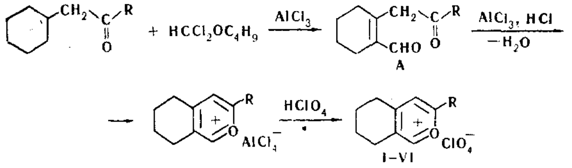
SYNTHESIS OF 3-ARYL-5,6,7,8-TETRAHYDRO-2-BENZOPYRILIUM SALTS AND CORRESPONDING ISOQUINOLINES

G. N. Dorofeenko and G. P. Safaryan

UDC 547.814.1'833.07:542.959.1

β,γ-Unsaturated ketones (such as cyclohexylideneacetophenone) are formylated with dichloromethyl butyl ether in the presence of anhydrous aluminum chloride. A method has been developed for the synthesis of 3-aryl-substituted 5,6,7,8-tetrahydro-2-benzopyrilium salts unsubstituted in 1 position. The thus-synthesized salts are converted into the corresponding 5,6,7,8-tetrahydroisoquinolines.

We have previously investigated the synthesis of 1,3-disubstituted 5,6,7,8-tetrahydro-2-benzopyrilium salts, and the corresponding isoquinoline derivatives, by acylation of β,γ-unsubstituted cyclic ketones [1-3]. However, until recently the α-unsubstituted derivatives of 5,6,7,8-tetrahydro-2-benzopyrilium salts have not been investigated. In continuation of this work we have suceeded in synthesizing some 3-aryl-substituted 5,6,7,8-tetrahydro-2-benzopyrilium salts by the formylation of β,γ-unsaturated cyclic ketones with dichloromethyl butyl ether in the presence of anhydrous aluminum chloride. This formylation method, which has found wide application for the preparation of aromatic aldehydes [4, 5], was first used by us for the formylation of activated double bonds in β,γ-unsaturated cyclic ketones. The resulting β,γ-unsaturated ketoaldehydes (A) cyclize in HCl solution in the presence of aluminum chloride to give the highly water-soluble 5,6,7,8-tetrahydro-2-benzopyrilium tetrachloroaluminates. The latter, on treatment with 70% perchloric acid, are converted into the sparingly soluble perchlorates which are isolated in the crystalline state in yields of 16-17%.



I R = C_6H_5, II p-$OCH_3C_6H_4$, III 3,4-$(OCH_3)_2C_6H_3$, IV α-C_4H_3S, V p-$CH_3C_6H_4$, VI p-ClC_6H_4.

The following characteristic bands occur in the IR spectra of the salts obtained: 1648-1621 cm^{-1} (symmetrical valence vibrations of the pyrilium cation [6, 7]), 1604-1599 cm^{-1} (symmetrical valence vibrations of the aromatic substituents linked to the pyrilium ring), 1090-1071 cm^{-1} (ClO_4^- [8]). Compounds II and III show bands at 1282-1269 cm^{-1} due to the valence vibrations of the ether bonds of the methoxy groups [9]. Compound IV absorbs at 1511 and 1444 cm^{-1}, indicating the presence of the thiophene ring [10].

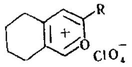
Compounds I, V, and VI, on treatment with an excess of concentrated aqueous ammonia, are readily converted in good yields (90%) into the corresponding 5,6,7,8-tetrahydroisoquinolines, which are of interest as potential starting materials for the preparation of analogs of naturally occuring alkaloids of the morphine series [11].

EXPERIMENTAL

ω-(1-Cyclohexenyl)-p-chloroacetophenone and ω-(1-Cyclohexenyl)-p-methylacetophenone. These compounds were obtained by the condensation of cyclohexanone with p-chloroacetophenone or p-methylacetophenone in the presence of 5% sodium ethoxide in ethanol by the method described previously [3, 12].

Rostov-on-Don State University. Translated from Khimiya Geterotsiklicheskikh Soedinenii, Vol. 6, No. 5, pp. 585-587, May, 1970. Original article submitted August 27, 1968.

TABLE 1



R	mp, °C	Characteristic bands in the spectra, cm^{-1}	Molecular formula	Found, %			Calculated, %			Yield, %
				C	H	Cl	C	H	Cl	
C_6H_5	204.5	1631, 1594, 1575, 1087	$C_{15}H_{15}ClO_5$	57,42	4,91	11,75	57,93	4,83	11,42	16
p-$CH_3OC_6H_4$	202	1648, 1603, 1572, 1282, 1083	$C_{16}H_{17}ClO_6$	56,28	5,22	10,00	56,36	5,03	10,45	16
3,4-$(CH_3O)_2 \cdot C_6H_3$	183	1625, 1599, 1561, 1269, 1087	$C_{17}H_{19}ClO_7$	55,51	5,17	9,46	55,04	5,17	9,58	16
α-C_4H_3S	>350	1623, 1511, 1444, 1071	$C_{13}H_{13}ClO_5S$**	49,40	4,29	10,91	49,26	4,14	11,21	17
p-$CH_3C_6H_4$	153	1621, 1604, 1571, 1090	$C_{16}H_{17}ClO_5$	58,98	5,45	11,04	59,14	5,27	10,93	16
p-ClC_6H_4	193.5	1626, 1593, 1570, 1083, 735	$C_{15}H_{14}Cl_2O_5$	51,90	4,32	20,49	52,15	4,12	20,57	16

---

*From glacial acetic acid.

