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Inclusion complex of Sulfathiazole Schiff base- Beta cyclodextrin

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Abstract
The interaction between Schiff base of Sulfathiazole and (β-CD) was investigated. The Inclusion complex was prepared followed freeze drying method and the mode of interaction was characterized by IR , 1HNMR and DSC analysis , the IR bands and 1HNMR signal undergo significant shifts or masked by host bands. The XRD patterns show the decrease of crystinality of the complex. The Phase solubility study was investigated following Higuchi and Connors method and the result indicated the enhancing the aqueous solubility by ~6 folds and the value of solubility constant (1131 M-1) indicate the formation of 1:1 Schiff : (β-CD) molar ratio.
Keywords: *Sulfathiazole , Schiff base , Inclusion complex , Phase solubility.*

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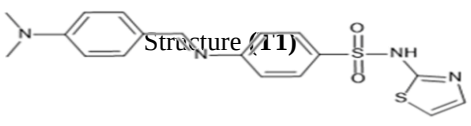
I. Introduction :

Inclusion complex (IC) a system consist of a guest molecules such as drug or any chemical compound interact with a host compound formed a specific structure and cyclodextrin where the CD have inner cavity has partial hydrophobic character and they can accommodate small lipophilicmolecules , beside that the cyclodextrin are nontoxic material[1][2][3][4][5] , in this regard cyclodextrin consider on of the best material for drug delivery.

II. Experimental :

Material : (β-CD) s commercially available purchased from Acros organic company , 4-(dimethyl amino)benzaldehyde was supplied from BDH company and recrystallized from hexane, Sulfathiazole was supplied from Sigma Aldrich company and used as received. Other Chemical were of the analytical grade and were used as received.

Instruments:
FT-IR spectra were recorded on a (SHIMADZU)spectrophotometer between 4000-400 cm^{-1} as KBr pellets. ^{1}HNMR spectra were recorded on Brucker 500 (500 MHZ) as DMSO-d_6 solution at room temperature. Images of the morphological surface of the samples under a scanning electron microscope (SEM) using a ZEISS SIGMA VP device from Carl Zeiss Microscopy Germany at the Laboratories of Day Petronic Company in the Islamic Republic of Iran / Tehran. XRD patterns of base and complexe was recorded using a Panalytscal X PERT PRO. Panalytical Company Netherlands at 2θfrom (5°-80°)using (1.5406 Å = λ).
Preparation:
Preparation of (E)-4-((4-(dimethylamino)benzlidene)amino)-N-(thiazol-2-yl)benzenesulfonamide(T1)


Structure (T1)

To a warm ethanol solution of sulfathiazole (3 mmole , 0.765 g) , 3 mmole of ethanolic solution of 4-(dimethyl amino)benzaldehyde was added drop wise and the resulting mixture was refluxed for 4 hrs and the resulting yellow precipitate which obtain filtered hot and the precipitate washed several times with cold ethanol and dried to afford a yellow crystal , m-p 206-208 $C^{o,}$ yield 72%.

Preparation of Schiff base- (β-CD) inclusion complex:
Freeze drying method was employed to prepare the inclusion complex between (β-CD) and (E)-4-((4-(dimethylamino)benzlidene)amino)-N-(thiazol-2-yl)benzenesulfonamide as following:-
Equimobr from (β-CD) and (E)-4-((4-(dimethylamino)benzlidene)amino)-N-(thiazol-2-yl)benzenesulfonamide was mixed in deionized water at room temperature and stirred for 72 hrs and then filtered and the filtered then lyophilized in a freeze drying type CHRIST model alpha LD plus until completely drying and the resulting fine powder kept in desiccator over silica gel.

III. Result and discussion :

The prepared Schiff base was characterized by **IR**[1]HNMR and **EI-mass** analysis. The mass spectrum Fig.1 Show the molecular ion at m/z= 386 which confirm the condensation of sulfa and aldehyde in 1:1 molar ratio.

