SYNTHESIS AND OXIDATION OF 2,6-DIMETHYL-1,4-DIHYDROPYRIDINE-3,5-DICARBOXYLIC ACID ESTERS

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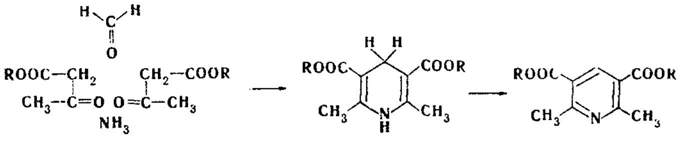
Twenty-six esters of 2,6-dihydropyridine-3,5-dicarboxylic acid were obtained by means of the Hantzsch pyridine synthesis. The synthesized compounds were oxidized by chloranil to the corresponding pyridine derivative.

1,4-Dihydropyridine derivatives [1] have recently acquired practical value as agents for the treatment of cardiovascular diseases [2] and as antioxidants [3, 4]. Dihydropyridines are generating great interest as analogs and model compounds of the redox coenzyme HAD • H [1, 5] and as reducing agents [6]. From this point of view, γ-unsubstituted 1,4-dihydropyridines, in which the electron- and hydrogen-donor properties are most markedly expressed, are of greatest interest. However, little study has been devoted to this group of compounds, and the investigations that have been made are extremely erratic. There are a rather large number of papers dealing with 1,4-dihydronicotinamide derivatives and 2,6-dimethyl-3,5-diethoxycarbonyl-1,4-dihydropyridine (the so-called "Hantzsch ester"), but only the methyl [1] and ethyl [4] esters of 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylic acid are known.



A B

We have proposed [3] a simple and convenient modification of the Hantzsch pyridine synthesis [1] for the synthesis of new esters of 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylic acid (A). The use of acetoacetic esters, hexamethylenetetramine (urotropin), and ammonium acetate in alcohol for the synthesis of such esters makes it possible to obtain them easily and in good yields. The amounts of urotropin and ammonium acetate (catalyst) can be varied over broad limits. In the presence of a larger excess of these reagents the reaction time is reduced to 5 min, and this may be extremely important in the case of unstable easily oxidized compounds. The following esters of 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylic acid were synthesized: alkyl up to C_{16} (I-XVI), hydroxyethyl (XVII), alkoxy- and phenoxy-ethyl (XVIII-XXII), benzyl (XXIII), cinnamyl (XXV), carbethoxymethyl (XXIV), and furfuryl (XXVI) (Table 1). Characteristic blue fluorescence in UV light [1] is observed for all esters A. The melting points decrease and pass through a minimum when $R = C_6H_{13}$ as the length of the alkyl grouping of the ester group becomes longer.

The UV spectra (Table 3) of all of the investigated alkyl and alkoxyalkyl esters (I-XXI) almost coincide with the spectrum of the "Hantzsch ester" (A, $R = C_2H_5$) [8, 9]. There are also characteristic maxima at 232, 251, and ~373 nm. A change in the ester group has little effect on the spectrum: A hypsochromic shift of the long-wave maximum of only ~1 nm (i.e., within the limits of the error in the measurements) is observed even on passing from the methyl or ethyl ester to tert-butyl ester V. The introduction of a strong electron acceptor – a carbethoxy group (XXIV) – in the ester group causes a bathochromic shift of the long-wave maximum of only 5 nm. The presence of phenyl groups in esters A (XXII, XXIII, and XXV) naturally

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TABLE 1. 2,6-Dimethyl-1,4-dihydropyridine-3,5-dicarboxylic Acid Esters (A)

