

SYNTHESIS AND CHARACTERIZATION OF DIALKYL ESTERS OF 1,2,4,5-TETRAZINE-3,6-DICARBOXYLIC ACID

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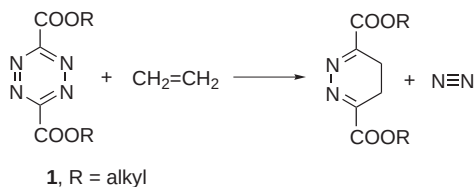
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Synthesis and characterization of a series of dialkyl esters of 1,2,4,5-tetrazine-3,6-dicarboxylic acid are reported. These compounds were prepared by a two-stage synthesis: re-esterification of dimethyl 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylate in the presence of aluminium triethoxide and subsequent dehydrogenation of dialkyl 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylates. The structures of the prepared compounds were confirmed by NMR and mass spectra.

Keywords: Tetrazines; Dihydropyridazines; Esterification; Aluminium triethoxide; Oxidation.

1,2,4,5-Tetrazines have been widely investigated because of the possibility of a large variety of practical applications. Investigations have led to their applications as biocides^{1–6}, high-nitrogen energetic materials^{7,8}, and intermediates for syntheses of a variety of heterocyclic compounds^{9–12}. Over the last twenty years, 3,6-disubstituted compounds of 1,2,4,5-tetrazine type **1** have been intensively studied^{9–15}. Dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate is the best-known compound of this type from the viewpoint of application and key intermediate in inverse-type Diels–Alder reaction^{9–15}. In the sense of this reaction, some dialkyl 1,2,4,5-tetrazine-3,6-dicarboxylates may have potential use for improving the shelf-life of fruits and vegetables by trapping the ethene gas generated by these crops¹⁶. Ethene rapidly reacts with 1,2,4,5-tetrazine compounds at room temperature and produces dihydropyridazine compounds with concomitant formation of nitrogen gas¹⁷

(Scheme 1). A characteristic colour change is typical of this reaction: the bright-red reactants turned to yellow products.



SCHEME 1

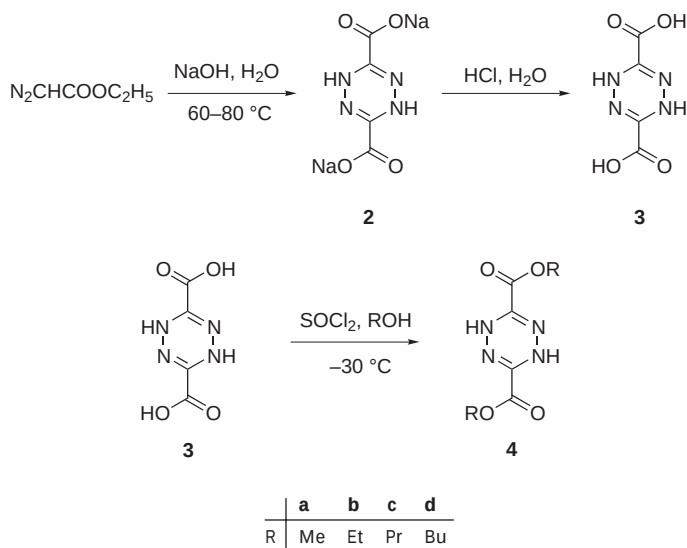
1,2,4,5-Tetrazines are unstable in the presence of water¹⁸, which is an impediment in their applications in moist or humid conditions, as it is the case of fruits and vegetables. Therefore the tetrazines are incorporated in a hydrofobic ethene-permeable substrate which does not contain hydroxy groups. The used hydrophobic polymeric materials include siliconepolycarbonate, polystyrene, polyethylene and polypropylene¹⁶. The preferred tetrazine esters used as active substances are dioctyl, didecyl and dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate¹⁶.

In spite of the wide range of applications mentioned above, these compounds have not received sufficient attention as far as their syntheses are concerned. Therefore, our initial studies were aimed at finding the optimum method for their preparation.