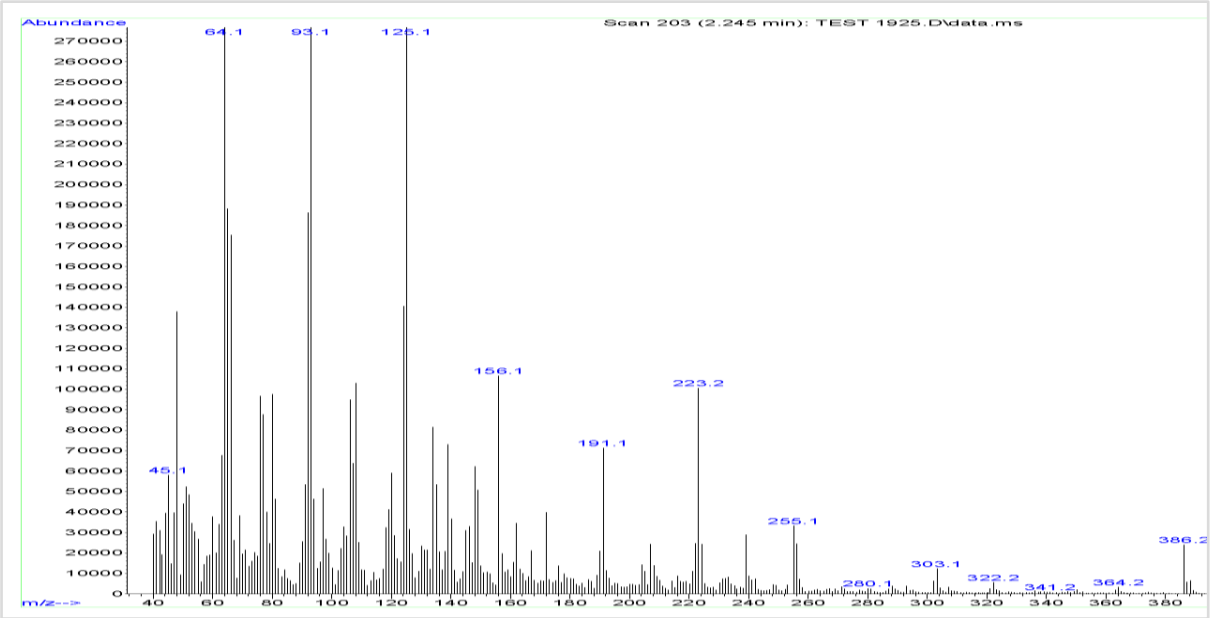


Fig (1) : EI-mass spectrum of (T1)

The IR spectrum show a strong band at 1608 cm^{-1} attributed to υC=N which indicated the formation of Schiff base[6]

