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Original Article

CATALYTIC SYNTHESIS OF TRIAZOLES AND TETRAZOLES BY COPPER TRIFLATE UNDER MICROWAVE IRRADIATION AND TO EVALUATE THEIR BIOLOGICAL ACTIVITIES

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ABSTRACT

An efficient synthetic approach of pharmacologically important diversely functionalized compounds (Triazoles and Tetrazoles) through the cycloaddition of Glucals, Azides and nitriles in presence of CuII(OTf) as a catalyst by conventional and microwave methods and to compare the yields. The antibacterial activity of the triazoles and tetrazole were tested by serial dilution method taking drug at a concentration of 150 mg/ml. The anti-fungal activies of the triazoles and tetrazole were tested by agar diffusion method (cup-plate method) taking drug at a concentration of 100 mg/ml and 150 mg/ml against five fungi (C.albicans, C.rugosa, S.cerevisiae, A.flavus and A.niger).

Keywords: *Cycloaddition, CuII(OTf), antibacterial activity & anti-fungal activity.*

1. INTRODUCTION:

1, 2, 3-Triazoles and tetrazoles have continued to attract considerable attention in the past decade. An enormous number of publications and patents appear every year.

The use of benzotriazole as a synthetic auxiliary in particular has been the focus of intensive studies since the start of the 1990s.

1,2,3-Triazole and tetrazoles are potential targets for drug discovery as they exhibit a broad spectrum of biological properties such as anti-viral, anti-bacterial, anti-epileptic, and anti-allergic behavior.

They have also found applications as optical brighteners, light stabilizers, fluorescent whiteners, and corrosion-retarding agents.

Not only the above mentioned properties but they posses some more activities such as antileukemic, antitumor, antiallergic, antihistaminic, anti-inflamatory etc and also posses aromatase inhibitory activity.

Since the early 1980, the growth of Tetrazole chemistry has continued unabated as judged by the number of publications and patents relating to various types of Tetrazoles.

Unlike the 1960s, and 1970s, most good heterocyclic chemistry books now contain considerable discussion of the tetrazole ring.

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The atmosphere of TITAN, the largest moon of saturn, appears to be compatible with Tetrazole chemistry and indeed the first claims of Tetrazole compounds on TITAN have appeared.

Tetrazoles are class of heterocyclics with a wide range of applications that are receiving considerable attention. This functional group has a role in coordination chemistry, as well as in various materials, science applications, including photography, and specialty explosives.

A wide range of tetrazole derivatives has been patented for anti hypertension activity and as angiotensin - II receptor antagonists.

Tetrazoles are class of heterocyclics[1] with a wide range of applications that are receiving considerable attention.

This functional group has a role in coordination chemistry, as well as in various materials, science applications, including photography, and specialty explosives.

More over extensive work has been carried out in the field of medicinal chemistry.

Tetrazoles and Triazoles are frequently used as metabolically stable surrogates for carboxylic acids, as the Tetrazoles and Triazoles generally offer a more favorable pharmacokinetic profile.

Driven in particular by the widespread incorporation of Tetrazole and Triazoles functionality into angiotensin-II antagonist structures (sartan).

Several methods have been described for the synthesis of Tetrazoles and Triazoles

Tetrazoles[2] were useful for treating congestive heart failure and preventing cardiac hypertrophy.

Azetidin-2-ones[3] displayed moderate to potent activity against a variety of bacteria.

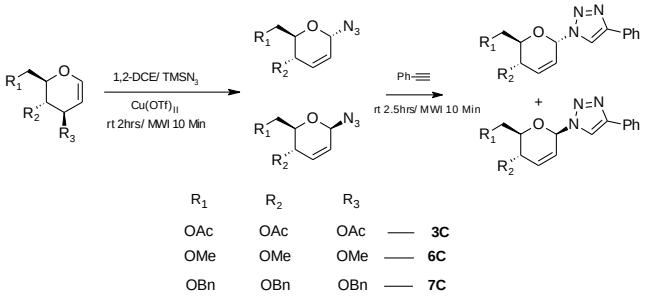
Tetrabutylammonium fluoride (TBAF)[4] is an efficient catalyst in the [3 + 2] cycloaddition reaction of organic nitriles with trimethylsilyl azide ($TMSN_3$) in solventless conditions. Nanocrystalline ZnO[5] is an effective heterogeneous catalyst for the [2+3]-cycloaddition of sodium azide with nitriles to afford 5-substituted 1H-tetrazoles in good yields. The addition of sodium azide to nitriles [6] to give 1H-tetrazoles is shown to proceed readily in water with zinc salts as catalysts. The scope of the reaction is quite broad; a variety of aromatic nitriles, activated and unactivated alkyl nitriles, substituted vinyl nitriles, thiocyanates, and cyanamides have all been shown to be viable substrates for this reaction. A simple, efficient and general method has been developed for the synthesis of 1-substituted-1H-1,2,3,4- tetrazoles[7] via a three-component condensation of amine, trimethylorthoformate and sodium azide in presence of a catalytic amount of indium triflate under solvent-free conditions. The reaction proceeds smoothly to generate the corresponding 1-substituted tetrazoles in moderate to excellent yields under heating. Cadmium chloride (CdCl2)[8] has been found to be an efficient for a neat [2+3]-cycloaddition of $NaN^3$with nitriles to afford 5-substituted 1H-tetrazoles in good yields..

