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AN EFFICIENT SYNTHESIS OF BENZOTRIAZEPINE FROM A COMPLEX ARYLHYDRAZONE BY CATALYTIC TRANSFER HYDROGENATION

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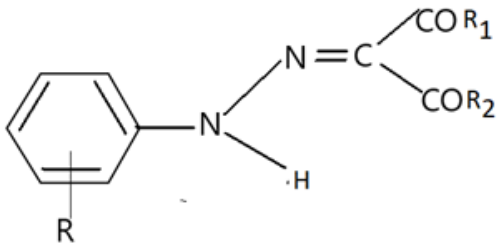
ABSTRACT

A new and efficient protocol is developed for the synthesis of benzotriazepine derivatives from 2-cyano-2-o-nitrophenylhydrazono ethanoic acid by catalytic transfer hydrogenation using 10% Pd-C as a catalyst, various hydrogen donors and solvents. The new synthesized compound has been characterized by IR, ^{1}HNMR and mass spectral studies.

KEYWORDS: Benzotriazepine Derivative, Electron Impact Studies, 2-Cyano-2-0-nitrophenylhydrazono ethanoic acid

Complex Hydrazones are aryl hydrazones (Armbruster *et al.*, 2006; bukhinghum, 1968; Prasad and Singh, 2004; Prasad, 2011) of the type.



(I)

Where the carbonyl gr. of side chain is capable of forming intramolecular hydrogen bonding with the arylamino H-atom

$R=NO_2$

$R_1=R_2=OC_2H_s$

$R_1=OC_2H_5$, $R_2=CH_3$

$R_1=OC_2H_5$, $COR_2=CN$

$R_1=OH$, $COR_2=CN$

The title compound(I) possessing multifunctional reactive sites are starting materials for the synthesis of different condensed nitrogen heterocycles by cyclization reactions (Chakarborty *et al.*, 2011; Robinson, B.,1963; Rogers, 1947)

This paper presents the synthesis of 4-amino, 3-carboxyl- IH-benzo-1,2.5-triazepine from 2-cyano-2-0-nitrophenylhydrazono ethanoic acid.(I,R_1=OH,COR_2 =CN)

In a search for more active hydrogen donors for transfer hydrogenation, it was found that formic, hypophosphorous and phosphoric acids or their salts in the presence of a catalyst would reduce nitro compounds to amines in high yield (Entwistle *et al.*, 1977) as alternative donors to cyclohexene and hydrazine, these acids and their salts have several advantages.

The effectiveness of catalytic transfer hydrogenation of aromatic nitro compounds to the corresponding amino compounds, utilizing unsaturated hydrocarbons as hydrogen donors was demonstrated ago (Braude *et al.*, 1954). Subsequent general application of this mild, convenient technique in synthesis was slow to follow (Hartner, 1980)

The earlier reported much wider use of hydrazine as hydrogen donor for reduction of nitro group with a variety of metal catalysts has been reviewed (Furst *et al.*, 1965)

The use of cyclohexene as hydrogen donor with catalyst-to-substrate ratio of 1:100 in earlier work (Hartner, 1980) resulted in inordinately long reduction times and many non-specific reductions were recorded.

Certainly these catalytic transfer reductions at the very least are a considerable technical improvement over the rather messy traditional reductions with metals and acids. The catalytic transfer reactions appear to be more selective than regular catalytic hydrogenation (Braude *et al.*, 1954)

N Heterocycles are abundant in nature and are of great significance to life, hence they have attracted considerable attention towards the design of biologically active molecules and advance organic materials. Benzotriazepines comprise an interesting class of

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heteroatomic compounds because of their significant biological and pharmaceutical properties such as antibacterial, antiviral psychotropic and antimalarial properties (A.Naraharibabu *et al.*, 2001; Reddy, Ch K, 1985)

Few attempts were made to reduce nitro group attached to the benzene ring of complex arylhydrazones (Braude, E.A. and Linstead, R.P., 1954) by catalytic transfer hydrogenation.

Therefore, We are describing in this communication interesting findings by CTH method by using 10% P-C as a catalyst, various H donors and solvent.

