Chemistry of Heterocyclic Compounds, Vol. 31, No. 5, 1995

NUCLEOPHILIC SUBSTITUTION REACTIONS OF 2,4,6-TRIS(TRINITROMETHYL)-1,3,5-TRIAZINE.

1. INTERACTION OF 2,4,6-TRIS(TRINITROMETHYL)-1,3,5-TRIAZINE WITH ALCOHOLS, DIOLS, AMMONIA, AND SECONDARY AMINES

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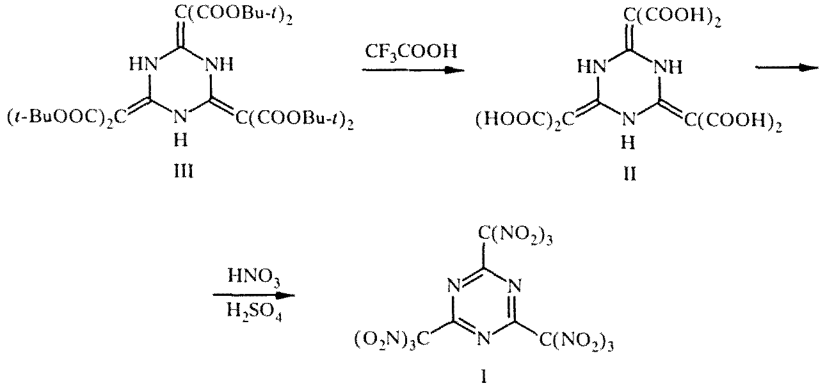
A study has been made of nucleophilic substitution reactions of 2,4,6-tris(trinitromethyl)-1,3,5-triazine with certain nucleophiles. The possibility of replacing one, two, or three trinitromethyl groups in this compound has been demonstrated.

We had reported previously [1] on the synthesis of 2,4,6-tris(trinitromethyl)-1,3,5-triazine (I) by the action of a mixture of concentrated sulfuric and nitric acids on 2,4,6-tris[di(carboxy)methylene]-1,3,5-hexahydrotriazine (II), which in turn was obtained by splitting the ester 2,4,6-tris[di(tert-butoxycarbonyl)methylene]-1,3,5-hexahydrotriazine (III) by the action of trifluoroacetic acid:



Compound I is of interest as the starting point for the synthesis of a large number of difficultly accessible products whose molecules include the 1,3,5-triazine ring with one or two trinitromethyl substituents. Such structures may be approached by means of nucleophilic substitution reactions. Since the triazine I has three reaction centers, the main task of the present work was to search for optimal conditions for the selective replacement of one or two trinitromethyl groups of this compound.

As nucleophilic reagents we used alcohols, diols, ammonia, and secondary amines. The interaction of compound I with sodium methylate in methanol (I:NaOMe = 1:3) proceeds at room temperature and affords 2,4,6-trimethoxy-1,3,5-triazine (IV) with a 75% yield. The use of excess methanol in CCl_4 without any base gave us the disubstituted product (V) with a 50% yield. Monosubstitution was accomplished successfully at 0-5°C with strictly dosed addition of a dilute solution of methanol in CCl_4, with the reaction monitored by means of TLC. The yield of the monosubstituted product (VI) was no greater than 35%. Analogously, using ethanol, the monoethoxy derivative (VII) was obtained with a 40% yield.

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*Deceased.

N. D. Zelinskii Institute of Organic Chemistry, Russian Academy of Sciences, Moscow 117913. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 674-678, May, 1995. Original article submitted February 28, 1995.

