# Solubility of 1*H*-1,2,4-Triazole in Ethanol, 1-Propanol, 2-Propanol, 1,2-Propanediol, Ethyl Formate, Methyl Acetate, Ethyl Acetate, and Butyl Acetate at (283 to 363) K

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The solubility of 1*H*-1,2,4-triazole in ethanol, 1-propanol, 2-propanol, 1,2-propanediol, ethyl formate, methyl acetate, ethyl acetate, and butyl acetate at (283 to 363) K was measured using a laser monitoring observation technique. Results of these measurements were correlated with a semi-empirical equation. For the eight group data studied, the semi-empirical equation provided an accurate mathematical representation of the experimental data.

## Introduction

1*H*-1,2,4-Triazole ($C_2H_3N_3$) (CAS Registry No. 288-88-0) is a white crystalline powder and a useful chemical for synthesis of antiasthmatic, antiviral, antifungal, antibacterial, and hypnotic drugs.[1] To determine the proper solvent and to design an optimized crystallization process, it is necessary to know the solubility in solvents. Viasov determined the solubility of 1*H*-1,2,4-triazole in $H_2O$, formamide, BuOH, *m*-xylene, and *o*-xylene by an isothermal method.[2] In this paper, the solubility of 1*H*-1,2,4-triazole in ethanol, 1-propanol, 2-propanol, 1,2-propanediol, ethyl formate, methyl acetate, ethyl acetate, and butyl acetate between (283 and 363) K was experimentally determined using a laser monitoring observation technique at atmospheric pressure. The method employed in this work was classed as a synthetic method, which was much faster, more reliable, and more stable than the analytical method.[3,4]

## Experimental Section[1]

***Materials.*** The 1*H*-1,2,4-triazole used during the solubility measurements had a mass purity of 0.992, purchased from Jintan Maolu Solvent Factory. Other reagents were analytical research grade reagents from Shanghai Chemical Reagent Co.

***Apparatus and Procedure.*** The solubility of 1*H*-1,2,4-triazole was measured using an apparatus similar to that described as the literature[4−6] and described briefly here (see Figure 1). A 500 mL jacketed vessel was used to determine the solubility; the temperature in the vessel was maintained at the desired value by continuous forced water circulation from a thermostat (uncertainty of temperature ± 0.05 K). A mercury in-glass thermometer (uncertainty of temperature ± 0.05 K) was used for the measurement of the temperature in the vessel. The dissolution of the solute was examined by the laser beam penetrating the vessel. To prevent the evaporation of the solvent, a condenser vessel was introduced. At high temperatures, some amount of solvent remains in the condenser vessel, but the solvent that remained in the condenser vessel is about (0.05 to 0.3) % of total solvent. The corresponding solute partly separates out on an inner wall of the dissolution vessel. So the effect of the remainer in the condenser vessel at high temperatures can be negligible for calculating the mole fraction solubility using eq 1. The masses of the samples and solvents were determined using an analytical balance (Sartorius CP124S, Germany) with an uncertainty of ± 0.1 mg.

Pre-determined excess amounts of the solvent and 1*H*-1,2,4-triazole of known mass were placed in the inner chamber of the vessel. The contents of the vessel were stirred continuously at the required temperature. In the early stage of the experiment, the laser beam was blocked by the undissolved particles of 1*H*-1,2,4-triazole in the solution, so the intensity of the laser beam penetrating the vessel was lower. As the particles of the solute dissolved, the intensity of the laser beam increased gradually. When the solute dissolves completely, the solution will be clear, and the laser intensity reached a maximum. Small amounts of the solute of known mass (1 to 3 mg) were introduced into the vessel at intervals, and the procedure was repeated until the penetrated laser intensity could not return maximum (i.e., the last added amount of the solute no longer dissolves completely in the solvent). The interval of addition was 90 min. The total amount of the solute consumed was recorded. In order to make the measurement more efficient and get more accurate results, it is better to mill the solute initially. The same solubility experiment was conducted three times, and the mean values were used to calculate the fractional mole fraction solubility of the 1*H*-1,2,4-triazole in the solvent, $x_1$, based on eq 1:

$$x_1 = \frac{m_1/M_1}{m_1/M_1 + m_2/M_2} \tag{1}$$

where $m_1$ and $m_2$ represent the masses of the solute and the solvent, respectively; and $M_1$ and $M_2$ are the molecular weight of the solute and the solvent, respectively. The estimated uncertainty of the solubility values based on error analysis and repeated observations was within 1.0 %.

