Taylor & Francis
Taylor & Francis Group

Synthetic Communications

An International Journal for Rapid Communication of Synthetic Organic Chemistry

ISSN: 0039-7911 (Print) 1532-2432 (Online) Journal homepage: http://www.tandfonline.com/loi/lsyc20

Design, synthesis and anticancer activity evaluation of novel aziridine-1,2,3-triazole hybrid derivatives

Hong-Ru Dong, Jian-Guo Wu & Zhong-Lian Gao

To cite this article: Hong-Ru Dong, Jian-Guo Wu & Zhong-Lian Gao (2017): Design, synthesis and anticancer activity evaluation of novel aziridine-1,2,3-triazole hybrid derivatives, Synthetic Communications, DOI: 10.1080/00397911.2017.1353632

To link to this article: http://dx.doi.org/10.1080/00397911.2017.1353632

Design, synthesis and anticancer activity evaluation of novel aziridine-1,2,3-triazole hybrid derivatives

Hong-Ru Dong*

School of Chemical Engineering, Lanzhou University of Arts and Science, Lanzhou, P.R. China

Jian-Guo Wu

School of Chemical Engineering, Lanzhou University of Arts and Science, Lanzhou, P.R. China

Zhong-Lian Gao

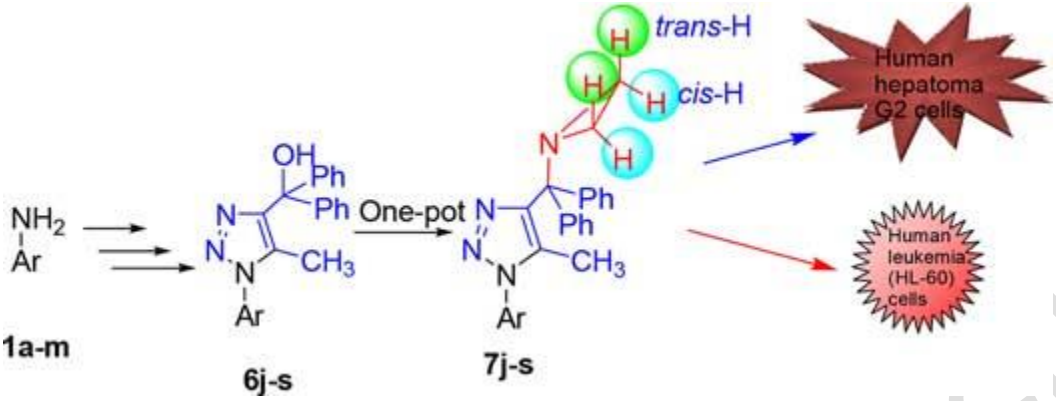
School of Chemical Engineering, Lanzhou University of Arts and Science, Lanzhou, P.R. China

Address correspondence to Hong-Ru Dong. E-mail: donghr@luas.edu.cn

ABSTRACT

Some new 1-aryl-4-[(aziridine-1-yl)diaryl-methyl]-5-methyl-1*H*-1,2,3-triazole derivatives **7j-s** were synthesized by a one-pot reaction of diaryl-(1-aryl-5-methyl-*1H*-1,2,3-triazol-4-yl)methanol compounds **6j-s** formed from 1-aryl-5-methyl-1*H*-1,2,3-triazole-4-carboxylic acid derivatives. The new compounds **7j-s** and **6j-s** are investigated by ^{1}H and ^{13}C NMR, MS, and IR. The anticancer activity of the synthesis target compounds was evaluated against human leukemia (HL-60) cells and human hepatoma G2 cells. Some of the compounds were highly efficient. The ^{1}H-NMR signals of the aziridine-ring *cis*-H/*trans*-H protons were found to be two group peaks at 1.800-1.884 and 1.183-1.327 ppm.

GRAPHICAL ABSTRACT



KEYWORDS: 1*H*-1,2,3-triazole, anticancer, aziridine, human hepatoma G2, human leukaemia (HL-60), synthesis

Introduction

Some reactions and synthetic methodologies have been accompanied by dramatic increases in molecular complexity and impressive selectivity.[1] The vast majority of reported biologically important molecules, such as drugs and natural products, contain nitrogen in their framework. Experience has shown that compounds with biological activity are often derived from heterocyclic structures. Aziridines are well known as important heterocycles in organic and medicinal chemistry. In addition to their utility as synthetic endpoints, aziridines are also important intermediates in organic chemistry.[2] Substituted aziridines are ubiquitous building blocks in natural products and have important biological activities (Scheme 1). The functionality of aziridine is present in a small number of naturally occurring molecules. The biological properties of aziridine-containing compounds such as azicemicins,[3] miraziridine,[4], [5] azinomycins,[6] ficellomycin,[7] FR-900482[8] and mitomycins[9] are of significant interest. The antibiotic and

antitumour properties of several such compounds are well-known. Mitomycin C has a broad activity against a range of tumours and has been applied clinically since the 1960s.

In addition to aziridine, molecules containing the 1,2,3-triazole nucleus are also important heterocycles and pharmacologically active molecules. Hence, they have been applied extensively to modify and potentiate anticancer,[10–12] antibacterial,[13], [14] antifungal,[15] antiviral,[16] anti-inflammatory and analgesic activities.[17] However, there is little information describing compounds containing these two heterocyclic moieties, aziridine and 1,2,3-triazole, in one molecule. Because compounds containing aziridines among several active functional groups are difficult to synthesize, we devoted our attention to the synthesis of this type of compound. Some new 1-aryl-4-[(aziridin-1-yl)diaryl-methyl]-5-methyl-1*H*-1,2,3-triazole derivatives have been synthesized by a one-pot reaction. Substituted 1,2,3-triazoles are often applied as building blocks in designing drugs to inhibit the growth, invasion and migration of cancer cells (Scheme 2).

Results and Discussion

Some new 1-aryl-4-[(aziridin-1-yl)diaryl-methyl]-5-methyl-1*H*-1,2,3-triazole derivatives **(7j-s)** have been synthesized by the one-pot reaction of diaryl-(1-aryl-5-methyl-*1H*-1,2,3-triazol-4-yl) methanol **(6j-s)** beginning from 1-aryl-5-methyl-1*H*-1,2,3-triazole-4-carboxylic acid derivatives. The synthetic route is shown in Scheme 3.

Our interest in the development of some new 1-aryl-4-[(aziridin-1-yl)diaryl-methyl]-5-methyl-1*H*-1,2,3-triazole derivatives **(7j-s)** with anticancer activities and in extending this type of one-pot reaction prompted us to examine potential applications and generalizations for the synthesis of compounds with substituted aziridine and 1,2,3-triazole.

When 1-aryl-4-[(aziridin-1-yl)diaryl-methyl]-5-methyl-1*H*-1,2,3-triazole derivatives were synthesized by a one-pot reaction, PCl_3/dry benzene followed by dry benzene, aziridine, Et_3N, and acetonitrile were applied to the reaction, and the yield was 32%. When PCl_3 was replaced by $POCl_3$ in dry benzene, and benzene, aziridine, Et_3N, and acetonitrile were applied to the reaction, the yield was 25%. When $SOCl_2$ was applied to the one-pot reaction in dry benzene, and then benzene, aziridine, Et_3N, and acetonitrile were applied to the reaction, the yield was 41%. When dry HCl/dry benzene were refluxed, and benzene, aziridine, Et_3N, and acetonitrile were applied to the reaction, the yield was a good 86%. If Et_3N was not applied to the reaction in the second step, the yield was relatively low.

As we know, aziridine and 1,2,3-triazole were the functional groups. Their main function was to provide high biological activity. In designing the new synthetic route, in this paper, we synthesized the new compounds **6j**-**s** and **7j**-**s**. Aziridine and 1,2,3-triazole were connected to one structure among compounds **7j-s** that had anticancer activity. This synthesis is the biggest bright spot in this paper.

A hydroxy compound was identified as showing IR absorption at 3320-3524 cm^{-1} in **6j**-**s**, but this signal disappeared in compounds **7j**-**s**. ^1H NMR showed the proton signals of the aziridine ring at 1.800-1.884 and 1.183-1.327 ppm in compounds **7j-s**.

Compound **7n** was characterized by 1D and 2D NMR (^1H, ^{13}C and ^{13}C -^1H COSY or gHSQC). The ^1H and ^{13}C NMR chemical shifts and coupling constant data for **7n** were determined (**Figures 1** and **2**). In the ^1H NMR spectrum, the signals of most protons were shown as general ^1H NMR spectrum absorption peaks and $J_{H\text{-}H}$ coupling patterns, except for the proton signal of the CH_2 group connected to the N atom in the aziridine-ring. In the normal case, it appeared as a sharp peak at ~2.50 ppm, according to earlier literature.[18], [19] We found two group peaks at 1.800-1.884

and 1.183-1.327 ppm in compounds **7j-s**. To determine the two group peaks, a ^{13}C-^{1}H one-bond correlation experiment (^{13}C -^{1}H COSY) was applied. From the ^{13}C -^{1}H COSY (**Figure 3**; **Table 1**) spectra and spectral data, we observed strong cross peaks for carbon and hydrogen. Then, we determined that the two group peaks at 1.800-1.884 and 1.183-1.327 ppm were the signal of the aziridine-ring *cis*-H/*trans*-H proton. Since we had achieved unambiguous assignments for all the ^{1}H signals, ^{13}C signals were assigned in a straightforward manner by analysis of the ^{13}C -^{1}H COSY spectra for the proton and carbon atoms. It is worth mentioning that the *cis*-H/*trans*-H protons of the methylene groups attached directly to the central N atom appear as two group peak signals, probably due to the presence of this central N atom in the aziridine-ring.