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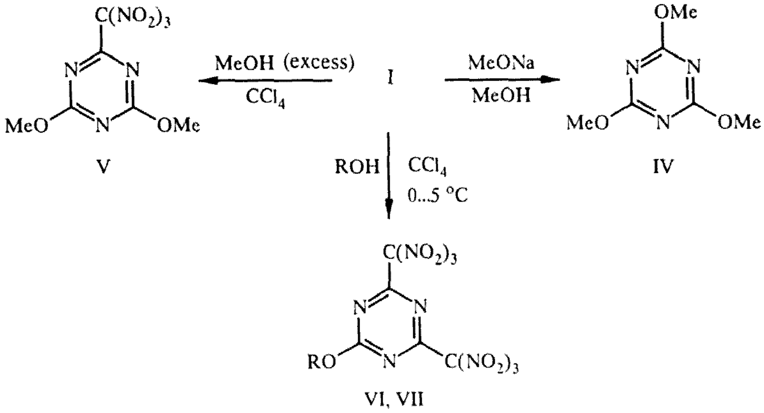
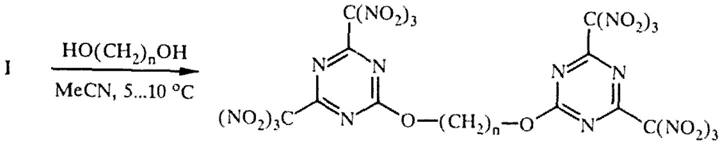


VI R = Me, VII R = Et

These reactions of the triazine I with alcohols were very rapid; the product of monosubstitution was already present in the reaction mixture immediately after adding the first drop of the solution of alcohol in CCl_4.

Here we must note that both the monosubstituted and disubstituted products contained nitroform as an impurity, which was removed by various purification methods (see Experimental section).

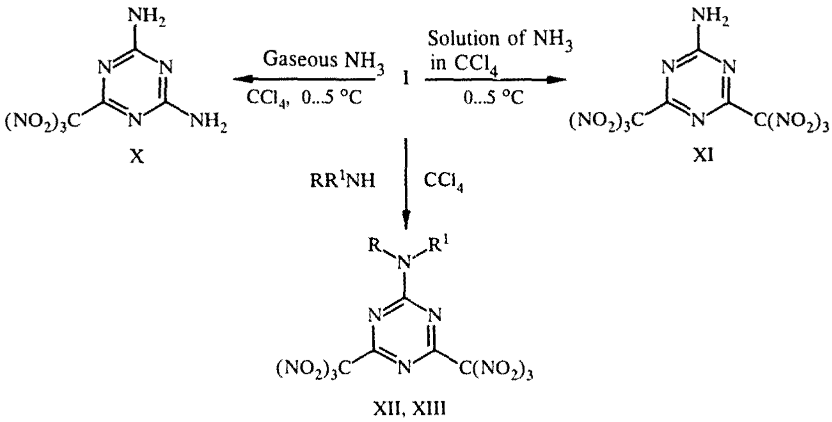
The interaction of I with 1,3-propanediol and 1,4-butanediol (I:diol = 2:1) proceeded with the replacement of one trinitromethyl group in the triazine ring and the formation of the corresponding ethers VIII and IX with respective yields of 66% and 70%:



VIII n = 3; IX n = 4

Treatment of I in CCl_4 solution with gaseous ammonia resulted in immediate replacement of two trinitromethyl groups and the formation of the diamine X with a 40% yield. By strictly controlled dosing of ammonia/CCl_4 solution while monitoring the reaction by means of TLC, we were able to obtain the monosubstituted product (XI) with a 50% yield.

Reaction of the triazine I with an accurately dosed solution of dimethylamine in CCl_4 gave 2-N,N-dimethylamino-4,6-bis(trinitromethyl)-1,3,5-triazine (XII) with a 72% yield. The use of a solution of methylphenylamine under analogous conditions gave 2-(methylphenylamino)-4,6-bis(trinitromethyl)-1,3,5-triazine (XIII) with a 50% yield.



XII R = R^1 = Me; XIII R = Me, R^1 = Ph

It should be emphasized that all of these reactions (other than the synthesis of compounds IV and XII) were performed with freshly prepared tris(trinitromethyl)triazine I, which was not separated from its solution in the organic solvent, but was immediately introduced into the nucleophilic substitution reaction. In all instances, the addition of the second component was terminated when the original I disappeared from the reaction mixture, as evidenced by TLC data.

The structures of the newly synthesized compounds V-XIII were confirmed by means of elemental analyses and by NMR and IR spectroscopy (see Experimental section).