Compound	R	mp, °C (crystallization solvent*)	Empirical formula	Found, %			Calc., %			Yield, %
				C	H	N	C	H	N	
I	n-C_3H_7	140—143	$C_{15}H_{23}NO_4$	64,0	8,5	4,9	64,0	8,2	5,0	71
II	i-C_3H_7	123—125	$C_{15}H_{23}NO_4$	64,1	8,6	5,2	64,0	8,2	5,0	63
III	n-C_4H_9	116—118	$C_{17}H_{27}NO_4$	65,8	9,0	4,7	66,0	8,8	4,5	65
IV	i-C_4H_9	128—129	$C_{17}H_{27}NO_4$	65,7	8,8	4,6	66,0	8,8	4,5	61
V	t-C_4H_9	152—154	$C_{17}H_{27}NO_4$	65,5	8,7	4,7	66,0	8,8	4,5	65
VI	n-C_5H_{11}	102—103 (ethanol—water)	$C_{19}H_{31}NO_4$	67,4	9,0	4,3	67,6	9,3	4,2	51
VII	i-C_5H_{11}	117—119 (ethanol—water)	$C_{19}H_{31}NO_4$	67,2	9,2	4,5	67,6	9,3	4,2	53
VIII	n-C_6H_{13}	86—89 (ethanol—water)	$C_{21}H_{35}NO_4$	69,0	9,9	3,8	69,0	9,7	3,8	47
IX	Cyclohexyl	104—107 (hexane)	$C_{21}H_{31}NO_4$	69,4	8,7	4,1	69,8	8,7	3,9	57
X	n-C_7H_{15}	90—92	$C_{23}H_{39}NO_4$	70,1	9,9	3,3	70,2	10,0	3,6	60
XI	n-C_8H_{17}	81—82	$C_{25}H_{43}NO_4$	71,4	10,6	3,5	71,2	10,3	3,3	50
XII	n-C_9H_{19}	89—90	$C_{27}H_{47}NO_4$	71,8	10,8	3,3	72,1	10,5	3,1	60
XIII	n-$C_{10}H_{21}$	86—90	$C_{29}H_{51}NO_4$	72,8	11,0	3,1	72,9	10,8	2,9	66
XIV	n-$C_{11}H_{23}$	89—92	$C_{31}H_{55}NO_4$	73,5	11,3	2,9	73,6	11,0	2,8	82
XV	n-$C_{12}H_{25}$	93—94	$C_{33}H_{59}NO_4$	73,7	10,9	2,5	74,3	11,1	2,6	82
XVI	n-$C_{16}H_{33}$	95—97	$C_{41}H_{75}NO_4$	77,1	11,8	2,2	76,2	11,7	2,2	76
XVII	C_2H_4OH	185—192 (methanol)	$C_{13}H_{19}NO_6$	54,5	7,0	4,8	54,7	6,7	4,9	49
XVIII	$C_2H_4OCH_3$	95—99 (ethanol—water)	$C_{15}H_{23}NO_6$	57,8	7,4	4,3	57,5	7,4	4,5	70
XIX	$C_2H_4OC_2H_5$	100—103 (ethanol—water)	$C_{17}H_{27}NO_6$	59,4	7,9	4,3	59,8	8,0	4,1	78
XX	$C_2H_4OC_4H_9$	85—86 (ethanol—water)	$C_{21}H_{35}NO_6$	63,5	9,3	3,7	63,5	8,9	3,5	82
XXI	$C_2H_4OC_6H_{13}$	84—85	$C_{25}H_{43}NO_6$	66,3	9,4	3,4	66,2	9,6	3,1	85
XXII	$C_2H_4OC_6H_5$	128—129	$C_{25}H_{27}NO_6$	68,9	6,2	3,1	68,6	6,2	3,2	90
XXIII	$CH_2C_6H_5$	113—115 (benzene)	$C_{23}H_{23}NO_4$	73,3	6,2	3,7	73,2	6,1	3,7	79
XXIV	$CH_2COOC_2H_5$	104—107 (ethanol—water)	$C_{17}H_{23}NO_8$	55,2	6.3	4,1	55,3	6,3	3,8	59
XXV	$CH_2CH{=}CHC_6H_5$	147—150 (benzene)	$C_{27}H_{27}NO_4$	75,7	6,2	3,5	75,5	6,3	3,3	73
XXVI	Furfuryl	130—131	$C_{19}H_{19}NO_6$	63,5	5,4	3,7	63,8	5,4	3,9	84

*If the solvent is not indicated, the compound was recrystallized from 95% ethanol.

complicates the spectrum, particularly in the case of the cinnamyl ester. A new absorption maximum at 200-220 nm appears in the spectra of these compounds, but the characteristic absorption is also simultaneously changed. The absorption bands at 220-230 nm are superimposed in the spectrum of furfuryl ester XXVI.