If the target compound was substituted at the 2-position of the Ar group attached to the triazole, the chemical shift of the triazole-ring methyl proton was decreased from ~2 ppm to 1.696-1.792 ppm in compounds **7j**, **7k**, **7m**, **7n**, **and 7r**, which was due-to the steric hindrance of the aromatic ring substituted at the 2-position and the triazole-ring, as the methyl proton was in the shielding environment of the aromatic ring current.

Experimental Section

5-Methyl-1-substituted-1,2,3-triazol-4-carboxylic acids were prepared by an existing literature method; ethyl 1-aryl-5-methyl-1H-1,2,3-triazol-4-carboxylate 5 was also prepared by a literature method.[20] ***Therefore, we used the same method to synthesize some new compounds, (1-aryl-5-methyl-1H-1,2,3-triazol-4-yl)diarylmethanols 6j-s***

A three-necked round-bottomed flask (250 mL) was fitted with an efficient stirrer unit, a dropping funnel and an efficient reflux condenser; calcium chloride guard-tubes were placed on the top of the funnel and on the condenser. All parts of the apparatus were thoroughly dry. First, 1.06 g (0.044mole) of fresh magnesium turnings and a few crystals of iodine were placed in the flask, 5 mL of sodium-dried diethyl ether was added, and then 2 mL of a mixture of 0.044 mole (4.4 mL) bromo-benzene and 30 mL sodium-dried diethyl ether was added directly to the flask. After the reaction had proceeded for a few minutes and the iodine colour had disappeared, the bottom of the flask was heated with a bath of hot water until the iodine began to vaporize and was then allowed to cool. The remainder of the bromo-benzene and ether were dropped into the flask through the dropping funnel under stirring. Stirring and refluxing were continued for an hour after the dropwise addition was completed.

A mixture of ethyl 1-aryl-5-methyl-1*H*-1,2,3-triazole-4-carboxylate (0.02 mole)[20] in benzene was added completely. Stirring was continued for 2~3 h at room temperature. The mixture was decomposed by a mixture of ice, water and ammonium chloride. The organic layer was separated, and the solvent was distilled off. The crude product was recrystallized from benzene to give **6j-s**. Some of the new compounds (1-aryl-5-methyl-1*H*-1,2,3-triazol-4-yl)diarylmethanols **6j-s** are shown below:

(5-Methyl-1-o-tolyl-1H-1, 2,3-triazol-4-yl)diphenylmethanol 6j,

Yield 84%, white flaky crystals, m.p. 127-128°C. ^{1}H NMR ($CDCl_3$-d_1), δ7.229-7.463(m, 4H, Ar_1-3,4,5,6), 7.327-7.360(m, 10H, Ar_2), 4.306(s, 1H, OH), 2.037 (s, 3H, Ar_1-CH_3), 1.528(s, 3H, TRZ-CH_3). ^{13}C NMR ($CDCl_3$-d_1), δ 148.7, 145.2, 135.6, 135.1, 131.1, 131.2, 130.4, 128.0, 127.8, 127.6, 127.4, 126.9, 17.1, 8.6; MS m/z: 355(6.8) (M^+), 326(100), 310(31), 250(12), 222(7.5),

207(12), 143(11), 132(26), 107(32), 105(66), 91(43), 77(52), 64(42). IR: 3385(b, OH), 3085, 3057, 3026(m, Ar-H), 2959, 2925, 2856(w, CH_3), 1598, 1551 (w), 1493, 1446(s, Ar), 1465, 1373(m, CH_3), 1317(m, OH), 1267, 1214(m), 1131, 1028, 894(s, triazole ring), 1166(s, C-O), 770, 760, 699(s, Ar-H) cm^{-1}. Calcd for $C_{23}H_{21}N_3O$: C, 77.72; H, 5.96; N, 11.82; Found: C, 77.75; H, 5.98; N, 11.86.

[1-(2-Chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]diphenylmethanol 6k,

Yield 83%, white flaky crystals, m.p. 157-158°C. ^{1}H NMR ($CDCl_3$-*d*$_1$), δ7.565-7.590(d, 1H, *J* = 7.5Hz, Ar_1-3), 7.432-7.524(m, 3H, Ar_1-4,5,6), 7.284-7.358(m, 10H, Ar_2), 4.288(s, 1H, OH), 1.574(s, 3H, TRZ-CH_3). ^{13}C NMR ($CDCl_3$-*d*$_1$), δ 148.7, 145.1, 133.8, 132.8, 131.9, 131.6, 130.4, 129.3, 128.0, 127.9, 127.8, 127.7, 8.6; MS m/z: 375(5.7) (M^+), 377(2.7), 348(30), 346(100), 332(11), 330(27), 294(10), 272(2.7), 270(9), 244(4.6), 242(13), 207(14), 167(8), 165(20), 154(13), 152(41), 129(14), 127(45), 113(18), 111(48), 105(66), 77(35). IR: 3400(b, OH), 3088, 3060, 3027(m, Ar-H), 2924(w, CH_3), 1596, 1552(w), 1491, 1447 (s, Ar), 1372(m, CH_3), 1321(m, OH), 1274, 1211, 1134(m), 1026, 895(s, triazole ring), 1167(s, C-O), 767, 699(s, Ar-H), 1083, 639(m) cm^{-1}. Calcd for $C_{22}H_{16}ClN_3O$: C, 70.32; H, 4.83; Cl, 9.43;N, 11.18; Found: C, 70.35; H, 4.84; N, 11.16.

[1-(3-Chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]diphenylmethanol 6l,

Yield 80%, white needle crystals, m.p. 156-157°C. ^{1}H NMR ($CDCl_3$-*d*$_1$), δ7.466-7.492(m, 3H, Ar_1-2,4,6), 7.250-7.434(m, 11H, Ar_1-5, Ar_2), 4.124(s, 1H, OH), 1.782(s, 3H, TRZ-CH_3). ^{13}C NMR ($CDCl_3$-*d*$_1$), δ 149.6, 145.0, 137.2, 135.2, 131.2, 130.4, 129.7, 128.1, 127.7, 125.8, 123.6, 9.5; MS m/z: 375(4.6) (M^+), 377(2.1), 348(31), 346(100), 332(8.6), 330(22), 294(5), 272(3), 270(10), 244(3), 242(11), 207(11), 167(4.8), 165(15), 154(10), 152(33), 129(11), 127(34), 113(10),

111(28), 105(53), 77(30). IR: 3443(b, OH), 3081, 3025(m, Ar-H), 2928(w, CH_3), 1591, 1550(w), 1489, 1445(s, Ar), 1393(m, CH_3), 1344(m, OH), 1273, 1221(m), 1140, 1047, 900(s, triazole ring), 1164(s, C-O), 875, 792, 769, 697(s, Ar-H), 1253, 1094, 630(s) cm^{-1}. Calcd for $C_{22}H_{18}ClN_3O$: C, 70.30; H, 4.83; Cl, 9.43;N, 11.18; Found: C, 70.32; H, 4.85; N, 11.20.

[1-(2,5-Dichlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]diphenylmethanol 6m,

Yield 92%, white flaky crystals, m.p. 166-167°C. ^{1}H NMR ($CDCl_3$-*d*$_1$), δ7.496(s, 3H, Ar_1-3,4,6), 7.260-7.420(m, 10H, Ar_2), 4.169(s, 1H, OH), 1.593(s, 3H, TRZ-CH_3). ^{13}C NMR ($CDCl_3$-*d*$_1$), δ 148.9, 144.9, 134.6, 133.6, 132.9, 131.8, 131.3, 130.4, 129.6, 128.6, 127.7, 8.6; MS m/z: 409(3.1) (M^+), 413(0.6), 411(2), 384(10), 382(53), 380(82), 368(2), 366(12), 364(17), 330(2), 328(7), 308(0.7), 306(3), 304(5), 280(2), 278(9), 276(12), 243(5), 241(13), 201(3), 199(5), 190(5), 188(19), 186(28), 161(17), 149(4), 147 (13), 145(18), 105(100), 77(46). IR: 3524(b, OH), 3055, 3027(m, Ar-H), 2926, 2852(w, CH_3), 1584(m), 1486, 1445(s, Ar), 1366(s, CH_3), 1304(m, OH), 1263, 1210(m), 1122, 1016, 908(s, triazole ring), 1164(s, C-O), 824, 763, 700(s, Ar-H), 1097, 578(s) cm^{-1}. Calcd for $C_{22}H_{17}Cl_2N_3O$: C, 64.40; H, 4.18; Cl, 17.28; N, 10.24; Found: C, 64.42; H, 4.16; N, 10.22.

