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# Heterocyclization of Functionalized Heterocumulenes with C,N-, C,O- , and C,S-Binucleophiles: XI.* Synthesis of Dialkyl 2-Oxo-3,6-diaryl-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylates by Cyclocondensation of 1-Chlorobenzyl Isocyanates with Dialkyl Anilinofumarates

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**Abstract**—1-Chlorobenzyl isocyanates react with *N*-arylfumarates with the formation of dialkyl 2-oxo-3,6-diaryl-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylates that on alkaline hydrolysis are converted into 6-alkoxycarbonyl-1,4-diaryl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic acids. The condensation of 1-chloro-1-phenyl-2,2,2-trifluoroethyl isocyanate with N-arylfumarates results in dialkyl 6-oxo-2,3-diaryl-2-trifluoromethyl-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylates.

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The cyclization of 1-chlorobenzyl isocyanates with deactivated enamines that we have formerly found is a convenient way of preparation of 3,4-dihydropyrimidine systems [2]. In particular, the employment as the C,N-binucleophilic component 2-aroyl(nitro)-S,N-ketenacetals [1, 3] made it possible to obtain previously unknown Biginelli compounds, 5,6-bifunctionally substituted 3,4-dihydropyrimidin-2(1*H*)-ones. In extension of the research on the design of the polyfunctional partially hydrogenated pyrimidines we report here on the new reaction involving deactivated enamines, dialkyl anilinofumarates. The latter are used in the syntheses of versatile heterocyclic compounds. For instance, their thermal intramolecular cyclization provides quinoline-2-carboxylic acids derivatives [4–7], the condensation with amines gives pyrrole-2,5-diones [8, 9]. The reactions with electrophilic reagents where the N-arylfumarates act as 1,3-binucleophiles, do not go beyond the examples of reactions with oxalyl chloride [10] and chlorocarbonylsulfophenyl chloride [11]. Quite recently [12] a publication appeared on the Mannich synthesis of 1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylic acid esters proceeding from the diethyl N-phenylfumarate.

We found that the reaction of 1-chlorobenzyl isocyanates **Ia–If** with dialkyl N-arylaminofumarates **IIa–IIf** in toluene at 15–20°C led to the formation of dialkyl 2-oxo-3,6-diaryl-1,2,3,6-tetrahydro-4,5-dicarboxylates **IIIa–IIIo** in 41–79% yields (Scheme 1). Apparently similarly to the cyclocondensation involving the S,N-ketenacetals [1, 3] the more nucleophilic carbon atom of the aminofumarate **II** attacks the activated C=N bond of the N-chloroformyl imine form of isocyanate **I** [13] resulting in the formation of intermediate A. Its structure originating from the prototropy in the triade N–C=C permits under relatively mild conditions the formation of the pyrimidine ring by the attack of the imine nitrogen on the chlorocarbamoyl group.

The structure of compounds **IIIa–IIIo** was confirmed by the combination of physicochemical investigations. Their $^1$H NMR spectra are characterized by the doublets of the proton H$^6$ at 5.27–5.55 ppm and of the NH proton at 8.31–8.62 ppm with the coupling constant 3.0–3.5 Hz. The methoxy groups of diesters **IIIa–IIIh** appear as

* For Communication X, see [1].

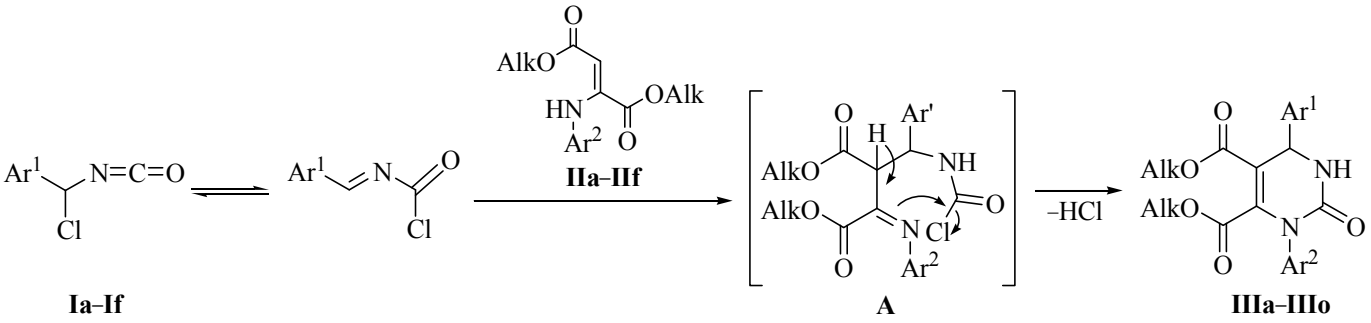
singlets at 3.36–3.47 and 3.54–3.62 ppm, and the ethoxy groups of diesters **IIIi–IIIo** give rise to triplets at 0.92–0.97 and 1.08–1.13 ppm and quartets at 3.87–3.93 and 4.00–4.06 ppm. In the $^{13}C$ NMR spectra the signals of the carbon atoms of the partially hydrogenated pyrimidine ring are observed in the regions 49–53 ($C^6$), 100–103 ($C^5$), 142–143 ($C^4$), and 150–151 ($C^2$) ppm.

The IR spectra of compounds **IIIa–IIIo** recorded in KBr pellets contain strong absorption bands of the C=O groups of the pyrimidine ring at 1700–1705 $cm^{-1}$ and of alkoxycarbonyl moieties at 1735–1745 $cm^{-1}$; the same bands are observed in the spectra of $CH_2Cl_2$ solutions. In the absorption range of the stretching vibrations of N–H bond in the spectra taken in KBr two broad bands are observed in the region 3120–3140 and 3235–3245 $cm^{-1}$ indicating that the compounds exist as dimers. In the $CH_2Cl_2$ solutions instead of these bands a single absorption band appears at 3420–3425 $cm^{-1}$ showing the decomposition of the intermolecular associates involving the NH groups.