All of the esters obtained (I-XXVI), like other γ-unsubstituted 1,4-dihydropyridines, are oxidized extremely readily to the corresponding pyridine derivatives (B). This oxidation occurs even under the influence of air oxygen on storage. The stabilities of I-XXVI differ. Among the alkyl esters (I-XVI), esters with a long alkyl chain (XII-XVI) are also stable in addition to the methyl and ethyl esters. These esters undergo little change even on prolonged storage. On the other hand, esters V-X and XVIII-XX are rapidly converted to the oxidized form on storage in air. The oxidation process is accelerated appreciably in light. It is assumed that the reason for this difference consists mainly in the different melting points of B. When the melting points of 1,4-dihydropyridines and pyridines are sufficiently high, the oxidation of the former occurs in the solid phase; in addition, the oxidized form partially protects the particles of esters A from further oxidation. The low melting points of pyridines B promote the formation of a liquid phase, and this facilitates oxidation. Photochemical processes [10] also play a certain role, as attested to by acceleration of autooxidation in light.

1,4-Dihydropyridines I-XXVI are oxidized very easily by the usual chemical methods: oxidation with sodium nitrite in acetic acid [7] does not even require heating. However, in some cases this method cannot be used. Thus, for example, ester XXV undergoes resinification during oxidation by this method. In cases such as this, a more suitable method is oxidation with chloranil [9] in benzene; this method makes it possible to avoid acidic media and carry out the reaction without heating or only with brief heating. Difficulties arise in the purification of pyridines B with low melting points. The oxidation products are obtained in relatively pure form (the UV spectra correspond exactly to the spectra of the

TABLE 2. 2,6-Dimethylpyridine-3,5-dicarboxylic Acid Esters (B)