RESULTS AND DISCUSSION

Because of the instability of 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylic acid (**3**) in acid media at enhanced temperatures¹¹, we failed to get dialkyl esters by using the standard esterification method. Therefore, we used the procedure described by Boger¹³ for synthesis of dimethyl 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylate (**4a**). According to this method, the diester was prepared by the three-step reaction of ethyl diazoacetate with sodium hydroxide in water at 70 °C giving sodium 1,2,4,5-tetrazine-3,6-dicarboxylate (**2**), which was treated with aqueous HCl to give **3**. The following reaction of **3** with thionyl chloride and methanol at -30 °C then gave **4a** (Scheme 2).

The same procedure was adopted for preparation of diethyl, dipropyl, and dibutyl esters **4b–4d**, but their reaction yields were very low (15, 10 and 6% for **4b**, **4c** and **4d**, respectively). The reaction yields drastically decrease with increasing alkyl chain length. So far our efforts to prepare

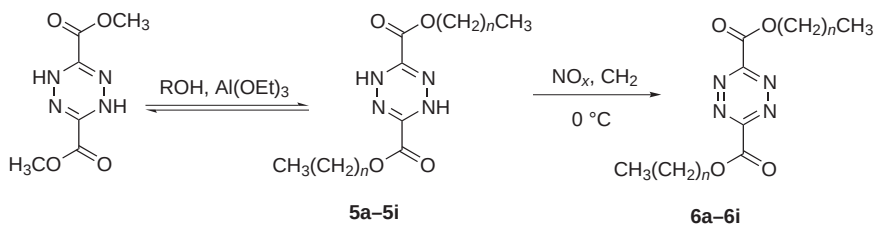


SCHEME 2

longer-chain esters using the same method have failed. Therefore, for the synthesis of these esters we have adopted a modification of the common procedure consisting in re-esterification of **4a** with various alcohols at boiling temperature in the presence of $\text{Al}(\text{OC}_2\text{H}_5)_3$ as a catalyst. In this way, a series of dialkyl 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylates **5a–5i** was prepared (Scheme 3). The equilibrium of this reaction is usually shifted towards the product by distilling off the methanol formed.

Generally, the re-esterification reactions of **4a** with long-chain alcohols were easy and without complications. However, with lower-boiling alcohols the re-esterification was difficult. Therefore, the re-esterification of **4a** with short-chain, e.g. ethyl, propyl and butyl, alcohols was performed in an autoclave. Our attempts at preparing such esters at normal atmospheric pressure led to very low yields and conversions. Usually, the products were present in a yield of ca. 50% together with the non-reacted starting material **4a**. The use of autoclave was successful: the reaction temperature increased, and hence also the yields and conversions. Nevertheless, the reaction yields and purity of products **5b–5d** were not as good as those of long-chain esters **5e–5i**. The reaction course and purity of products were checked by HPLC with acetonitrile–water (4:1) as the mobile phase.

The oxidation method adopted for all the dihydro compounds **4** was identical with the procedures described in the literature¹³. The synthesis is shown in Scheme 3. The prepared compounds were characterized by ¹H, ¹³C, and ¹⁵N NMR spectra, elemental analysis and mass spectra. The molecular weights (MW) of all the studied compounds were confirmed by the measurement of their atmospheric-pressure chemical ionization (APCI) mass spectra in both polarity modes. Positive-ion APCI mass spectra show mainly peaks of protonated molecules [M + H]⁺, while the negative-ion APCI spectra provide complementary information with [M – H][–] ions. In addition to these even-electron ions, typical of soft ionization mass spectra, the odd-electron molecular radical ions M[•] in the positive-ion mode and M^{•–} in the negative-ion mode are observed as well, which is quite unusual in APCI¹⁹. The type of alkyl substituent can be identified on the basis of neutral losses of side chain, as reported earlier²⁰.