We formerly showed [1] that the regiodirection of the cyclocondensation changed in the reaction of S,N-ketenacetals with 1-aryl-1-chloro-2,2,2-trifluoroethyl isocyanates. We demonstrated by examples of reactions of 1-chloro-1-phenyl-2,2,2-trifluoroethyl isocyanate (**IV**) with anilinofumarates **IIb** and **IIf** that unlike the process involving 1-chlorobenzyl isocyanates **I** at the room temperature products B formed from C-carbamoylation which was detected by the presence in the $^{19}F$ NMR spectra of the reaction mixture of signals in the region –69...–70 ppm. Intermediates B only at heating for 12 h in the boiling toluene were converted into dialkyl 6-oxo-2,3-diaryl-2-trifluoromethyl-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylates **Va** and **Vb** in 20–22% yield that evidently was caused by the low nucleophilicity of the secondary amino group insufficient for the easy intramolecular cyclization (Scheme 2).

The most compelling proves of the structure of compounds **Va** and **Vb** are the $^{19}F$ NMR spectra where the signals at –75...–74 ppm correspond to the $CF_3$ group

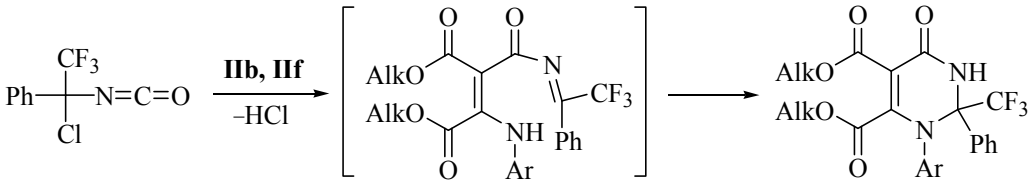
**Scheme 1.**




**Ia–If**

**I**, $Ar^1$ = Ph (**a**), 2-$FC_6H_4$ (**b**), 3-$BrC_6H_4$ (**c**), 3-$NO_2C_6H_4$ (**d**), 4-$NO_2C_6H_4$ (**e**), 3,4-$Cl_2C_6H_3$ (**f**); **II**, Alk = Me, $Ar^2$ = Ph (**a**), 4-$MeC_6H_4$ (**b**), 4-$ClC_6H_4$ (**c**), 4-$BrC_6H_4$ (**d**); Alk = Et, $Ar^2$ = 4-$ClC_6H_4$ (**e**), 4-$BrC_6H_4$ (**f**); **III**, Alk = Me: $Ar^1$ = $Ar^2$ = Ph (**a**); $Ar^1$ = Ph, $Ar^2$ = 4-$BrC_6H_4$ (**b**); $Ar^1$ = 2-$FC_6H_4$, $Ar^2$ = 4-$ClC_6H_4$ (**c**); $Ar^1$ = 3-$BrC_6H_4$, $Ar^2$ = 4-$MeC_6H_4$ (**d**); $Ar^1$ = 4-$NO_2C_6H_4$, $Ar^2$ = Ph (**e**), 4-$ClC_6H_4$ (**f**), 4-$BrC_6H_4$ (**g**), 4-$MeC_6H_4$ (**h**); Alk = Et: $Ar^1$ = Ph, $Ar^2$ = 4-$ClC_6H_4$ (**i**); $Ar^1$ = 2-$FC_6H_4$, $Ar^2$ = 4-$ClC_6H_4$ (**j**), 4-$BrC_6H_4$ (**k**); $Ar^1$ = 3-$BrC_6H_4$, $Ar^2$ = 4-$ClC_6H_4$ (**l**); $Ar^1$ = 3-$NO_2C_6H_4$, $Ar^2$ = 4-$BrC_6H_4$ (**m**); $Ar^1$ = 4-$NO_2C_6H_4$, $Ar^2$ = 4-$ClC_6H_4$ (**n**); $Ar^1$ = 3,4-$Cl_2C_6H_4$, $Ar^2$ = 4-$ClC_6H_4$ (**o**).

**Scheme 2.**




**IV**

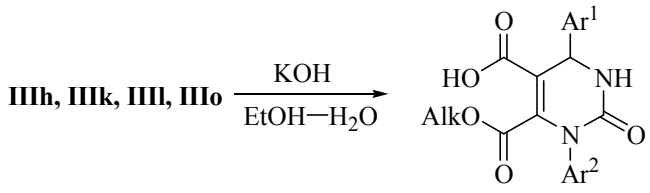
**V**, Alk = Me, Ar = 4-$MeC_6H_4$ (**a**); Alk = Et, Ar = 4-$BrC_6H_4$ (**b**).

in the aminal fragment $NC(CF_3)PhNH$, and the $^{13}C$ NMR spectra containing a characteristic quartet of atom $C^2$ in the region 79–80 ppm [14]. In the IR spectra of these compounds recorded in the KBr pellets the C=O bond of the lactam fragment gives rise to two bands at 1670 and 1690–1695 $cm^{-1}$, and of the exocyclic ester groups, to the band at 1742–1745 $cm^{-1}$. The vibrations of the N–H bond are characterized by the bands at 3095 and 3190 $cm^{-1}$, which in the $CH_2Cl_2$ solution transform into the band of the monomer structure at 3400 $cm^{-1}$.

The observed recently high interest directed on the polyfunctional 3,4-dihydropyrimidin-2(1*H*)-ones is due in a large measure to the pharmacological properties of this unique structure [15–17]. Among the common initial compounds for the synthesis of these derivatives 4-aryl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic acids should be mentioned [18–21] that as a rule are obtained from the corresponding esters by hydrogenolysis or alkaline hydrolysis [22]. Therefore we deemed useful to investigate the behavior of diesters **IIIh, IIIk, IIIl**, and **IIIo** under the conditions of alkaline hydrolysis.