Compound	R	mp, °C (crystallization solvent*)	Empirical formula	Found, %			Calc., %			Yield, %
				C	H	N	C	H	N	
XXVII	*n*-C_3H_7	44—50 (ethanol—water)	$C_{15}H_{21}NO_4$	64,4	7,7	5,3	64,5	7,6	5,0	67
XXVIII	*i*-C_3H_7	65—66 (ethanol—water)	$C_{15}H_{21}NO_4$	64,3	7,7	5,1	64,5	7,6	5,0	82
XXIX	*n*-C_4H_9	29—30	$C_{17}H_{25}NO_4$	66,8	7,9	4,5	66,4	8,2	4,6	37
XXX	*i*-C_4H_9	33—34	$C_{17}H_{25}NO_4$	66,8	8,0	4,5	66.4	8,2	4,6	49
XXXI	t-C_4H_9	108—109 (ethanol—water)	$C_{17}H_{25}NO_4$	67,1	8,4	4.3	66,4	8,2	4,6	62
XXXII	*n*-C_5H_{11}	33—34	$C_{19}H_{29}NO_4$	68,3	8,2	4.1	68,0	8,7	4,2	60
XXXIII	*i*-C_5H_{11}	~20	$C_{19}H_{29}NO_4$							72
Picrate XXXIII		77—78	$C_{19}H_{29}NO_4 \times$ $\times C_6H_3N_3O_7$	53.2	5,8	10,0	53,2	5.7	9,9	—
XXXIV	*n*-C_6H_{13}	31—32								52
Picrate XXXIV		80—81.5	$C_{21}H_{33}NO_4 \times$ $\times C_6H_3N_3O_7$	54,4	6,1	9,2	54,7	6,2	9,5	—
XXXV	Cyclohexyl	51—52	$C_{21}H_{29}NO_4$	70.3	8,3	3.9	70,2	8,1	3,9	66
XXXVI	*n*-C_7H_{15}	22—23								60
Picrate XXXVI		65—66	$C_{23}H_{37}NO_4 \times$ $\times C_6H_3N_3O_7$	56,3	6.9	9,0	56,1	6,5	9,0	—
XXXVII	*n*-C_8H_{17}	28—29								77
Picrate XXXVII		69—70	$C_{25}H_{41}NO_4 \times$ $\times C_6H_3N_3O_7$	57,2	7.1	8,8	57,4	6,8	8,6	—
XXXVIII	*n*-C_9H_{19}	23—24								80
Picrate XXXVIII		72—73	$C_{27}H_{45}NO_4 \times$ $\times C_6H_3N_3O_7$	58,7	7,5	8,6	58,6	7,2	8,3	—
XXXIX	*n*-$C_{10}H_{21}$	26—27								63
Picrate XXXIX		72—73	$C_{29}H_{49}NO_4 \times$ $\times C_6H_3N_3O_7$	59,6	7,7	8,0	59,6	7.4	8,0	—
XL	*n*-$C_{11}H_{23}$	38—39 (ethanol)								84
Picrate XL		72—73	$C_{31}H_{54}NO_4 \times$ $\times C_6H_3N_3O_7$	60,3	7.9	7.9	60,6	7.7	7,7	—
XLI	*n*-$C_{12}H_{25}$	36—37 (ethanol)	$C_{33}H_{57}NO_4$	74,4	11,1	3,0	74,5	10,8	2,6	88
XLII	*n*-$C_{16}H_{33}$	53—54 (dioxane)	$C_{41}H_{73}NO_4$	76,7	11,9	2,4	76,5	11,4	2,2	60
XLIII	C_2H_4OH	151—152 (ethyl acetate)	$C_{13}H_{17}NO_6$	54,8	6,2	5.3	55,1	6,1	5,0	72
XLIV	$C_2H_4OCH_3$	30—31								70
Picrate XLIV		96—98	$C_{15}H_{21}NO_6 \times$ $\times C_6H_3N_3O_7$	46,5	4,4	10,3	46,7	4,5	10,4	—
XLV	$C_2H_4OC_6H_{13}$	from 0 to 3	$C_{25}H_{41}NO_6$	66.1	9.0	3,0	66,5	9,2	3,1	76
XLVI	$C_2H_4OC_6H_5$	62—63 (hexane)	$C_{25}H_{25}NO_6$	68,9	5,7	3,0	69,0	5,8	3,2	89
XLVII	$CH_2C_6H_5$	88—89 (hexane)	$C_{23}H_{25}NO_4$	73,6	5,6	3,8	73,6	5,6	3,7	96
XLVIII	$CH_2COOC_2H_5$	76—77 (hexane)	$C_{17}H_{21}NO_8$	55,3	5,6	3,7	55,6	5,8	3,8	70
XLIX	$CH_2CH{=}CHC_6H_5$	85—86 (hexane)	$C_{27}H_{25}NO_4$	76,1	6,0	3,5	75,9	5,9	3,3	90
L	Furfuryl	69—71 (hexane)	$C_{19}H_{17}NO_6$	64.2	5,0	3.7	64,2	4,8	3,9	72

* If the solvent is not indicated, the compound was recrystallized from 95% ethanol by cooling (except for the picrates).

known analogs [8, 9]), but it is impossible to subject them to further purification by dissolving the pyridine bases in acid because of their lyophilic character, and distillation requires the use of a very high vacuum. Some pyridines B were purified by crystallization (with cooling), while others were characterized in the form of their picrates (Table 2).