SCHEME 3

5,6	a	b	c	d	e	f	g	h	i
n	1	2	3	4	5	6	7	8	9

CONCLUSIONS

Aluminium triethoxide was used successfully as a catalyst for the re-esterification of dimethyl 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylate with various alcohols. It was found that the re-esterification with longer-chain alcohols (C₅–C₁₀) is easier than that with shorter-chain alcohols (C₁–C₄). The corresponding dialkyl 1,2,4,5-tetrazine-3,6-dicarboxylates **6** were obtained by oxidation of the 1,4-dihydro compounds with nitrogen oxides (NO_x).

EXPERIMENTAL

The chemicals used were purchased from Fluka and their melting points were checked on a hot-stage microscope. The ¹H, ¹³C and ¹⁵N NMR spectra (δ, ppm; J, Hz) were recorded on a Bruker Avance 500 spectrometer operating at 500.13 MHz for ¹H, 125.76 MHz for ¹³C and

50.68 MHz for ^{15}N . The samples were dissolved in deuterochloroform and measured at room temperature. The ^1H and ^{13}C chemical shifts were referenced to internal TMS. The ^{15}N chemical shifts were referenced to external nitromethane in coaxial capillary (δ 0.0). The positive values of chemical shifts denote shifts of signals to higher frequencies with respect to the standard. The ^{13}C chemical shifts of COO groups were assigned having analysed proton-coupled ^{13}C NMR spectra in which these groups form broadened triplets due to $^3J(^{13}\text{C},\text{H})$ coupling constants from OCH_2 groups (in contrast to singlets of aromatic). Mass spectrometry analyses were performed on an Esquire 3000 ion trap analyzer (Bruker Daltonics, Bremen, Germany). Atmospheric-pressure chemical ionization (APCI) mass spectra were recorded in the mass range m/z 50–1000 using both positive- and negative-ion modes and the following setting of tuning parameters: target mass m/z 250 and compound stability 20% for the alkyl series $\text{C}_2\text{--C}_4$, m/z 350 and compound stability 100% for the alkyl series $\text{C}_5\text{--C}_{10}$, pressure of the nebulizing gas 103.4 kPa, the drying gas flow rate 4 l/min, ion source temperature 350 °C and drying gas temperature 300 °C. The samples were dissolved in acetonitrile and delivered into the system with infusion pump at a flow rate of 5 $\mu\text{l}/\text{min}$.

The analytical HPLC was performed with a Thermo separation products PC 1000, equipped with a reverse-phase column (250 $\times$ 4 mm) Nucleosil C18. The elemental analyses were performed by the Central Analytical Service of Department of Organic Chemistry, University of Pardubice.

1,4-Dihydro-1,2,4,5-tetrazine-3,6-dicarboxylic acid (**3**) and dimethyl 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylate (**4a**) were prepared by known methods¹².

Synthesis of Compounds **5a–5c**. General Procedure

An amount of 1 g (5.0 mmol) of **4a**, 60 ml of corresponding alcohol and a catalytic amount of aluminium triethoxide were placed into an autoclave. The autoclave was heated to 180 °C until maximum conversion was reached (HPLC, $\text{MeCN--H}_2\text{O}$ 4:1). During 1 h alcohol vapours were gradually released (45 ml of the condensate was collected). The autoclave was then cooled to room temperature, the crude product was filtered off and purified by recrystallization from hexane.

Diethyl 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylate (5a; R = C₂H₅). Yield 46%. M.p. 104–108 °C (ref.¹ 101–102 °C). ^1H NMR: 7.51 (NH); 4.39 (OCH_2); 1.39 (CH_3). Positive-ion APCI-MS: m/z 229 $[\text{M} + \text{H}]^+$ (100%), 228 $[\text{M}]^+$, 201 $[\text{M} + \text{H} - \text{C}_2\text{H}_4]^+$. Positive-ion APCI-MS/MS of m/z 229: m/z 201 $[\text{M} + \text{H} - \text{C}_2\text{H}_4]^+$ (100%), 173 $[\text{M} + \text{H} - \text{C}_4\text{H}_8]^+$. Negative-ion APCI-MS: m/z 226 $[\text{M} - 2]^-$ (100%). For $\text{C}_8\text{H}_{12}\text{N}_4\text{O}_4$ (228.2) calculated: 42.10% C, 5.30% H, 24.55% N; found: 41.71% C, 5.38% H, 25.14% N.