## Results and Discussion

The measured solubility data of 1*H*-1,2,4-triazole in ethanol, 1-propanol, 2-propanol, 1,2-propanediol, ethyl formate, methyl acetate, ethyl acetate, and butyl acetate between (283 and 363) K are presented in Table 1. The temperature dependency of the

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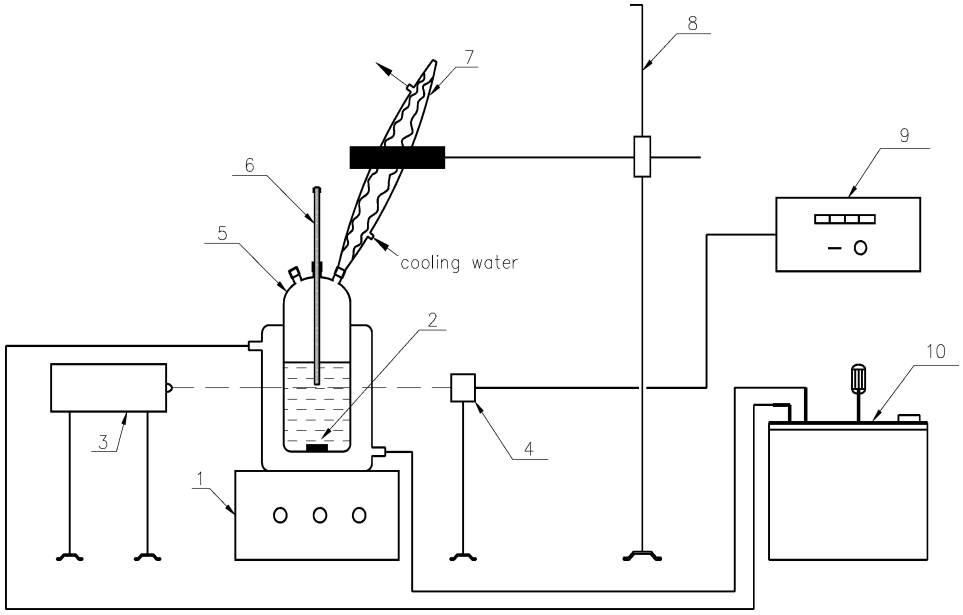


**Figure 1.** Schematic setup for the solubility measure: 1, magnetic stirrer; 2, stir bar; 3, laser generator; 4, photoelectric converter; 5, dissolution vessel; 6, thermometer; 7, condenser; 8, a ring stand and clamp; 9, digital display; 10, thermostat.