It was established that the presence in the structure of compounds **III** of two ester groups and an N-aryl substituent makes them relatively inert to the treatment with water-alcoholic alkali solution. For instance, the mentioned compounds were not hydrolyzed by boiling over 7 h with an equimolar amount of KOH in a water-alcohol mixture. A selective hydrolysis of a single ester group was achieved by boiling for 3 h with the double excess of alkali in a mixture ethanol–water, 5 : 1. As a result 6-alkoxycarbonyl-1,4-diaryl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic acids **VIa–VId** were obtained (Scheme 3). Analysis of their $^1H$ NMR spectra lacking the downfield signals of alkoxy groups indicated that the ester group in the position 5 of the pyrimidine ring underwent the hydrolysis. This conclusion was confirmed by the $^{13}C$ NMR spectra recorded without decoupling

**Scheme 3.**




**VIa–VId**

**VI**, Alk = Me, $Ar^1$ = 4-$NO_2C_6H_4$, $Ar^2$ = 4-$MeC_6H_4$ (**a**); Alk = Et: $Ar^1$ = 2-$FC_6H_4$, $Ar^2$ = 4-$BrC_6H_4$ (**b**); $Ar^1$ = 3-$BrC_6H_4$, $Ar^2$ = 4-$ClC_6H_4$ (**c**); $Ar^1$ = 3,4-$Cl_2C_6H_3$, $Ar^2$ = 4-$ClC_6H_4$ (**d**).

from protons. In this spectrum of compound **VIc** the most downfield signal appears at 165.17 ppm as a doublet, $^3J_{C–H}$ 3.0 Hz, and corresponds to the carbon atom of the carboxy group coupled with the proton in the position *4* of the heterocycle, whereas the triplet with $^3J_{C–H}$ 3.7 Hz at 162.00 ppm corresponds to the carbonyl carbon of the ester group.

The longer heating at the alkaline hydrolysis according to the data of GC-MS analysis provided a complex mixture of mono- and diacids and their decarboxylation products.

The $^1H$ NMR spectra of acids **VIa–VId** alongside the signals of the alkoxy substituents [3.39 (s), 0.94–0.99 (t), 3.85–3.89 ppm (q)] contain doublets of the proton $H^4$ of the hydrogenated pyrimidine ring with the coupling constant 1.0–1.8 Hz. In the $^{13}C$ NMR spectra of compounds **VIa** and **VId** the corresponding atom $C^4$ gives rise to the signal at 49–53 ppm. The IR spectra in the absorption region of C=O bonds are characterized by a strong wide band with weakly pronounced maxima at 1650, 1680–1685, 1705–1710, and 1730–1735 $cm^{-1}$, in the absorption range of the OH bond a wide band is present at 2400–2650 $cm^{-1}$, the vibrations of the NH bond appear as two bands at 3085 and 3235 $cm^{-1}$.

## EXPERIMENTAL

IR spectra compounds in KBr pellets were recorded on a spectrophotometer UR-20. $^1H$ and $^{13}C$ NMR spectra were registered on a spectrometer Bruker Avance DRX-500 (500.13, 125.75 MHz respectively), internal reference TMS. GC-MS analysis was performed on an instrument Aligent 1100/DAD/HSD/VLG 119562. 1-Chlorobenzyl isocyanates **Ia–If** and 1-aryl-2,2,2-trifluoro-1-chloroethyl isocyanate (**IV**) were prepared by procedures [2] and [15] respectively.

**Dialkyl 3,6-diaryl-2-oxo-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylates IIIa–IIIo**. To a solution of 5 mmol of N-arylaminofumarate **IIa–IIf** in 20 ml of anhydrous toluene was added 5 mmol of isocyanate **Ia–If**, and the mixture was left standing at room temperature for 24 h. The separated precipitate was filtered off, dried, and recrystallized from ethanol.

**Dimethyl 2-oxo-3,6-diphenyl-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate** (**IIIa**). Yield 46%, mp 239–241°C. IR spectrum, ν, $cm^{-1}$: 3240, 3120 (NH), 1740, 1702 (C=O). $^1H$ NMR spectrum, δ, ppm: 3.36 s (3H, $CH_3O$), 3.59 s (3H, $CH_3O$), 5.28 d (1H, $H^6$, *J* 3.0 Hz), 7.18–7.41 m ($10H_{arom}$), 8.35 d (1H, NH, *J* 3.0 Hz). $^{13}C$ NMR spectrum, δ, ppm: 51.98 ($CH_3O$), 52.41

($CH_3O$), 53.07 ($C^6$), 102.79 ($C^5$), 126.26, 128.05, 128.66, 128.73, 128.93, 129.67, 136.13, 142.76 ($C_{arom}$), 143.03 ($C^4$), 150.98 ($C^2$), 162.14 (C=O), 163.88 (C=O). Found, %: C 65.83; H 5.07; N 7.41. $[M + 1]^+$ 367. $C_{20}H_{18}N_2O_5$. Calculated, %: C 65.57; H 4.95; N 7.65. M 366.

**Dimethyl 3-(4-bromophenyl)-2-oxo-6-phenyl-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (IIIb).** Yield 49%, mp 191–193°C. IR spectrum, ν, $cm^{-1}$: 3235, 3130 (NH), 1737, 1700 (C=O). $^1H$ NMR spectrum, δ, ppm: 3.47 s (3H, $CH_3O$), 3.62 s (3H, $CH_3O$), 5.31 d (1H, $H^6$, *J* 3.3 Hz), 7.17 d ($2H_{arom}$, *J* 8.5 Hz), 7.35–7.44 m ($5H_{arom}$), 7.60 d ($2H_{arom}$, *J* 8.5 Hz), 8.41 d (1H, NH, *J* 3.3 Hz). $^{13}C$ NMR spectrum, δ, ppm: 52.04 ($CH_3O$), 52.64 ($CH_3O$), 53.12 ($C^6$), 103.24 ($C^5$), 121.95, 126.29, 128.08, 128.93, 131.74, 131.80, 135.48, 142.43 ($C_{arom}$), 142.59 ($C^4$), 150.64 ($C^2$), 162.08 (C=O), 163.79 (C=O). Found, %: C 53.73; H 3.97; N 6.48. $[M + 1]^+$ 446. $C_{20}H_{17}BrN_2O_5$. Calculated, %: C 53.95; H 3.85; N 6.29. M 445.