The UV spectra of pyridines XXVII-L have three absorption bands: An intense maximum at 207 nm, a band at 236 nm, and a low-intensity absorption band (double maximum) at 270-280 nm (Table 3). More complex spectra are observed in the case of XLVI, XLIX, and L. In the case of L, the band at 236 nm is almost unnoticeable because of absorption of the furan ring.

Because of the specific character of the structure of the 1,4-dihydropyridines (a complex aminovinylcarbonyl system) these compounds display peculiar chemical properties: The presence of β-carbonyl groups deprives these compounds of the basicity characteristic for secondary amines, and they do not display the usual properties of carbonyl groups. This structural peculiarity also affects the IR spectrum. Some investigators [11] assert that because of conjugation of the aminovinylcarbonyl sys-

TABLE 3. Electronic Spectra of A and B

Compound	R	λ_{max}, nm (lg ε)
I[*]	n-C_3H_7	231 (4,12); 250 sh (3,85); 373 (3,74)
XXII	$C_2H_4OC_6H_5$	202 (4,48); 222 (4,51); 234 sh (4,33); 252 sh (4,09); 270 sh (3,74); 278 (3,58); 376 (3,95)
XXIII	$CH_2C_6H_5$	211 (4,38); 230 (4,33); 251 sh (4,04); 374 (3,85)
XXIV	$CH_2COOC_2H_5$	233 (4,15); 251 sh (3,94); 378 (3,83)
XXV	$CH_2CH{=}CHC_6H_5$	204 (4,72); 210 sh (4,69); 216 sh (4,55); 251 (4,66); 283 (3,60); 292 (3,51); 377 (3,86)
XXVI	Furfuryl	221 (4,41); 252 sh (3,97); 378 (3,86)
XXVII[†]	n-C_3H_7	207 (4,47); 235 (4,03); 274 (3,56); 282 (3,48)
XLVI	$C_2H_4OC_6H_5$	207 (4,63); 221 sh (4,39); 236 sh (4,11); 271 (3,86); 277 (3,81)
XLVII	$CH_2C_6H_5$	207 (4,59); 236 (4,09); 274 (3,62); 282 (3,56)
XLVIII	$CH_2COOC_2H_5$	207 (4,59); 236 (4,12); 274 (3,60); 282 (3,51)
XLIX	$CH_2CH{=}CHC_6H_5$	204 (4,91); 210 sh (4,89); 216 sh (4,67); 250 (4,66); 282 (3,92); 292 (3,56)
L	Furfuryl	207 (4,65); 236 sh (4,23); 274 (3,64); 282 (3,56)

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[*] Esters II-XXI have practically identical spectra: 232 ± 1 (4.11-4.29); sh 251 ± 1 (3.85-4.03) and 373 ± 2 (3.75-3.88).

[†] Pyridines XXVIII-XLV have practically identical spectra: 207 ± 1 (4.41-4.59); 235 ± 1 (3.89-4.13); 274 ± 1 (3.48-3.62); 282 ± 1 (3.40-3.56).

tem, the absorption peaks should be assigned to the vibrations of the entire conjugated system rather than to the vibrations of definite bonds. However, the absorption associated with the stretching vibrations of the NH group and, to a certain degree, of the CO group can be indicated sufficiently definitely (although there are, of course, deviations from the expected values), and the absorption caused by substituents that do not enter into conjugation with the ring or the carbonyl group can be indicated completely definitely.

The IR spectra of esters A (I-XXVI and the methyl and ethyl esters) are extremely similar to one another (Table 4). The intensity of the ν_{CH_2} vibrations increase as the alkyl or alkoxyethyl grouping of the ester group of esters A becomes longer, and ν_{asCH_3} (~2970 cm^{-1}), ν_{asCH_2} (~2950 cm^{-1}), ν_{sCH_3} (~2890 cm^{-1}), and ν_{sCH_2} (~2870 cm^{-1}) can be distinguished. The isopropyl and tert-butyl groups (esters II and V) give increased ν_{asCH_3} values. The intensity of the ν_{sCH_2} band increases in the spectra of compounds in which the number of methylene groups is higher than four, and one observes superimposition on the ν_{sCH_3} band; of course, cyclohexyl ester IX does not give a ν_{CH_3} band. The introduction of a phenyl group in the ester grouping (esters XXII, XXIII, and XXV) is also reflected in the IR spectra: the absorption at 3000 cm^{-1} is overlapped, but characteristic maxima appear at ~700, ~750, and ~1600 cm^{-1}.