The reduction of an organic compound with an organic molecule as the hydrogen donor and a solvent in the presence of a catalyst is called catalytic transfer hydrogenation (Braude *et al.* 1954; Braude *et al.*, 1952)

$$DHx+nA \rightarrow nAHx+D$$

Where DH_x = a donor Compound

A = hydrogen acceptor

The reaction conditions are the following:-

i. Nature of donor
ii. Effect of solvents
iii. Effect of temperature
iv. Other variables

The donor compound can be any organic compound whose oxidation potential is sufficiently slow so that the hydrogen transfer can occur under mild condition.

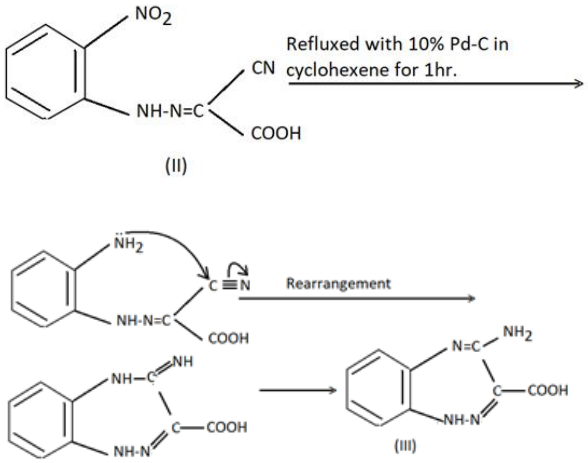
A wide range of conditions for carrying out heterogeneous hydrogen transfer reductions of arenes has been applied. (Hartner,1980; Furst 1965 Barber *et al.*, 1961; Brieger *et al.*, 1974)

It was thought worthwhile to prepare o-amino derivative of

I ($R=NO_2$,R_1,=OH and R_2=CN)

The E-form of 2-cyano-2-0-nitrophenyhydrozono ethanoic acid, on reduction with 10% Pd-C by refluxing with cyclohexene acting both as a solvent and as a H donor gave 4-amino-3-carboxy-1-hydro-1,2,5-benzotriazepine III, a deep red oil.

The same product was obtained on reduction with 10% Pd-C and hydrazine hydrate acting both as a solvent and as H donor at room temp.



10%Pd-C in hydrazine hydrate at room temp.

II ⟶ III

The identity of the cyclic compound (III) is confirmed by its IR, ^{1}HNMR and by examining the fragmentation pattern in its mass spectrum.

EXPERIMENTAL METHODOLOGY

Melting points were measured in sulphuric acid bath in open capillaries and are uncorrected. Infrared spectra were recorded on Perkin Elmer spectrum version and in Startech Labs Pvt. Ltd. using KBr pellets. The NMR spectrum was, recorded on Bruker AvII-400MHz FTNMR with VT. The DART-Mass was recorded on a JEOL-Accu-TOF JMS- T100LC Mass spectrometer having a DART source. The given samples were subjected as such in front of DART source. Dry Helium was used with 4LPM flow rate for ionization of 350^{o}C. The orifice I was set at 28V and spectra were collected and print outs are averaged spectra of 6-8 scans.

Preparation of 2-cyano-2-o-nitrophenylhydrazono Ethanoic acid.,II

0-Nitroaniline (6.9g, 0.05 mol) was dissolved in conc. hydrochloric acid (12.5mL) and diazotized by gradual addition of sodium nitrite (13.5g) in water (4mL) at o-5^{o}c. The filtered benzene diazonium salt soln. was run drop wise into the cooled soln of cyanoacetic acid (4.25mL) in 100 mL of water- acetone (50:50, v/v) mixture containing sodium acetate (Brieger and Nestrick, 1974; Prasad and Singh, 2004) The deep red ppt. was collected by filtration after stirring the mixture for Ihr, in 90% yield, having m.p. 215^{o}C. The main product showed two spots on TLC of which the intensity of the slower moving component was greater than that of faster moving one.