EXPERIMENTAL

The IR spectra were taken on a Specord instrument in KBr tablets. The ^1H, ^{13}C, and $^{14/15}N$ NMR spectra were obtained on a Bruker AM-300 instrument (300, 75.5, and 21.67 MHz, respectively), internal standard TMS. The melting points were determined on a Boetius heating stage with a heating rate of 4°C/min at the melting point. For the column chromatography we used Grade L silica gel, 100/160 μ. The course of the reactions and the product purities were monitored by means of TLC on Silufol UV-254 plates, solvent CH_2Cl_2 or $CHCl_3$, with detection in UV light at 254 nm, and also by development of the spots with a 1% alcoholic solution of diphenylamine. The yields of the compounds were calculated in relation to the triazine III.

The results from elemental analyses of compounds V-XIII for C, H, and N matched the calculated values (see below).

2,4,6-Tris[di(tert-butoxycarbonyl)methylene]-1,3,5-hexahydrotriazine (III). A solution of 17.3 g (80 mmoles) of di(tert-butyl)malonic ester, obtained by a method described in [2], in 30 ml of absolute tetrahydrofuran, was stirred at room temperature and then mixed vigorously with 0.64 g (80 mmoles) of finely divided lithium hydride. The reaction mass was stirred 2 h at 50-60°C and then cooled to 10-12°C (ice bath). Then, a solution of 1.85 g (10 mmoles) of recrystallized cyanuric chloride in 10 ml of absolute THF was added at a rate such that the temperature did not rise above 15°C. This mixture was stirred for 1 h at room temperature and then refluxed for 12-14 h and cooled to 18-20°C, after which the THF was removed in a rotary evaporator. To the residue, 100 ml of $CHCl_3$ and 100 ml of a saturated aqueous NH_4Cl solution were added; this mixture was shaken in a separatory funnel until a uniform mass was obtained, after which the organic layer was separated, washed with water (100 ml), and dried with calcined $MgSO_4$; then the chloroform was removed in a rotary evaporator. The excess malonic ester was taken off by heating on a water bath while drawing vacuum down to 1 mm Hg; 50 ml of ethanol was added to the residue, and the residue was filtered off, washed with ethanol (2 × 25 ml), and oven-dried at 80°C. Obtained 6.58-6.72 g (91-93%) of the product III, mp 203-205°C (decomp.).*

2,4,6-Tris[di(carboxy)methylene]-1,3,5-hexahydrotriazine (II). To 20 ml of trifluoroacetic acid, 1.45 g (2 mmoles) of compound III was added at 0-5°C while stirring. Then the cooling was discontinued, and the stirring was continued another 30 min. The precipitate was filtered off, washed with dry ether (2 × 10 ml), and dried on the filter. Obtained 0.77-0.8 g (~100%) of compound II, T_{decomp} 120°C. Decomposes upon extended standing at room temperature.

2,4,6-Tris(trinitromethyl)-1,3,5-triazine (I). Compound II was chilled to 0-5°C and stirred while adding a mixture of 8 ml of H_2SO_4 (d 1.84) and 6 ml of HNO_3 (d 1.5) (**CAUTION:** violent gas evolution!). After the evolution of CO_2 had ended, the reaction mixture was allowed to stand overnight at room temperature. The precipitate was filtered off, washed with concentrated H_2SO_4, and extracted with 20-30 ml of hot CCl_4; the extract was shaken with freshly calcined magnesium sulfate to remove traces of H_2SO_4. The crystals that were formed upon cooling the filtrate were filtered off; after recrystallization from CCl_4, obtained 0.52-0.62 g (50-60%) of the product I, mp 90-91°C. Compound I is unstable in air. **EXPLOSIVE**! It is stored at 5-10°C in the form of a solution in absolute CCl_4.

2,4,6-Trimethoxy-1,3,5-triazine (IV). To a solution of 69 mg (3 mmoles) of Na in 10 ml of absolute MeOH, at room temperature, 528 mg (1 mmole) of compound I was added. The reaction mixture was stirred for 1 h, the solvent was evaporated, and the residue was recrystallized from water. Obtained 128 mg (75%) of the product IV, mp 134-136°C. Literature mp 135°C [3].

