intensity ratio of 3:1, indicate the presence of a CH_3–CH fragment. However, these spectral characteristics are not sufficient to elucidate the structure of perchlorate IV. Transformation of compound IV by the action of lithium aluminum chloride into benzoindenopyran V and recording the mass spectrum of the latter, made it possible to calculate the molecular weight of the initial perchlorate, which was found to be equal to 409. The above data unequivocally showed that in the starting molecule of III a cyclization takes place with the participation of the acetyl group and one of the phenyl substituents, i.e., the structure of the compound obtained is described by formula IV or VI:



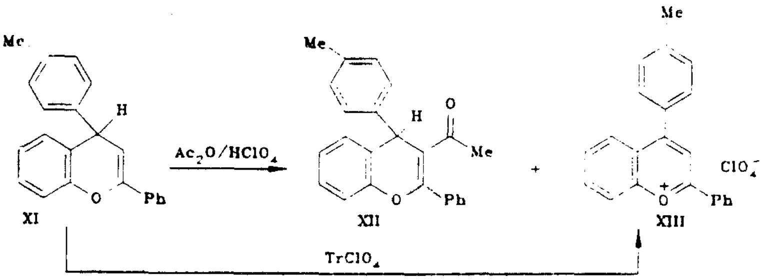
VI

To find out which of the possible structures is formed, a countersynthesis of compound IV was carried out from ketone VII obtained by the method described in [6].



The condensation of 3-methyl-1-indanone (VII) with salicylaldehyde VIII in the presence of perchloric acid led to the formation of salt IX, in the reaction of which with phenylmagnesium bromide, 10-methyl-10H-11-phenyl-11H-benzo[b]indeno[2,1-e]pyran (X) was obtained [isomeric with compound (V)] in the form of one diastereomer. The determination of the steric configuration of compound X for the purpose of a countersynthesis is not of prime importance, since the oxidative dehydrogenation of both the diastereomers gives one and the same salt. As a result of the reaction of the benzoindenopyran X with trityl perchlorate, a pyrylium salt is formed, which does not give a depression of the melting point with a perchlorate isolated from the reaction of chromene I with acetic anhydride and perchloric acid. The IR spectra of the salts are absolutely identical. Thus, the alternative structure VI could be dismissed.

It has been stated above that the oxidation of chromene I into salt II in an Ac_2O–$HClO_4$ mixture is not observed and is suppressed by the acylation of the starting compound. We found that these two processes may compete with one another. Thus, 2-phenyl-4-(tolyl-4)-4H-chromene (XI), under the same conditions as chromene I, forms a mixture of 2-phenyl-3-acetyl-4-(tolyl-4)-4H-chromene (XII) and 2-phenyl-4-(tolyl-4)-1-benzopyrylium perchlorate (XIII). The latter is also obtained by the action of trityl perchlorate on chromene XI in a 97% yield.



In this case, the salt corresponding to the cyclization of compound XII, analogous to perchlorate IV, could not be isolated. The fact of formation of compound XIII indicates a more rapid oxidative dehydrogenation of compound XI compared with chromene I, which is possibly due to the electron-donor influence of the methyl group, which promotes a more ready oxidation of the C–H bond.

Thus, the action of an Ac_2O–$HClO_4$ mixture on 4H-chromenes causes not only their acylation, but also the formation of either an indenobenzopyrylium or 2,6-diaryl-1-benzopyrylium salt, depending on the structure of the starting compound.

EXPERIMENTAL

The PMR spectra were run on a Tesla BS-487C spectrometer (80 MHz), using HMDS as an internal standard, the IR spectra on a Specord IR-75 spectrophotometer in mineral oil, and the mass spectra on an MS-30 spectrometer.

The initial 2,4-diaryl-4H-chromenes were obtained by the reaction of 2-phenyl-1-benzopyrylium perchlorate with Grignard reagents [7].

The data of the elemental analyses for compounds IV for C, H coincide with the calculated values.