[1-(2-Bromophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]diphenylmethanol 6n,

Yield 82%, white flaky crystals, m.p. 158-159°C. ^{1}H NMR ($CDCl_3$-*d*$_1$), δ7.737-7.762(d, 1H, *J* = 7.5Hz, Ar_1-3), 7.395-7.501(m, 3H, Ar_1-4,5,6), 7.315-7.344(m, 10H, Ar_2), 4.279(s, 1H, OH), 1.555(s, 3H, TRZ-CH_3). ^{13}C NMR ($CDCl_3$-*d*$_1$), δ 148.8, 145.1, 135.5, 133.6, 132.6, 131.9, 129.4, 128.5, 128.1, 127.8, 127.7, 121.9, 8.7; MS m/z: 419(2.8) (M^+), 421(2.7), 392(46), 390(53), 376(9), 374(12), 316(1.6), 314(2.3), 288(7.2), 286(7.8), 234(14), 207(15), 198(15), 196(17), 173(18), 171(20), 157(13), 155(15), 129(26), 105(100), 77(52). IR: 3395(b, OH), 3086, 3059,

3026(w, Ar-H), 2924(w, CH_3), 1596, 1551(w), 1489, 1447 (m, Ar), 1373(m, CH_3), 1322(m, OH), 1273, 1212, 1130(m), 1026, 894(s, triazole ring), 1166(m, C-O), 768, 749, 698(s, Ar-H), 1068, 639, 567(m) cm^{-1}. Calcd for $C_{22}H_{18}BrN_3O$: C, 62.87; H, 4.32; Br, 19.01; N, 10.00; Found: C, 62.88; H, 4.34; N, 10.01.

[1-(4-Bromophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]diphenylmethanol 6o,

Yield 91%, white needle crystals, m.p. 159-160°C. ^{1}H NMR ($CDCl_3$-*d*$_1$), δ7.628-7.682(d, 2H, *J* = 8.1Hz, Ar_1-3,5), 7.272-7.350(m, 12H, Ar_1-2,6, Ar_2), 4.165(s, 1H, OH), 1.773(s, 3H, TRZ-CH_3). ^{13}C NMR ($CDCl_3$-*d*$_1$), δ 149.6, 145.0, 135.1, 132.6, 131.1, 128.3, 128.1, 127.7, 126.9, 123.6, 9.5; MS m/z: 419(1.4) (M^+), 421(1.3), 392(98), 390(100), 376(20), 374(22), 316(6), 314(6.5), 288(6), 286(6.9), 234(17), 207(33), 198(32), 196(34), 173(39), 171(44), 157(27), 155(19), 129(16), 105(90), 77(45). IR: 3320(b, OH), 3089, 3055, 3025(w, Ar-H), 2930(w, CH_3), 1596, 1551(w), 1493, 1446 (s, Ar), 1398(m, CH_3), 1349(m, OH), 1273, 1222, 1137(m), 1048, 901(s, triazole ring), 1184(m, C-O), 827, 759, 699(s, Ar-H), 1073, 731, 630(m) cm^{-1}. Calcd for $C_{22}H_{16}BrN_3O$: C, 62.87; H, 4.32; Br, 19.01; N, 10.00; Found: C, 62.89; H, 4.34; N, 10.02.

[1-(4-Methoxyphenyl)-5-methyl-1H-1,2,3-triazol-4-yl]diphenylmethanol 6p,

Yield 89%, white needle crystals, m.p. 167-168°C. ^{1}H NMR ($CDCl_3$-*d*$_1$), δ7.268-7.370(m, 12H, Ar_1-2,6, Ar_2), 7.000-7.030(d, 2H, *J* = 9.0Hz, Ar_1-3,5), 4.198(s, 1H, OH), 3.868(s, 3H, Ar_1-OCH_3), 1.699(s, 3H, TRZ-CH_3). ^{13}C NMR ($CDCl_3$-*d*$_1$), δ 160.3, 149.0, 145.2, 131.2, 129.1, 128.0, 127.8, 127.6, 126.9, 114.5, 55.6, 9.4; MS m/z: 371(0.8) (M^+), 342(100), 326(14), 266(6), 238(14), 223(7.9), 161(4.6), 148(23), 123(28), 108(9), 105(40), 92(6), 77(26). IR: 3373(b, OH), 3078, 3018(w, Ar-H), 2971, 2941, 2845(w, CH_3), 1610, 1551(w),1515, 1448(s, Ar), 1383(w, CH_3), 1348(m, OH), 1254, 1044(s, C-O-C), 1165(s, C-O),1304, 1223, 1135, 1021, 902(s, triazole ring),

837, 758, 702(s, Ar), 731, 629(m) cm^{-1}. Calcd for $C_{23}H_{21}N_3O_2$: C, 74.37; H, 5.70; N, 11.31; Found: C, 74.35; H, 5.72; N, 11.29.

[1-(4-Ethoxyphenyl)-5-methyl-1H-1,2,3-triazol-4-yl]diphenylmethanol 6q,

Yield 78%, white needle crystals, m.p. 117-118°C. ^{1}H NMR ($CDCl_3$-*d*$_1$), δ7.270-7.379(m, 12H, Ar_1-2,6, Ar_2), 6.975-7.004(d, 2H, *J* = 8.7Hz, Ar_1-3,5), 4.284(s, 1H, OH), 4.038-4.109(q, 2H, *J* = 6.9Hz, Ar_1-OCH_2-), 1.705(s, 3H, TRZ-CH_3), 1.418- 1.463(t, 3H, *J* = 6.9Hz, Ar_1-OCH_2CH_3). ^{13}C NMR ($CDCl_3$-*d*$_1$), δ 159.7, 149.0, 145.2, 131.2, 128.9, 128.0, 127.8, 127.6, 126.9, 114.9, 63.9, 14.7, 9.4; MS m/z: 385(0.4) (M^+),356(100), 340(18), 280(5), 252(18), 224(4.3), 175(4.7), 162(22), 137(26), 121(2), 105(52), 93(4), 91(5), 77(22). IR: 3335(b, OH), 3084, 3060, 3024(w, Ar-H), 2975, 2930(w, CH_3), 2759(w, OCH_2), 1605, 1553(w), 1515, 1446(s, Ar), 1389(m, CH_3), 1251, 1044(s, C-O-C), 1172(s, C-O), 1298, 1210, 1139, 1025, 899(m, triazole ring), 838, 763, 703(s, Ar), 636(m) cm^{-1}. Calcd for $C_{24}H_{23}N_3O_2$: C, 74.78; H, 6.01; N, 10.90; Found: C, 74.77; H, 6.00; N, 10.92.

[5-Methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl]diphenylmethanol 6r,

Yield 84%, white flaky crystals, m.p. 153-154°C. ^{1}H NMR ($CDCl_3$-*d*$_1$), δ8.001-8.027(d, 1H, *J* = 7.8Hz, Ar_1-5), 7.923-7.948(d, 1H, *J* = 7.5Hz, Ar_1-8), 7.480- 7.560(m, 4H, Ar_1-2,3,6,7), 7.302-7.429(m, 10H, Ar_2), 7.153-7.181(d, 1H, *J* = 8.4Hz, Ar_1-4), 4.365(s, 1H, OH), 1.528(s, 3H, TRZ-CH_3). ^{13}C NMR ($CDCl_3$-*d*$_1$), δ 148.8, 145.2, 134.1, 133.1, 132.3, 130.7, 129.8, 128.3, 128.1, 128.0, 127.8, 127.7, 127.1, 125.4, 125.0, 122.0, 8.8; MS m/z: 391(0.5) (M^+), 362(100), 346(30), 286(10), 258(41), 243(23), 180(45), 168(29), 143(41), 127(63), 105(40), 101(6), 77(27). IR: 3406(b, OH), 3090, 3058, 3006(w, Ar-H), 2928(w, CH_3), 1596, 1558(w), 1489, 1444 (m, Ar), 1379(w, CH_3), 1305(m, OH), 1256, 1202, 1046, 884(m, triazole ring), 1128 (m, C-O), 820, 774,

697(s, Ar) cm^{-1}. Calcd for $C_{26}H_{21}N_3O$: C, 79.77; H, 5.41; N, 10.73; Found: C, 79.76; H, 5.43; N, 10.76.

[5-Methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl]diphenylmethanol 6s,

Yield 84%, white flaky crystals, m.p. 133-134°C. ^{1}H NMR ($CDCl_3$-*d*$_1$), δ7.882-7.999(m, 4H, Ar_1-5,6,7,8), 7.515-7.618(m, 3H, Ar_1-1,3,4), 7.288-7.401(m, 10H, Ar_2), 4.261(s, 1H, OH), 1.803(s, 3H, TRZ-CH_3). ^{13}C NMR ($CDCl_3$-*d*$_1$), δ 149.4, 145.2, 133.5, 133.2, 132.9, 131.3, 129.6, 128.3, 128.1, 127.9, 127.8, 127.6, 127.4, 127.3, 124.4, 123.0, 9.6; MS m/z: 391(1) (M^+), 362(100), 346(31), 286(14), 258(60), 243(32), 180(18), 168(31), 143(47), 127(64), 105(57), 101(6), 77(36). IR: 3492(b, OH), 3059, 3028(w, Ar-H), 2924(w, CH_3), 1600, 1553(w), 1510, 1446(m, Ar), 1387(w, CH_3), 1356(m, OH), 1250, 1126, 1045, 894(m, triazole ring), 1167(m, C-O), 859, 814, 755, 699(s, Ar) cm^{-1}. Calcd for $C_{26}H_{21}N_3O$: C, 79.77; H, 5.41; N, 10.73; Found: C, 79.76; H, 5.43; N, 10.75.

