DOI: 10.1002/ejoc.201100710

Temperature-Dependent Regioselective Synthesis of 1,2,4-Triazino[2,3-*b*]indazoles and 3*H*-1,4-Benzodiazepines by Domino-Staudinger/Aza-Wittig/Isomerization Reaction

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Keywords: Nitrogen heterocycles / Fused ring systems / Aza-Wittig reaction / Isomerization / Azides

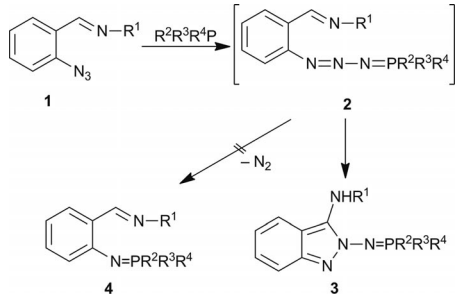
o-Azidobenzaldimine **8** reacted with triphenylphosphane at 0 °C with warming to room temperature to give 1,2,4-triazino[2,3-*b*]indazoles **12** by a domino-Staudinger/aza-Wittig/isomerization reaction. However, when heated to 80 °C the same reaction mixture afforded 3*H*-1,4-benzodiazepines **14** by a tandem-Staudinger/aza-Wittig reaction.

Introduction

Domino reactions have attracted significant attention from the synthetic organic chemistry community because of their utility in the creation of structurally diverse and complex molecules from simple precursors in an efficient manner.[1] The value of domino processes can be greatly enhanced when divergence from an intermediate is made possible with different reaction conditions.

Indazoles play an increasingly important role in drug discovery because of their structural similarity with indoles and benzimidazoles.[2] Many indazole derivatives have exhibited anti-HIV,[3] antiplatelet,[4] anticancer,[5] antimicrobial,[6,7] and antifungal activities.[8,9] Much effort has been invested in the synthesis of derivatives of these compounds to deduce structure–activity relationships and to discover new analogues with improved properties, especially in medicinal chemistry.

There are several regioselective methods for the preparation of 2*H*-indazoles.[10] Among them, a simple but effective route for the synthesis of indazoles was provided by Molina et al. (Scheme 1).[10b] The (indazolylimino)phosphorane derivative **3** was directly obtained from Staudinger reaction of *o*-azidobenzaldimines **1** through the intermediacy of phosphazide **2** instead of the expected *o*-(triphenylphosphoranylidene)aminobenzaldimine **4**. Further aza-Wittig reactions of **3** with isocyanates or acyl chlorides gave various fused indazoles in good yields. Aza-Wittig reactions have recently received increased attention in view of their utility in the synthesis of many nitrogen-containing heterocycles.[11,12] We envisioned that a domino-Staudinger/aza-Wittig reaction of suitably functionalized *o*-azidobenzaldimines **1** would provide access to fused indazoles in only one step. In support of our continued interest in the synthesis of N-heterocycles by application of the aza-Wittig reaction,[13] we report here a temperature-dependent regioselective synthesis of previously unreported 1,2,4-triazino[2,3-*b*]indazole ring systems and 3*H*-1,4-benzodiazepines by a domino-Staudinger/aza-Wittig/isomerization reaction.



Scheme 1. Literature preparation of the (indazolylimino)phosphorane **3** by abnormal Staudinger reaction.

Results and Discussion

Vinyl azides **6**, obtained easily from condensation of azides **5** with aromatic aldehydes in the presence of piperidinium acetate,[14] reacted with triphenylphosphane or methyldiphenyl phosphane to give iminophosphoranes **7**. Initially, aza-Wittig reactions of (triphenylimino)phosphorane **7** (R = Ph) with 2-azidobenzaldehyde were examined in ethanol, but low yields (32–35%) of **8** were obtained due to the low reactivity of **7** (R = Ph) with 2-azidobenzaldehyde. However, when more reactive (methyldi-

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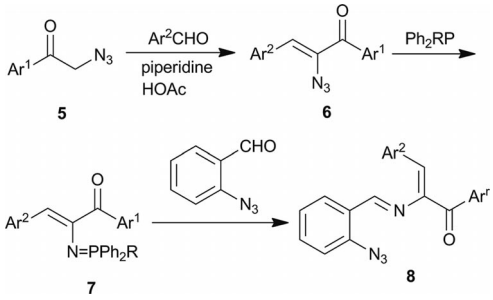
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201100710.

phenylimino)phosphorane **7** (R = Me) was used at 50 °C, good yields (82–92%) of condensed *o*-azidobenzaldimines **8** were obtained (Scheme 2, Table 1).



Scheme 2. Preparation of *o*-azidobenzaldimine **8**.