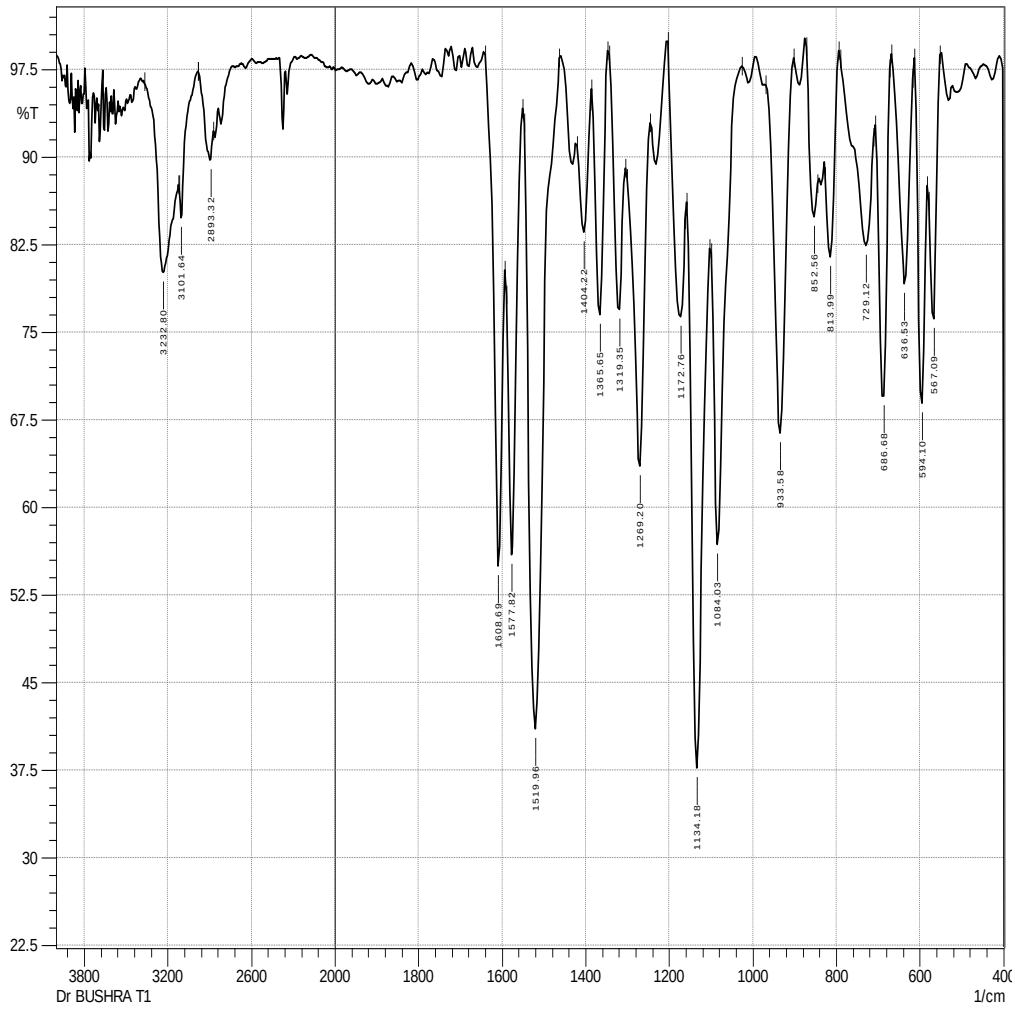


Fig (2) :IR spectrum of (T1)

The ^{1}HNMR spectrum show a signal characteristic to azomethine proton (HC=N) at δ8.3 ppm. Interaction between Schiff base and (β-CD) were studied by a comparison of IR ^{1}HNMR as well as XRD and DSC analysis , a significant change in IR bands position of Schiff base were observed , were the strong vibration of C=N at 1597 cm^{-1} in pure Schiff base was shifted to lower frequency ($\Delta\upsilon$=-11 cm^{-1}). Also the two bands attributed to o=s=o are shifted where asymmetric band at 1365 cm^{-1} was shifted to higher frequency (+8 cm^{-1}) and the other strong band at 1134 cm^{-1} was shifted also to higher frequency (+ 23 cm^{-1}). The ^{1}HNMR spectrum of the inclusion complex (Fig. 3)show the shift of the signals attributed at aromatic protons as well as the protons of (β-CD) compered with the pure (β-CD)[7][8].