2. MATERIALS AND METHODS

Catalyst: Copper (II) triflate [Cu(OTf)2], Copper (I) triflate [Cu(OTf)1]

Chemicals: Tri-O-acetyl-D-glucal, Tri-O-methyl-D-glucal, Tri-O-benzyl-D-glucal, 1,2-di chloro ethane, Acetonitrile, $TMSN_3$ – Tri-methyl silyl azide, Phenyl acetylene, Ethyl acetate, Hexane, Sodium sulphate [Na_2SO^4].

SCHEME: TRIAZOLES

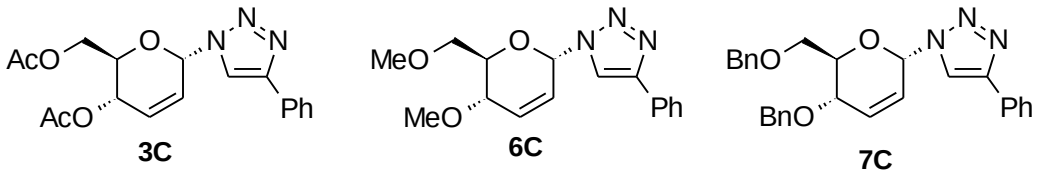


R_1	R_2	R_3	
OAc	OAc	OAc	3C
OMe	OMe	OMe	6C
OBn	OBn	OBn	7C

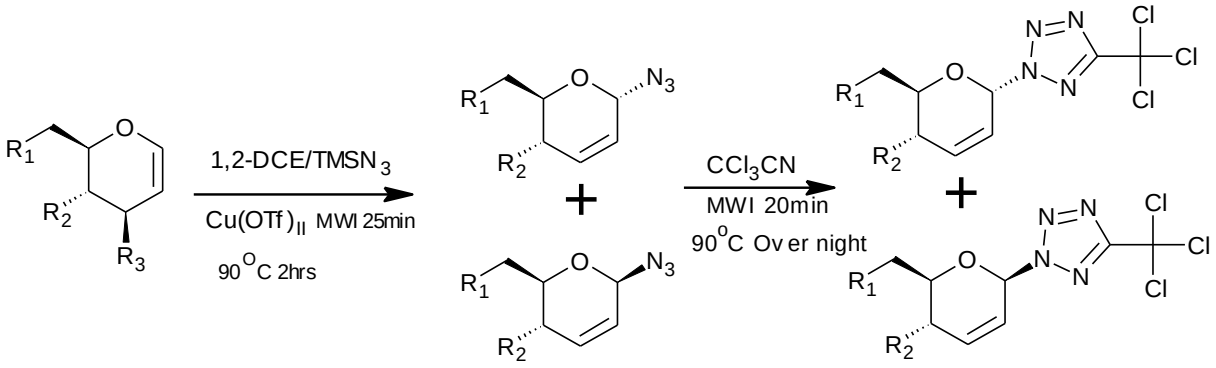
Procedure for the synthesis of triazoles from substituted glucals:

A mixture of Tri-*O*-substituted-D-glucals (0.5mmol), $TMSN_3$ (0.6mmol) and Cu(OTf)II (5mol%) in 1,2-dichloro ethane (2ml) was stirred at room temperature for 2h/ MWI 10 Min. Then phenyl acetylene (0.55mmol) and Cu powder (10 mol %) were added and the resulting mixture was stirred at rt for 2.5h/MWI 10 Min. After the completion of the reaction, as monitored by TLC, the product was extracted with ethyl acetate (3×10 ml) and dried over anhydrous Na2SO4. Removals of the solvent by reduced pressure, followed by purification on the silica gel using acetae (4:1) afford the pure 1,2,3-triazoles.

DERIVATIVES:



SCHEME: TETRAZOLES



R_1	R_2	R_3		
OAc	OAc	OAc	------	12C
H	OAc	OAc	------	14C
OTBS	OTBS	OTBS	------	15C
OAllyl	OAllyl	OAllyl	------	16C
OBn	OBn	OBn	------	17C
OBz	OBz	OBz	------	18C

Procedure for 12C-18C:

Tetrazoles are the Heterocyclic compounds which are synthesized from Nitriles and Organic Azides using Glucal's as starting materials which undergo cycloadition catalysed by Copper Triflate [Cu(OTf)II].