Some new 1-aryl-4-[(aziridin-1-yl)diaryl-methyl]-5-methyl-1H-1,2,3-triazole derivatives 7j-s were prepared by one-pot synthesis

A mixture of 0.04 mole (1-aryl-5-methyl-1*H*-1,2,3-triazol-4-yl)diphenylmethanol **6j-s**, 20 mL benzene was placed in a 50 mL three-necked round-bottomed flask equipped with an automatic water separator carrying a reflux condenser with calcium chloride guard-tubes. All parts of the apparatus were thoroughly dry. The bottom of the flask was refluxed with a bath of hot oil under rapid stirring. Dry hydrogen chloride was passed into the three-neck bottle until the lighter benzene passed back into the flask. The reaction device was changed to a distillation apparatus, and the solvent benzene was evaporated. The heating device was removed, 10 mL anhydrous benzene was added, and 0.06 mole aziridine was added under rapid stirring. When the solution turned yellow, 0.08 mole triethylamine was added. After the mixture solution was stirred at 45 °C for

approximately an hour, the solvent was evaporated, and the raw product was given. Either it was recrystallized with ethyl acetate, or the crude product was purified by column chromatography with silica gel as the adsorbent and ethyl acetate/petroleum ether as the eluent. Compounds **7j-s** were given. The physical constants and yields of compounds **7j-s** are shown below:

4-[(Aziridin-1-yl)diphenylmethyl]-5-methyl-1-(2-tolyl)-1H-1,2,3-triazole 7j,

Yield 87%, white flaky crystals, m.p. 170-171 °C. ^{1}H NMR ($CDCl_3$-d_1), δ7.587-7.616(m, 4H, Ar_1-3,4,5,6), 7.204-7.419(m, 10H, Ar_2), 1.979(s, 3H, TRZ-CH_3), 1.837-1.843(d, 2H, J = 1.8Hz, AZI-CH_2-), 1.696(s, 3H, Ar-CH_3), 1.241-1.252(d, 2H, J = 3.3Hz, AZI-CH_2-); ^{13}C NMR ($CDCl_3$-d_1), δ144.5, 144.1, 135.6, 135.3, 134.1, 131.0, 130.1, 128.8, 127.5, 127.4, 126.73, 126.71, 69.6, 21.8, 17.0, 9.6. MS m/z: 380(M^+), 0.74), 351(0.61), 338(7.5), 323(0.39), 310(0.76), 247(0.36), 232(0.41), 217 (0.69), 204(0.57), 190(0.85), 178(4.5), 165(2.8), 152(1.5), 132(100), 117(4), 91(45), 77(8), 65(22). IR: 3054, 3019(m, Ar-H), 2988, 2922, 2852(m, CH_3, CH_2), 1596(w), 1491, 1444(s, Ar), 1382(m, CH_3), 1261, 993, 903(s, triazole ring), 1116(m, C-N), 768,745, 699(s, Ar-H) cm^{-1}. Anal. Calcd for $C_{25}H_{24}N_4$: C, 78.92; H, 6.36; N, 14.73; Found: C, 78.67; H, 6.08; N, 14.56.

4-[(Aziridin-1-yl)diphenylmethyl]-5-methyl-1-(2-chlorophenyl)-1H-1,2,3-triazole 7k,

Yield 88%, white flaky crystals, m.p. 171-172 °C. ^{1}H NMR ($CDCl_3$-d_1), δ7.558-7.618(m, 4H, Ar_1-3,4,5,6), 7.200-7.450(m, 10H, Ar_2), 1.850(s, 2H, AZI-CH_2-), 1.725(s, 3H, TRZ-CH_3), 1.270(s, 2H, AZI-CH_2-); ^{13}C NMR ($CDCl_3$-d_1), δ144.4, 135.1, 134.1, 132.1, 131.5, 130.4, 129.4, 128.8(×2), 127.8, 127.6, 126.8, 69.6, 21.9, 9.6. MS m/z: 400(M^+, 0.26), 371(0.14), 360(1.1), 358(4.5), 346(0.89), 330(0.72), 267(0.14), 252 (0.23), 217(0.66), 203(0.9), 190(1.6), 178(7.8),

165(4.9), 154(32), 152(100), 113(9.4), 111(29), 75(17). IR: 3051, 3022(m, Ar-H), 2990, 2921, 2851(m, CH_3, CH_2), 1595(w), 1491, 1444(s, Ar), 1385(m, CH_3), 1256, 989, 903(s, triazole ring), 1117(s, C-N), 767, 744, 697(s, Ar- H), 1081(m) cm^{-1}. Anal. Calcd for $C_{24}H_{21}ClN_4$: C, 71.90; H, 5.28; Cl, 8.84; N, 13.98; Found: C, 71.76; H, 5.08; Cl, 8.63; N, 14.06.

4-[(Aziridin-1-yl)diphenylmethyl]-5-methyl-1-(3-chlorophenyl)-1H-1,2,3-triazole 7l,

Yield 90%, white flaky crystals, m.p. 149-150 ^oC. ^1H NMR ($CDCl_3$-d_1), δ7.441-7.562(m, 7H, Ar_1-2,4,5,6, Ar_2), 7.255-7.336(m, 7H, Ar_2), 2.098(s, 3H, TRZ- CH_3), 1.803-1.822(t, 2H, *J* = 1.9Hz, AZI-CH_2-), 1.185-1.205(t, 2H, *J* = 1.9Hz, AZI-CH_2-); ^{13}C NMR ($CDCl_3$-d_1), δ146.6, 143.2, 137.4, 135.0, 132.8, 130.3, 129.4, 129.2, 127.5, 126.9, 125.9, 123.7, 70.0, 21.7, 10.5. MS m/z: 400(M^+, 0.72), 402(0.24), 371(0.5), 360(2.1), 358(4.7), 343(0.72), 330(0.52), 267(0.15), 252(0.74), 219(2.9), 202(0.87), 190(1.2), 178(5.8), 165(3.8), 154(25), 152(100), 113(11), 111(33), 75(12). IR: 3059, 3022(m, Ar-H), 2989, 2925, 2850(m, CH_3, CH_2), 1592, 1489, 1441(s, Ar), 1388(m, CH_3), 1263, 1013, 902(s, triazole ring), 1118(m, C-N), 873, 783, 748, 703(s, Ar-H), 1089(s) cm^{-1}. Anal. Calcd for $C_{24}H_{21}ClN_4$: C, 71.90; H, 5.28; Cl,8.84; N, 13.98; Found: C, 71.82; H, 5.02; Cl,8.70; N, 14.03.

4-[(Aziridin-1-yl)diphenylmethyl]-5-methyl-1-(2,5-dichlorophenyl)-1H-1,2,3-triazole 7m,

Yield 89%, white needle crystals, m.p. 159-160^oC. ^1H NMR ($CDCl_3$-d_1), δ 7.450-7.598(m, 7H, Ar_1-3,4,6, Ar_2), 7.195-7.356(m, 6H, Ar_2), 1.834-1.853(t, 2H, *J* = 1.9Hz, AZI-CH_2-), 1.792(s, 3H, TRZ-CH_3), 1.253(s, 2H, AZI-CH_2-); ^{13}C NMR ($CDCl_3$-d_1), δ145.0, 143.9, 135.0, 134.9, 133.5, 131.6, 131.1, 130.5, 129.6, 128.8, 127.6, 126.9, 69.6, 21.8, 9.7. MS m/z: 434(M^+, 0.24), 405(0.13),

396(0.37), 394(2.7), 392(4.3), 374(0.37), 366(0.45), 364(0.7), 328(0.17), 252(0.59), 217(0.75), 202(1.6), 198(2.9), 196(2.7), 190(13), 188(65), 186(100), 178(14), 165(6.4), 151(5.1), 147(13), 145(20), 109 (13), 77(16). IR: 3061, 3024(m, Ar-H), 2984, 2924(m, CH_3, CH_2), 1586(m), 1487, 1446(s, Ar), 1384 (m, CH_3), 1262, 1019, 902(s, triazole ring), 1117(m, C-N), 876, 829, 748, 703(s, Ar- H), 1095(s)cm^{-1}. Anal. Calcd for $C_{24}H_{20}Cl_2N_4$: C, 66.21; H, 4.63; Cl, 16.29; N, 12.87; Found: C, 66.34; H, 4.82; Cl, 16.35; N, 12.63.