**Dimethyl 2-oxo-6-(2-fluorophenyl)-3-(4-chlorophenyl)-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (IIIc).** Yield 41%, mp 255–257°C. IR spectrum, ν, $cm^{-1}$: 3245, 3135 (NH), 1740, 1705 (C=O). $^1H$ NMR spectrum, δ, ppm: 3.43 s (3H, $CH_3O$), 3.54 s (3H, $CH_3O$), 5.51 d (1H, $H^6$, *J* 3.0 Hz), 7.21–7.47 m ($8H_{arom}$), 8.33 d (1H, NH, *J* 3.0 Hz). $^{13}C$ NMR spectrum, δ, ppm: 49.48 ($C^6$), 51.92 ($CH_3O$), 52.58 ($CH_3O$), 100.83 ($C^5$), 115.95 d ($J_{C–F}$ 21.2 Hz), 124.76, 128.75, 129.31, 129.55 d ($J_{C–F}$ 19.4 Hz), 130.30, 131.60, 133.40, 135.12, 160.26 d ($C_{arom}$, $J_{C–F}$ 245.0 Hz), 142.90 ($C^4$), 150.19 ($C^2$), 162.01 (C=O), 163.61 (C=O). Found, %: C 57.61; H 3.72; N 6.47. $[M + 1]^+$ 419.6. $C_{20}H_{16}ClFN_2O_5$. Calculated, %: C 57.36; H 3.85; N 6.69. M 418.6.

**Dimethyl 6-(3-bromophenyl)-2-oxo-3-(4-tolyl)-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (IIId).** Yield 67%, mp 199–200°C. IR spectrum, ν, $cm^{-1}$: 3235, 3125 (NH), 1739, 1703 (C=O). $^1H$ NMR spectrum, δ, ppm: 2.35 s (3H, $CH_3$), 3.41 Cs(3H, $CH_3O$), 3.61 s (3H, $CH_3O$), 5.27 d (1H, $H^6$, *J* 3.3 Hz), 7.03 d ($2H_{arom}$, *J* 8.4 Hz), 7.30 d ($2H_{arom}$, *J* 8.4 Hz), 7.39 d ($2H_{arom}$, *J* 8.4 Hz), 7.49–7.55 m ($2H_{arom}$), 8.36 d (1H, NH, *J* 3.3 Hz). $^{13}C$ NMR spectrum, δ, ppm: 20.66 ($CH_3$), 52.05 ($CH_3O$), 52.46 ($CH_3O$), 52.50 ($C^6$), 101.91 ($C^5$), 121.90, 125.12, 129.15, 129.25, 129.40, 130.91, 131.33, 133.32, 138.35, 143.52 ($C_{arom}$), 145.26 ($C^4$), 150.81 ($C^2$), 161.95 (C=O), 163.69 (C=O). Found, %: C 55.24; H 4.03; N 6.25. $[M + 1]^+$ 460. $C_{21}H_{19}BrN_2O_5$. Calculated, %: C 54.92; H 4.17; N 6.10. M 459.

**Dimethyl 6-(4-nitrophenyl)-2-oxo-3-phenyl-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (IIIe).** Yield 58%, mp 242–244°C. IR spectrum, ν, $cm^{-1}$: 3240, 3125 (NH), 1735, 1705 (C=O). $^1H$ NMR spectrum, δ, ppm: 3.38 s (3H, $CH_3O$), 3.60 s (3H, $CH_3O$), 5.44 d (1H, $H^6$, *J* 3.3 Hz), 7.21 m ($2H_{arom}$), 7.42 m ($3H_{arom}$), 7.68 d ($2H_{arom}$, *J* 8.7 Hz), 8.30 d ($2H_{arom}$, *J* 8.7 Hz), 8.51 d (1H, NH, *J* 3.3 Hz). $^{13}C$ NMR spectrum, δ, ppm: 52.08 ($CH_3O$), 52.48 ($CH_3O$), 52.74 ($C^6$), 101.74 ($C^5$), 124.27, 127.78, 128.64, 128.86, 129.76, 135.90, 143.56, 147.21, 149.73 ($C_{arom}$), 143.56 ($C^4$), 150.64 ($C^2$), 161.85 (C=O), 163.61 (C=O). Found, %: C 58.18; H 4.04; N 10.37. $[M + 1]^+$ 412. $C_{20}H_{17}N_3O_7$. Calculated, %: C 58.39; H 4.17; N 10.21. M 411.

**Dimethyl 6-(4-nitrophenyl)-2-oxo-3-(4-chlorophenyl)-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (IIIf).** Yield 71%, mp 218–220°C. IR spectrum, ν, $cm^{-1}$: 3235, 3130 (NH), 1745, 1705 (C=O). $^1H$ NMR spectrum, δ, ppm: 3.45 s (3H, $CH_3O$), 3.60 s (3H, $CH_3O$), 5.47 d (1H, $H^6$, *J* 3.5 Hz), 7.28 d ($2H_{arom}$, *J* 8.7 Hz), 7.48 d ($2H_{arom}$, *J* 8.7 Hz), 7.67 d ($2H_{arom}$, *J* 8.7 Hz), 8.29 d ($2H_{arom}$, *J* 8.7 Hz), 8.59 d (1H, NH, *J* 3.5 Hz). $^{13}C$ NMR spectrum, δ, ppm: 52.12 ($CH_3O$), 52.69 ($CH_3O$), 52.80 ($C^6$), 102.18 ($C^5$), 124.24, 127.85, 128.75, 131.62, 133.56, 134.82, 147.23, 149.56 ($C_{arom}$), 143.07 ($C^4$), 150.39 ($C^2$), 161.81 (C=O), 163.53 (C=O). Found, %: C 54.06; H 3.57; N 9.31. $[M + 1]^+$ 446. $C_{20}H_{16}ClN_3O_7$. Calculated, %: C 53.88; H 3.62; N 9.43. M 445.