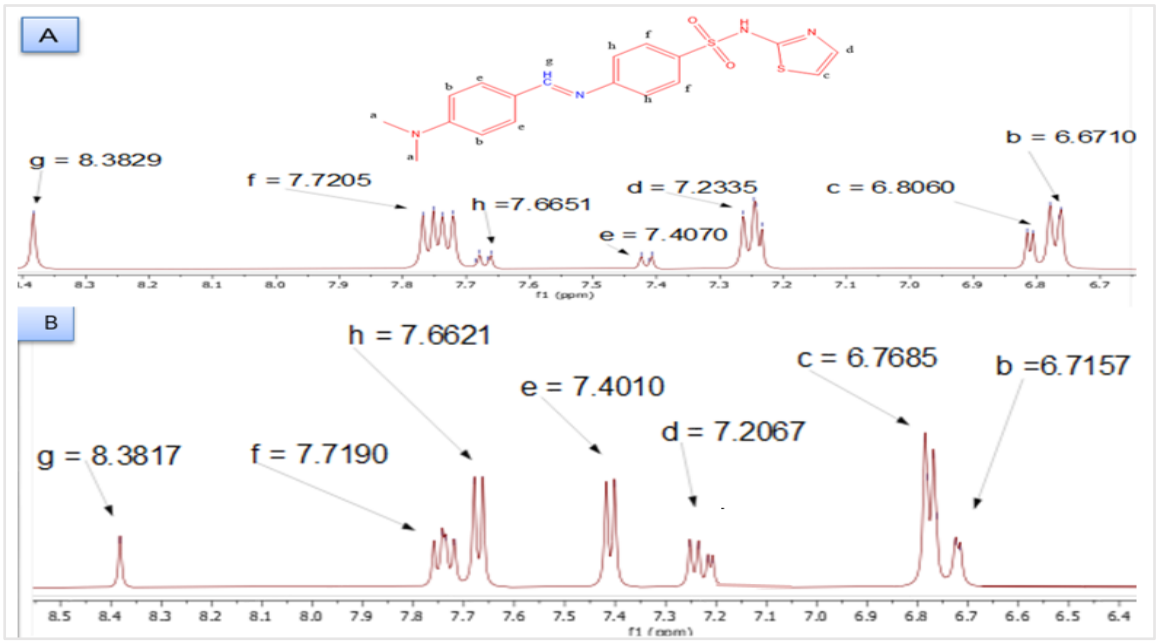


Fig. 3: [1]HNMR spectra of (a)- Schiff base (b)- Schiff base- β-CD inclusion complex

SEM : The SEM figures,of Schiff base and their inclusion complex are depicted in(Fig. 4). it can be noted that the Schiff base particle a block like shape in micrometer size while the inclusion complex have a amorphous shape which indicate the formation of complex[9].

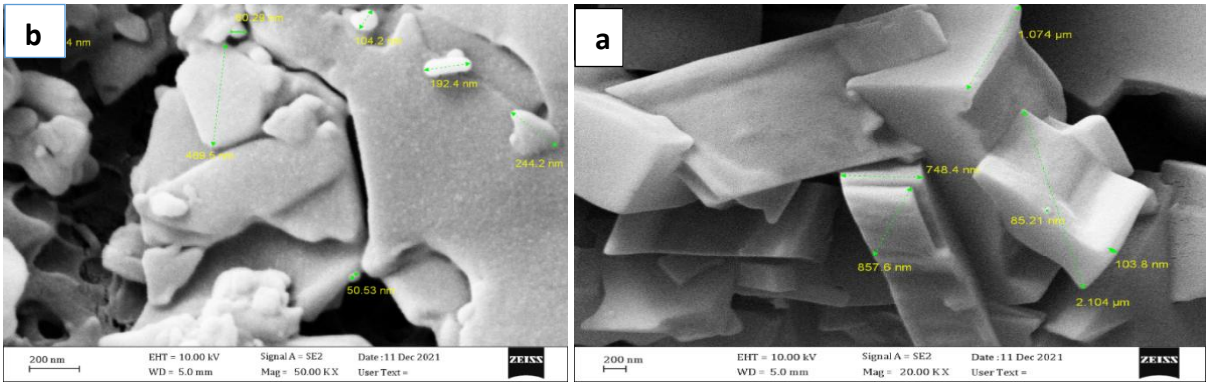


Fig. 4: SEM images of (a)Schiff base (b)- Schiff base- β-CD inclusion complex

XRD : the XRD pattern of Schiff base show an intense peaks at 2θ = 19.34 , 22.4 and 24.74 , which indicted the crystanility of the schiff base , when compered XRD pattern with inclusion complex the later show a change in the position of the peaks compared with pure (β-CD) and pure Schiff base and decrease in intensity as show in (fig. 5)and this confirmed the formation of inclusion complex [10][11][12].

