24. K. Sato and S. Morii, Ashahi Garasu Kogyo Gijutsu Shoreikai Kenkyu Hokoku, 29, 199 (1976); Chem. Abs., 89, 197734j (1978).

SYNTHESIS OF ACETYL DERIVATIVES OF 2,2-BIS(4'-HYDROXYPHENYL)PROPANE

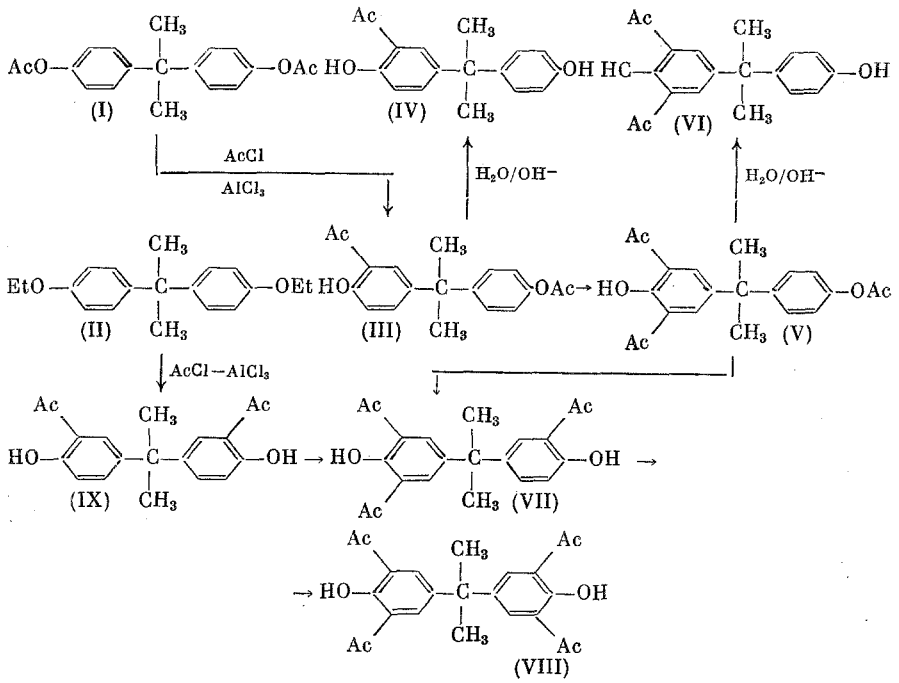
L. G. Fedenok, R. N. Myasnikova, and M. S. Shvartsberg

UDC 542.951.1:547.638.1

The Friedel—Crafts acetylation of dimethyl and diethyl ethers of diphenylolpropane is accompanied by dealkylation, leading to 2,2-bis(3'-acetyl-4'-hydroxyphenyl)propane [1, 2]. The free diphenylopropane under these conditions undergoes phenolic cleavage [3].

We have studied the influence of the character of protection of the hydroxyl groups in diphenylolpropane on the orientation of the entering groups during the acetylation. We expected that the reaction course can be altered by replacing the alkoxy groups by acetoxy groups.

2,2-Bis(4'-acetoxyphenyl)propane (I), synthesized by reaction of diphenylolpropane with Ac_2O in the presence of H_3PO_4, was acetylated analogously to 2,2-bis(4'-ethoxyphenyl)propane (II) [2] with an excess of AcCl—$AlCl_3$ in dichloroethane at 50°C. The reaction product, diketone (VI), was isomeric to 2,2-bis(3'acetyl-4'-hydroxyphenyl)propane (IX) obtained from (II)