In a 25 ml round bottomed flask 250 mg (1 eq) of Tri-O-substituted-D-glucal was taken with 5 ml of 1, 2-dicholoro ethane fitted to a mechanical stirrer. To this reaction mixture 1.2 eq of $TMSN_3$ was added dropwise at rt then allowed the reaction mixture to stir for about 2hrs (MWI 25min). Then 1.2 eq of tri-chloro acetonitrile was added to the reaction mixture and allowed it to reflux for over night (MWI 20min) at 90^0C and progress of the reaction was monitored by TLC (hexane: ethyl acetate; 70:30). After the completion of the reaction the solvent was removed, and the organic mixture was extracted with water and ethylacetate. The organic layer was separated, dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography.

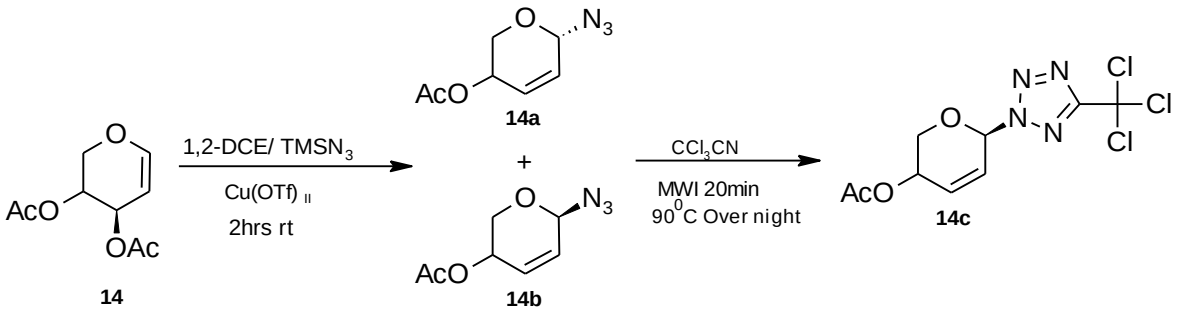
Procedure for the synthesis of Arabinal(14) from D-glucal:

The syrupy di-*O*-acetyl-L-arabinal was added to enough of the chilled barium methoxide solution to make an approximately 10% solution. The hydrolysis was allowed to proceed for about 24hrs at refrigerator temperature, shaking the reaction

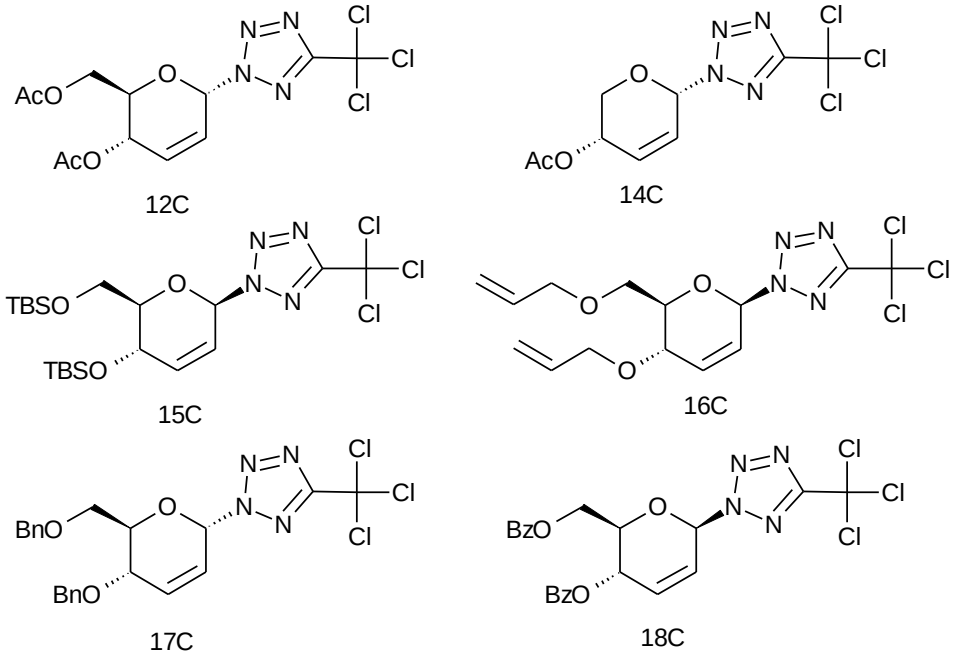
mixture occasionally. At this time, all the diacetyl derivative should have gone into the solution. With rapid stirring the calculated amount of cold 0.5N sulphuric acid (0^oC) was added inorder to precipitate barium quantitatively. Barium sulphate was removed by filtration through thick carbon pad. The nearly colourless filtrate was concentrated to thick syrup under reduced pressure and at a temperature not higher than 50^0C. The residual syrup usually crystallizes spontaneously in the distilling flag. The residue was taken up in warm absolute ethanol remove the last traces of water. After distilling the ethanol under reduced pressure, the residue was extracted with three 250ml portions of benzene. The combined extracts are filtered and placed in the refrigerator to crystallize. Next morning, L-arabinal crystals are filtered, washed with cold benzene (0^0C), and dried at room temperature under reduced pressure.