2,4-Dimethoxy-6-trinitromethyl-1,3,5-triazine (V). To a CCl_4 solution of the triazine I obtained from 2 mmoles of the hexaester III, 5 ml of absolute methanol was added at room temperature while stirring. The solution took on a yellow color that disappeared rapidly. The reaction mass was stirred for 15-20 min and then evaporated in a rotary evaporator. In order to remove the nitroform present as an impurity, the residue was treated with 20 ml of CCl_4 and 2-3 g of finely powdered, freshly calcined K_2CO_3; the resulting mixture was stirred for 15 min and then filtered. The filter was evaporated down and the residue was recrystallized from hexane, obtaining 0.58 g (50%) of the product V, mp 61°C. IR spectrum, cm^{-1}: 2900, 1580, 1520, 1480, 1370, 1260, 940, 900, 790. ^{13}C NMR spectrum ($CDCl_3$), ppm: 172.72 (N=C—O), 164.13 (—C=N), 122.79 [$C(NO_2)_3$],

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*For spectra of compounds I-III, see [1].

58.69 (CH_3O). ^{14}N NMR spectrum ($CDCl_3$), ppm: −37.65 (NO_2). Found, %: C 25.05, H 2.29, N 29.11. $C_6H_6N_6O_8$. Calculated, %: C 24.83; H 2.09; N 28.97.

2-Methoxy-4,6-bis(trinitromethyl)-1,3,5-triazine (VI). To a CCl_4 solution of compound I, obtained from 2 mmoles of the hexaester III, while holding the solution at 0-5°C, 1 ml of absolute MeOH in 20 ml of CCl_4 was added dropwise with stirring. The reaction mixture was evaporated in a rotary evaporator and then held at 30°C under vacuum (1 mm Hg) for 0.5-1.0 h to remove the nitroform. After two recrystallizations of the residue from hexane, obtained 0.28 g (35%) of the product VI, mp 100°C. IR spectrum, cm^{-1}: 2880, 1570, 1520, 1400, 1260, 1110, 990, 770, 680. PMR spectrum ($CDCl_3$), ppm: 4.32 (3H, s, CH_3). ^{13}C NMR spectrum ($CDCl_3$), ppm: 171.59 (N═C−O), 164.55 (−C═N), 121.53 [$C(NO_2)_3$], 58.91 (CH_3O). ^{14}NMR spectrum ($CDCl_3$), ppm: −40.53 (NO_2). Found, %: C 17.69; H 0.75; N 31.03. $C_6H_3N_9O_{13}$. Calculated, %: C 17.60; H 0.73; N 30.81.

4,6-Bis(trinitromethyl)2-ethoxy-1,3,5-triazine (VII). Under the conditions described above for the synthesis of VI, by washing the reaction mixture with cold water to remove nitroform and drying with calcined $MgSO_4$, from the triazine I and ethanol, after recrystallization from hexane, obtained 0.34 g (40%) of the product VII, mp 84-85°C. IR spectrum, cm^{-1}: 2900, 1595, 1500, 1450, 1280, 790. PMR spectrum ($CDCl_3$), ppm: 1.55 (3H, t, CH_3), 4.71 (2H, q, CH_2). ^{13}N NMR spectrum ($CDCl_3$), 170.91 (N═C−O), 164.54 (C═N), 121.60 [$C(NO_2)_3$], 69.69 (CH_2), 13.59 (CH_3). ^{14}N NMR spectrum ($CDCl_3$), ppm: −40.44 (NO_2). Found, %: C 19.83; H 1.25; N 29.83. $C_7H_5N_9O_{13}$. Calculated, % C 19.86; H 1.19; N 29.79.