4-[(Aziridin-1-yl)diphenylmethyl]-5-methyl-1-(2-bromophenyl)-1H-1,2,3-triazole 7n,

Yield 91%, white flaky crystals, m.p. 164-165ºC. ^{1}H NMR ($CDCl_3$-d_1), δ 7.604-7.740(m, 5H, Ar_1-3,4,5,6, Ar_2), 7.216-7.462(m, 9H, Ar_2), 1.843(s, 2H, AZI-CH_2-), 1.707(s, 3H, TRZ-CH_3), 1.283(s, 2H, AZI-CH_2-); ^{13}C NMR ($CDCl_3$-d_1), δ144.3, 135.7, 134.9, 133.5, 131.7, 129.4, 128.7, 128.4, 127.6(×2), 126.8, 122.1, 69.6, 21.9, 9.8. MS m/z: 444(M^+, 0.25), 446(0.24), 417(0.25), 415(0.29), 404(5.6), 402(4), 387(0.11), 374(1.1), 311(0.13), 294(2.1), 252(1), 217(1.8), 208(0.85), 202(2.4), 198(95), 196 (100), 190(3.1), 178(17), 165(8.6), 157(26), 155(28), 152(6.5), 77(27). IR: 3087, 3054, 3018(m, Ar-H), 2990, 2926(m, CH_3, CH_2), 1583(w), 1489, 1443(s, Ar), 1384(m, CH_3), 1253, 993, 903(s, triazole ring), 1120(s, C-N), 766, 745, 698(s, Ar- H), 1071(m)cm^{-1}. Anal. Calcd for $C_{24}H_{21}BrN_4$: C, 64.73; H, 4.75; Br, 17.94; N, 12.58; Found: C, 64.56; H, 4.55; Br, 17.76; N, 12.32.

4-[(Aziridin-1-yl)diphenylmethyl]-5-methyl-1-(4-bromophenyl)-1H-1,2,3-triazole 7o,

Yield 91%, white flaky crystals, m.p. 178-179ºC. ^{1}H NMR ($CDCl_3$-d_1), δ 7.632-7.660(d, 2H, J = 8.4Hz, Ar_1-3,5), 7.517-7.544(d, 4H, J = 8.1Hz, Ar_2-2,6), 7.210-7.360(m, 8H, Ar_2), 2.083(s,

3H, TRZ-CH_3), 1.800(s, 2H, AZI-CH_2-), 1.183(s, 2H, AZI-CH_2-); ^{13}C NMR ($CDCl_3$-*d*$_1$), δ146.6, 143.2, 135.4, 132.7, 132.5, 129.2, 127.4, 127.0, 126.8, 123.3, 70.0, 21.7, 10.5. MS m/z: 444(M^+, 0.13), 446(0.12), 417(0.27), 415(0.13), 404(3.8), 402(4.4), 387(0.28), 374(0.5), 294(0.97), 252(1), 217(1.4), 208(0.92), 202(2.1), 198(89), 196(100), 190 (2.5), 178(20), 165(8.8), 157(30), 155(32), 152(5.5), 76(31). IR: 3055, 3023(m, Ar-H), 2987, 2922, 2851(m, CH_3, CH_2), 1595(w), 1491, 1446(s, Ar), 1397(m, CH_3), 1261, 1004, 906(s, triazole ring), 1120(m, C-N), 831, 749, 706(s, Ar-H), 1070(s) cm^{-1}. Anal. Calcd for $C_{24}H_{21}BrN_4$: C, 64.73; H, 4.75; Br, 17.94; N, 12.58; Found: C, 64.60; H, 4.65; Br, 17.80; N, 12.30.

4-[(Aziridin-1-yl)diphenylmethyl]-5-methyl-1-(4-methoxyphenyl)-1H-1,2,3-triazole 7p,

Yield 89%, white flaky crystals, m.p. 152-153ºC. ^{1}H NMR ($CDCl_3$-*d*$_1$), δ7.547-7.583(d, 4H, *J* = 7.2Hz, Ar_2-2,6), 7.219-7.348(m, 8H, Ar_1-2,6, Ar_2), 6.970- 7.014(d, 2H, *J* = 8.8Hz, Ar_1-3,5), 3.851(s, 3H, Ar_1-OCH_3), 1.967(s, 3H, TRZ-CH_3), 1.804-1.819(t, 2H, *J* = 1.5Hz, AZI-CH_2-), 1.218(s, 2H, AZI-CH_2-); ^{13}C NMR ($CDCl_3$-*d*$_1$), δ160.1, 145.6, 143.7, 133.1, 129.3, 129.1, 127.4, 127.0, 126.7, 114.3, 69.9, 55.6, 21.7, 10.4. MS m/z: 396(M_+, 1.1), 367(1.7), 354(11), 341(5.6), 326(7.3), 294(0.18), 237(0.38), 219(24), 202 (0.5), 191(1.2), 178(5.8), 165(4), 152(3.2), 148(100), 107(6.3), 92(20), 77(47), 43(46). IR: 3052, 3024(m, Ar-H), 2987, 2922, 2844(m, CH_3, CH_2), 1607(m), 1517, 1443(s, Ar), 1490(s, CH_2), 1254(s, C-O-C), 1125(s, C-N), 1007, 905(s, triazole ring), 835, 753, 705(s, Ar-H) cm^{-1}. Anal. Calcd for $C_{25}H_{24}N_4O$: C, 75.73; H, 6.10; N, 14.13; Found: C, 75.57; H, 5.98; N, 14.06.

4-[(Aziridin-1-yl)diphenylmethyl]-5-methyl-1-(4-ethoxyphenyl)-1H-1,2,3-triazole 7q,

Yield 90%, white flaky crystals, m.p. 148-149°C. ^{1}H NMR ($CDCl_3$-d_1), δ7.549-7.589(d, 4H, J = 8Hz, Ar_2-2,6), 7.218-7.334(m, 8H, Ar_1-2,6, Ar_2), 6.955-7.000 (d, 2H, J = 9Hz, Ar_1-3,5), 4.018-4.123(q, 2H, J = 7Hz, Ar_1-OCH_2-), 1.959(s, 3H, TRZ-CH_3), 1.803-1.821(t, 2H, J = 1.8Hz, AZI-CH_2-), 1.403-1.473(t, 3H, J = 7Hz, Ar_1-CH_3), 1.202-1.220(t, 2H, J = 1.8Hz, AZI-CH_2-); ^{13}C NMR ($CDCl_3$-d_1), δ159.5, 145.5, 143.8, 133.1, 129.13, 129.07, 127.4, 126.9, 126.7, 114.9, 69.9, 63.8, 21.7, 14.7, 10.4. MS m/z: 410(M^+, 2), 381(2.9), 368(15), 353(1.5), 340(14), 312(3.4), 219(10), 208(1.5), 202 (0.6), 190(0.98), 178(7.3), 165(5.5), 162(100), 152(2.7), 134(16), 105 (13), 93(8.4), 91(8.1), 77(25), 65(24), 43(24). IR: 3056(m, Ar-H), 2982, 2930(s, CH_3, CH_2), 1608, 1517, 1442(s, Ar), 1487, 1395(m, CH_3, CH_2), 1252, 1044(s, C-O-C), 1111(s, C-N), 1008, 900(s, triazole ring), 830, 751, 702(s, Ar-H) cm^{-1}. Anal. Calcd for $C_{26}H_{26}N_4O$: C, 76.07; H, 6.38; N, 13.65; Found: C, 76.27; H, 6.21; N, 13.46.

4-[(Aziridin-1-yl)diphenylmethyl]-5-methyl-1-α-naphthalenyl-1H-1,2,3-triazole 7r,

Yield 89%, white flaky crystals, m.p. 134-136°C. ^{1}H NMR ($CDCl_3$-d_1), δ7.906-8.016(m, 2H, Ar_1), 7.630-7.670(m, 4H, Ar_1), 7.502-7.567(m, 4H, Ar_2), 7.236-7.364(m, 6H, Ar_2), 7.047-7.099(d, 1H, J = 10.4Hz, Ar_1), 1.868-1.884(t, 2H, J = 1.6 Hz, AZI-CH_2-), 1.734(s, 3H, TRZ-CH_3), 1.321-1.327(d, 2H, J = 0.6Hz, AZI-CH_2-); ^{13}C NMR ($CDCl_3$-d_1), δ144.9, 144.0, 135.2, 134.1, 132.6, 130.5, 129.9, 129.0, 128.3, 127.9, 127.6, 126.9, 126.8, 125.4, 125.0, 122.0, 69.8, 21.9, 9.9. MS m/z: 416(M^+, 1.6), 387(3.4), 374(14), 359(0.63), 346(3), 330(0.44), 283(0.17), 268(0.69), 215(0.58), 208(1.1), 202(0.77), 190(0.71), 178(5.1), 168(100), 165(3.5), 152(2.4), 127(47), 77(14). IR: 3053(m, Ar-H), 2992, 2923(m, CH_3, CH_2), 1596, 1487, 1445(s, Ar), 1392(m, CH_3), 1263, 999, 901(s, triazole ring), 1113(s, C-N), 771, 743, 704(s, Ar-H) cm^{-1}. Anal. Calcd for $C_{28}H_{24}N_4$: C, 80.74; H, 5.81; N, 13.45; Found: C, 80.67; H, 5.88; N, 13.26.