†Found, %: S 9.72. Calculated, %: S 10.12.

ω-(Cyclohexenyl)-p-chloroacetophenone (yield 15%); bp 154-156° C (5 mm). Found, %: C 71.26; H 6.36. Calculated for $C_{14}H_{15}ClO$, %: C 72.00; H 6.48.

ω-(Cyclohexenyl)-p-methylacetophenone (yield 18%); bp 164-167° C (6 mm). Found, %: C84.60; H 8.65. Calculated for $C_{15}H_{18}O$, %: C 84.05; H 8.47.

3-(p-Chlorophenyl)-5,6,7,8-tetrahydro-2-benzopyrilium Perchlorate. A solution of 2.3 g (0.01 mole) of ω-(1-cyclohexenyl)-p-chloroacetophenone in 5-7 ml of methylene chloride was cooled to 0° C, and 1.3 g (0.01 mole) of anhydrous aluminum chloride added with stirring, followed by the rapid dropwise addition of 3.2 g (0.02 mole) of dichloromethyl butyl ether with continued stirring. The reaction began immediately with vigorous evolution of HCl, and the reaction mixture darkened in color. The mixture was kept for 10-15 min, until the evolution of HCl had largely ceased, then it was poured onto ice and HCl. The aqueous emulsion was extracted with ether, the aqueous layer was separated, and acidified with 70% perchloric acid. The colorless, crystalline precipitate was filtered off, washed with a mixture of alcohol and ether (1 : 5), followed by ether. Yield 0.54 g (16%). The other salts were obtained in a similar manner (see Table 1).

3-(p-Chlorophenyl)-5,6,7,8-tetrahydroisoquinoline. To 0.5 g (0.0016 mole) of 3-(p-chlorophenyl)-5,6,7,8-tetrahydro-2-benzopyrilium perchlorate was added an excess (4-5 ml) of a 22% solution of ammonia, and the mixture was kept for 3 days. The reaction product was filtered off, dried,and purified by chromatography on an alumina column (solvent, benzene—chloroform, 2 : 3), giving 0.32 g (91%) of bright-yellow crystals, mp 97° C. Found, %: C 73.42; H 5.96; N 5.80. Calculated for $C_{15}H_{14}ClN$, %: C 73.88; H 5.79; N 5.74.

The following were similarly obtained: 3-Phenyl-5,6,7,8-tetrahydroisoquinoline (yield 91%, mp 130° C after purification on an alumina column). Found, %: C 87.10; H 7.64; N 6.50. Calculated for $C_{15}H_{15}N$, %: C 86.75; H 7.23; N 6.69. 3-(p-Tolyl)-5,6,7,8-tetrahydroisoquinoline (yield 90%, mp 63° C after purification on an alumina column). Found, %: C 85.88; H 7.87; N 5.82. Calculated for $C_{16}H_{17}N$, %: C 86.04; H 7.67; N 6.27.

The IR spectra of the pyrilium salts were taken on an IKS-14 spectrophotometer with NaCl prisms, in the form of pastes in Vaseline oil.

LITERATURE CITED

1. G. N. Dorofeenko and V. I. Dulenko, DAN, 157, 361, 1964.
2. L. V. Dulenko, V. I. Dulenko, and G. N. Dorofeenko, ZhOKh, 34, 3588, 1964.
3. G. N. Dorofeenko, G. P. Safaryan, and V. I. Dulenko, ZhOKh, 36, 811, 1966.
4. A. Rieche, H. Gross,and E. Höft, Chem. Ber. 93, 88, 1960.

5. V. V. Moiseev and L. P. Zalukaev, Izvestiya Vuz. ser. khim., 8, 945, 1967.
6. A. D. Semenov, G. N. Dorofeenko, and V. I. Dulenko, KhGS [Chemistry of Heterocyclic Compounds], 14, 1966.
7. A. T. Balaban, G. D. Mateescu, and M. Elian, Tetrah., 18, 1053, 1962.
8. A. Cross, Introduction to Practical Infrared Spectroscopy [Russian translation], IL, Moscow, 106, 1961.
9. L. Bellamy, The Infrared Spectra of Complex Molecules, Methuen, 1958.
10. A. R. Katritzky, ed., Physical Methods in Heterocyclic Chemistry [Russian translation], Khimiya, Moscow, 506, 1966.
11. R. Grew, Naturwiss., 33, 333, 1946; Ber., 81, 279, 1948.
12. M. D. Jarrow and G. A. R. Kon, J. Chem. Soc., 128, 2188, 1926.