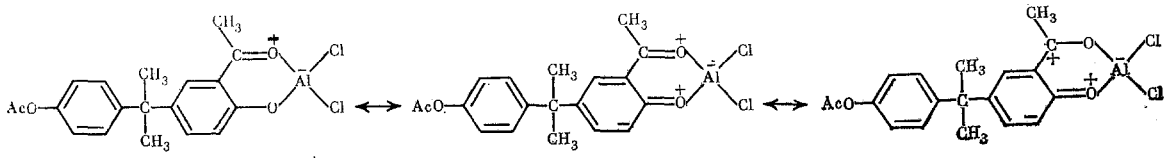
The IR spectrum of diketone (VI) in the region of stretching vibrations contains two absorption bands at 1645 and 1680 cm^{-1} instead of one at 1650 cm^{-1} in (IX) [4], which indicates the nonequivalence of these groups in (VI). The presence of two doublets in the NMR spectrum at 7.06 and 6.73 ppm (J = 8.8 Hz), corresponding to 4H, and a singlet at 7.94 ppm, corresponding to 2H, allow one to determine the structure of (VI) as 2-(3',5'-diacetyl-4'-hydroxyphenyl)-2-(4"-hydroxyphenyl)propane. Indeed, with the location of the acetyl substituents in different

Institute of Chemical Kinetics and Combustion, Siberian Branch, Academy of Sciences of the USSR, Novosibirsk. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 8, pp. 1836-1839, August, 1985. Original article submitted April 12, 1984.

0568-5230/85/3408-1685$09.50

rings (positions 2' and 3") the spectra would display an unavoidable complication as a result of differences in the chemical shifts of nonequivalent $H^{3'}$ and $H^{2''}$, $H^{5'}$ and $H^{5''}$, $H^{6'}$ and $H^{6''}$, as well as the change in the multiplicity of interacting $H^{3'}$ and $H^{5'}$ and $H^{2''}$ and $H^{6''}$ signals ($J_{meta} > 1$ Hz). On the other hand, the spectrum of symmetrically substituted (IX), the aromatic rings of which, similarly to (VI), contain six pairs of equivalent protons, differs from the spectrum of (VI) in the multiplicity of these proton signals (ppm): 6.76 d ($H^{5'}$, $J_{5',6'} = 8.8$ Hz), 7.26 d.d ($H^{6'}$, $J_{6',5'} = 8.8$, $J_{6',2'} = 1.8$ Hz), and 7.69 d ($H^{2'}$, $J_{2',6'} = 1.8$ Hz). For the diketone, in which the acetyl groups occupy the 2' and 5' positions in one of the rings, the magnetic equivalence of $H^{3'}$ and $H^{6'}$ has a very low probability, and therefore this structure is not consistant with the NMR spectrum of (VI). The structure of the 2',6'-diacetyl isomer contradicts the IR spectrum data of (VI).

Hence, the directions of diacetylation of diphenylolpropane derivatives (I) and (II) are different. Moreover, introduction of both acetyl groups to the same ring of diester (I) in the absence of the monoketone in the reaction products and in the presence of a considerable amount of unreacted I compels us to assume that in this case the intermediate monoketone manifests a higher reactivity than the starting (I). This result can be explained by assuming that the introduction of one acetyl substituent in the ring is accompanied by the cleavage of the ester group in which $AlCl_3$ participates. This process could be the Fries rearrangement. It has been reported [5] about the rearrangement of compound (I) in the presence of $AlCl_3$ at 120-130°C in $PhNO_2$; however, the structure of the product has been apparently established incorrectly. We failed to effect this reaction at 20-50°C in dichloroethane, and at elevated temperatures it was complicated by the phenolic cleavage of (I). Supported by this evidence, we assume that the proposed isomerization involves the acetylation of (I) with AcCl—$AlCl_3$ with the consecutive cleavage of the acetyl group. One way or another, the transfer of the acetyl group ends with the formation of a chelate complex in which, due to a donor—acceptor interaction of the carbonyl oxygen and aluminum, the +C effect of the phenolic oxygen increases, which in the final account determines the orientation and the relative activation of the monoacylation of the ring during the introduction of the second acetyl group



It is noteworthy that an analogous chelate formation is apparently also responsible for the anomalous orientation during the Gatterman formylation of polyhydroxyl phenols with a functional group containing a carbonyl substituent [6].