**Dimethyl 3-(4-bromophenyl)-6-(4-nitrophenyl)-2-oxo-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (IIIg).** Yield 76%, mp 224–226°C. IR spectrum, ν, $cm^{-1}$: 3245, 3130 (NH), 1740, 1703 (C=O). $^1H$ NMR spectrum, δ, ppm: 3.46 s (3H, $CH_3O$), 3.61 s (3H, $CH_3O$), 5.55 d (1H, $H^6$, *J* 3.0 Hz), 7.27 d ($2H_{arom}$, *J* 8.5 Hz), 7.64 d ($2H_{arom}$, *J* 8.5 Hz), 7.71 d ($2H_{arom}$, *J* 8.5 Hz), 8.32 d ($2H_{arom}$, *J* 8.5 Hz), 8.62 d (1H, NH, *J* 3.0 Hz). $^{13}C$ NMR spectrum, δ, ppm: 52.11 ($CH_3O$), 52.67 ($CH_3O$), 52.80 ($C^6$), 102.17 ($C^5$), 122.08, 124.20, 127.83, 131.69, 131.87, 135.26, 147.19, 149.53 ($C_{arom}$), 142.97 ($C^4$), 150.31 ($C^2$), 161.79 (C=O), 163.50 (C=O). Found, %: C 49.18; H 3.41; N 8.40. $[M]^+$ 490. $C_{20}H_{16}BrN_3O_7$. Calculated, %: C 49.00; H 3.29; N 8.57. M 490.

**Dimethyl 6-(4-nitrophenyl)-2-oxo-3-(4-tolyl)-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (IIIh).** Yield 62%, mp 275–277°C. IR spectrum, ν, $cm^{-1}$: 3230, 3130 (NH), 1730, 1705 (C=O). $^1H$ NMR spectrum, δ, ppm: 2.35 s (3H, $CH_3$), 3.40 s (3H, $CH_3O$), 3.59 s (3H, $CH_3O$), 5.43 d (1H, $H^6$, *J* 3.3 Hz), 7.09 d ($2H_{arom}$, *J* 8.1 Hz), 7.20 d ($2H_{arom}$, *J* 8.1 Hz), 7.66 d ($2H_{arom}$,

*J* 8.4 Hz), 8.29 d (2$H_{arom}$, *J* 8.4 Hz), 8.47 d (1H, NH, *J* 3.3 Hz). $^{13}$C NMR spectrum, δ, ppm: 20.64 ($CH_3$), 52.05 ($CH_3O$), 52.50 ($C^6$), 52.73 ($CH_3O$), 101.51 ($C^5$), 124.24, 127.76, 129.11, 129.46, 133.30, 138.39, 147.19, 149.78 ($C_{arom}$), 143.76 ($C^4$), 150.73 ($C^2$), 161.87 (C=O), 163.62 (C=O). Found, %: C 59.53; H 4.27; N 9.99. $[M + 1]^+$ 426. $C_{21}H_{19}N_3O_7$. Calculated, %: C 59.29; H 4.50; N 9.88. M 425.

**Diethyl 2-oxo-6-phenyl-3-(4-chlorophenyl)-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (IIIi).** Yield 44%, mp 185–186°C. IR spectrum, ν, $cm^{-1}$: 3235, 3140 (NH), 1730, 1700 (C=O). $^1$H NMR spectrum, δ, ppm: 0.92 t (3H, $CH_3$, *J* 7.5 Hz), 1.10 t (3H, $CH_3$, *J* 7.2 Hz), 3.87 q (2H, $CH_2O$, *J* 7.5 Hz), 4.02 q (2H, $CH_2O$, *J* 7.2 Hz), 5.28 d (1H, $H^6$, *J* 3.3 Hz), 7.23 d (2$H_{arom}$, *J* 8.7 Hz), 7.32–7.46 m (7$H_{arom}$), 8.38 d (1H, NH, *J* 3.3 Hz). $^{13}$C NMR spectrum, δ, ppm: 13.10 ($CH_3$), 13.71 ($CH_3$), 53.26 ($C^6$), 60.66 ($CH_2O$), 61.73 ($CH_2O$), 103.22 ($C^5$), 126.36, 128.03, 128.69, 128.85, 131.83, 133.45, 135.02, 142.30 ($C_{arom}$), 142.80 ($C^4$), 150.83 ($C^2$), 161.47 (C=O), 163.27 (C=O). Found, %: C 61.35; H 5.07; N 6.69. $[M]^+$ 429.2. $C_{22}H_{21}ClN_2O_5$. Calculated, %: C 61.61; H 4.94; N 6.53. M 428.9.

**Diethyl 2-oxo-6-(2-fluorophenyl)-3-(4-chlorophenyl)-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (IIIj).** Yield 51%, mp 184–186°C. IR spectrum, ν, $cm^{-1}$: 3240, 3135 (NH), 1735, 1704 (C=O). $^1$H NMR spectrum, δ, ppm: 0.92 t (3H, $CH_3$, *J* 7.5 Hz), 1.08 t (3H, $CH_3$, *J* 8.0 Hz), 3.89 q (2H, $CH_2O$, *J* 7.5 Hz), 4.00 q (2H, $CH_2O$, *J* 8.0 Hz), 5.51 d (1H, $H^6$, *J* 3.0 Hz), 7.27–7.55 m (8$H_{arom}$), 8.31 d (1H, NH, *J* 3.0 Hz). $^{13}$C NMR spectrum, δ, ppm: 13.06 ($CH_3$), 13.57 ($CH_3$), 49.56 ($C^6$), 60.50 ($CH_2O$), 61.65 ($CH_2O$), 100.74 ($C^5$), 115.86 d ($J_{C–F}$ 21.3 Hz), 124.64, 128.65, 129.48, 129.68 d ($J_{C–F}$ 12.6 Hz), 130.14, 131.91, 133.44, 135.09, 160.18 d ($C_{arom}$, $J_{C–F}$ 245.0 Hz), 142.79 ($C^4$), 150.27 ($C^2$), 161.39 (C=O), 163.07 (C=O). Found, %: C 58.88; H 4.64; N 6.39. $[M + 1]^+$ 447. $C_{22}H_{20}ClFN_2O_5$. Calculated, %: C 59.13; H 4.51; N 6.27. M 446.