4-[(Aziridin-1-yl)diphenylmethyl]-5-methyl-1-β-naphthalenyl-1H-1,2,3-triazole 7s,

Yield 90%, white needle crystals, m.p. 180-181°C. ^{1}H NMR ($CDCl_3$-*d*$_1$), δ7.860-7.982(m, 4H, Ar_1), 7.494-7.610(m, 7H, Ar_1, Ar_2), 7.197-7.349(m, 6H, Ar_2), 2.089(s, 3H, TRZ-CH_3), 1.836(s, 2H, AZI-CH_2-), 1.255(s, 2H, AZI-CH_2-); ^{13}C NMR ($CDCl_3$-*d*$_1$), δ146.1, 143.6, 133.8, 133.2, 133.1, 133.0, 129.4, 129.2, 128.2, 127.8, 127.5, 127.3, 127.2, 126.8, 124.5, 123.5, 70.0, 21.8, 10.6. MS m/z: 416(M^+, 0.43), 387(1), 374(6.6), 359(0.7), 346(1.1), 330(0.29), 283(0.51), 268(0.73), 215(0.88), 208(0.76), 202(1.1), 190(1.7), 178(17), 168(100), 165(5.7), 152(4.7), 127(82), 77(21). IR: 3052, 3028(m, Ar-H), 2983, 2920, 2850(m, CH_3, CH_2), 1598, 1486, 1444(m, Ar), 1386(m, CH_3), 1261, 1010, 898(s, triazole ring), 1112(s, C-N), 811,750,702(s, Ar-H) cm^{-1}. Anal. Calcd for $C_{28}H_{24}N_4$: C, 80.74; H, 5.81; N, 13.45; Found: C, 80.62; H, 5.78; N, 13.36.

Biological evaluation of target compounds.

The potential effects on cell viability were investigated under our previously reported conditions,[21], [22] using the MTT assay [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide, Sigma, France] as an indicator of metabolically active cells.

Human leukaemia cells and human hepatoma G2 cells was plated into 96-well plates at a density of 5×10^3 cells/well and incubated for 12 h before the addition of test compounds. Cells were then exposed for 48 h at 37 °C to known concentrations of the compound to be tested (10 or 160 μM, expressed as final concentration). After drug exposure, the culture medium was removed, and 200 mL of MTT reagent (diluted in culture medium, 0.25 mg/mL) was added. After incubation for 4 h, the MTT/medium was removed, and DMSO (200 mL) was added to dissolve the formazan deposits or crystals. The absorbance of the coloured solution was measured on a microplate

photometer (PerkinElmer Victor3) using a test wavelength of 570 nm and a reference wavelength of 630 nm. The results were evaluated by comparing the absorbance of the wells containing compound-treated cells with the absorbance of wells containing 0.1% DMSO alone (solvent control). Conventionally, cell viability was determined for each assay by including wells that did not contain cells as blank wells. All experiments were performed at least twice in triplicate. The anticancer activity (IC_{50}) of the synthesized compounds in two cancer cell lines (μM) is shown in **Table 2**. The resulting effectiveness was as follows: (+) reflects an inhibition rate >50% for the growth of tumour cells at 10^{-5} mol/L; (++++) reflects an inhibition rate >90% at 10^{-5} mol/L.

Conclusions

Some new 1-aryl-4-[(aziridin-1-yl)diaryl-methyl]-5-methyl-1*H*-1,2,3-triazole derivatives **(7j-s)** were synthesized by a one-pot reaction of diaryl-(1-aryl-5-methyl-*1H*-1,2,3-triazol-4-yl)methanol. The synthesis of 1-aryl-4-[(aziridin-1-yl)diaryl-methyl]-5-methyl-1*H*-1,2,3-triazole derivatives is a highly efficient one-pot reaction. The anticancer activity of the synthesized compounds was evaluated. Compound **7j** was highly efficient in inhibiting human hepatoma G2 cells, and the compounds **7j**, **7m** and **7n** were highly efficient in inhibiting human leukaemia cells. Thus, the synthesis and testing in vitro show that the compounds **7j-s** can be applied successfully to design and develop better anticancer agents.

Acknowledgements

The authors wish to acknowledge the funding support by the education department in Gansu province (2016B-124) and by the Lanzhou University of Arts and Science (High levels of achievement projects 2015GSP05).

References

[1] (a) Dong, H. R.; Chen, Z. B.; Li, R. S.; Dong, H. S.; Xie, Z. X. *RSC Adv.* **2015**, *5*, 10768–10772. (b) Hoveyda; *J. Am. Chem. Soc.* **2004**, *126*, 3734. (c) Smith; *J. Am. Chem. Soc.* **2016**, *138*, 3675.

[2] Jamookeeah, C. E.; Beadle, C. D.; Harrity, J. P. A. *Synthesis* **2009**, 133–137.

[3] Watson, I. D. G.; Yudin, A. K. *J. Org. Chem.*, **2003**, *68*, 5160–5167.

[4] Nakao, Y.; Fusetani, N. *J. Nat. Prod.* **2007**, *70*, 689–710.

[5] Plaza, A.; Gustchina, E.; Baker, H. L.; Kelly, M.; Bewley, C. A. *J. Nat. Prod.* **2007**, *70*, 1753–1760.

[6] Sharma, V.; Kelly, G. T.; Foulke-Abel, J.; Watanabe, C. M. H. *Org. Lett.* **2009**, *11*, 4006–4009.

[7] Han, H.; Park, S. B.; Kim, S. K.; Chang, S. *J. Org. Chem.* **2008**, *73*, 2862–2870.

[8] Judd, T. C.; Williams, R. M. *J. Org. Chem.* **2004**, *69*, 2825–2830.

[9] Galm, U.; Hager, M. H.; Van Lanen, S. G.; Ju, J.; Thorson, J. S.; Shen, B. *Chem. Rev.* **2005**, *105*, 739–758.

[10] (a) Miyakoshi, H.; Miyahara, S.; Yokogawa, T. *J. Med. Chem.* **2012**, *55*, 6427–6437. (b) Zheng, Y. C.; Duan, Y. C.; Ma, J. L. *J. Med. Chem.* **2014**, *56*, 8543–8560.

[11] Zhang, W. J.; Li, Z.; Zhou, M.; Wu, F.; Hou, X. Y.; Luo, H.; Liu, H.; Han, X.; Yan, G. Y.; Ding, Z. Y.; et al. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 799–807.

[12] Sambasiva Rao, P.; Kurumurthy, C.; Veeraswamy, B.; Santhosh, K. G.; Poornachandra, Y.; Ganesh, K. C.; Vasamsetti, S. B.; Kotamraju, S.; Narsaiah, B. *Eur. J. Med. Chem.* **2014**, *80*, 184–191.

[13] Reck, F.; Zhou, F.; Girardot, M.; Kern, G.; Eyermann, C. J.; Hales, N. J.; Ramsay, R. R.; Gravestock, M. B. *J. Med. Chem.* **2005**, *48*, 499–506.

[14] Liang, C. H.; Yao, S.; Chiu, Y. H.; Leung, P. Y.; Robert, N.; Seddon, J.; Sears, P.; Hwang, C. K.; Ichikawa, Y.; Romero. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1307–1310.

[15] Chen, H.; Taylor, J. L.; Abrams, S. R. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 1979–1983.

[16] Maurya, S. K.; Gollapalli, D. R.; Kirubakaran, S.; Zhang, M. J.; Johnson, C. R.; Benjamin, N. N.; Hedstrom, L.; Cuny, G. D. *J. Med. Chem.* **2009**, *52*, 4623–4630.

[17] Youcef, R. T.; Santos, M. D.; Roussel, S.; Baltaze, J.; Lubin-Germain, N.; Uziel, J. *J. Org. Chem.* **2009**, *74*, 4318–4323.

[18] (a) Dong, H. R.; Dong, W. J.; Li, R. S.; Hu, Y. M.; Dong, H. S.; Xie, Z. X. *Green Chem.* **2014**, *16*, 3454–3457. (b) Dong, H. S.; Wang, B. *J. Chin. Chem. Soc.* **2005**, *52*, 103–108.

[19] Dong, H. S.; Quan, B.; Zhu, D. W.; Li, W. D. *J. Mol. Struct.* **2002**, *613*, 1–5.

[20] Dong, H. S.; Huo, G. Y.; Ma, Z. T. *Indian J. Chem., Sect. B* **2008**, *47*, 171–174.

[21] Wang, H.; Gao, H. H.; Wang, Q.; Gao, Q. X.; Lin, C. J. *Pharmazie* **2007**, *62*(9), 699–704.

[22] Iyengar, B. S.; Dorr, R. T.; Remers, W. A. *J. Med. Chem.* **2004**, *47*, 218–223.

Table 1. Yield and structure of compounds **6j–s** and **7j–s**.

Entry	Ar	Yield(%)[a]	Yield(%)[b]	-CH_3	Aziridine-δ_H	Aziridine-δ_H
1	2-$CH_3C_6H_4$	**6j** 84	**7j** 92	1.696	1.837–1.843d1.8	1.241–1.252d3.3
2	2-ClC_6H_4	**6k** 83	**7k** 88	1.725	1.850	1.270
3	3-ClC_6H_4	**6l** 80	**7l** 90	2.098	1.803–1.822t1.9	1.185–1.205t1.9
4	2,5-$Cl_2C_6H_3$	**6m** 92	**7m** 89	1.792	1.834–1.853t1.9	1.253
5	2-BrC_6H_4	**6n** 82	**7n** 91	1.707	1.843	1.283
6	4-BrC_6H_4	**6o** 91	**7o** 90	2.083	1.800	1.183
7	4-$CH_3OC_6H_4$	**6p** 89	**7p** 89	1.967	1.804–1.819t1.5	1.218
8	4-$C_2H_5OC_6H_4$	**6q** 78	**7q** 90	1.959	1.803–1.821t1.8	1.202–1.220t1.8
9	α-$C_{10}H_7$	**6r** 84	**7r** 89	1.734	1.868–1.884t1.8	1.321–1.327d0.6
10	β-$C_{10}H_7$	**6s** 84	**7s** 91	2.089	1.836	1.255

[a]Isolated yield.

