AROXYDIHYDROPYRANS

XI.* SYNTHESIS OF 3,4-DIHYDRO-2-PYRANYLOXY(MERCAPTO)QUINOLINES AND THEIR PRINCIPAL PROPERTIES

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UDC 547.831.7'811:543.422.4

The reaction of vinyl ethers and vinyl sulfides of the quinoline series with unsaturated aldehydes gives 3,4-dihydro-2-pyranyloxy(mercapto)quinolines, in the hydrogenation of which, depending on the conditions, the multiple bonds in the pyran or pyridine ring are reduced. The ionization constants of the adducts were established by potentiometry. The vinyl ethers of 6-hydroxyquinoline, 8-hydroxy-1,2,3,4-tetrahydroquinoline, and 8-(S-vinyl)mercaptoquinoline were obtained for the first time.

In order to synthesize adducts of unsaturated aldehydes with vinyl ethers and vinyl sulfides of the quinoline series (potential antioxidants and biologically active substances) we studied the reaction of 6- and 8-vinyloxyquinolines (I, II), 8-vinyloxy-1,2,3,4-tetrahydroquinoline (III), and 8-(S-vinyl)mercaptoquinoline (IV) with acrolein and its homologs. The previously undescribed starting dienophiles were obtained by reaction of the appropriate hydroxy- and mercaptoquinolines with acetylene, in analogy with the method in [2].

The reaction of vinyl ethers I and II with α,β-unsaturated aldehydes takes place on prolonged heating (at 150-190°C) without the addition of a catalyst. The yields of the adducts (Table 1) in this case range from 50 to 75%. Acrolein reactions under milder conditions and condensation with crotonaldehyde and cinnamaldehyde take place at higher temperatures.

Ether III, which reacts under the investigated conditions to give 8-(3,4-dihydro-2-pyranyloxy)-1,2,3,4-tetrahydroquinoline (IX) in only 15% yield, is less reactive with unsaturated aldehydes. The low yield in this case is possibly due to an increase in the lability of the proton of the NH bond (pK_a of III in methanol 3.91, as compared with 4.82 for II), because of which the intra- and intermolecular hydrogen bonds, which hinder condensation of the associated molecules of vinyl ether III with aldehydes, are strengthened, although the steric effect of the hydrogenated pyridine ring of ether III also is not excluded. Vinyl sulfide IV is a more active dienophile than ether II, and reaction with it is therefore realized under relatively mild conditions (140-145°).

The proton of the quinoline H-2 fragment (8,76 ppm, dd, $J_1 = 2.0$ and $J_2 = 4.2$ Hz) resonates at weak field in the PMR spectrum of 8-(3,4-dihydro-2-pyranyloxy)quinoline (V). The H-4 signal of the quinoline ring is found at 7.75 ppm ($J_1 = 2.0$, $J_2 = 7.0$ Hz). The signals of the remaining protons of the quinoline fragment give a narrow multiplet at 6.9-7.3 ppm. The protons of the pyran ring resonate at stronger fields: H-6 (6.14 ppm, d, $J = 6.5$ Hz), H-2 (6.05 ppm, t, $J = 2.5$ Hz), and H-5 (4.7 ppm, m). The protons attached to C-3 and C-4 of the pyran ring form a complex multiplet at 1.5-2.8 ppm.

The usual absorption bands of the quinoline and pyran rings are present in the IR spectra of the adducts. On the basis of previous studies [1], it might be supposed that the band at 1230-1260 cm^{-1} corresponds to the stretching vibrations of the ether C—O—C group in V-IX and that the C—O—C group of the pyran ring is characterized by frequencies at 1040-1115 cm^{-1}. The intense absorption band at 1650 cm^{-1} constitutes evidence

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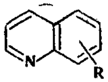
*See [1] for communication X.

Irkutsk Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 375-378, March, 1976. Original article submitted April 7, 1975.