**Table 1. Mole Fraction $x_1$ of 1*H*-1,2,4-Triazole in Pure Solvents**

| *T*/K | $x_1$ | $x_1^{calc}$ | *T*/K | $x_1$ | $x_1^{calc}$ |
|---|---|---|---|---|---|
| Ethanol | | | | | |
| 283.18 | 0.1314 | 0.1309 | 313.21 | 0.2531 | 0.2526 |
| 288.25 | 0.1471 | 0.1473 | 318.23 | 0.2799 | 0.2793 |
| 293.21 | 0.1643 | 0.1649 | 323.22 | 0.3084 | 0.3079 |
| 298.18 | 0.1836 | 0.1841 | 328.27 | 0.3389 | 0.339 |
| 303.15 | 0.2047 | 0.2050 | 333.28 | 0.3709 | 0.3721 |
| 308.14 | 0.2278 | 0.2276 | | | |
| 1-Propanol | | | | | |
| 283.17 | 0.1205 | 0.1201 | 318.20 | 0.2557 | 0.2554 |
| 288.18 | 0.1345 | 0.1346 | 323.22 | 0.2830 | 0.2825 |
| 293.27 | 0.1504 | 0.1508 | 328.28 | 0.3127 | 0.3122 |
| 298.19 | 0.1675 | 0.1679 | 333.18 | 0.3437 | 0.3434 |
| 303.21 | 0.1867 | 0.1870 | 338.23 | 0.3780 | 0.3782 |
| 308.23 | 0.2078 | 0.2080 | 343.29 | 0.4149 | 0.4161 |
| 313.27 | 0.2310 | 0.2309 | | | |
| 2-Propanol | | | | | |
| 283.17 | 0.1294 | 0.1301 | 318.22 | 0.2537 | 0.2543 |
| 288.21 | 0.1441 | 0.1439 | 323.27 | 0.2779 | 0.2786 |
| 293.16 | 0.1592 | 0.1585 | 328.20 | 0.3036 | 0.3043 |
| 298.23 | 0.1756 | 0.1749 | 333.19 | 0.3320 | 0.3324 |
| 303.27 | 0.1930 | 0.1926 | 338.18 | 0.3629 | 0.3626 |
| 308.19 | 0.2114 | 0.2113 | 343.26 | 0.3972 | 0.3957 |
| 313.24 | 0.2318 | 0.2321 | | | |
| 1,2-Propanediol | | | | | |
| 283.16 | 0.1745 | 0.1805 | 323.21 | 0.4511 | 0.4571 |
| 288.27 | 0.2125 | 0.2120 | 328.22 | 0.4827 | 0.4905 |
| 293.26 | 0.2488 | 0.2448 | 333.23 | 0.5137 | 0.522 |
| 298.16 | 0.2837 | 0.2785 | 338.29 | 0.5446 | 0.5514 |
| 303.19 | 0.3187 | 0.3142 | 343.21 | 0.5742 | 0.5774 |
| 308.18 | 0.3527 | 0.3502 | 348.23 | 0.6039 | 0.6009 |
| 313.20 | 0.3862 | 0.3865 | 353.24 | 0.6333 | 0.6213 |
| 318.28 | 0.4194 | 0.4228 | | | |

| *T*/K | $x_1$ | $x_1^{calc}$ | *T*/K | $x_1$ | $x_1^{calc}$ |
|---|---|---|---|---|---|
| Ethyl Formate | | | | | |
| 283.21 | 0.02083 | 0.02100 | 308.17 | 0.04459 | 0.04478 |
| 288.23 | 0.02460 | 0.02434 | 313.24 | 0.05235 | 0.05251 |
| 293.29 | 0.02864 | 0.02833 | 318.27 | 0.06168 | 0.06159 |
| 298.24 | 0.03309 | 0.03293 | 323.31 | 0.07295 | 0.07236 |
| 303.26 | 0.03838 | 0.03843 | | | |
| Methyl Acetate | | | | | |
| 283.27 | 0.0968 | 0.0972 | 308.29 | 0.1552 | 0.1558 |
| 288.21 | 0.1064 | 0.1063 | 313.18 | 0.1710 | 0.1716 |
| 293.19 | 0.1168 | 0.1166 | 318.16 | 0.1892 | 0.1896 |
| 298.21 | 0.1282 | 0.1281 | 323.24 | 0.2104 | 0.2101 |
| 303.20 | 0.1408 | 0.1410 | | | |
| Ethyl Acetate | | | | | |
| 283.21 | 0.0268 | 0.0277 | 313.20 | 0.0578 | 0.0588 |
| 288.29 | 0.0320 | 0.0313 | 318.21 | 0.0660 | 0.0671 |
| 293.21 | 0.0365 | 0.0353 | 323.16 | 0.0759 | 0.0767 |
| 298.19 | 0.0410 | 0.0399 | 328.17 | 0.0884 | 0.0878 |
| 303.18 | 0.0457 | 0.0453 | 333.27 | 0.1040 | 0.1010 |
| 308.27 | 0.0513 | 0.0516 | | | |
| Butyl Acetate | | | | | |
| 283.20 | 0.0141 | 0.0148 | 328.24 | 0.0586 | 0.0596 |
| 288.23 | 0.0166 | 0.0171 | 333.19 | 0.0688 | 0.0703 |
| 293.26 | 0.0202 | 0.0198 | 338.18 | 0.0809 | 0.0832 |
| 298.22 | 0.0240 | 0.0229 | 343.23 | 0.0955 | 0.0987 |
| 303.24 | 0.0279 | 0.0267 | 348.18 | 0.1130 | 0.1170 |
| 308.17 | 0.0320 | 0.0311 | 353.19 | 0.1359 | 0.1391 |
| 313.28 | 0.0370 | 0.0366 | 358.18 | 0.1667 | 0.1654 |
| 318.21 | 0.0428 | 0.0429 | 363.26 | 0.2111 | 0.1975 |
| 323.16 | 0.0498 | 0.0504 | | | |