Preparation of Benzotriazepine derivative,III

Method-a

2-cyano-2-o-nitrophenylhydrazono ethanoic acid II (250mg) was mixed with cyclohexene (50ml) and then added portion wise 10% Pd-C(100mg) with occasional stirring. The content was refluxed for 1hr. and filtered hot. On evaporation of the solvent, a deep red oil was obtained, Yield, 80%. The compound gave a single spot on TLC.

Method-b

2-cyano-2-o-nitrophenylhydrazono ethanoic acid II (250mg) was dissolved in hydrazine hydrate (50mL) and then added 10% Pd-C (100mg) portion wise with occasional stirring. A vigorous reaction occurred with evolution of heat. The mixture was cooled for some 20 minutes and filtered. On evaporation of the solvent, a deep red oil was obtained which gave a single spot on TLC, yield, 80%.

RESULTS AND DISCUSSION

IR spectral studies of III-

The two NH stretching frequencies of the amino derivative were observed in the region 3391.29 cm^{-1} and 2900 cm^{-1} as a broad band and as a medium band respectively. These bands were assigned as NH stretching frequencies of (NH_2) and (-NH-N=C) groups respectively.

The bands at 1643.48cm^{-1} and 1638cm^{-1} (s) can be assigned as vC=O and vC-O stretching vibrations respectively.

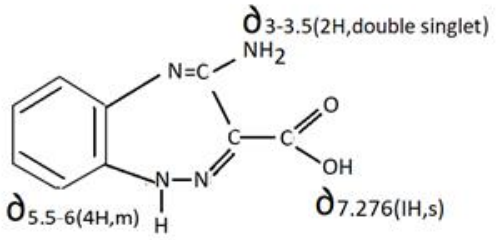
The absence of C≡N stretching frequency in the ir spectrum obviously shows that the reduction product was not the free amino compound.

The Characteristic ir absorptions are in confirmity of the structure (Robinson, 1963; Srivastava, A.K.,1989; Sarokin, V.J., 1974)

Table 1: Elemental analysis

Compound (Colour)	% analysis Found (Calculated)			%yield	Molecular Formula
(II)	C	H	N		
Adeep red Solid	46.15	2.56	25.158	90%	$C_9H_6N_4O_4$
	(46.05)	(2.5)	(23.81)		
(III)	52.06	3.69	27.05	80%	$C_9H_8N_4O_2$
Adeep red Oil	(52.94)	(3.92)	(27.45)		

^{1}HNMR spectral studies of III-



The ^{1}HNMR spectrum of amino derivative showed resonances at δ7.275(IH,s) as a singlet (carboxyl proton). Four aromatic protons in the form of multiplet showed resonances at δ 5.5-6.0.

The resonances at δ3-3.5(2H,s) and δ3.494(IH,s) were assigned as amino and imino groups protons respectively.