A change in the ester group apparently has little effect on the absorption band of the CO group at 1700 cm^{-1}. The unexpected decrease in the frequency of these vibrations in the case of the isopropyl ester (II) apparently should be explained by intermolecular interaction, inasmuch as this sort of decrease in the frequency is not observed in acetonitrile solution.

The presence in XXIV of ester groups that are not conjugated with the aminovinylcarbonyl system of the dihydropyridine brings about the appearance of an absorption band of CO groups at 1753 cm^{-1}, and maxima at 1714 and 1688 cm^{-1} are observed in place of the absorption at 1700 and 1650 cm^{-1}. It seems likely that the absorption at ~1125 and ~1220 cm^{-1} corresponds to the stretching vibrations of the ester group.

The absorption at ~3360 cm^{-1} is due to vibrations of the N–H bond of esters A, on which changes in the ester group have little effect.

Judging from the IR spectrum, hydroxyethyl ester XVII has a strong intermolecular hydrogen bond. Vibrations of the OH group at 3400-3700 cm^{-1} are therefore not observed in the spectrum of solid XVII (KBr pellet on Nujol suspension), and this band appears only as a shoulder at 3260 cm^{-1} on the absorption band of the NH group.

A strong absorption band at ~ 760 cm^{-1} is observed in all of the spectra of esters A, probably because of vibrations of the ring C–H bonds.

The IR spectra of the oxidized products are similar to the spectrum of the known ethyl ester of 2,6-dimethylpyridine-3,5-dicarboxylic acid (Table 4). The absorption in the region of vibrations of double bonds changes markedly. The frequency of the vibrations of the CO group increases. In the investigated cases