Synthesis of (3S,6S)-6-[5-(trichloromethyl)-2H-1,2,3,4-tetraazol-2-yl]-3,6-dihydro-2H-3-pyranyl acetate (14C):

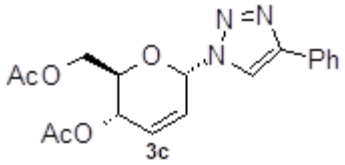
In a 25 ml round-bottomed flask 250 mg (1 eq) of Di-*O*-arabinol-D-glucal was taken with 5 ml of 1,2-dichloro ethane fitted to a mechanical stirrer. To this reaction mixture 1.2 eq of $TMSN_3$ was added dropwise at rt then allowed the reaction mixture to stir for about 2hrs/ MWI 10 Min. Then 1.2 eq of Tri-chloroaceto nitrile was added to the reaction mixture and allowed it to reflux for over night at 90^0C (MWI 20min) and progress of the reaction was monitored by TLC (hexane: ethyl acetate; 70:30). After the completion of the reaction the solvent was removed and the organic mixture was extracted with water and ethylacetate. The organic layer was separated, dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography.



DERIVATIVES:



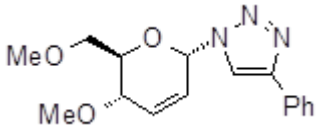
3. RESULTS AND DISCUSSION



3c

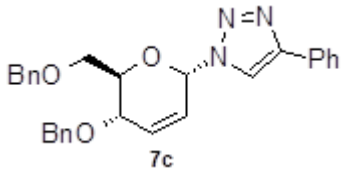
(2R,3S,6S)-2-[(acetyloxy)methyl]-6-(4-phenyl-1H-1,2,3-triazol-1-yl)-3,6-dihydro-2H-pyran-3-yl acetate:(3C)

Molecular Formula: $C_{18}H_{19}N_3O_5$, Molecular Weight: 357, Yeild: 85% Solid; M.P. 104-106°C, [α]D20 = +210.7 (c = 0.7 in chloroform); I.R. (KBr) $\upsilon_{(max)}$: 3452, 3136, 2925, 2854, 1745, 1652, 1458, 1370, 1227, 1076, 1048, 892, 768 cm-1. LC-MS: m/z: 380 (M+Na).HRMS ($C_{18}H_{19}N_3O_5Na$) (M+Na+): 380.1222; found, 380.1215. 1H NMR (300 MHz, CDCl3): δ 7.76-7.90(m, 3H), 7.19-7.51(m, 3H), 6.80(d, J=6.0Hz, 1H), 5.60(t, J=5.2 Hz, 1H), 5.23(dd, J=5.2, 6.5 Hz, 1H), 5.09(t, J=5.28 Hz, 1H), 4.09-4.35(m, 3H), 2.05(s, 3H), 2.04(s, 3H), 13C NMR (75 MHz, CDCl3): δ 170.3, 169.6, 148.2, 128.8, 128.2, 125.6, 119.5, 95.2, 70.2, 66.5, 61.7, 52.1, 29.6, and 20.5.



1-[(2S,5S,6S)-5,6-dimethoxy-5,6-dihydro-2H-pyran-2-yl]-4-phenyl-1H-1,2,3-triazole: (6C)

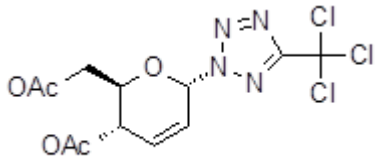
Molecular Formula: $C_{16}H_{19}N_3O_3$, Molecular Weight: 301, Yeild:85% Solid; m.p. 102-104 °C.[α]D20 = +198 (c = 0.5 in chloroform); I.R. (KBr) $\upsilon_{(max)}$: 3421, 2923, 2853, 1726, 1652, 1460, 1215, 1091, 1043, 761, cm-1. LC-MS: m/z: 324 (M+Na).HRMS calcd for C16H19N3O3Na: 324.1324; found, 324.1327. 1H NMR (300 MHz, CDCl3): δ 7.79-7.86 (m, 3H), 7.24-7.43(m, 3H), 6.55-6.59(m, 1H), 5.27-5.32(m, 2H), 4.80-4.84(m, 1H), 3.63-3.99(m, 3H), 3.42(s, 3H), 3.15(s, 3H). 13C NMR (75 MHz, CDCl3): δ 148.0, 128.7, 127.9, 128.2, 125.8, 125.5, 119.4, 95.2, 74.1, 72.9, 70.6, 59.4, and 57.9.