Dipropyl 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylate (5b; R = n-C₃H₇). Yield 39%. M.p. 78–81 °C. ^1H NMR: 7.53 (NH); 4.28 (OCH_2); 1.76 (CH_2); 0.99 (CH_3). Positive-ion APCI-MS: m/z 257 $[\text{M} + \text{H}]^+$ (100%), 256 $[\text{M}]^+$, 215 $[\text{M} + \text{H} - \text{C}_3\text{H}_6]^+$. Positive-ion APCI-MS/MS of m/z 257: m/z 215 $[\text{M} + \text{H} - \text{C}_3\text{H}_6]^+$ (100%), 173 $[\text{M} + \text{H} - \text{C}_6\text{H}_{12}]^+$. Negative-ion APCI-MS: m/z 254 $[\text{M} - 2]^-$ (100%). For $\text{C}_{10}\text{H}_{16}\text{N}_4\text{O}_4$ (256.3) calculated: 46.87% C, 6.29% H, 21.86% N; found: 46.72% C, 6.27% H, 22.02% N.

Dibutyl 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylate (5c; R = n-C₄H₉). Yield 42%. M.p. 56–61 °C. ^1H NMR: 7.49 (NH); 4.31 (OCH_2); 1.73, 1.43 ($(\text{CH}_2)_2$); 0.95 (CH_3). Positive-ion APCI-MS: m/z 285 $[\text{M} + \text{H}]^+$ (100%), 284 $[\text{M}]^+$. Positive-ion APCI-MS/MS of m/z 285: m/z 229 $[\text{M} + \text{H} - \text{C}_4\text{H}_8]^+$ (100%), 173 $[\text{M} + \text{H} - \text{C}_8\text{H}_{16}]^+$. Negative-ion APCI-MS: m/z 282 $[\text{M} - 2]^-$.

(100%). For $C_{12}H_{20}N_4O_4$ (284.3) calculated: 50.69% C, 7.09% H, 19.71% N; found: 50.76% C, 7.04% H, 20.11% N.

Synthesis of Compounds **5d–5i**. General Procedure

An amount of 5 g (24.98 mmol) of **4a** was heated with 100 ml of corresponding alcohol and catalytic amount of aluminum triethoxide. A part of the alcohol formed was distilled off from the reaction mixture during 1 h. The rusty brown reaction mixture was then allowed to cool in refrigerator. The obtained crystals were filtered off, recrystallized from hexane and dried in vacuum at 55 °C.

Dipentyl 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylate (5d; R = n-C₅H₁₁). Yield 71%. M.p. 50–52 °C. ¹H NMR: 7.63 (NH); 4.30 (OCH₂); 1.14–1.76 ((CH₂)₃); 0.89 (CH₃). ¹³C NMR: 158.6 (COO); 138.2 (N=C-N); 67.1 (OCH₂); 28.1, 25.2, 22.3 ((CH₂)₃); 13.8 (CH₃). Positive-ion APCI-MS: *m/z* 313 [M + H]⁺ (100%), 312 [M]⁺⁺, 243 [M + H – C₅H₁₀]⁺, 173 [M + H – C₁₀H₂₀]⁺. Positive-ion APCI-MS/MS of *m/z* 313: *m/z* 243 [M + H – C₅H₁₀]⁺ (100%), 173 [M + H – C₁₀H₂₀]⁺. Negative-ion APCI-MS: *m/z* 310 [M – 2][–] (100%). For C₁₄H₂₄N₄O₄ (312.4) calculated: 53.83% C, 7.74% H, 17.94% N; found: 54.15% C, 7.58% H, 17.73% N.