10-Methyl-10H-11-phenylbenzo[b]indeno[2,1-e]pyrylium Perchlorate (IV, $C_{23}H_{17}ClO_5$) and 2,4-Diphenyl-3-acetyl-4H-chromene (III, $C_{23}H_{18}O_2$) from 2,4-Diphenyl-4H-chromene (I). A 1-ml portion (10 mmoles) of a 70% perchloric acid was added dropwise to 10 ml of acetic anhydride cooled by ice water, and the mixture was allowed to stand at room temperature for 20 min. A 2.84-g portion (10 mmoles) of chromene I was then added, which gradually dissolved. After 2 h, the dark reaction mixture was diluted with 300 ml of ether. Salt IV was thus separated out in the form of an oily mixture. The ether layer was then decanted, and the residue reprecipitated with ether from 20 ml of acetone to give a brown precipitate. Yield 1.06 g (29%). Salt IV can be further purified with larger losses. After adding 5 ml of acetone, the salt dissolved, and then a yellow crystalline precipitate separated out which was filtered off and recrystallized from acetic acid to give 0.3 g of yellow crystals, mp 261-262°C. IR spectrum: 1615 (pyrylium cation); 1605 and 1580 (C-C$_{ar}$); 1100 cm^{-1} (ClO_4^-). PMR spectrum (CF_3COOH): 0.70 (3H, d, CH_3); 4.20 (1H, q, CH); 7.10-8.20 ppm (13H, m, H$_{ar}$).

To separate **compound III**, the ether solution, obtained on dilution of the reaction mixture with ether, was neutralized with aqueous ammonia, dried over Na_2SO_4, and the solvent was distilled on a water bath. The remaining yellow oil was dissolved in 5 ml of benzene and chromatographed on a column with Al_2O_3 (height of the Al_2O_3 layer 30 cm, diameter 1.8 cm, eluent benzene). A fraction with R_f 0.5 was collected. The solvent was distilled off on a water bath. The residue was twice recrystallized from ethanol and cream-colored needlelike crystals were obtained. Yield 1.12 g (36%), mp 133-134°C. IR spectrum: 1680 (C=O), 1635 (C=C), 1580 (C-C$_{ar}$); 1220 cm^{-1} (C–O–C). PMR spectrum (CCl_4): 1.5 (3H, s, CH_3), 5.05 (1H, s, 4-H), 6.60-7.65 ppm (14H, m, H$_{ar}$).

10-Methyl-10H-11-phenylbenzo[b]indeno[2,1-e]pyrylium Perchlorate (IV) from 2,4-Diphenyl-3-acetyl-4H-chromene (III). A 0.31-g portion (1 mmole) of compound III was added to a mixture of 2.5 ml of acetic anhydride and 0.2 ml (2 mmoles) of 70% $HClO_4$, and the reaction mixture was allowed to stand overnight. On dilution with ether, 0.30 g (82%) of perchlorate IV was isolated, which in its physicochemical characteristics was identical to the compound described above.

2,4-Diphenyl-1-benzopyrylium Perchlorate (II). A mixture of 5.68 g (20 mmoles) of chromene I, 6.86 g (20 mmoles) of trityl perchlorate, and 30 ml of glacial acetic acid was boiled for 20 min. After cooling, crystals of salt II separated out. The mixture was diluted with ether and the yellow precipitate was filtered off. Yield 7.45 g (97%), mp 216-217°C; according to the data in [5], mp 217°C.

5*a*H-10-Methyl-10H-11-phenylbenzo[b]indeno[2,1-e]-pyran (V, $C_{23}H_{18}O$). A 1.44-g portion (3.52 mmoles) of perchlorate IV was added to a suspension of 0.2 g (5.26 mmoles) of lithium aluminum hydride in 20 ml of absolute ether cooled by ice water. The pyrylium salt dissolved immediately. The excess of lithium aluminum hydride was decomposed by adding water dropwise. The ether layer was washed with a saturated solution of NH_4Cl, dried over Na_2SO_4 and ether was evaporated on a water bath. The remaining oil was chromatographed on a column with Al_2O_3 (height of the sorbent layer 10 cm, diameter 1.8 cm, eluent a 1:1 benzene–hexane mixture. The fraction with R_f 0.7 was collected. After distillation of solvents under vacuum on a water bath, the remaining oil was dissolved with heating in 2 ml of isopropanol, 2 ml of methanol was added, and the solution was cooled with ice water. The colorless crystals that separated out were filtered off. Yield 0.30 g (28%), mp 107-108°C. IR spectrum: 1645 (C=C), 1585 and 1570 ($C–C_{ar}$), 1220 cm^{-1} (C–O–C). PMR spectrum (CCl_4): 0.77 (3H, d, CH_3), 3.93 (1H, q, 10-H), 5.74 (1H, s, 5*a*-H), 6.40-7.70 ppm (13H, m, H_{ar}). Mass spectrum: M^+ 310.