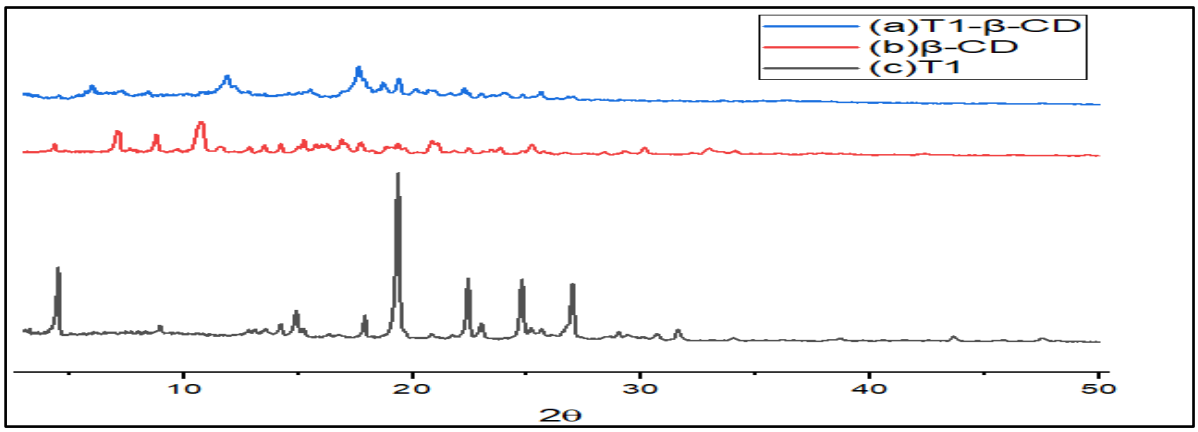


Fig. 5: XRD patterns (a)Schiff base (b)- β-CD (c)- Schiff base- β-CD inclusion complex

DSC : DSC curve displayed and endothermic of fusion at 212.56 C^o with ΔH = +11.73 KJ/mole and broad exothermic peak onset at 232.4 C^o end at 265.6 C^o which may be attributed to decomposition while the DCS of inclusion complex Fig. 6 show no endothermic of Schiff base (guest) was observed which provided the formation of inclusion complex[12][13].

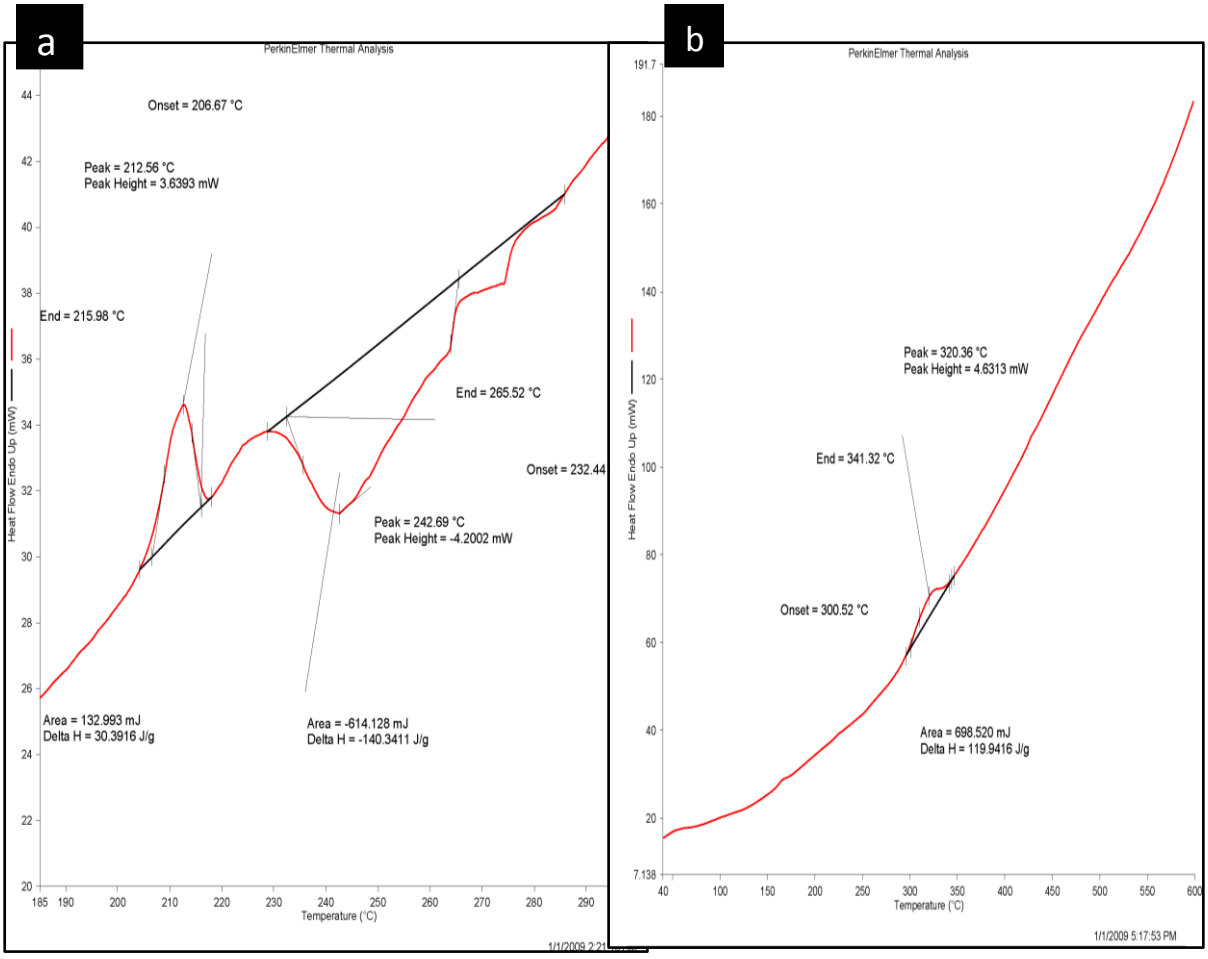
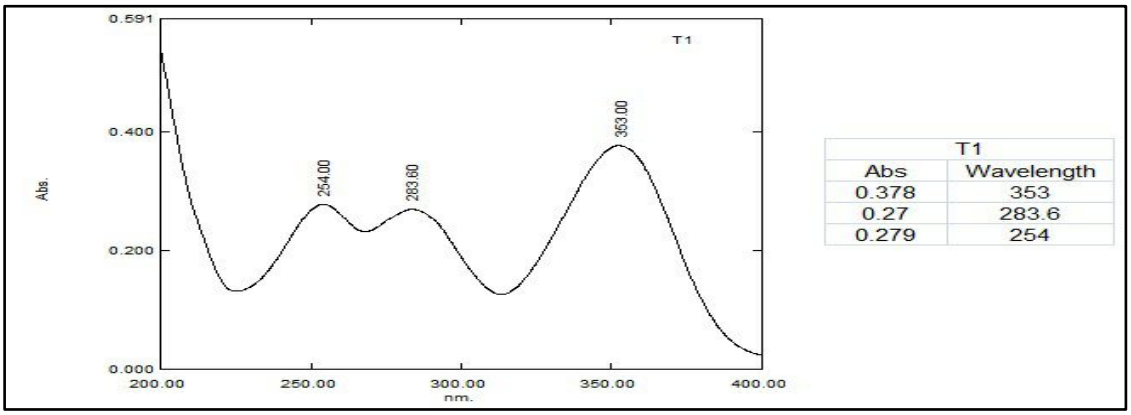