7c

1-((2S,5S,6R)-5-(benzyloxy)-6-(benzyloxymethyl)-5,6-dihydro-2H-pyran-2-yl)-4-phenyl-1H-1,2,3-triazole: (7C)

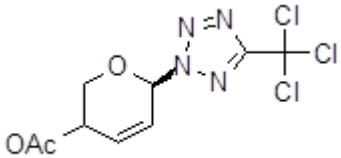
Molecular Formula: $C_{26}H_{31}N_3O_3$, Molecular Weight: 453, Yeild: 80% Solid; m.p. 100-102°C. [α]D20 = +169.1 (c = 0.75 in chloroform); I.R. (KBr) $\upsilon_{(max)}$: 3064, 3031, 2924, 2856, 1725, 1652, 1454, 1364, 1256, 1114, 1046, 744, 699 cm-1 , LC-MS: m/z: 238 (M+).HRMS calcd for C26H31N3O3Na: 456.2263; found, 456.2265.1H NMR (300 MHz, CDCl3): δ 6.96-7.39(m, 10H), 6.67(d, J=6.0Hz, 1H), 5.47(t, J=5.2Hz, 1H), 4.82-4.94(m, 1H), 4.44-4.67 (m, 3H), 3.97-4.14(m, 2H), 3.7(d, J=3.0Hz, 2H), 2.71(t, J=7.5Hz, 2H), 1.60-1.73(m, 2H), 1.26-1.47(m, 2H), 0.88-1.02(m, 5H). 13C NMR (75 MHz, CDCl3): δ 147.6, 146.4, 132.9, 128.4, 128.4, 127.9, 127.8, 127.7, 120.5, 119.9, 95.48, 73.6, 73.2, 72.1, 71.8, 68.4, 52.2, 31.4, 25.3, 22.3, and 13.7.



12c

((2R,3S,6S)-3-acetoxy-6-(5-(trichloromethyl)-2H-tetrazol-2-yl)-3,6-dihydro-2H-pyran-2-yl)methyl acetate: (12C)

Molecular Formula: $C_{12}H_{13}Cl_3N_4O_5$, Molecular weight: 399, Yeild:85% I.R. (KBr) $\upsilon_{(max)}$: 3354, 2925, 2853, 2108, 1743, 1599, 1371, 1253, 1049, 816, 727, 606 cm-1 ,LC-MS: m/z: 400 (M+), H1 NMR(300 MHz, CDCl3): δ 5.63(d, 1H), 5.96 (t, 1H), 5.9(t, 1H), 5.46 (t, 1H) 5.06 (q, 1H),4.89(d, 2H), 2.61(s, 3H), 2.60(s, 3H). 13C NMR (75 MHz, CDCl3): δ 183,182, 98,137.1, 136.3, 102, 90.9, 84.4, 79.4, 67.9, 31.4, 22.4 and 22.3.



14c

(6R)-6-(5-(trichloromethyl)-2H-tetrazol-2-yl)-3,6-dihydro-2H-pyran-3-yl acetate: (14C)

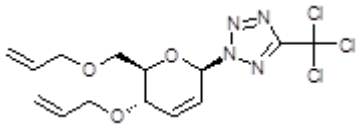
Molecular Formula: $C_9H_9Cl_3N_4O_3$, molecular weight: 327, Yeild:82% I.R. υ (max): 2924, 2853, 2109, 1747, 1463, 1369, 1221, 1021, 936, 869, 803, 772, 727, 574 cm-1LC-MS: m/z: 329 (M+), H1 NMR(300 MHz, CDCl3): δ 5.80(d, 1H), 5.94 (t, 1H), 5.92(t, 1H), 4.26 (q, 1H) 4.07 (d, 1H), 2.24(s, 3H). 13C NMR (75 MHz, CDCl3): δ 185, 106, 98, 138.1, 136.03, 83.9, 74.9 and 22.93.

15c

2-[5-[1-(tert-butyl)-1, 1-dimethylsilyl] oxy-6- ([1-(tert-butyl)-1, 1-dimethylsilyl]oxymethyl)-5, 6-dihydro-2H-2-pyranyl]-5-(trichloromethyl)-2H-1, 2, 3, 4-tetraazole: (15C)

molecular formula: $C_{20}H_{37}Cl_3N_4O_3Si_2$, Molecular Weight: 544, Yeild:70% I.R. (KBr) $\upsilon_{(max)}$: 2930, 2857, 2102, 1655, 1466,

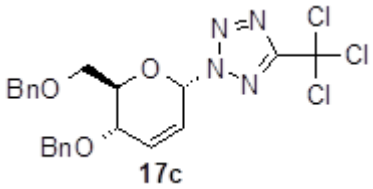
1255, 1126, 1005, 837, 779, 727, 672 cm-1 , LC-MS: m/z: 545 (M+), H1 NMR(300 MHz, CDCl3): δ 5.52(d, 1H), 5.74 (t, 1H), 5.72(t, 1H), 4.26 (t, 1H) 3.87 (q, 3H), 0.4(s, 3H), 0.94(s, 12H), 0.94(s, 18H). 13C NMR (75 MHz, CDCl3): δ 135, 109, 92, 90, 128.11, 126.21, 83.9, 72.01,71, 64,26.11, 18.41 and 7.19.