10-Methyl-10H-benzo[b]indeno[2,1-e]pyrylium Perchlorate (IX, $C_{17}H_{13}ClO_5$). A 6.4-ml portion (64 mmoles) of 70% $HClO_4$ was added dropwise to a mixture of 7.8 g (53 mmoles) of 3-methyl-1-indanone [6], 6.5 ml (53 mmoles) of salicylaldehyde, 27 ml of acetic anhydride and 55 ml of ether, cooled by ice water. The mixture was allowed to stand for 2 h at room temperature, the salt that separated out was filtered off and washed with ether. Yield 12.9 g (73%), mp 218°C. IR spectrum: 1625 (the pyrylium cation), 1595 ($C–C_{ar}$), 1100 cm^{-1} (ClO_4^-). PMR spectrum (CF_3COOH): 1.38 (3H, d, CH_3), 4.13 (1H, q, CH), 7.13-8.25 (8H, m, H_{ar}), 8.83 ppm (1H, s, 11-H).

10-Methyl-10H-11-phenyl-11H-benzo[b]indeno[2,1-e]pyran (X, $C_{23}H_{18}O$). A 3.33-g (10 mmoles) of perchlorate IX was added with ice-water cooling to a Grignard reagent prepared from 0.72 g (30 mmoles) of magnesium, 15 ml of absolute ether, and 3 ml (30 mmoles) of bromobenzene. After dissolution of the pyrylium salt, the excess of phenylmagnesium bromide was decomposed by adding a saturated solution of NH_4Cl. The ether layer was dried over Na_2SO_4 and the solvent was distilled off on a water bath. The residue was recrystallized from 15 ml of n-propanol. Yield 2.42 g (78%), mp 124-125°C. IR spectrum: 1670 (C=C), 1610 and 1580 ($C–C_{ar}$), 1230 cm^{-1} (C–O–C). PMR spectrum (CCl_4): 1.14 (3H, d, CH_3), 2.94 (1H, q, 10-H), 4.85 (1H, s, 11-H), 6.43-7.58 ppm (13H, m, H_{ar}).

10-Methyl-10H-11-phenylbenzo[b]indeno[2,1-e]pyrylium Perchlorate (IV) from Benzoindenopyran (X). A mixture of 0.31 g (1 mmole) of benzoindenopyran X and 0.34 g (1 mmole) of trityl perchlorate was boiled for 5 min in 3 ml of glacial acetic acid. After cooling, a precipitate separated out and was washed with ether. Yield 0.39 g (95%), mp 261-262°C, with no melting point depression for a mixed sample with a product obtained by another method (see above).

2-Phenyl-4-(tolyl-4-)-1-benzopyrylium Perchlorate (XIII, $C_{22}H_{17}ClO_5$) and 2-Phenyl-3-acetyl-4-(tolyl-4-)-4H-chromene (XII, $C_{24}H_{20}O_2$). The reaction was carried out in the same way as when chromene I was used. From 2.98 g (0.01 mole) of 2-phenyl-4-(tolyl-4)-4H-chromene (XI), 0.55 g (14%) of salt XIII was obtained after its reprecipitation from chloroform by ethyl acetate, mp 172-175°C. IR spectrum: 1620 (pyrylium cation), 1605 and 1585 ($C–C_{ar}$), 1100 cm^{-1} (ClO_4^-). PMR spectrum (CF_3COOH): 2.07 (3H s, CH_3), 6.90-8.25 ppm (14H, m, H_{ar}, and 3-H).

After chromatography on a column filled with Al_2O_3, 1.11 g (33%) of acetylchromene XII was isolated, mp 125°C (from ethanol). IR spectrum: 1680 (C=C), 1635 (C=C), 1580 ($C–C_{ar}$), 1220 cm^{-1} (C–O–C). PMR spectrum ($CDCl_3$): 1.34 (3H, s, CH_3CO), 2.95 (3H, s, $\underline{H}_3C_6H_4$), 4.86 (1H, s, 4-H), 6.55-7.30 ppm (13H, m, H_{ar}).

Perchlorate XIII was also formed in a 97% yield by the action of trityl perchlorate on chromene XI by a method analogous to the synthesis of salt II (see above).

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