**Diethyl 3-(4-bromophenyl)-2-oxo-6-(2-fluorophenyl)-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (IIIk).** Yield 47%, mp 195–196°C. IR spectrum, ν, $cm^{-1}$: 3245, 3128 (NH), 1735, 1700 (C=O). $^1$H NMR spectrum, δ, ppm: 0.97 t (3H, $CH_3$, *J* 7.0 Hz), 1.11 t (3H, $CH_3$, *J* 7.5 Hz), 3.91 q (2H, $CH_2O$, *J* 7.0 Hz), 4.01 q (2H, $CH_2O$, *J* 7.5 Hz), 5.54 d (1H, $H^6$, *J* 3.0 Hz), 7.22–7.45 m (6$H_{arom}$), 7.62 d (2$H_{arom}$, *J* 8.5 Hz), 8.30 d (1H, NH, *J* 3.0 Hz). $^{13}$C NMR spectrum, δ, ppm: 13.05 ($CH_3$), 13.57 ($CH_3$), 49.55 ($C^6$), 60.50 ($CH_2O$), 61.66 ($CH_2O$), 100.75 ($C^5$), 115.79 d ($J_{C–F}$ 21.3 Hz), 121.92, 124.66, 129.50 ($J_{C–F}$ 12.5 Hz), 129.70, 130.15, 131.63, 132.20, 135.54, 160.25 d ($C_{arom}$, $J_{C–F}$ 245.0 Hz), 142.71 ($C^4$), 150.21 ($C^2$), 161.37 (C=O), 163.06 (C=O). Found, %: C 54.05; H 4.22; N 5.89. $[M + 1]^+$ 492. $C_{22}H_{20}BrFN_2O_5$. Calculated, %: C 53.78; H 4.10; N 5.70. M 491.

**Diethyl 6-(3-bromophenyl)-2-oxo-3-(4-chlorophenyl)-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (IIIl).** Yield 79%, mp 202–204°C. IR spectrum, ν, $cm^{-1}$: 3238, 3125 (NH), 1738, 1703 (C=O). $^1$H NMR spectrum, δ, ppm: 0.93 t (3H, $CH_3$, *J* 7.5 Hz), 1.13 t (3H, $CH_3$, *J* 7.5 Hz), 3.87 q (2H, $CH_2O$, *J* 7.5 Hz), 4.04 q (2H, $CH_2O$, *J* 7.5 Hz), 5.31 d (1H, $H^6$, *J* 3.0 Hz), 7.22 d (2$H_{arom}$, *J* 8.4 Hz), 7.39–7.54 m (6$H_{arom}$), 8.44 d (1H, NH, *J* 3.0 Hz). $^{13}$C NMR spectrum, δ, ppm: 13.09 ($CH_3$), 13.70 ($CH_3$), 52.81 ($C^6$), 60.77 ($CH_2O$), 61.81 ($CH_2O$), 102.50 ($C^5$), 121.77, 125.26, 128.73, 129.54, 130.89, 131.37, 131.78, 133.54, 134.85, 145.34 ($C_{arom}$), 142.63 ($C^4$), 150.57 ($C^2$), 161.29 (C=O), 163.10 (C=O). Found, %: C 52.36; H 4.12; N 5.37. $[M + 1]^+$ 509. $C_{22}H_{20}BrClN_2O_5$. Calculated, %: C 52.04; H 3.97; N 5.52. M 508.

**Diethyl 3-(4-bromophenyl)-6-(3-nitrophenyl)-2-oxo-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (IIIm).** Yield 69%, mp 229–231°C. IR spectrum, ν, $cm^{-1}$: 3240, 3130 (NH), 1730, 1705 (C=O). $^1$H NMR spectrum, δ, ppm: 0.97 t (3H, $CH_3$, *J* 7.0 Hz), 1.15 t (3H, $CH_3$, *J* 7.0 Hz), 3.93 q (2H, $CH_2O$, *J* 7.0 Hz), 4.07 q (2H, $CH_2O$, *J* 7.0 Hz), 5.49 d (1H, $H^6$, *J* 3.0 Hz), 7.21 d (2$H_{arom}$, *J* 8.0 Hz), 7.61 d (2$H_{arom}$, *J* 8.0 Hz), 7.76 t (1$H_{arom}$, *J* 6.5 Hz), 7.87 d (1$H_{arom}$, *J* 7.5 Hz), 8.22 d (1$H_{arom}$, *J* 8.0 Hz), 8.28 C (1$H_{arom}$), 8.56 d (1H, NH, *J* 3.0 Hz). $^{13}$C NMR spectrum, δ, ppm: 13.05 ($CH_3$), 13.63 ($CH_3$), 52.72 ($C^6$), 60.82 ($CH_2O$), 61.83 ($CH_2O$), 102.24 ($C^5$), 121.26, 122.08, 122.98, 130.74, 131.68, 132.10, 133.03, 135.21, 144.80, 147.86 ($C_{arom}$), 142.86 ($C^4$), 150.42 ($C^2$), 161.16 (C=O), 163.01 (C=O). Found, %: C 51.26; H 3.75; N 8.22. $[M + 1]^+$ 519. $C_{22}H_{20}BrN_3O_7$. Calculated, %: C 50.98; H 3.89; N 8.11. M 518.

**Diethyl 6-(4-nitrophenyl)-2-oxo-3-(4-chlorophenyl)-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (IIIn).** Yield 47%, mp 229–231°C. IR spectrum, ν, $cm^{-1}$: 3240, 3135 (NH), 1743, 1702 (C=O). $^1$H NMR spectrum, δ, ppm: 0.94 t (3H, $CH_3$, *J* 7.5 Hz), 1.12 t (3H, $CH_3$, *J* 7.5 Hz), 3.88 t (2H, $CH_2O$, *J* 7.5 Hz), 4.05 t (2H, $CH_2O$, *J* 7.5 Hz), 5.45 d (1H, $H^6$, *J* 3.3 Hz), 7.28 d (2$H_{arom}$, *J* 8.4 Hz), 7.45 d (2$H_{arom}$, *J* 8.4 Hz), 7.68 d (2$H_{arom}$, *J* 8.7 Hz), 8.29 d (2$H_{arom}$, *J* 8.7 Hz), 8.55 d

(1H, NH, *J* 3.3 Hz). $^{13}$C NMR spectrum, δ, ppm: 13.08 ($CH_3$), 13.68 ($CH_3$), 52.93 ($C^6$), 60.84 ($CH_2O$), 61.83 ($CH_2O$), 102.05 ($C^5$), 124.18, 127.92, 128.66, 131.95, 133.59, 134.78, 147.17, 149.77 ($C_{arom}$), 142.91 ($C^4$), 150.48 ($C^2$), 161.18 (C=O), 163.01 (C=O). Found, %: C 55.57; H 3.36; N 8.98. $[M]^+$ 474. $C_{22}H_{20}ClN_3O_7$. Calculated, %: C 55.76; H 4.25; N 8.87. M 474.