[b]Isolated yield.

Table 2. Anticancer activity of synthesized compounds in two cancer cell lines.

No	**7j**	**7k**	**7l**	**7m**	**7n**	**7o**	**7p**	**7q**	**7r**
HL-60	+++	+	+	+++	++++	+	+	+	++
hepG2	++	+	+	+	+	+	+	+	+

Figure 1. ^{1}H NMR spectra of compound **7n**.

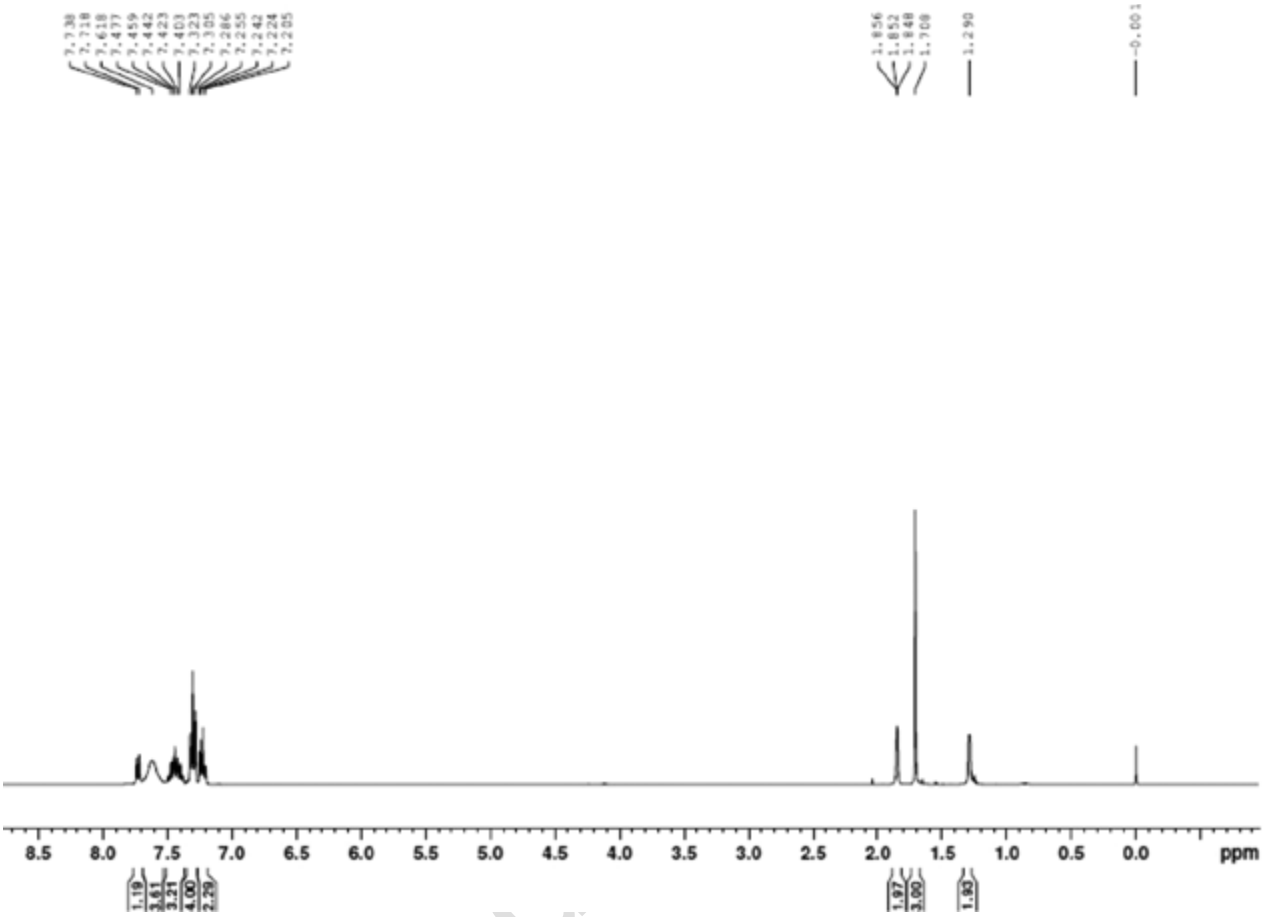


Figure 2. ^{13}C NMR spectra of compound **7n**.