16c

2-{(2R,5S,6R)-5-(prop-2-en-1-yloxy)-6-[(prop-2-en-1-yloxy)methyl]-5,6-dihydro-2H-pyran-2-yl}-5-(trichloromethyl)-2H-tetrazole: (16C)

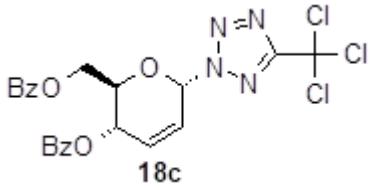
Molecular Formula: $C_{14}H_{17}Cl_3N_4O_3$, Molecular Weight: 395, Yeild:65% I.R. $\upsilon_{(max)}$: 3750, 3448, 2923, 2854, 2370, 1736, 1647, 1461, 1219, 1098, 771 cm-1, LC-MS: m/z: 396 (M+), H1 NMR(300 MHz, CDCl3): δ 6.11(s,2H), 5.96 (t, 1H), 5.92(t, 1H), 5.69(d, 2H),5.55(d, 2H), 5.35(d, 2H),4.41 (t, 1H) 4.06 (q, 1H),3.79(d, 2H), 4.21(s, 4H). 13C NMR (75 MHz, CDCl3): δ 139,132, 128, 120, 119, 113, 96.3, 92, 90.9, 84.4, 79.4, 72,70 and 67.9.



17c

2-5-(benzyloxy)-6-[(benzyloxy)methyl]-5,6-dihydro-2H-2-pyranyl-5-(trichloromethyl)-2H-1,2,3,4-tetraazole: (17C)

Molecular Formula: $C_{22}H_{21}Cl_3N_4O_3$, Molecular Weight: 495, Yeild:85% I.R. (KBr) $\upsilon_{(max)}$ 3031, 2923, 2865, 2106, 1653, 1454, 1362, 1241, 1111, 866, 803, 730, 699 cm-1, LC-MS: m/z: 496 (M+).1H NMR (300 MHz, CDCl3): δ 6.98-7.39(m, 10H), 5.67(d, 1H), 5.87(t,1H), 5.82(t,1H),4.89(s,4H), 3.82(t, 1H), 3.44(q, 1H), 3.27(d, 2H), 13C NMR (75 MHz, CDCl3): δ 138, 129,128,127,126,125,106,92, 74,71,70 and 69,



18c

2-5-(benzoyloxy)-6-[(benzoyloxy)methyl]-5,6-dihydro-2H-2-pyranyl-5-(trichloromethyl)-2H-1,2,3,4-tetraazole: (18C)

Molecular formula: $C_{22}H_{17}Cl_3N_4O_5$, Molecular Weight: 523, Yeild:85% I.R. (KBr) $\upsilon_{(max)}$: 3031, 2923, 2865, 2106, 1653, 1454, 1362, 1241, 1111, 866, 803, 730, 699 cm-1LC-MS: m/z: 524 (M+), H1 NMR(300 MHz, CDCl3): δ 7.90-7053(m, 10H), 5.94 (t, 1H), 5.92(t, 1H) 5.90(t, 1H), 4.26 (t, 1H) 4.67 (t, 2H), 4.24(q, 1H). 13C NMR (75 MHz, CDCl3): δ 169,166, 138,135, 130, 128, 127,126, 125, 10, 92, 74, 71,70 and 69,

PHARMACOLOGICAL ACTIVITY:

Antimicrobial activity10:

Procedure: The antibacterial activity of synthesized triazoles and tetrazoles had been assayed against six different strains of bacteria by serial dilution method.

Gram positive bacteria	Gram negative bacteria
Bacillus subtilis	**Pseudomonas aeruginosa**
Staphylococcus aureus	**Escherichia coli**
Staphylococcus epidermidis	**Klebsella pneumoniae**

Generally, the antibacterial activity of a compound was expressed in terms of its ability to inhibit the growth of bacteria in nutrient broth or agar. The bacterial growth inhibition can be measured by two methods: serial dilution and cup plate methods.

Serial dilution method is very much useful for the determination of the levels of resistance to antibiotic. The method adopted in this investigation was serial dilution method. In this method serial dilutions of the antibiotic/test compounds were made in a liquid medium which was inoculated separately with six strains of bacteria and incubated at 37 ± 1oC for 24h. The lowest concentration (higher dilution) of compound preventing the appearance of turbidity is considered to be the minimal inhibitory concentration (MIC). At this dilution the compound is known to be bacteriostatic.

The method is carried under aseptic conditions, sterile capped numbered tubes from 1-9 were taken and added 1ml of sterile broth to each of them. To the first tube 2 ml of stock solution (150µg/ml) was added and then transferred 1ml from first tube to the second tube. The contents were mixed and 1ml of it was transferred to the third tube. Likewise dilutions were continued and 1ml from 8th tube was discarded. The 9th tube served as control. The final concentration of the compound was now are one-half of the original concentration in each tube. These tubes were incubated at 35^{o}C for 24hrs.