Dihexyl 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylate (5e; R = n-C₆H₁₃). Yield 70%. M.p. 56–60 °C. ¹H NMR: 7.61 (NH); 4.30 (OCH₂); 1.34–1.77 ((CH₂)₄); 0.91 (CH₃). ¹³C NMR: 158.6 (COO); 138.3 (N=C-N); 67.2 (OCH₂); 27.9, 27.7, 22.1 ((CH₂)₄); 13.7 (CH₃). Positive-ion APCI-MS: *m/z* 341 [M + H]⁺ (100%), 340 [M]⁺⁺, 257 [M + H – C₆H₁₂]⁺. Positive-ion APCI-MS/MS of *m/z* 341: *m/z* 257 [M + H – C₆H₁₂]⁺ (100%), 173 [M + H – C₁₂H₂₄]⁺. Negative-ion APCI-MS: *m/z* 338 [M – 2][–] (100%). For C₁₆H₂₈N₄O₄ (340.4) calculated: 56.45% C, 8.29% H, 16.46% N; found: 56.95% C, 8.22% H, 16.20% N.

Diheptyl 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylate (5f; R = n-C₇H₁₅). Yield 66%. M.p. 58–61 °C. ¹H NMR: 7.60 (NH); 4.30 (OCH₂); 1.24–1.74 ((CH₂)₅); 0.88 (CH₃). ¹³C NMR: 158.6 (COO); 138.3 (N=C-N); 67.3 (OCH₂); 31.5, 29.0, 28.9, 28.3, 25.6, 22.5 ((CH₂)₅); 14.0 (CH₃). Positive-ion APCI-MS: *m/z* 369 [M + H]⁺ (100%), 368 [M]⁺⁺, 271 [M + H – C₇H₁₄]⁺. Positive-ion APCI-MS/MS of *m/z* 369: *m/z* 271 [M + H – C₇H₁₄]⁺ (100%), 173 [M + H – C₁₄H₂₈]⁺. Negative-ion APCI-MS: *m/z* 366 [M – 2][–] (100%). For C₁₈H₃₂N₄O₄ (368.5) calculated: 58.67% C, 8.75% H, 15.20% N; found: 58.94% C, 8.81% H, 15.27% N.

Diocetyl 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylate (5g; R = n-C₈H₁₇). Yield 70%. M.p. 67–69 °C. ¹H NMR: 7.57 (NH-, ¹J(¹⁵H, ¹H) = 87.9); 4.30 (OCH₂); 1.24–1.74 ((CH₂)₆); 0.88 (CH₃). ¹³C NMR: 158.6 (COO); 138.3 (N=C-N); 67.3 (OCH₂); 31.5, 29.0, 28.9, 28.3, 25.6, 22.5 ((CH₂)₆); 14.0 (CH₃). ¹⁵N NMR: –251.4 (–NH–); –102.8 (–N=). Positive-ion APCI-MS: *m/z* 397 [M + H]⁺ (100%), 396 [M]⁺⁺, 285 [M + H – C₈H₁₆]⁺. Positive-ion APCI-MS/MS of *m/z* 397: *m/z* 285 [M + H – C₈H₁₆]⁺ (100%), 173 [M + H – C₁₆H₃₂]⁺. Negative-ion APCI-MS: *m/z* 394 [M – 2][–] (100%). For C₂₀H₃₆N₄O₄ (396.5) calculated: 60.58% C, 9.15% H, 14.13% N; found: 60.98% C, 8.99% H, 13.92% N.

