SYNTHESIS OF 4H-PYRANS BY O-CYCLIZATION OF 1,5-DIKETONES

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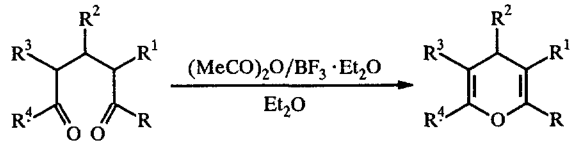
Substituted 4H-pyrans were obtained in high preparative yields by the reaction of 1,5-diketones with acetic anhydride and boron trifluoride etherate in diethyl ether. It is assumed that the heterocyclization of 1,5-diketones includes a step involving the formation and transformations of an acyloxy carbonium ion.

The most efficient method for the synthesis of 4H-pyrans is the well-known acid-catalyzed O-cyclization of 1,5-diketones [1]. The principal advantages of this method as compared with methods based on the use of pyrylium salts as the starting compounds are the availability of diverse 1,5-diketones [2] and the absence of 2H-pyrans in the reaction products. Nevertheless, this method has not been practiced on a large scale and has been used only in some cases for the synthesis of unreactive 4H-pyrans containing strong electron-acceptor substituents [3]. There is some doubt about the similar production of pyrans having only alkyl or aryl groups as substituents in view of the known ability of these compounds to undergo subsequent heteroaromatization, as well as decyclization to the starting 4,5-dicarbonyl compounds, under the influence of acidic reagents [3].

We have found that the preparative synthesis of a number of tri-, tetra-, and pentaalkyl(aryl)-substituted 4H-pyrans can be easily accomplished by the action of boron trifluoride etherate and acetic anhydride in diethyl ether on the corresponding 1,5-diketones. Under these conditions the cyclization of 1,5-diketones proceeds irreversibly and much faster than the subsequent heteroaromatization of the resulting pyrans. Appreciable (4-13%) formation of pyrylium salts occurs only in the production of IIh-j. In the remaining cases heteroaromatization takes place to a very insignificant extent, and pyrylium salts are formed only in trace amounts. The reason for this is evidently the high degree of steric shielding of the tetragonal carbon atom of the pyran ring by the substituents attached to the $C_{(2)}$, $C_{(3)}$, and $C_{(4)}$ atoms and, in the case of IIa-g, also by the brief time of their contact with the reaction mixture.



Ia-n IIa-n

I, II a $R+R^1=R^3+R^4=(CH_2)_3$, $R^2=H$; b $R+R^1=(CH_2)_3$, $R^3+R^4=(CH_2)_4$, $R^2=H$; c-g $R+R^1=R^3+R^4=(CH_2)_4$; c $R^2=H$; d $R^2=CH_3$; e $R^2=C_3H_7$; f $R^2=C_6H_5$; g $R^2=4\text{-}CH_3OC_6H_4$; h $R=R^2=C_6H_5$, $R^3+R^4=(CH_2)_3$, $R^1=H$; i $R=R^2=C_6H_5$, $R^3+R^4=(CH_2)_4$, $R^1=H$; j $R=R^2=R^4=C_6H_5$, $R^1=R^3=H$; k $R=R^4=C_6H_5$, $R^1=R^3=H$, $R^2=4\text{-}CH_3OC_6H_4$; ℓ $R=R^2=R^4=C_6H_5$, $R^1=CH_3$, $R^3=H$; m $R=R^4=C_6H_5$, $R^1=R^3=H$, $R^2=2\text{-}ClC_6H_4$; n $R=C_6H_5$, $R^1=H$, $R^2=3,4\text{-}(CH_3O)_2C_6H_3$, $R^3+R^4=o\text{-}CH_2C_6H_4$

Heteroaromatization of the 4H-pyrans is also undoubtedly hindered by dilution of the reaction mixture with ether, which ties up the boron trifluoride and hinders the ionization of its complexes with acetic anhydride. Attempts to carry out the reactions without this solvent and also when it is replaced by petroleum ether, hexane, and benzene lead in most cases to the quantitative formation of pyrylium salts.