TABLE 1. Characteristics of the Synthesized Compounds 

Compound	R	bp, °C (mm)	d_4^{20}	n_D^{20}	pK_a (CH_3OH)	Empirical formula	Found				Calculated				Yield, %
							C, %	H, %	N, %	MR_D	C, %	H, %	N, %	MR_D	
V	8-(3,4-Dihydro-2-pyranyloxy)	170 (2,5)	1,2044	1,6112	5,13	$C_{14}H_{13}NO_2$	73,8	5,6	6,2	65,6	74,0	5,8	6,2	65,1	76
VI	8-(4-Methyl-3,4-dihydro-2-pyranyloxy)	175—177 (2)	1,1531	1,5936	5,18	$C_{15}H_{15}NO_2$	74,8	6,4	5,6	70.9	74,7	6,3	5,8	69,8	52
VII	8-(4-Phenyl-3,4-dihydro-2-pyranyloxy)	209—210 (0,5)	1,1964	1,6312	5,09	$C_{20}H_{17}NO_2$	80,0	5,7	4,6	90,3	79,2	5,6	4,6	89,5	31
VIII	6-(3,4-Dihydro-2-pyranyloxy)	154—155 (1)	1,1911	1,6100	5,06	$C_{14}H_{13}NO_2$	73,9	5,7	6,1	66,2	74,0	5,8	6,2	65,1	75
IX*	8-(3,4-Dihydro-2-pyranyloxy)	160—161 (2)	1,1396	1,5721	4,50	$C_{14}H_{17}NO_2$	72,9	7,5	5,7	66,8	72,7	7,4	6,1	67,1	15
X	8-(3,4-Dihydro-2-pyranylmercapto)	67†	—	—	4,31	$C_{14}H_{13}NOS$	68,5	5,1	13,2 S, %	—	68,8	5,3	13,1 S, %	—	64
XI	8-(Tetrahydro-2-pyranyloxy)	136—137 (0,5)	1,1684	1,5920	5,37	$C_{14}H_{15}NO_2$	72,9	6,8	6,1	66,4	73,3	6,6	6,1	65,6	82
XII*	8-(Tetrahydro-2-pyranyloxy)	141—142 (1)	1,1303	1,5679	4,98	$C_{14}H_{19}NO_2$	72,2	8,2	6,1	67,5	72,1	8,2	6,0	67,6	85

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*This is R for 1,2,3,4-tetrahydroquinoline.

†Melting point.

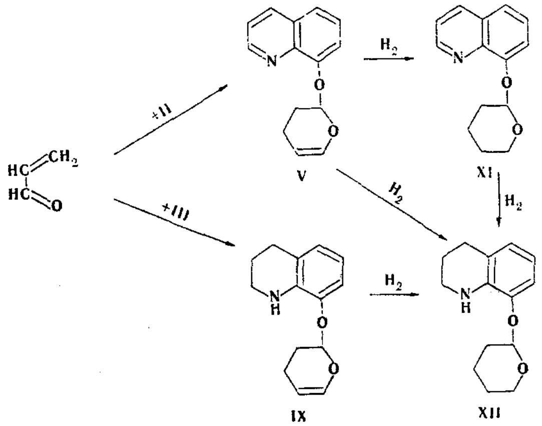
for the presence of a C = C bond in the pyran ring. The stretching vibrations of the C—H bonds attached to the C = C bond are characterized by absorption at 3060 cm^{-1}, whereas the deformation vibrations of this bond are found at 955-970 cm^{-1}. The stretching vibrations of the CH_2 group of the dihydropyran or quinoline ring of the adducts are observed at 2850-2940 cm^{-1}.

The ionization constants were determined for adducts V-XII (Table 1). 3,4-Dihydro-2-pyranyloxyquinolines V-VIII are stronger bases than quinoline (pK_a 4.99). A hydroxydihydropyran substituent in the 6 and 8 positions of the quinoline ring has an electron-donor effect, although it is smaller than that of the completely hydrogenated pyran ring. This sort of change in the basic properties of adducts V and XI is evidently due to an increase in the electronegativity of the ring oxygen atom due to $p-\pi$ overlapping. The presence of substituents in the 4 position of the pyran ring (adducts V-VII) changes the basicity only slightly, and the order of change in the basic properties of these compounds is in conformity with the polar effects of the substituents.

The weakest base in the investigated series is 8-(3,4-dihydro-2-pyranyloxy)-1,2,3,4-tetrahydroquinoline (IX), the basicity of which is considerably lower than the basicity of 1,2,3,4-tetrahydroquinoline (pK_a 5.55); this would seem to contradict the conclusion regarding the electron-donor character of the hydroxydihydropyran grouping. The analogy with dialkylanilines is usually drawn upon to explain the basic properties of these two-ring systems [3]. In particular, tetrahydroquinoline adduct IX is similar to N-alkylaniline with an o-alkyl substituent with specific shielding of the basicity center during its solvation, which also leads to its low basicity. However, this sort of ortho effect is weakened in unsubstituted tetrahydroquinoline.