The chelate complex of the mixed aluminum phenolate of 2-(3',5'-diacetyl-4'-hydroxyphenyl)-2-(4"-acetoxyphenyl)propane is converted, after decomposition with an acid, into the monoester (V), which due to the intramolecular hydrogen bond preserves its chelating structure, similar to its predecessor. Compound (V) dissolved in ether during treatment with 10-15% aqueous KOH forms a phenolate, goes into the aqueous basic phase, and hydrolyzes to disphenol (VI). The unreacted (I) left in the organic solvent, hydrolyzes much slower, and this allows one to separate it from (VI). When instead of ether $CHCl_3$ is used as solvent, the monoester (V) is converted into its phenolate much slower during shaking it with 10% aqueous KOH. The monoester (V), not converted into its phenolate, similarly to (I), does not dissolve in water and can be easily identified chromatographically in the organic phase. This shows that during the acetylation process only one ester group is cleaved.

Since the alteration of the character of substituents in one ring (I) should not decisively influence the reactivity of the second ring, it was reasonable to expect that in the presence of an excess of AcCl—$AlCl_3$ it will undergo acetylation. Indeed, the increase of the reaction time to 30 h leads to the formation of triketone (VII) and tetraketone (VIII) in a 25% yield. They can be extracted from the $CHCl_3$ solution of the reaction products with 10% aqueous KOH easier than (V), and are removed sufficiently completely before (V) hydrolyzes to (VI). With this isolation method the chloroform solution retains the principal amount of (V) (yield 22%). A prolonged heating of the reaction mixture induces the phenolic cleavage of diphenylolpropane derivatives and a considerable formation of tars. The reduction of the

amount of AcCl and $AlCl_3$ from >6 to ∿2 moles per mole of (I) allows one to obtain under the same conditions a small yield (∿10%) of 2-(3'-acetyl-4'-hydroxyphenyl)-2-(4"-hydroxyphenyl)-propane (IV).

The principal possibility of the introduction of four acetyl groups into the aromatic rings of diphenylolpropane, demonstrated on ester (I), could be expediently applied for the acetylation of the more reactive diethoxy derivative (II). The reaction was carried out at 60°C for 7 h, using the reagents in the ratio recommended in [2] for obtaining (IX). Tetraketone (VIII) was separated from the accompanying compounds (IX) and (VII) by recrystallization from ethyl acetate. The yield of (VIII) was 52%. Diketone (IX) was synthesized with a yield of 61% by acetylation of (II) at 0-30°C with the amounts of AcCl and $AlCl_3$ reduced ∿3 times.

EXPERIMENTAL

The NMR spectra were taken on a Varian XL-200 spectrometer. The IR spectra were recorded on a UR-20 instrument.

2,2-Bis(4'-acetoxyphenyl)propane (I). Diphenylolpropane (45.6 g), Ac_2O (40.8 g), and H_3PO_4 (0.8 g) were refluxed for 5 h. AcOH was distilled off (∿16 g), and the mixture was diluted with $CHCl_3$, washed with a 5% aqueous solution of NaOH, and then with water, and dried with $CaCl_2$. Yield 57.4 g (91.8%) of (I), mp 91.5-92.5°C (EtOH) (compare [7]). NMR spectrum ($CDCl_3$, δ, ppm: 1.65 (CH_3CCH_3), 2.27 (CH_3COO), 6.97 d and 7.22 d ($H^{2',3',5',6'}$). IR spectrum ($CHCl_3$, ν, cm^{-1}): 1765 (C=O).

2-(3',5'-Diacetyl-4'-hydroxyphenyl)-2-(4"-hydroxyphenyl)propane (VI). To a solution of (I) (141 g) and AcCl (221 g) in dichloroethane (540 ml) freshly sublimed $AlCl_3$ (390 g) was added gradually during 1.5 h at 0-2°C. The mixture was heated to 50°C, stirred for 5 h, and poured on a mixture of conc. HCl and ether with ice. The ether extract was washed with a few portions of 10% aqueous KOH, then with water, and dried with $CaCl_2$. The solvent was evaporated, and the residue (64.6 g) was recrystallized from EtOH. Yield 57.3 g (40.6%) of (I). The alkaline extracts were acidified with HCl and extracted with ether; the extract was washed with water and dried with $CaCl_2$. After evaporation of the solvent the residue (72.1 g) was recrystallized from benzene. Yield 53 g (37.6%) of (VI), mp 151-152°C. Found, %: C 72.99; H 6.51. $C_{19}H_{20}O_4$. Calculated, %: C 73.06; H 6.45. NMR spectrum ($CDCl_3$, δ, ppm): 1.64 (CH_3CCH_3), 2.62 (CH_3CO), 5.99 ($C^{4"}OH$), 6.75 d, and 7.05 d ($H^{2",3",5",6"}$), 7.85 ($H^{2",6"}$), 13.18 ($C^{4'}OH...OC$). IR spectrum ($CHCl_3$, ν, cm^{-1}); 1645 and 1680 (C=O), 3610 (OH).