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TABLE 1. Results of the O-Cyclization of 1,5-Diketones Ia-n

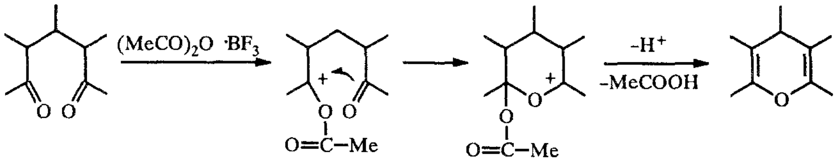
Initial compound I and product II	Length of experiment, h	Yield II, %	Initial compound I and product II	Length of experiment, h	Yield II, %
a	0,5	84	h	4	87
b	0,5	92	i	3	94
c	0,3	96	j	6	76
d	0,5	87	k	6	71
e	0,5	89	l	5	94
f	0,5	83	m	10	96
g	0,5	70	n	10	82

TABLE 2. Characteristics of the Synthesized IIa, h, i, m, n

Compound	Tmp, °C	IR spectra, cm^{-1}
a	55...56	1675, 1710
h	107...108	1640, 1710
i	72...74	1650, 1715
m	106...107	1645, 1690
n	96...98	1645, 1685

Alkylidene- and arylalkylidenedicyloalkanones Ia-g undergo cyclization most readily, while aryl aliphatic 1,5-diketones Ij-m undergo cyclization with the greatest difficulty. The facile conversion of diketone Ia to pyran IIa should especially be noted. Previous attempts at the O-cyclization of this diketone using other cyclizing agents were unsuccessful [4, 5].

The known data on the catalysis of the transformations of carbonyl compounds by acyl cations [6] make it possible to assume that the high efficiency of the cyclization of 1,5-diketones in the reaction that we developed is due to the formation and rapid transformations of the highly reactive acyloxy carbonium ion:



Similar character of the transformations probably also occurs in the case of the unusually facile O-cyclization of 1,5-diaryl(alkyl)-3-carboranylpentane-1,5-diones under the influence of acetic anhydride [7]. The carboranyl substituent evidently acts as a Lewis acid.

The IIb-g and IIj-l obtained by the new method are known, and their IR spectra and physicochemical constants are identical to those presented in the literature [8-12]. We synthesized 4H-pyrans IIa, h, i, m, n for the first time. Their structure is confirmed by the IR spectra, which contain two absorption bands at 1645-1710 cm^{-1}, which are characteristic for the C=C bonds of the 4H-pyran ring [3].

EXPERIMENTAL

The IR spectra of suspensions of the compounds in mineral oil were recorded with a Specord 75-IR spectrometer. The progress of the transformations and the individuality of the compounds obtained were monitored by TLC on Silufol UV-254 plates. The starting 1,5-diketones I were obtained by the methods presented in [2].

The results of elementary analysis of IIa, h, i, m, n were in agreement with the calculated values.

General Method for the Synthesis of 4H-Pyrans IIa-n. A 10-mmole sample of boron trifluoride etherate was added to a stirred solution (suspension) of 10 mmole of 1,5-diketone I in 50 ml of ether and 10 ml of acetic anhydride. After 0.5-10 h, the reaction mixture was diluted with 50 ml of hexane, and the precipitated pyrylium salt, when necessary, was removed by filtration. The filtrate was washed successively with water (2 × 100 ml), 10% aqueous NaOH solution (100 ml), and 100 ml of water. The organic layer was dried with sodium sulfate, and the solvent was removed by distillation. The oily residue was purified by chromatography with a column packed with aluminum oxide, while the solid products were recrystallized from methanol.

The reaction times and yields and constants of pyrans II are presented in Tables 1 and 2.

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