The sub-cultures were prepared by suspending several colonies of the culture that were to be tested in 5ml of nutrient broth to give a slightly turbid suspension. This suspension was diluted by aseptically pipetting 0.2 ml of suspension in to 40 ml of nutrient broth. Stock solutions of the test compounds were

prepared by dissolving 10mg each in dimethyl sulfoxide (DMSO-d6, 10 ml) further required dilution were made to prepare 150 μg/ml. A reference standard was prepared by dissolving weighed quantities of streptomycin, pencillin in DMSO to obtain 50 μg/ml.

Procedure for antifungal activity 11:

For the antifungal screening of synthesized compounds Saccharomyces cerevisiae, Aspergillus niger, Aspergillus flavus, Candida albicans, and Candida rugosa were used. The tubes containing sterilized medium were inoculated with test fungi and after inoculation at 25^{0}C for 48 hrs, they were stored at 4^{0}C in refrigerator. The inoculum was prepared by taking a loopful of stock culture to about 5 ml of potato dextrose broth in a test tube. The tubes were incubated at 25^{0}C for 48 hrs before use. Stock solutions of the test compounds were prepared by dissolving 10 mg each in dimethyl sulfoxide (DMSO-d6, 10 ml) further required dilution were made to prepare 100 μg/ml, 150 μg/ml. A reference standard solution of Amphotericin-B was prepared from stock solution containing (150 μg/ml), which was prepared by dissolving 10 mg of Amphotericin-B(50) in 1 ml of dimethyl sulfoxide (DMSO).

The PDA medium was sterilized by autoclaving at 121^{0}C (15 lb/sq. inches) for 15 min; the Petri-plates were sterilized in hot-air oven at 16^{0}C for an hour. Into each sterilized Petri-plate about 27 ml of molten PDA medium was poured. The plates were separated with 100 ml of 48 h old culture. After spreading of inoculum, cups of 6 mm diameter were made in each plate with sterile borer. Accurately 100 μg concentration of test solution was transferred to the respective Petri-plates aseptically and labeled accordingly. The reference standard (Amphotericin-B) was also added to the wells in each plate. The plates were incubated at 25^{0}C for 48 hrs. After incubation, the diameter of zone of inhibition was read with the help of an antibiotic zone reader. The experiment was performed in triplicate and the results are tabulated.

Antibacterial activity of triazoles and tetrazoles:

The antibacterial activity of the test compounds were tested by serial dilution method taking drug at a concentration of 150 mg/ml. The minimum inhibitory concentration (MIC) was taken as a parameter of antibacterial activity. The MIC of the test compounds is compared to that of the standard drugs i.e., Streptomycin and Penicillin. Both the compounds triazoles and tetrazoles showed somewhat activity against six strains of bacteria

Minimum Inhibitory concentration (μg/ml)						
	Gram positive organisms			Gram negative organisms		
Compound no.	B.subtilis	S.aureus	S.epidermidis	E.coli	P.aeroginosa	K.pneumoniae
3C	150	150	150	150	150	150
6C	150	37.5	37.5	150	37.5	37.5
7C	150	150	150	150	150	150
14C	150	150	75	75	75	75
15C	150	150	150	150	150	150
12C	150	150	150	150	150	150
16C	150	150	150	150	150	150
17C	37.5	75	75	150	75	75
18C	150	150	150	150	150	150
Streptomycin	6.25	1.56	1.562	3.125	3.125	3.125
Penicillin	1.526	6.25	3.125	6.25	12.5	6.25

The compounds 6C, 14C and 17C showed significant activity against six strains of bacteria.

The MIC exhibited by the compounds 6C against S.aureus, S.epidermidis, P.aeroginosa and K.pneumoniae was at 37.5 mg/ml where as for the B.subtilis and E.colis it was observed at 150 mg/ml.

The MIC exhibited by the compound 14C against S.epidermidis, E.coli, P.aeroginosa and K.pneumoniae was at 75 mg/ml where as for the other two strains B.subtilis and S.aureus was observed at 150 mg/ml.

The MIC exhibited by compound 17C against B.subtilis was at 37.5 mg/ml whereas for E.coli it was observed at 150 mg/ml and for other four strains it was observed at 75 mg/ml.

The compounds 3C, 7C, 15C, 12C, 16C and 18C showed MIC at 150mg/ml against all the six straina of bacteria

Antifungal activity of triazoles and tetrazoles:

The anti-fungal activies of the triazoles and tetrazole were tested by agar diffusion method (cup-plate method) taking drug at a concentration of 100 mg/ml and 150 mg/ml against five fungi (C.albicans, C.rugosa, S.cerevisiae, A.flavus and A.niger). The area of zone of inhibition (ZOI) was taken as a parameter for this antifungal activity. The ZOI of the test compound is compared to that of the standard drug i.e, Amphotericin-B.