2,2-Bis(3',5'-diacetyl-4'-hydroxyphenyl)propane (VIII) and 2-(3',5'-Diacetyl-4'-hydroxyphenyl)-2-(3"-acetyl-4"-hydroxyphenyl)propane (VII). Compound (I) (4.6 g) was acetylated in the same manner as (VI), however, during 30 h (50°C). The reaction mixture was poured on HCl, $CHCl_3$, and ice, then it was worked up with a 10% aqueous solution of KOH. The product remaining in the chloroform solution and containing a considerable amount of tars after removing $CHCl_3$ was filtered in benzene through a small layer of silica gel. Yield 1.1 g (21.1%) of (V), mp 102.5-103.5°C (EtOH). Found, %: C 70.97; H 6.50. Calculated, %: C 71.17; H 6.26. NMR spectrum ($CDCl_3$, δ, ppm): 1.67 (CH_3CCH_3), 2.27 (CH_3COO), 2.60 (CH_3CO), 6.99 d, 7.20 d ($H^{2",3",5",6"}$), 7.83 ($H^{2',6'}$), 13.17 (OH...OC). IR spectrum ($CHCl_3$, ν, cm^{-1}): 1645, 1680, and 1170 (C=O). The alkaline extracts were acidified and extracted with $CHCl_3$. After evaporation of the solvent the residue (2.5 g) was triturated with CCl_4. The precipitated compound (VIII) was isolated; yield 0.6 g (10.1%), mp 204.5-205°C (EtOAc). Found, %: C 69.37; H 6.07. $C_{23}H_{24}O_6$. Calculated, %: C 69.98; H 6.10. NMR spectrum ($CDCl_3$, δ, ppm): 1.69 (CH_3CCH_3), 2.63 (CH_3CO), 7.82 ($H^{2',6'}$), 13.23 (OH...OC). IR spectrum ($CHCl_3$, ν, cm^{-1}): 1645 and 1680 (C=O).

CCl_4 was evaporated from the filtrate, and the residue was separated by preparative TLC on silica gel (eluent $CHCl_3$). Obtained 0.8 g (15.3%) of (VII), mp 111.5-112°C (EtOH). Found, %: C 71.40; H 6.10. $C_{21}H_{22}O_5$. Calculated, %: C 71.17; H 6.26. NMR spectrum ($CDCl_3$, δ, ppm): 1.68 (CH_3CCH_3), 2.58 (3H, CH_3CO), 2.61 (6H, CH_3CO), 6.86 d ($H^{5"}$), 7.23 d.d ($H^{6"}$), 7.61 d ($H^{2"}$), 7.83 ($H^{2',6'}$), 12.19 ($C^{4"}OH...OC$), 13.19 ($C^{4'}OH...OC$). IR spectrum (CCl_4, ν, cm^{-1}): 1655, 1690 (C=O). Besides (VII) also 0.1 g of (VI) and 0.13 g (5%) of 2,4-diacetylphenol, mp 91.5-92°C (EtOH) (see [8]), were isolated. NMR spectrum ($CDCl_3$, δ, ppm) 2.32 and 2.66 (CH_3CO), 6.94 d (H^6), 7.98 d.d. (H^5), 8.35 d (H^3).

2-(3'-Acetyl-4'-hydroxyphenyl)-2-(4"-hydroxyphenyl)propane (IV). The reaction between (I) (2.0 g), AcCl (1 g), and $AlCl_3$ (1.9 g) in dichloroethane (15 ml) was carried out at 50°C for 30 h. The mixture was quenched with HCl, ether, and ice. The phenolic fraction was separated by washing the ether extract several times with a 10% aqueous solution of NaOH.