Dinonyl 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylate (5h; R = n-C₉H₁₉). Yield 85%. M.p. 67–70 °C. ¹H NMR: 7.59 (NH); 4.30 (OCH₂); 1.26–1.76 ((CH₂)₇); 0.88 (CH₃). ¹³C NMR: 158.6 (COO); 138.2 (N=C-N); 67.1 (OCH₂); 31.7, 29.3, 29.1, 29.0, 28.3, 25.6, 22.5 ((CH₂)₇); 14.0 (CH₃). Positive-ion APCI-MS: *m/z* 425 [M + H]⁺ (100%), 424 [M]⁺⁺, 299 [M + H – C₉H₁₈]⁺. Positive-ion APCI-MS/MS of *m/z* 425: *m/z* 299 [M + H – C₉H₁₈]⁺ (100%), 173 [M + H – C₁₈H₃₆]⁺. Negative-ion APCI-MS: *m/z* 422 [M – 2][–] (100%). For C₂₂H₄₀N₄O₄ (424.6) calculated: 62.24% C, 9.50% H, 13.20% N; found: 62.58% C, 9.46% H, 13.22% N.

Didecyl 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylate (5i; R = n-C₁₀H₂₁). Yield 79%. M.p. 76–77 °C. ¹H NMR: 7.54 (NH); 4.30 (OCH₂); 1.26–1.76 ((CH₂)₈); 0.88 (CH₃). ¹³C NMR: 158.6 (COO); 138.3 (N=C-N); 67.2 (OCH₂); 31.8, 29.4, 29.3, 29.2, 29.1, 28.3, 25.6, 22.6 ((CH₂)₈); 14.0 (CH₃). Positive-ion APCI-MS: *m/z* 453 [M + H]⁺ (100%), 452 [M]⁺⁺, 313 [M + H – C₁₀H₂₀]⁺. Positive-ion APCI-MS/MS of *m/z* 453: *m/z* 313 [M + H – C₁₀H₂₀]⁺ (100%), 173 [M + H – C₂₀H₄₀]⁺. Negative-ion APCI-MS: *m/z* 450 [M – 2][–] (100%). For C₂₄H₄₄N₄O₄ (452.6) calculated: 63.69% C, 9.80% H, 12.38% N; found: 63.52% C, 9.98% H, 12.41% N.

Synthesis of Compounds **6a–6i**. General Procedure

A solution of 5 g of **5a–5i** in 100 ml of dry dichloromethane was cooled to 0 °C. A stream of nitrous gases was bubbled into the reaction mixture with stirring for 30 min. The reaction mixture was stirred for another 1 h. The clear yellow solution gradually turned to bright red. A large part of the solvent was removed, and the red precipitate was filtered off.

Diethyl 1,2,4,5-tetrazine-3,6-dicarboxylate (6a; R = C₂H₅). Yield 96%. M.p. 103–106 °C (ref.²¹ 105–106 °C). ¹H NMR: 4.69 (OCH₂); 1.54 (CH₃). Positive-ion APCI-MS: *m/z* 227 [M + H]⁺ (100%), 226 [M]⁺⁺, 199 [M + H – C₂H₄]⁺. Positive-ion APCI-MS/MS of *m/z* 227: *m/z* 199 [M + H – C₂H₄]⁺ (100%). Negative-ion APCI-MS: *m/z* 226 [M][–] (100%).

Dipropyl 1,2,4,5-tetrazine-3,6-dicarboxylate (6b; R = n-C₃H₇). Yield 94%. M.p. 72–76 °C. ¹H NMR: 4.56 (OCH₂); 1.95 (CH₂); 1.09 (CH₃). Positive-ion APCI-MS: *m/z* 255 [M + H]⁺ (100%), 254 [M]⁺⁺. Positive-ion APCI-MS/MS of *m/z* 255: *m/z* 213 [M + H – C₃H₆]⁺ (100%). Negative-ion APCI-MS: *m/z* 254 [M][–] (100%). For C₁₀H₁₄N₄O₄ (254.3) calculated: 47.24% C, 5.55% H, 22.04% N; found: 47.83% C, 5.45% H, 21.94% N.