2,2′-(Trimethylenedioxy)bis[4,6-bis(trinitromethyl)-1,3,5-triazine (VIII) and **2,2′-(Tetramethylenedioxy)bis[4,6-bis(trinitromethyl)-1,3,5-triazine] (IX).** To a solution of compound I in CCl_4, obtained from 12 g (16 mmoles) of the hexaester III, at 5-10°C, a solution of 1,3-propanediol in absolute acetonitrile was added slowly while stirring. The reaction mass was evaporated down, and the residue was dissolved in CH_2Cl_2, filtered, and passed through 400/100 μ silica gel. After removing the solvent, obtained 2.3 g (66%) of the product VIII, mp 138-140°C (from CCl_4, decomp.). IR spectrum, cm^{-1}: 2900, 1630, 1600, 1540, 1500, 1460, 1380, 1320, 1290, 1200, 1130, 1030, 1000, 900, 860, 840, 800. PMR spectrum (CD_2Cl_2), ppm: 2.51 (2H, m, $CH_2\underline{CH_2}CH_2$), 4.82 [4H, t, $2(-O-CH_2)$]. ^{13}C NMR spectrum (CD_2Cl_2), ppm: 171.392 (C−O), 164.915 [$\underline{C}-C(NO_2)_3$], 121.735 [$C(NO_2)_3$], 69.187 ($O-CH_2-$), 27.288 ($CH_2\underline{C}H_2CH_2$). ^{14}N NMR spectrum (CD_2Cl_2), ppm: −40.258 (NO_2). Found, %: C 18.73: H 0.86; N 30.60. $C_{13}H_6N_{18}O_{26}$. Calculated, %: C 18.81; H 0.73; N 30.37. Analogously, starting with 1,4-butanediol, synthesized 2.6 g (70%) of the product IX, mp 143-144°C (from CCl_4, decomp.). IR spectrum, cm^{-1}: 2900, 1630, 1600, 1520, 1500, 1360, 1340, 1310, 1290, 1180, 1130, 1120, 1040, 1000, 970, 900, 860, 840, 800. PMR spectrum (CD_2Cl_2), ppm: 2.09 [4H, m, $2(CH_2\underline{C}H_2CH_2)$], 4.67 [4H, t, $2(-O-CH_2-)$]. ^{13}C NMR spectrum (CD_2Cl_2), ppm: 171.482 (C−O), 164.902 [$\underline{C}-C(NO_2)_3$], 121.997 [$C-(NO_2)_3$], 72.895 ($-O-CH_2-$), 24.992 ($CH_2\underline{C}H_2CH_2$). ^{14}N NMR spectrum (CD_2Cl_2), ppm: 40.179 (NO_2). Found, %: C 19.95; H 0.81; N 30.05. $C_{14}H_8N_{18}O_{26}$. Calculated, %: C 19.92; H 0.96; N 29.86.

2,4-Diamino-6-trinitromethyl-1,3,5-triazine (X). A solution of the triazine I (from 2 mmoles of the hexaester III) in CCl_4 was held at 0-5°C and stirred while passing in a slow stream of dry ammonia until there was no more precipitation of $NH_4C(NO_2)_3$. The nitroform salt was filtered off, the residue on the filter was washed with 10 ml of dry $CHCl_3$, and the filtrate was evaporated in a rotary evaporator. This residue was recrystallized from CCl_4, obtaining 0.21 g (40%) of the product X, mp 145°C. IR spectrum, cm^{-1}: 3520, 3410, 3220, 1580, 1500, 1450, 1260, 1120, 950, 780. PMR spectrum [$(CD_3)_2CO$], ppm: 6.43 (4H, br.s, $2NH_2$). ^{13}C NMR spectrum [$(CD_3)_2CO$], ppm: 166.40 (CNH_2), 161.60 [$\underline{C}C(NO_2)_3$], 123.70 [$C(NO_2)_3$]. ^{14}N NMR spectrum [$(CD_3)_2CO$], ppm: −35.58 (NO_2). ^{15}N NMR spectrum [$(CD_3)_2CO$], ppm: −285.17 (NH_2, $^1J_{NH}$ = 63 Hz). Found, %: C 19.09; H 1.62; N 43.35. $C_4H_4N_8O_6$. Calculated, %: C 18.47; H 1.55; N 43.08.

2-Amino-4,6-bis(trinitromethyl)-1,3,5-triazine (XI). A solution of the triazine I (from 2 mmoles of the hexaester III) in CCl_4 was held at 0-5°C and stirred while adding dropwise a saturated solution of dry ammonia in 50 ml of CCl_4, monitoring the course of the reaction by means of TLC. The precipitated nitroform salt was filtered off, the residue was washed on the filter with 10 ml of dry $CHCl_3$, and the filtrate was evaporated in a rotary evaporator. After recrystallizing this residue from hexane, obtained 0.4 g (50%) of the product XI, mp 123-124°C. IR spectrum, cm^{-1}: 3510, 3390, 1640, 1620, 1580, 1510, 1270, 1220, 980, 790. ^{13}C NMR spectrum ($CDCl_3$), ppm: 166.02 ($C-NH_2$), 162.92 [$\underline{C}-C(NO_2)_3$], 121.82 [$C(NO_2)_3$]. ^{14}N NMR spectrum ($CDCl_3$), ppm: −39.76 (NO_2). ^{15}N NMR spectrum ($CDCl_3$): −293.13 (NH_2, $^1J_{NH}$ = 61 Hz). Found, %: C 15.48; H 10.49; N 35.70. $C_5H_6N_{10}O_{12}$. Calculated, %: C 15.23; H 0.51; N 35.54.