The basicity of 8-(3,4-dihydro-2-pyranylmercapto)quinoline X is considerably lower than the basicity of oxygen analog V; this is due to the strongly expressed electron-acceptor effect of the SR group, included in the π system of the aromatic ring, as compared with the OR group [3].

Adducts V and IX were hydrogenated in order to prove their structure. In this case it was noted that not only the double bond but also the quinoline fragment of the adducts are reduced to give, ultimately, 8-(tetrahydro-2-pyranyloxy)-1,2,3,4-tetrahydroquinoline (XII). In the case of V it was shown that the pyran ring is hydrogenated initially, after which the pyridine ring undergoes hydrogenation.



The properties of the product of exhaustive hydrogenation (XII) obtained by various methods are in complete agreement. A band of vibrations of an NH group appears in its IR spectrum at 3430 cm^{-1}, and the band of stretching vibrations of the C = C bond in the pyran ring (1650 cm^{-1}) vanishes.

EXPERIMENTAL

The IR spectra of KBr pellets of the solids and of thin layers of the liquids were obtained with a UR-20 spectrometer. The PMR spectra of CCl_4 solutions were recorded with a BS-487 B spectrometer with hexamethyldisiloxane as the internal standard. The ionization constants in methanol were measured potentiometrically [4].

8-Vinyloxyquinoline (II) was obtained by the method described in [2].

6-Vinyloxyquinoline (I). A 1-liter autoclave was charged with 15 g of 6-hydroxyquinoline, 6 g of KOH, and 100 ml of dioxane, acetylene was fed in at an initial pressure of 14-16 atm up to the saturation point, and the mixture was then heated at 200-210° for 1 h. Workup of the vinylation products gave 5.4 g (31%) of

I with bp 92° (1 mm), d_4^{20} 1.1288, and n_D^{20} 1.6228. Found: C 76.9; H 5.3; N 7.9%; MR_D 53.5. $C_{11}H_9NO$. Calculated: C 77.2; H 5.3; N 8.2%; MR_D 53.1.

8-Vinyloxy-1,2,3,4-tetrahydroquinoline (III). A 0.5-liter autoclave was charged with 20 g of 8-hydroxy-1,2,3,4-tetrahydroquinoline, 6 g of KOH, and 120 ml of dioxane, acetylene (at 20 atm) was fed into the autoclave, and the mixture was then heated at 210-220° for 45 min. Vacuum distillation of the reaction mixture yielded 10.3 g (43%) of III with bp 93° (0.5 mm), d_4^{20} 1.0924, and n_D^{20} 1.5825. Found: C 75.5; H 7.4; N 7.8%; MR_D 54.0. $C_{11}H_{13}NO$. Calculated: C 75.4; H 7.5; N 8.0%; MR_D 53.4.

8-(S-Vinyl)mercaptoquinoline (IV). This compound, with mp 36°, was obtained in 87% yield. Found: C 70.3; H 4.8; S 16.5%. $C_{11}H_9NS$. Calculated: C 70.5; H 4.8; S 17.1%.

Adducts V-X. A mixture of 8 g of 6-vinyloxyquinoline and 2.6 g of acrolein (equimolecular amounts) was heated in an autoclave at 150-155° for 10 h, after which it was vacuum distilled to give 7.9 g (75%) of adduct VIII.

Compounds V (reaction temperature 150-155°), VI (165-170°), VII (185-190°), IX (155-160°), and X (140-145°) were similarly isolated from the appropriate ether. The synthesized adducts were obtained as viscous yellowish oils or white crystalline substances that were quite soluble in organic solvents and insoluble in water.

8-(Tetrahydro-2-pyranyloxy)quinoline (XI). A mixture of 4 g of ether V in 10 ml of absolute ethanol and 2 g of Raney nickel catalyst were placed in a hydrogenation flask, and the reaction was carried out until 1 mole of H_2 per mole of V had been absorbed. The mixture was then filtered, the alcohol was removed by distillation, and the residue was vacuum fractionated to give 3.3 g (82%) of XI. Further hydrogen absorption to produce XII took place slowly (36 h) at room temperature and atmospheric pressure, whereas XII was formed in 85% yield after 4 h in an autoclave at 60-70° with an H_2 pressure 50 atm.

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