Fig (6) DSCthermogram of (a)Schiff base (b)- Schiff base- β-CD inclusion complex

Phase solubility : Phase solubility study was performed following the Higuchi and Connors method[14]. First the UV-visible spectrum of Schiff base in water (10^{-4} M) was measured (Fig.7) to find the λ max (nm) and the molar absorptivityε was determined(3780 $L.m^{-1}.cm^{-1}$) the second step preparation a series of (β-CD) solution in water (0.002 – 0.015 M) and for each solution an excess of Schiff base were added and shaken for 72 hrs and then filtered and the UV spectra were recorded after sutible dilution. The phase solution diagram (Fig. 8) show the increasing in solubility linearly and classified as A_L. And the solubility increased by ~6 fold.



T1	
Abs	Wavelength
0.378	353
0.27	283.6
0.279	254

Fig (7) UV-visible spectrum of Schiff base

CD (M)	T1 SOLUBILITY (M)	T1(mg)
0.001	0.0028	1080
0.003	0.00467	1802
0.006	0.0058	2238
0.009	0.0081	3126
0.012	0.0112	4323
0.015	0.0125	4825

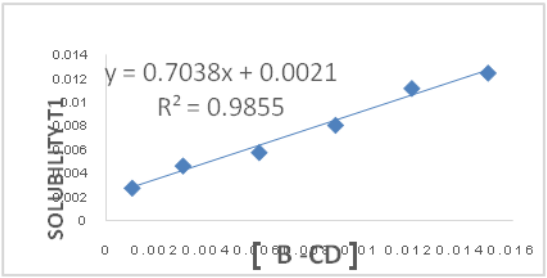


Fig (8)Phase solubility digram

Phase solubility analysis yielded additional information such as association constant were association constant determined form the relation

Where S_O is the solubility in the distilled water and obtained from the intercept the value of K_C was found to be 1131 M^{-1} and indicated the 1:1 molar ratio.

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