2-N,N-Dimethylamino-4,6-bis(trinitromethyl)-1,3,5-triazine (XII). A solution of 1.0 g (1.9 mmole) of the triazine I in 40 ml of dry CCl_4 was chilled to −15 to −20°C, and a solution of dimethylamine in dry chloroform was added slowly, dropwise. The chloroform was saturated at 18-20°C with dimethylamine obtained by boiling an aqueous solution of the dimethylamine while the vapor was passed through solid KOH. The precipitate formed in this operation was filtered off, washed with water until the nitroform salt of dimethylamine was completely dissolved, and then air-dried. The mother liquor was evaporated down, the residue was combined with the above-indicated residue, and this combined residue was dissolved in $CHCl_3$ and purified in a column (400/100 μ silica gel, eluent CCl_4—$CHCl_3$, 7:3). Obtained 0.57 g (72%) of the product XII, mp 144-145°C (from hexane, decomp.). IR spectrum, cm^{-1}: 2990, 2920, 1630, 1580, 1500, 1420, 1350, 1280, 1100, 980, 850, 820, 800. PMR spectrum ($CDCl_3$), ppm: 3.30 (6H, s, $2CH_3$). ^{13}C NMR spectrum ($CDCl_3$), ppm: 162.75 $[\underline{C}-C(NO_2)_3]$, 161.96 $[\underline{C}-N(CH_3)_2]$, 122.38 $[C(NO_2)_3]$, 37.80 (CH_3). ^{14}N NMR spectrum ($CDCl_3$), ppm: −38.85 (NO_2). Found, %: C 20.32; H 1.58; N 32.92. $C_7H_6N_{12}O_{12}$. Calculated, %: C 19.91; H 1.43; N 33.18.

2-(Methylphenylamino)-4,6-bis(trinitromethyl)-1,3,5-triazine (XIII). A solution of compound I, obtained from 4 mmoles of the hexaester III, in 100 ml of absolute CCl_4, was held at 0-5°C and stirred while adding dropwise a solution of methylphenylamine in CCl_4. The reaction mixture was treated by one of two alternative methods, designated A and B. ***A***) The precipitated nitroform salt of the amine was filtered off and washed with CCl_4, after which this was combined with the main filtrate. The solvent was driven off, and the residue was recrystallized from hexane, obtaining 1 g (52%) of the product XIII. ***B***) The reaction mixture was washed successively with water until the water layer no longer showed any color. The organic layer was separated off and dried with calcined $MgSO_4$, the solvent was driven off, and the residue was recrystallized from hexane. Obtained 0.96 g (50%) of the product XIII, mp 162°C. IR spectrum, cm^{-1}: 2980, 1630, 1605, 1585, 1500, 1495, 1415, 1385, 1335, 1315, 1285, 1205, 1175, 1125, 1100, 1080, 1065, 1025, 985, 925, 860, 855, 820, 800, 790 PMR spectrum ($CDCl_3$), ppm: 7.48-7.25 (5H, m, Ph), 3.63 (3H, s, CH_3). ^{13}C NMR spectrum ($CDCl_3$), ppm: 163.186 $[\underline{C}-N(Me)Ph]$, 162.462 and 161.799 $[\underline{C}-C(NO_2)_3]$, 140.060 ($N-C_{Ph}$), 129.857 ($o$-$C_{Ph}$), 129.132 ($m$-$C_{Ph}$), 124.343 ($p$-$C_{Ph}$), 122.362 and 122.051 $[C(NO_2)_3]$, 39.527 (CH_3). Found, %: C 29.87; H 1.59; N 28.87. $C_{12}H_8N_{10}O_{12}$. Calculated, %: C 29.75; H 1.65; N 28.92.

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