The triazole compounds showed significant activity whereas the tetrazoles showed somewat less activity.

The compounds showed different ZOI against the five fungi at 100 and 150 mg/ml concentrations. Among the compounds screened the maximum zone of inhibition were observed against Candida albicans and Candida rugosa and the compounds were inactive against Staphylococcus cerevisiae, Aspergillus flavus and Aspergillus niger.

Zone of inhibition in mm										
	C.albicans		C.rugosa		S.cerevisiae		A.flavus		A.niger	
Compound no.	100 µg	150 µg	100 µg	150 µg	100 µg	150 µg	100 µg	150 µg	100 µg	150 µg
3C	14	18	10	14	0	0	0	0	0	0
6C	0	0	0	0	0	0	0	0	0	0
7C	8	10	9	14	0	0	0	0	0	0
14C	0	0	7	10	0	0	0	0	0	0
15C	0	0	0	0	0	0	0	0	0	0
12C	0	8	0	0	0	0	0	0	0	0
16C	0	0	8	10	0	0	0	0	0	0
17C	10	8	7	10	0	0	0	0	0	0
18C	0	0	0	0	0	0	0	0	0	0
Amphotericin-B	23.5		24		22		24		2.5	

The compounds 3C, 7C, 14C, 16C, 17C were active against Candida albicans and Candida rugosa and the compounds are inactive anainst S.cerevisiae, A.flavus and A.niger.

Among the active compounds the compound 3C showed zone of inhibition (ZOI) 14 mm and 18 mm against C.albicans at 100 mg/ml and 150 mg/ml concentration respectively. Whereas it showed ZOI 10 mm and 14 mm against C.rugosa at 100 and 150 mg/ml respectively. And it is inactive agaist S.cerevisiae, A.flavus and A.niger.

The ZOI for the compound 7C is 8 mm for 100 mg/ml concentration and 10 mm for 150 mg/ml concentration against C.albicans whereas against C.rugosa the ZOI is 9 mm for 100 mg/ml concentration and 14 mm for 150 mg/ml concentration. And the compound 7C is inactive against and Cerevisiae, A.flavus and A.niger.

The compound 14C showed ZOI 7 mm and 10 mm against C.rugosa at 100 mg/ml and 150 mg/ml concentration whereas inactive against the other four fungi.

The compound 12C showed ZOI 8 mm at 150 mg/ml concentration against C.albicans and is inactive against the other four fungi and C.albicans at 100 mg/ml concentration.

The compound 16C showed ZOI 8 mm and 10 mm for 100 mg/ml and 150 mg/ml concentration against C.rugosa where as it is inactive against other four fungi.

The compound 17C showed ZOI 10 mm and 8 mm against C.albicans at 100 and 150 mg/ml concentration where as it is 7 mm and 10 mm against C.rugosa at 100 and 150 mg/ml. And the compound is inactive against the other three fungi.

4. CONCLUSION

We developed an efficient synthetic approach of pharmacologically important diversely functionalized compounds (Triazoles) through the cycloaddition of Glucals, Azides and nitriles in prence of CuII(OTf) as a catalyst at room temperature.

We also developed another efficient process for the synthesis of tetrazoles through the cycloaddition of Glucals, Azides and

Phenyl acetylene in prence of catalyst CuII(OTf) at room temperature.

The methodology involved in both the synthesis is click chemistry which offered very attractive features such as reduced reaction times, higher yields and has a wide scope in organic synthesis.

This simple procedure combined with ease of recovery and reuse of the catalyst made this method economic and a waste free chemical process for the synthesis of triazoles and Tetrazoles.

The compounds 6C, 14C and 17C showed significant activity against six strains of bacteria.

The MIC exhibited by the compounds 6C against S.aureus, S.epidermidis, P.aeroginosa and K.pneumoniae was at 37.5 mg/ml where as for the B.subtilis and E.colis it was observed at 150 mg/ml.

The MIC exhibited by compound 17C against B.subtilis was at 37.5 mg/ml whereas for E.coli it was observed at 150 mg/ml and for other four strains it was observed at 75 mg/ml.

Among the active compounds the compound 3C showed zone of inhibition (ZOI) 14 mm and 18 mm against C.albicans at 100 mg/ml and 150 mg/ml concentration respectively.

The compound 14C showed ZOI 7 mm and 10 mm against C.rugosa at 100 mg/ml and 150 mg/ml concentration where as inactive against the other four fungi.

The compound 16C showed ZOI 8 mm and 10 mm for 100 mg/ml and 150 mg/ml concentration against C.rugosa where as it is inactive against other four fungi.

The compound 17C showed ZOI 10 mm and 8 mm against C.albicans at 100 and 150 mg/ml concentration where as it is 7 mm and 10 mm against C.rugosa at 100 and 150 mg/ml. And the compound is inactive against the other three fungi

5. AKNOWLEDGMENTS

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