Dibutyl 1,2,4,5-tetrazine-3,6-dicarboxylate (6c; R = n-C₄H₉). Yield 95%. M.p. 50–53 °C. ¹H NMR: 4.60 (OCH₂); 1.90, 1.45 ((CH₂)₂); 0.95 (CH₃). Positive-ion APCI-MS: *m/z* 283 [M + H]⁺, 282 [M]⁺⁺ (100%), 227 [M + H – C₄H₈]⁺, 171 [M + H – C₈H₁₆]⁺. Positive-ion APCI-MS/MS of *m/z* 282: *m/z* 226 [M – C₄H₈]⁺⁺ (100%), 172 [M – C₈H₁₄]⁺⁺. Negative-ion APCI-MS: *m/z* 282 [M][–] (100%). For C₁₂H₁₈N₄O₄ (282.3) calculated: 51.06% C, 6.43% H, 19.85% N; found: 50.88% C, 6.56% H, 19.73% N.

Dipentyl 1,2,4,5-tetrazine-3,6-dicarboxylate (6d; R = n-C₅H₁₁). Yield 87%. M.p. 42–45 °C. ¹H NMR: 4.62 (OCH₂); 1.35–1.92 ((CH₂)₃); 0.93 (CH₃). ¹³C NMR: 160.2 (COO); 159.3 (N=C-N); 68.4 (OCH₂); 28.1, 27.9, 22.3 ((CH₂)₃); 13.9 (CH₃). Positive-ion APCI-MS: *m/z* 311 [M + H]⁺, 310 [M]⁺⁺ (100%). Positive-ion APCI-MS/MS of *m/z* 310: *m/z* 240 [M – C₅H₁₀]⁺⁺ (100%), 172 [M – C₁₀H₁₈]⁺⁺. Negative-ion APCI-MS: *m/z* 310 [M][–] (100%). For C₁₄H₂₂N₄O₄ (310.4) calculated: 54.18% C, 7.15% H, 18.05% N; found: 55.17% C, 7.42% H, 16.83% N.

Dihexyl 1,2,4,5-tetrazine-3,6-dicarboxylate (6e; R = n-C₆H₁₃). Yield 94%. M.p. 44–47 °C. ¹H NMR: 4.61 (OCH₂); 1.31–1.94 ((CH₂)₄); 0.91 (CH₃). ¹³C NMR: 160.2 (COO); 159.1 (N=C-N); 68.2 (OCH₂); 31.3, 28.3, 25.4, 22.1 ((CH₂)₄); 14.0 (CH₃). Positive-ion APCI-MS: *m/z* 339 [M + H]⁺, 338 [M]⁺⁺ (100%), 256 [M – C₆H₁₀]⁺⁺. Positive-ion APCI-MS/MS of *m/z* 338: *m/z* 256 [M – C₆H₁₀]⁺⁺, 254 [M – C₆H₁₂]⁺⁺, 172 [M – C₁₂H₂₂]⁺⁺ (100%). Negative-ion APCI-MS: *m/z* 338 [M][–] (100%). For C₁₆H₂₆N₄O₄ (338.4) calculated: 56.79% C, 7.74% H, 16.56% N; found: 57.05% C, 7.79% H, 16.19% N.

Diheptyl 1,2,4,5-tetrazine-3,6-dicarboxylate (6f; R = n-C₇H₁₅). Yield 92%. M.p. 52–55 °C. ¹H NMR: 4.61 (OCH₂); 1.30–1.92 ((CH₂)₅); 0.89 (CH₃). ¹³C NMR: 160.2 (COO); 159.3 (N=C-N); 67.2 (OCH₂); 31.7, 28.6, 28.4, 25.7, 22.6 ((CH₂)₅); 14.1 (CH₃). Positive-ion APCI-MS: *m/z* 367 [M + H]⁺, 366 [M]⁺⁺ (100%), 270 [M – C₇H₁₂]⁺⁺, 172 [M – C₁₄H₂₆]⁺⁺. Positive-ion APCI-MS/MS of *m/z* 366: *m/z* 270 [M – C₇H₁₂]⁺⁺ (100%), 172 [M – C₁₄H₂₆]⁺⁺.