TABLE 4. IR Spectra of Esters A and Pyridines B*

Compound	R	2800-3600 cm^{-1}	1500-1750 cm^{-1}
I	n-C_3H_7	3363 vs, 2980 s, 2950 m, 2895 m	1700 vs, 1661 vs, sh 1635 s, 1510 vs
II	i-C_3H_7	3373 vs, 2990 s, 2947 m, 2888 w	1673 vs, 1650 vs, 1508 vs,
III	n-C_4H_9	3355 vs, 2973 s, sh 2948m, 2887m	1702 vs 1661vs, sh 1650 s, sh 1635s, 1507 vs,
IV	i-C_4H_9	3358 vs, 2975 s, 2948 m, 2887 m	1703 vs, 1661 vs, 1507 vs
V	tert-C_4H_9	3335 vs, 3114 w, 2980 m, 2944w	1697 vs, 1647 vs, 1500 vs
VI	n-C_5H_{11}	3356 vs, 2972 s, 2944 s, 2883 m	1698 vs, 1660 vs, 1649 vs, 1508vs,
VII	i-C_5H_{11}	3353 vs, 2971 s, 2945s, 2885 m	1702 vs, 1660vs, sh 1650 vs, sh 1635 s,1508 vs
VIII	n-C_6H_{13}	3363 vs, 2970 s, 2941 s, sh, 2884 w, 2870 m	1700 vs, 1664 vs, sh, 1655vs, sh, 1635 s, 1517 vs,
IX	Cyclohexyl	3363vs, 2949 vs, 2870vs,	1701 vs, 1661vs, sh, 1635s, 1505 vs,
X	n-C_7H_{15}	3363 vs, 2970 vs, 2940 vs, 2868s,	1698vs, 1663vs, sh, 1635 s, 1518 vs
XI	n-C_8H_{17}	3363 vs, 2968 vs, 2937 vs, 2867 s,	1699 vs, 1662vs, sh, 1635s, 1517 vs,
XII	n-C_9H_{19}	3362 vs, 2968 vs, 2933 vs, 2862 vs	1698 vs, 1660vs, sh, 1635s, 1518 vs
XIII	n-$C_{10}H_{21}$	3359vs, 2968 s, 2933 vs, 2861 vs,	1697 vs, 1660 vs, sh, 1635 s, 1517 vs,
XIV	n-$C_{11}H_{23}$	3360 vs, 2968 s, 2934 vs, 2861 vs,	1697 vs, 1661 vs, sh, 1635 s, 1520 vs,
XV	n-$C_{12}H_{25}$	3358 vs, 2969s, 2932 vs, 2862 vs,	1697 vs, 1660vs, sh, 1635 s, 1517 vs,
XVI	n-$C_{16}H_{33}$	3357 vs, 2967 s, 2932 vs, 2861 vs,	1697 vs, 1660vs, sh, 1634 s, 1520 vs,
XVII	C_2H_4OH	3360 vs, 2974 m, 2940 m, 2887 m, 2875 m,	1702 s, 1659 vs, sh, 1635 s, 1508 vs,
XVIII	$C_2H_4OCH_3$	3363 vs, 2998 m, 2955 m, 2910 m, 2875 m, 2833 w,	1699 vs, 1661 vs, sh, 1635 s, 1517 vs
XIX	$C_2H_4OC_2H_5$	3363 vs, 2987 m, 2875 m,	1699 vs, 1663 vs, sh, 1633 s, 1519 vs
XX	$C_2H_4OC_4H_9$	3365 vs, 2973 s, 2945 s, 2877 s,	1700 s, 1663 vs, sh, 1633 s, 1518 vs,
XXI	$C_2H_4OC_6H_{13}$	3363 vs, 2970 s, 2943 vs, 2870 vs	1700 vs, 1660vs, sh 1635 s, 1518 vs
XXII	$C_2H_4OC_6H_5$	3365 vs, 3078 w, 2988 w, 2953 w, 2890 w, 2865w,	1705 vs, 1650 vs, 1603 s, 1589 m, 1500 vs
XXIII	$CH_2C_6H_5$	3360vs (Weak absorption without distinct maxima)	1703m, 1645 vs, sh, 1635 vs, sh, 1588 m, 1500 vs,
XXIV	$CH_2COOC_2H_5$	3402 vs, 3000 w, 2955 w, 2875 w,	1753 vs, 1714 vs, 1688 vs, 1662 s, 1635 m, 1500 vs,
XXV	$CH_2CH{=}CHC_6H_5$	3362 vs, 2936 w, 2888 w, 2870 w	sh,1695 s, 1670 vs, 1650 vs, sh, 1635 s, sh, 1600 m, 1515 vs
XXVI†	Furfuryl	3375 vs, 3168 w, 2970 w, 2935 w, 2900 w, 2875 w,	1698 vs, 1660 vs, sh, 1635 vs, sh, 1615m, 1507 vs,
XXVIII	i-C_3H_7	2997 s, 2948 w,	1720 vs, 1598m, 1553 m,
XXXI	tert-C_4H_9	3015w, 2991m, 2950 w	1717 vs, 1599m, 1551 m,
XXXII	n-C_5H_{11}	2973 s, 2947 s, 2885 w	1728 vs, 1600 m, 1558 w,
XLVIII	$CH_2COOC_2H_5$	3025 w, 2992 m	1752 vs, 1731 vs, 1603 w, 1557m