**Diethyl 2-oxo-6-(3,4-dichlorophenyl)-3-(4-chlorophenyl)-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (IIIo).** Yield 53%, mp 199–201°C. IR spectrum, ν, cm$^{-1}$: 3240, 3120 (NH), 1735, 1700 (C=O). $^1$H NMR spectrum, δ, ppm: 0.94 t (3H, $CH_3$, *J* 7.2 Hz), 1.13 t (3H, $CH_3$, *J* 7.2 Hz), 3.87 q (2H, $CH_2O$, *J* 7.2 Hz), 4.06 q (2H, $CH_2O$, *J* 7.2 Hz), 5.32 d (1H, $H^6$, *J* 3.3 Hz), 7.24 d ($2H_{arom}$, *J* 8.7 Hz), 7.38 d ($1H_{arom}$, *J* 8.4 Hz), 7.45 d ($2H_{arom}$, *J* 8.7 Hz), 7.55 C ($1H_{arom}$), 7.65 d ($1H_{arom}$, *J* 8.4 Hz), 8.46 d (1H, NH, *J* 3.3 Hz). $^{13}$C NMR spectrum, δ, ppm: 13.04 ($CH_3$), 13.65 ($CH_3$), 52.43 ($C^6$), 60.76 ($CH_2O$), 61.80 ($CH_2O$), 102.05 ($C^5$), 126.56, 128.66, 128.80, 130.64, 131.19, 131.30, 131.81, 133.55, 134.79, 143.64 ($C_{arom}$), 142.79 ($C^4$), 150.42 ($C^2$), 161.18 (C=O), 163.03 (C=O). Found, %: C 53.39; H 3.96; N 5.50. $[M]^+$ 498. $C_{22}H_{19}Cl_3N_2O_5$. Calculated, %: C 53.09; H 3.85; N 5.63. M 498.

**Dialkyl 2,3-diaryl-6-oxo-2-trifluoromethyl-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylates Va and Vb.** To a solution of 5 mmol of N-arylaminofumarate **IIb** or **IIf** in 20 ml of anhydrous toluene was added dropwise at stirring 0.7 ml (5 mmol) of triethylamine, and then over 30 min, 5 mmol (1.2 g) of isocyanate **IV**. The reaction mixture was stirred for 8 h and the precipitate of the triethylamine hydrochloride was filtered off. In the $^{19}$F NMR spectrum containing compound **Va** or **Vb** a signal was observed in the region –70...–69 ppm. The filtrate was boiled for 12 h, the solvent was evaporated, the residue was subjected to column chromatography on silica gel, eluent ethyl acetate–hexane, 1:1.

**Dimethyl 3-(4-methylphenyl)-6-oxo-2-phenyl-2-trifluoromethyl-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (Va).** Yield 22%, mp 181–183°C. IR spectrum, ν, cm$^{-1}$: 3190, 3095 (NH), 1742, 1690, 1670 (C=O). $^1$H NMR spectrum, δ, ppm: 2.16 s (3H, $CH_3$), 3.32 s (3H, $CH_3O$), 3.64 s (3H, $CH_3O$), 7.01 d ($2H_{arom}$, *J* 8.2 Hz), 7.26–7.44 m ($5H_{arom}$), 7.44–7.51 m ($2H_{arom}$), 9.13 s (1H, NH). $^{13}$C NMR spectrum, δ, ppm: 20.40 ($CH_3$), 51.62 ($CH_3O$), 52.57 ($CH_3O$), 79.32 q ($C^2$, $J_{C–F}$ 29.1 Hz), 99.34 ($C^5$), 123.79 q ($CF_3$, $J_{C–F}$ 278.5 Hz), 128.15, 128.87, 129.53, 130.01, 130.95, 132,38, 135.21, 138.44 ($C_{arom}$), 153.11 ($C^4$), 159.83 ($C^6$), 162.04 (C=O), 163.88 (C=O). $^{19}$F NMR spectrum, δ, ppm: –74.09. Found, %: C 59.16; H 2.17; N 6.42. $[M + 1]^+$ 449. $C_{22}H_{19}F_3N_2O_5$. Calculated, %: C 58.93; H 4.27; N 6.25. M 448.

**Diethyl 3-(4-bromophenyl)-6-oxo-2-phenyl-2-trifluoromethyl-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (Vb).** Yield 20%, mp 169–170°C. IR spectrum, ν, cm$^{-1}$: 3190, 3095 (NH), 1745, 1695, 1670 (C=O). $^1$H NMR spectrum, δ, ppm: 0.92 t (3H, $CH_3$, *J* 7.2 Hz), 1.13 t (3H, $CH_3$, *J* 7.2 Hz), 3.83 q (2H, $CH_2O$, *J* 7.2 Hz), 3.98 q (2H, $CH_2O$, *J* 7.2 Hz), 7.26 d ($2H_{arom}$, *J* 8.4 Hz), 7.38–7.44 m ($3H_{arom}$), 7.56 d ($2H_{arom}$, *J* 8.4 Hz), 7.61–7.63 m ($2H_{arom}$), 9.03 s (1H, NH). $^{13}$C NMR spectrum, δ, ppm: 13.29 C ($CH_3$), 13.43 C ($CH_3$), 61.18 ($CH_2O$), 62.57 ($CH_2O$), 79.64 q ($C^2$, $J_{C–F}$ 29.0 Hz), 102.81 ($C^5$), 124.40 q ($CF_3$, $J_{C–F}$ 280.4 Hz), 123.54, 127.45, 128.51, 129.00, 131.27, 132.15, 134.45, 137.33 ($C_{arom}$), 150.8 ($C^4$), 156.74 ($C^6$), 161.41 (C=O), 162.76 (C=O). $^{19}$F NMR spectrum, δ, ppm: –74.45. Found, %: C 50.76; H 3.89; N 5.24. $[M]^+$ 541. $C_{23}H_{20}BrF_3N_2O_5$. Calculated, %: C 51.03; H 3.72; N 5.17. M 541.