Negative-ion APCI-MS: m/z 366 $[M]^-$ (100%). For $C_{18}H_{30}N_4O_4$ (366.5) calculated: 59.00% C, 8.25% H, 15.29% N; found: 59.14% C, 8.17% H, 15.08% N.

Diocetyl 1,2,4,5-tetrazine-3,6-dicarboxylate (6g; R = n-C₈H₁₇). Yield 98%. M.p. 63–67 °C. ¹H NMR: 4.56 (OCH₂); 1.26–1.89 ((CH₂)₆); 0.86 (CH₃). ¹³C NMR: 160.0 (COO); 159.2 (N=C-N); 68.3 (OCH₂); 31.6, 29.0, 28.3, 28.2, 25.7, 22.6 ((CH₂)₆); 14.0 (CH₃). ¹⁵N NMR: 14.1 (-N=). Positive-ion APCI-MS: m/z 395 $[M + H]^+$, 394 $[M]^{++}$ (100%), 284 $[M - C_8H_{14}]^{++}$. Positive-ion APCI-MS/MS of m/z 394: m/z 284 $[M - C_8H_{14}]^{++}$ (100%), 172 $[M - C_{16}H_{30}]^{++}$. Negative-ion APCI-MS: m/z 394 $[M]^-$ (100%). For $C_{20}H_{34}N_4O_4$ (394.5) calculated: 60.89% C, 8.69% H, 14.20% N; found: 61.11% C, 8.59% H, 14.32% N.

Dinonyl 1,2,4,5-tetrazine-3,6-dicarboxylate (6h; R = n-C₉H₁₉). Yield 97%. M.p. 67–69 °C. ¹H NMR: 4.61 (OCH₂); 1.25–1.92 ((CH₂)₇); 0.87 (CH₃). ¹³C NMR: 160.1 (COO); 159.3 (N=C-N); 68.4 (OCH₂); 31.8, 29.4, 29.2, 29.1, 28.4, 25.7, 22.6 ((CH₂)₇); 14.0 (CH₃). Positive-ion APCI-MS: m/z 423 $[M + H]^+$, 422 $[M]^{++}$ (100%). Positive-ion APCI-MS/MS of m/z 422: m/z 298 $[M - C_9H_{16}]^{++}$ (100%), 172 $[M - C_{18}H_{34}]^{++}$. Negative-ion APCI-MS: m/z 422 $[M]^-$ (100%). For $C_{22}H_{38}N_4O_4$ (422.6) calculated: 62.53% C, 9.06% H, 13.26% N; found: 62.70% C, 9.04% H, 12.95% N.

Didecyl 1,2,4,5-tetrazine-3,6-dicarboxylate (6i; R = n-C₁₀H₂₁). Yield 89%. M.p. 76–78 °C. ¹H NMR: 4.60 (OCH₂); 1.24–1.89 ((CH₂)₈); 0.86 (CH₃). ¹³C NMR: 160.2 (COO); 159.3 (N=C-N); 68.4 (OCH₂); 31.9, 29.5, 29.4, 29.3, 29.2, 28.4, 25.8, 22.7 ((CH₂)₈); 14.0 (CH₃). Positive-ion APCI-MS: m/z 451 $[M + H]^+$ (100%), 450 $[M]^{++}$. Positive-ion APCI-MS/MS of m/z 451: m/z 313 $[M + H - C_{10}H_{18}]^+$ (100%), 172 $[M - C_{20}H_{38}]^{++}$. Negative-ion APCI-MS: m/z 450 $[M]^-$ (100%). For $C_{24}H_{42}N_4O_4$ (450.6) calculated: 63.97% C, 9.39% H, 12.43% N; found: 64.17% C, 9.48% H, 12.35% N.

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