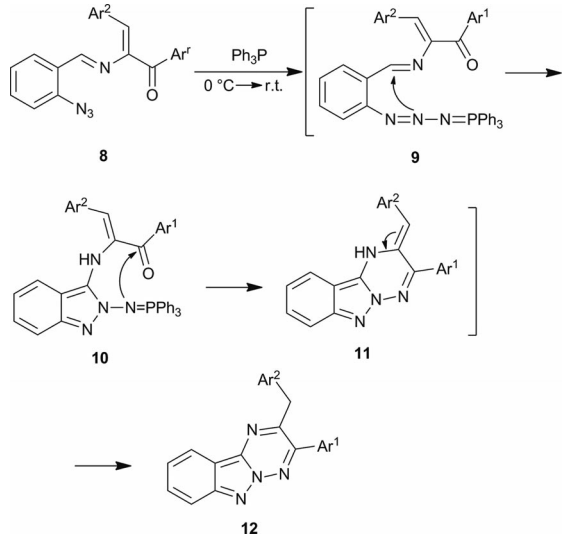
Table 1. Preparation of *o*-azidobenzaldimine **8**.

Entry		R	Ar^1	Ar^2	Conditions	Yield (%)[a]
1	**8a**	Ph	Ph	Ph	50 °C/8 h	35
2		Me			50 °C/4 h	90
3	**8b**	Ph	Ph	4-ClC_6H_4	50 °C/7 h	32
4		Me			50 °C/4 h	92
5	**8c**	Me	Ph	4-FC_6H_4	50 °C/6 h	75
6	**8d**	Me	Ph	4-$CH_3C_6H_4$	50 °C/4 h	88
7	**8e**	Me	4-ClC_6H_4	Ph	50 °C/4 h	86
8	**8f**	Me	4-ClC_6H_4	4-ClC_6H_4	50 °C/5 h	84
9	**8g**	Me	4-ClC_6H_4	4-FC_6H_4	50 °C/6 h	83
10	**8h**	Me	4-ClC_6H_4	4-$CH_3C_6H_4$	50 °C/4 h	90

[a] Isolated yields.

When *o*-azidobenzaldimines **8** were treated with triphenylphosphane in CH_2Cl_2 at 0 °C for 2 h, and then at room temperature for another 2 h, previously unreported 1,2,4-triazino[2,3-*b*]indazoles **12** were isolated directly in high yields (84–91%) (Scheme 3, Table 2). The domino formation of 1,2,4-triazino[2,3-*b*]indazoles **12** can be viewed as an initial Staudinger reaction between *o*-azidobenzaldimine **8** and triphenylphosphane to create phosphazide intermediate **9**, which cyclizes to give iminophosphorane **10**. Further intramolecular aza-Wittig reaction of **10** produces cyclized compound **11**, in which an isomerization reaction takes place to give 1,2,4-triazino[2,3-*b*]indazole **12**. It is noteworthy that the reaction proceeds under mild conditions to give various substituted 1,2,4-triazino[2,3-*b*]indazoles, and the overall transformation is run in a simple one-pot procedure from azides **8**.

It is interesting to note that 3*H*-1,4-benzodiazepines **14** were obtained instead when *o*-azidobenzaldimines **8** were allowed to react with triphenylphosphane in toluene at 80 °C for 8 h (Scheme 4, Table 3). The formation of 3*H*-1,4-benzodiazepines **14** can be viewed as an initial Staudinger reaction between *o*-azidobenzaldimine **8** and triphenylphosphane to give the iminophosphorane **13**, through loss of N_2 from phosphazide intermediate **9** under higher temperature. Further intramolecular aza-Wittig reaction of **13** produces 3*H*-1,4-benzodiazepine **14**. It is deduced that phosphazide intermediate **9** tends to decompose at higher temperature to give the iminophosphorane **13** instead of the (indazolyl-

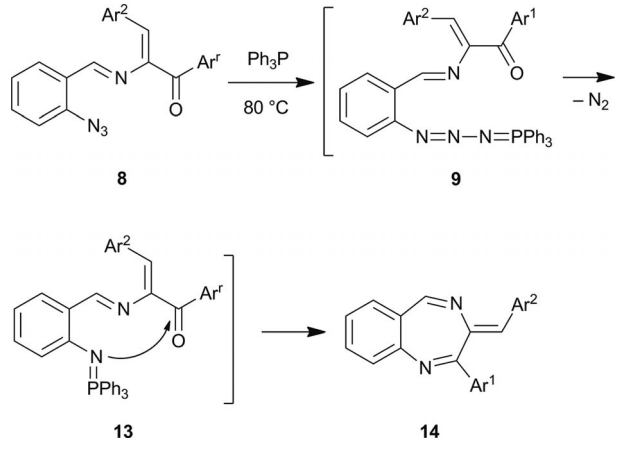


Scheme 3. Preparation of 1,2,4-triazino[2,3-*b*]indazoles **12** by a domino-Staudinger/aza-Wittig/isomerization reaction.

Table 2. Preparation of 1,2,4-triazino[2,3-*b*]indazoles **12**.