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*The IR spectra were recorded at 700-3600 cm^{-1} but are presented completely for ethyl esters A and B: A, R=C_2H_3–3364 vs, 3130 w, 2998–2990 m, 2950 w, 2935 w, 2910 w, 2875 w, 1695 vs, 1659 vs, sh, 1635 s, 1510 vs, 1473 w, 1450 w, 1392 w, 1370 m, 1323 s, 1303 vs, 1268 m, 1217 vs, 1154 w, 1121 w, 1095 s, 1062 s, 1025–1015 w, 850 w, 760 S; B, R=C_2H_5– 2297–2990 m, 2946 W, 1726 vs, 1595 m, 1558 w, 1479 w, 1447 m, sh, 1400 m, 1382 m, 1370 S, 1299 vs, 1256 s, 1226 vs, 1209 m, 1163 w, 1128 vs, 1113 s, 1050 m, 1030 w, 970 w, 870 w, 777 s.
The spectra were taken in nujol and hexachlorobutadiene (1500-1300 cm^{-1}).

(XXVIII, XXXI, XXXII, and XLVIII) it is noted that transition from the ethyl or pentyl ester (XXXII) to the isopropyl ester (XXVIII) and then to the tert-butyl ester (XXXI) is accompanied by a shift of this band from 1726 to 1714 cm^{-1}, and a small shift to the opposite side is observed in the case of carbethoxymethyl ester XLVIII. Another ester carbonyl group at 1752 cm^{-1} is also observed in the spectrum of XLVIII. All pyridines B absorb at 777 cm^{-1}, and this probably corresponds to the vibrations of the γ-CH bond. In contrast to esters A, these vibrations are observed at higher frequencies.

EXPERIMENTAL

The IR spectra were recorded with a UR-20 spectrometer. Most of the spectra were obtained from KBr pellets (1.0 mg of the compound per 500 mg of KBr). The UV spectra of ethanol solutions were recorded with a Specord UV-vis spectrophotometer.

The starting reagents for the synthesis of the dihydropyridines – acetoacetic esters – were obtained by known methods: from the appropriate alcohols (hydroxy compounds) and diketene [12] for the synthesis of I-VIII, XVII-XX, XXIV, and XXVI, and from ethyl acetoacetate by transesterification [13] for the remaining acetoacetic esters.

2,6-Dimethyl-1,4-dihydropyridine-3,5-dicarboxylic Acid Esters (Table 1). A mixture of 0.2 mole of acetoacetic ester, 4.2 g (0.03 mole) of hexamethylenetetramine, 3.9 g (0.05 mole) of ammonium acetate, and 50 ml of ethanol was refluxed for 20 min. The mixture was then cooled, and the light-yellow* precipitate was removed by filtration and recrystallized.

In the preparation of V-VIII and XVIII-XX the reaction mixtures were diluted with water for more complete isolation of the products. Ester IX was obtained as an oil, which slowly began to crystallize. It is preferable to synthesize ester XVII in 90% dioxane. The synthetic results and the physical constants for the esters obtained in this research are given in Tables 1, 3, and 4.

2,6-Dimethylpyridine-3,5-dicarboxylic Acid Esters (Table 2). A mixture of 0.03 mole of 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylic acid ester (A) and 7.38 g (0.03 mole) of chloranil in 50 ml of benzene was heated to the boiling point. After the solid dihydropyridine had dissolved completely and the yellow color of the solution (from chloranil) had disappeared, the solution was cooled, and the resulting precipitate of tetrachlorohydroquinone was removed by filtration and washed with a cold 10% solution of NaOH and water. The solution was dried with anhydrous sodium sulfate, and the benzene was evaporated to give colorless pyridines B.

Compound XLIII was only slightly soluble in benzene, and it was therefore isolated from the reaction mixture with hydrochloric acid. Purification by dissolving in acid can be also be used for XXVII-XXX. The physical constants, yields, and spectral characteristics of B are given in Tables 2-4.

Preparation of Picrates. A hot 5% solution of picric acid in absolute ethanol was mixed with a hot solution of pyridine base B in ethanol. The mixture was then cooled, and the resulting bright-yellow picrate was removed by filtration and recrystallized from ethanol.

The melting points and results of microanalyses of the picrates are given in Table 2.

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* Ester XXV was bright-yellow.

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