1*H*-1,2,4-triazole solubility in pure solvents is described by the modified Apelblat equation, which is a semi-empirical equation:[6−9]

$$\ln x_1 = A + \frac{B}{T/\mathrm{K}} + C \ln(T/\mathrm{K}) \qquad (2)$$

where *T* is the absolute temperature, and *A*, *B*, and *C* are dimensionless fitting parameters. The corresponding calculated solubility of 1*H*-1,2,4-triazole are also given in Table 1. The values of the parameters *A*, *B*, and *C* and the root-mean-square deviations (RMSDs) are listed in Table 2. The RMSD is defined as

$$\mathrm{RMSD} = \left[\frac{\sum_{j=1}^{N}(x_{1,j} - x_{1,j}^{calc})^2}{N-1}\right]^{1/2} \qquad (3)$$

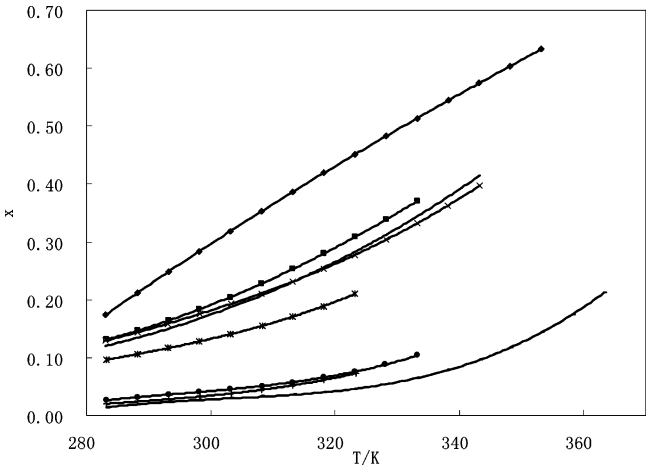


**Figure 2.** Mole fraction solubility ($x_1$) of 1*H*-1,2,4-triazole in different solvents: ◆, 1,2-propanediol; ■, ethanol; ▲, 1-propanol; ×, 2-propanol; ∗, methyl acetate; ●, ethyl acetate; +, ethyl formate; −, butyl acetate.

**Table 2. Parameters of Equation 2 for the Solubility of 1*H*-1,2,4-Triazole in Pure Solvents**

| solvent | *A* | *B* | *C* | $10^3$ rmsd |
|---|---|---|---|---|
| ethanol | −14.81 | −1068.8 | 2.9314 | 0.58 |
| 1-propanol | −36.107 | −112.8 | 6.0903 | 0.48 |
| 2-propanol | −41.518 | 316.05 | 6.7946 | 0.69 |
| 1,2-propanediol | 186.84 | −10276 | −26.968 | 5.93 |
| ethyl formate | −162.58 | 4772.2 | 25.126 | 0.28 |
| methyl acetate | −111.98 | 3453.7 | 17.26 | 0.39 |
| ethyl acetate | −154.42 | 4833.1 | 23.692 | 1.27 |
| butyl acetate | −194.25 | 6199.2 | 29.781 | 3.85 |

$N$ is the number of experimental points, $x_{1,j}^{calc}$ is the calculated solubility from eq 2, and $x_{1,j}$ is the corresponding experimental solubility.

## Conclusions

From the data listed in Tables 1 and 2, one can draw the following conclusions: (i) The solubility of 1*H*-1,2,4-triazole increases with the increasing of temperature for eight pure solvents studied in this work (see Figure 2). The solubility of 1*H*-1,2,4-triazole in butyl acetate is the lowest and largest in 1,2-propanediol. (ii) The butyl acetate may be used as a dilution in order to increase the yield of the product in the crystallization process of 1*H*-1,2,4-triazole. (iii) The experimental solubility data and the correlation equation tested in this work are essential in the purification process of 1*H*-1,2,4-triazole. (iv) Last, the calculated solubilities are in very good agreement with the experimental data.

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