**6-Alkoxycarbonyl-1,4-diaryl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic acids VIa–VId**. To a solution of 1 mmol of diester **IIIh, IIIk, IIIl, IIIo** in 25 ml of ethanol was added 0.12 g (2.2 mmol) of KOH in 5 ml of water, and the mixture was boiled for 3 h. On cooling the reaction mixture was poured into 50 ml of water and neutralized with dilute hydrochloric acid. The separated precipitate was filtered off, dried, and recrystallized from acetonitrile.

**1-(4-Methylphenyl)-6-methoxycarbonyl-4-(4-nitrophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid (VIa).** Yield 80%, mp 282–284°C. IR spectrum, ν, cm$^{-1}$: 3235, 3085 (NH), 2420–2630 (OH), 1735, 1705, 1680, 1650 (C=O). $^1$H NMR spectrum, δ, ppm: 2.37 s (3H, $CH_3$), 3.39 s (3H, $CH_3O$), 5.42 d (1H, $H^6$, *J* 1.2 Hz), 7.09 d ($2H_{apOm}$, *J* 7.0 Hz), 7.20 d ($2H_{arom}$, *J* 7.0 Hz), 7.70 d ($2H_{arom}$, *J* 8.5 Hz), 8.14 br.s (1H, NH), 8.31 d ($2H_{arom}$, *J* 8.5 Hz), 12.63 br.s (1H, COOH). Found, %: C 58.63; H 4.27; N 10.01. $[M]^+$ 411. $C_{20}H_{17}N_3O_7$. Calculated, %: C 58.39; H 4.17; N 10.21. M 411.

**1-(4-Bromophenyl)-2-oxo-4-(2-fluorophenyl)-6-ethoxycarbonyl-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid (VIb).** Yield 88%, mp 203–205°C. IR spectrum, ν, cm$^{-1}$: 3235, 3085 (NH), 2400–2650 (OH), 1730, 1710, 1685, 1650 (C=O). $^1$H NMR spectrum, δ, ppm: 0.99 t (3H, $CH_3$, *J* 6.8 Hz), 3.89 q (2H, $CH_2O$, *J* 6.8 Hz), 5.50 d (1H, $H^6$, *J* 1.0 Hz), 7.23–7.60 m ($8H_{arom}$, $7H_{arom}$, NH), 8.20 s ($1H_{arom}$), 12.67 br.s (1H, COOH).

$^{13}$C NMR spectrum, δ, ppm: 13.10 ($CH_3$), 49.57 ($C^6$), 61.50 ($CH_2O$), 100.79 ($C^5$), 115.85 d ($J_{C–F}$ 21.2 Hz), 121.82, 124.69, 129.24 ($J_{C–F}$ 12.6 Hz), 130.09, 131.33, 131.62, 132.23, 135.71, 159.28 d ($C_{arom}$, $J_{C–F}$ 242.2 Hz), 142.40 ($C^4$), 150.45 ($C^2$), 161.63 (C=O), 164.63 (C=O). Found, %: C 52.07; H 3.28; N 6.26. $[M]^+$ 463. $C_{20}H_{16}BrFN_2O_5$. Calculated, %: C 51.85; H 3.48; N 6.05. M 463.

**4-(3-Bromophenyl)-2-oxo-1-(4-chlorophenyl)-6-ethoxycarbonyl-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid (VIc).** Yield 90%, mp 206–207°C. IR spectrum, ν, cm$^{-1}$: 3235, 3085 (NH), 2420–2650 (OH), 1735, 1705, 1685, 1650 (C=O). $^1$H NMR spectrum, δ, ppm: 0.94 t (3H, $CH_3$, *J* 7.0 Hz), 3.85 q (2H, $CH_2O$, *J* 7.0 Hz), 5.26 d (1H, $H^6$, *J* 1.8 Hz), 7.20 d ($2H_{arom}$, *J* 8.7 Hz), 7.41–7.54 m ($6H_{arom}$, $5H_{arom}$, NH), 8.36 d ($1H_{arom}$, *J* 3.6 Hz), 12.74 br.s (1H, COOH). Found, %: C 50.35; H 3.32; N 5.97. $[M]^+$ 480. $C_{20}H_{16}BrClN_2O_5$. Calculated, %: C 50.07; H 3.36; N 5.84. M 480.

**2-Oxo-4-(3,4-dichlorophenyl)-1-(4-chlorophenyl)-6-ethoxycarbonyl-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid (VId).** Yield 92%, mp 204–206°C. IR spectrum, ν, cm$^{-1}$: 3235, 3085 (NH), 2470–2640 (OH), 1730, 1705, 1680, 1650 (C=O). $^1$H NMR spectrum, δ, ppm: 0.99 t (3H, $CH_3$, *J* 6.4 Hz), 3.89 q (2H, $CH_2O$, *J* 6.4 Hz), 5.31 d (1H, $H^6$, *J* 1.5 Hz), 7.22 d ($2H_{arom}$, *J* 8.5 Hz), 7.41–7.67 m ($5H_{arom}$, $4H_{arom}$, NH), 8.32 s ($1H_{arom}$), 12.75 br.s (1H, COOH). $^{13}$C NMR spectrum, δ, ppm: 13.25 ($CH_3$), 52.93 ($C^6$), 61.76 ($CH_2O$), 103.66 ($C^5$), 125.40, 128.85, 129.51, 130.85, 131.45, 131.91, 132.01, 133.55, 135.15, 145.56 ($C_{arom}$), 142.48 ($C^4$), 150.98 ($C^2$), 163.01 (C=O), 165.09 (C=O). Found, %: C 51.43; H 3.17; N 6.08. $[M]^+$ 469. $C_{20}H_{15}Cl_3N_2O_5$. Calculated, %: C 51.14; H 3.22; N 5.96. M 469.

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