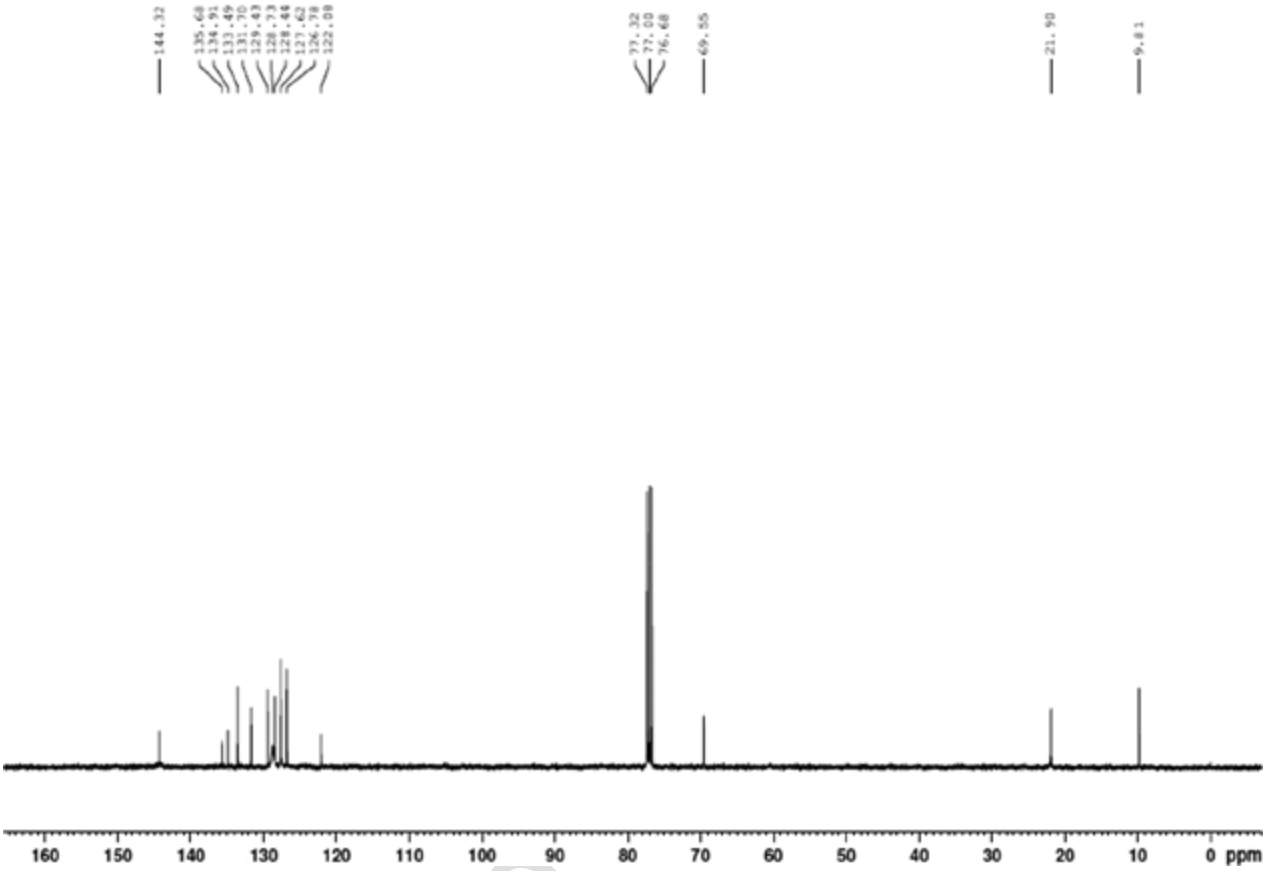
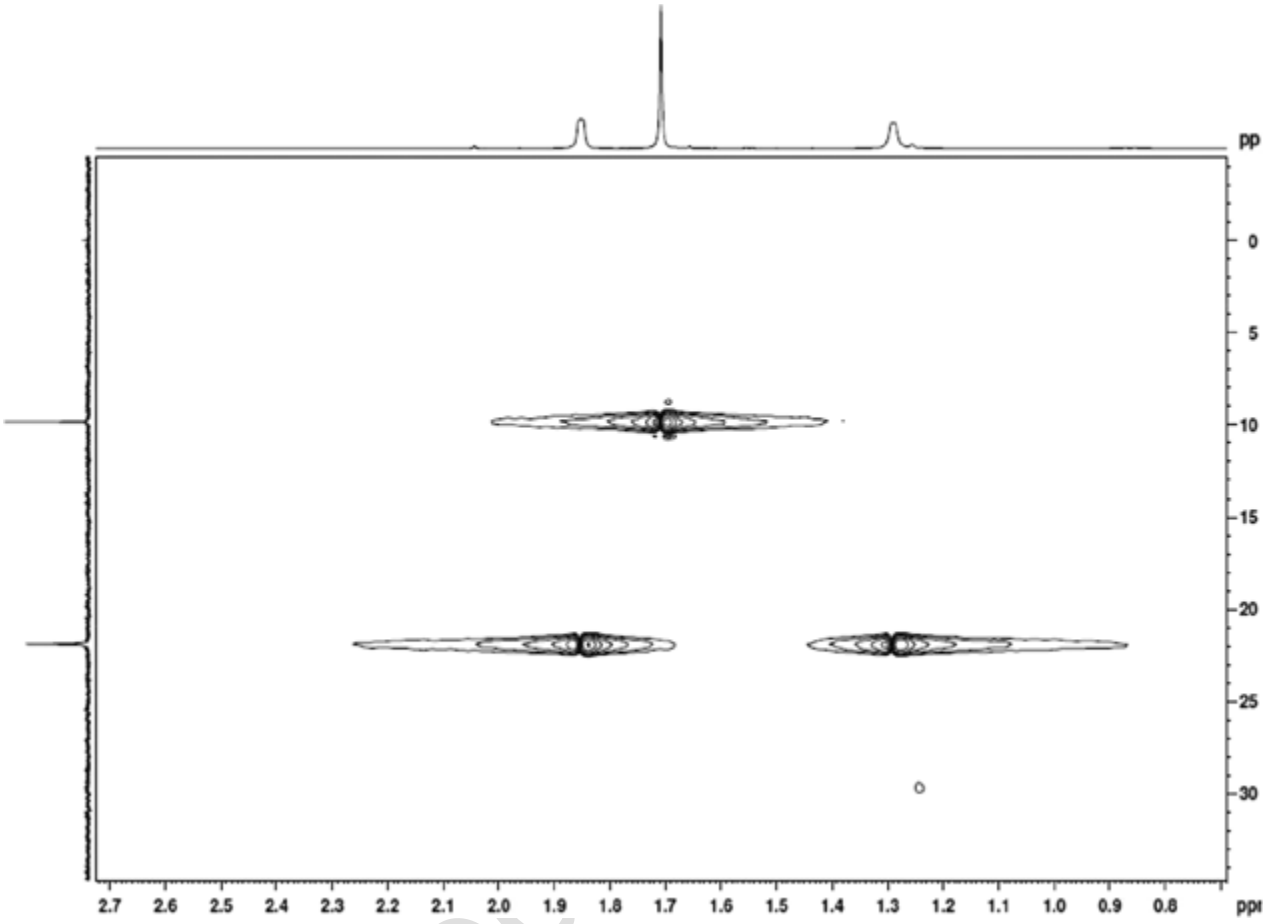
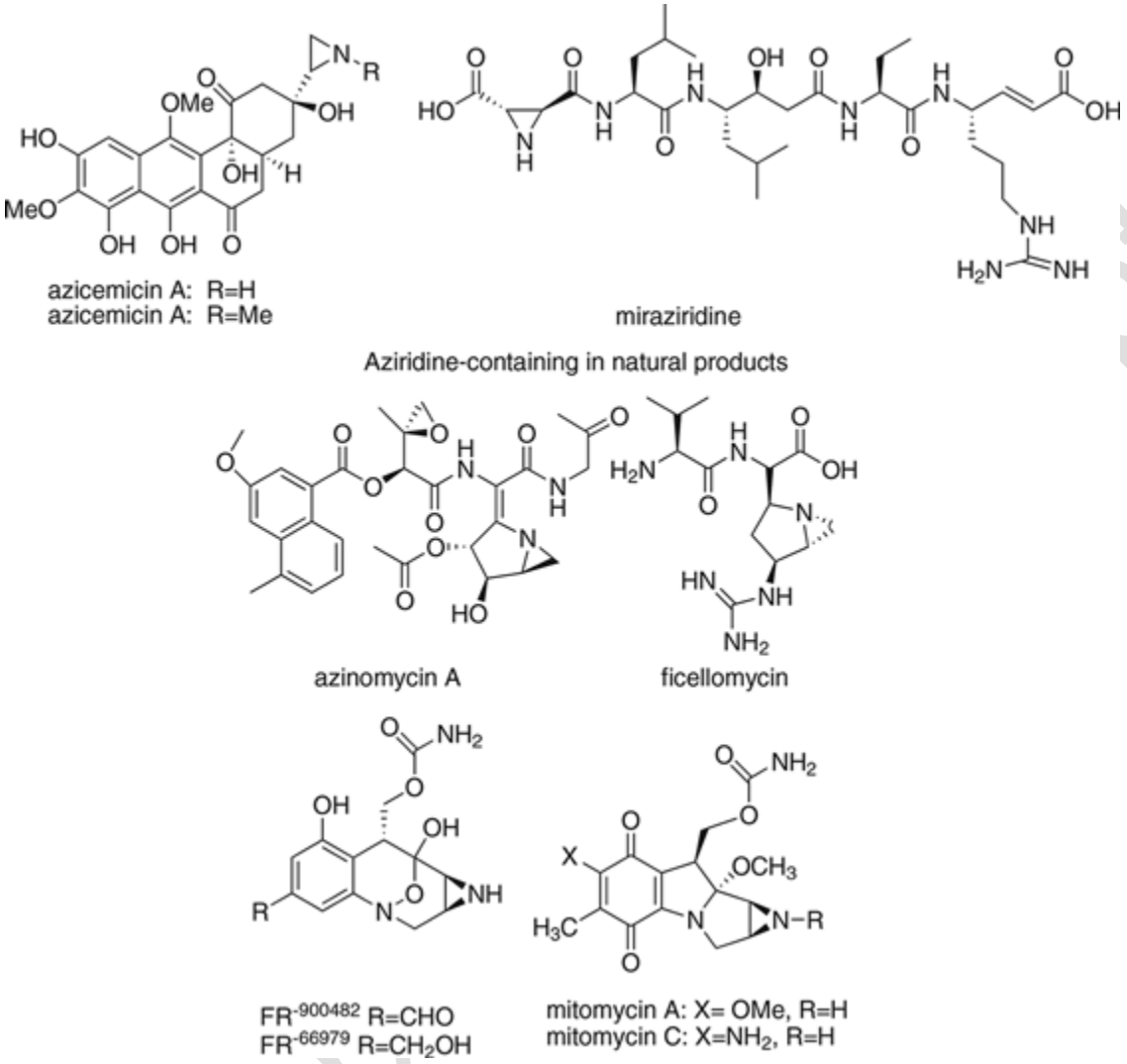


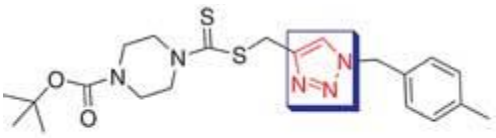
Figure 3. Part 2D NMR(^{1}H, ^{13}C and gHSQC) spectra of compound **7n**.



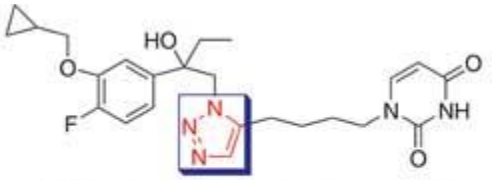
Scheme 1. Fuse-aziridine-containing in natural products.



Scheme 2. Anticancer compounds containing 1,2,3-triazole.

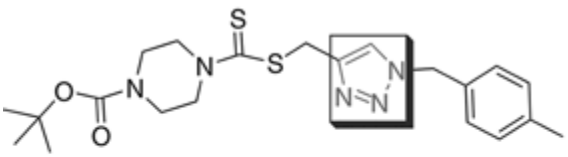


1-(4-methylbenzyl)-4-[4-(*tert*-butoxycarbonyl)piperazine-1-(carbonothioyl)thiomethyl]-1*H*-1,2,3-triazole

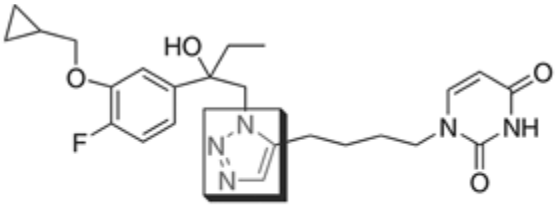


1-{2-[3-(cyclopropylmethoxy)-4-fluorophenyl]-2-hydroxybutane-1-yl}-5-[4-(3,4-dihydro-2,4-dioxopyrimidin-1(2*H*)-yl)butane-1-yl]-1*H*-1,2,3-triazole

Scheme 3. The synthesis of compounds 7j-s.



1-(4-methylbenzyl)-4-[4-(*tert*-butoxycarbonyl)piperazine-1-(carbonothioyl)thiomethyl]-1*H*-1,2,3-triazole



1-{2-[3-(cyclopropylmethoxy)-4-fluorophenyl]-2-hydroxybutane-1-yl}-5-{4-(3,4-dihydro-2,4-dioxopyrimidin-1(2*H*)-yl)butane-1-yl}-1*H*-1,2,3-triazole