Compound (IV) (0.34 g) containing an admixture of (VI) was obtained from it in the usual way. After recrystallization from CCl_4, the yield of (IV) was 0.17 g (9.8%), mp 139-140°C. Found, %: C 75.55 H 6.96. $C_{17}H_{18}O_3$. Calculated, %: C 75.53 H 6.71. NMR spectrum ($CDCl_3$, δ, ppm): 1.63 (CH_3CCH_3), 2.57 (CH_3CO), 5.53 br ($C^{4''}$–OH), 6.75 d and 7.07 d ($H^{2'',3'',5'',6''}$), 6.86 d ($H^{5'}$), 7.30 d.d ($H^{6'}$), 7.59 d ($H^{2'}$), 12.19 ($C^{4'}$OH...OC). IR spectrum ($CHCl_3$, ν, cm^{-1}): 1645 (C=O), 3610 (OH).

2,2-Bis(3'-acetyl-4'-hydroxyphenyl)propane (IX). $AlCl_3$ (10.8 g) was added during 0.5 h at 0-2°C to (II) (10 g) and AcCl (6 g) in dichloromethane (25 ml). The reaction was stirred for 0.5 h at 30°C. The solidified mixture was quenched with a mixture of dilute HCl (1:1) and ether with cooling. The aqueous layer was extracted with ether. Yield 6.7 g (61%) of (IX), mp 141-142°C (EtOH) (see [2]). NMR spectrum ($CDCl_3$, δ, ppm): 1.67 (CH_3CCH_3), 2.58 (CH_3CO), 6.87 d ($H^{5'}$), 7.28 d.d ($H^{6'}$), 7.60 d ($H^{2'}$), 12.18 (OH...OC) (see [4]). IR spectrum ($CHCl_3$, ν, cm^{-1}): 1650 (C=O). Acetylation of (II) (5 g) with AcCl (8.8 g) in the presence of $AlCl_3$ (15.2 g) in 20 ml of dichloroethane at 60°C for 7 h yielded 6.8 g of a mixture of (VIII), (VII), and (IX) from which 3.6 g (51.6%) of (VIII) was obtained, mp 204.5-205°C.

CONCLUSIONS

1. The Friedel–Crafts acetylation of 2,2-bis(4'-acetoxyphenyl)- and 2,2-bis(ethoxyphenyl)-propane allows one to introduce up to four substituents into the aromatic rings. The reaction is accompanied with the cleavage of the ether groups located in the ortho positions of the entering acetyl groups.

2. The regioselectivity of the acetylation of diesters and diethers of diphenylolpropane is different. The acetyl group enters successively the 3', 5', 3", and 5" positions of the ester, and the 3', 3", 5', and 5" positions of the ether.

LITERATURE CITED

1. I. L. Kotlyarevskii, A. S. Zanina, N. M. Gusenkova, I. E. Sokolov, and E. I. Cherepov, Vysokomol. Soedin., Kratkie Soobshch., 9B, 468 (1967).
2. E. I. Sokolov, A. S. Zanina, and I. L. Kotlyarevskii, Vysokomol. Soedin., Kratkie Soobshch., 14, 311 (1972).
3. G. A. Olah, J. Kaspi, and D. Meidar, Synthesis, 1978, 396.
4. A. S. Zanina, L. Ya. Al't, S. I. Shergina, and I. L. Kotlyarevskii, Izv. Akad. Nauk SSSR, Ser. Khim., 1970, 459.
5. E. Crescenzi, A. Mantegani, and G. Coppi, Farmaco Ed. Sci., 20, 491 (1965).
6. W. E. Truce, Org. React., 9, 37 (1957).
7. B. B. Corson, W. J. Heintzelman, L. H. Schwartzman, H. E. Tiefenthal, R. J. Lokken, J. E. Nickels, G. R. Atwood, and F. J. Pavlik, J. Org. Chem., 23, 544 (1958).
8. M. R. Bhatt and N. M. Shah, J. Ind. Chem. Soc., 33, 318 (1956).