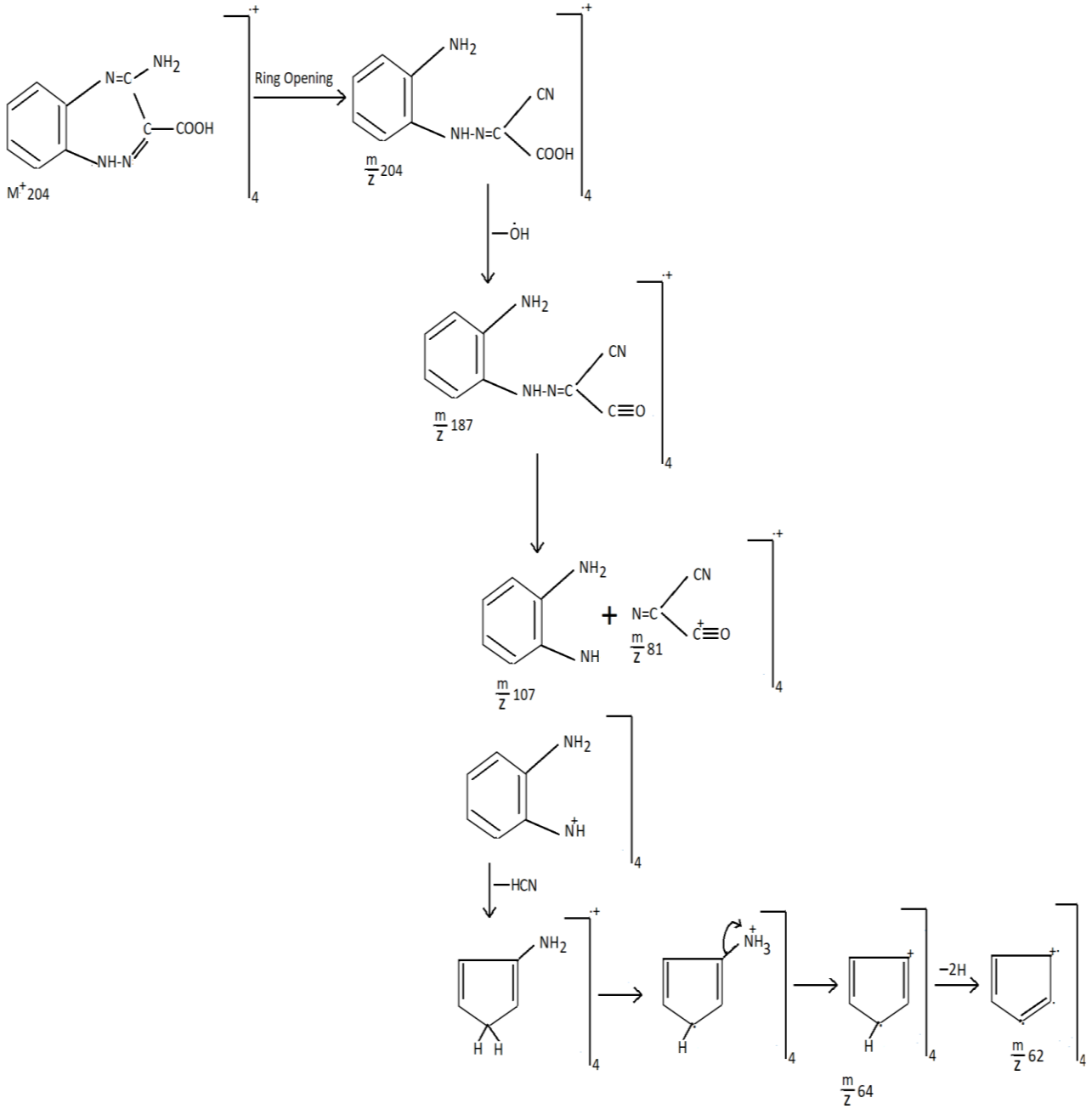
The relative intensity of the ions excluding ions of low abundance in case of III are as follows:

Table 2: MASS Spectral data of III-

m/z	Relative Intensity%
816	.8196
750	.8196
652	24.9
474	40.98
443	32.78
344	12.29
326	27.09
295	16.39
(B.P.) 248	100.00
229	40.98
214	14.75

The mass spectrum of the compound III was examined and showed that M^+ appears at 204 as a tetramer. The observed mass was found to be in agreement and in confirming the molecular formula $C_9H_8N_4O_2$.

The formation of the base peak at m/z,$(62)_4$ =248 is due to the ring opening by thermal isomerisation followed by cleavage of N-N bond of hydrazo gr.



CONCLUSION

We can say that we have designed an easy and eco-friendly method for the synthesis of benzotriazepine derivative by catalytic transfer hydrogenation which provided direction for the design of molecules in future.

We have endeavored to show that an interesting alternative to conventional catalytic hydrogenation with an organic molecule as H donor. This reaction, using predominantly Pd, permits the reduction of a wide variety of olefins, nitriles, nitro compounds and other N-containing unsaturated functional groups. The donors are readly available organic compounds such as cyclohexene, alcohols. The yields are in most cases excellent and fully comparable to those of normal catalytic hydrogenation. The reductions are generally stereospecific. The only major difference, in fact, is the slower rate, which could be an asset to experimental investigation. The catalyst was reused at least two times with no appreciable loss of reactivity. Prospects for the future work include the development of catalyst – donor system capable of reducing carbonyl functions under mild conditions, wider studies on the applicability of this reaction.

All the spectroscopic data were found to be in good agreement with the structure.

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