Entry		Ar^1	Ar^2	Yield (%)[a]
1	**12a**	Ph	Ph	91
2	**12b**	Ph	4-ClC_6H_4	90
3	**12c**	Ph	4-FC_6H_4	84
4	**12d**	Ph	4-$CH_3C_6H_4$	86
5	**12e**	4-ClC_6H_4	Ph	89
6	**12f**	4-ClC_6H_4	4-ClC_6H_4	86
7	**12g**	4-ClC_6H_4	4-FC_6H_4	88
8	**12h**	4-ClC_6H_4	4-$CH_3C_6H_4$	87
9	**12i**	4-ClC_6H_4	4-$CH_3OC_6H_4$	89
10	**12j**	4-ClC_6H_4	4-$CF_3C_6H_4$	90

[a] Isolated yields.



Scheme 4. Preparation of 3*H*-1,4-benzodiazepines **14** by a tandem-Staudinger/aza-Wittig reaction.

imino)phosphorane **10**. Notably, 1,4-benzodiazepine skeletons are one of the most important and central building blocks in medicinal and pharmaceutical chemistry. Many 1,4-benzodiazepines are found in a wide variety of biologically active substances, which show sedative, anxiolytic, anticonvulsant, hypnotic, raf protein kinase and cysteine

protease inhibitory activities.[15–17] The above tandem-Staudinger/aza-Wittig reaction provides an efficient synthesis of 3*H*-1,4-benzodiazepines under mild reaction conditions. Analogous 1,4-benzodiazepin-5-ones have also been prepared previously by application of the tandem-Staudinger/aza-Wittig reaction by other groups.[18]

Table 3. Preparation of 3*H*-1,4-benzodiazepines **14**.

Entry		Ar^1	Ar^2	Yield (%)[a]
1	**14a**	Ph	Ph	91
2	**14b**	Ph	4-ClC_6H_4	90
3	**14c**	Ph	4-FC_6H_4	84
4	**14d**	Ph	4-$CH_3C_6H_4$	86
5	**14e**	4-ClC_6H_4	Ph	89
6	**14f**	4-ClC_6H_4	4-ClC_6H_4	86
7	**14g**	4-ClC_6H_4	4-FC_6H_4	88
8	**14h**	4-ClC_6H_4	4-$CH_3C_6H_4$	87
9	**14i**	4-ClC_6H_4	4-$CH_3OC_6H_4$	82
10	**14j**	4-ClC_6H_4	4-$CF_3C_6H_4$	90

[a] Isolated yields.

The structures of the 1,2,4-triazino[2,3-*b*]indazoles **12** and 3*H*-1,4-benzodiazepines **14** were confirmed on the basis of spectroscopic data. Furthermore, single crystals of **12i** and **14j** were obtained from the CH_2Cl_2 solution of **12i** and **14j** and X-ray structure analysis verified the proposed structures (Figures 1 and 2).

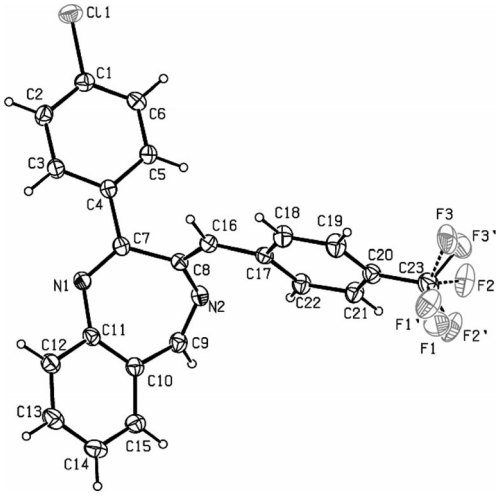


Figure 1. ORTEP diagram of the crystal structure of **14j** (30% thermal ellipsoids).

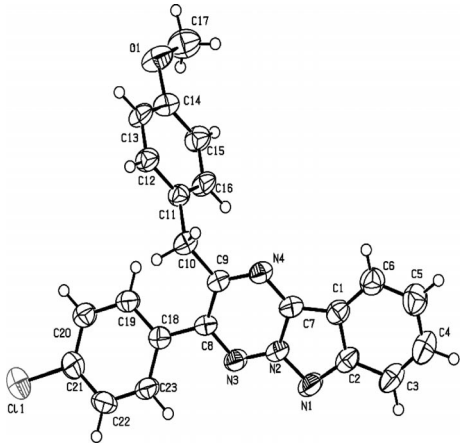


Figure 2. ORTEP diagram of the crystal structure of **12i** (30% thermal ellipsoids).

Conclusions

In conclusion, we report here a new temperature-dependent regioselective synthesis of 1,2,4-triazino[2,3-*b*]indazoles or 3*H*-1,4-benzodiazepines, by using a domino-Staudinger/aza-Wittig/isomerization reaction or tandem-Staudinger/aza-Wittig reaction. Due to the availability of the synthetic approach and the neutral ring closure conditions, this new synthetic approach has potential applications in the synthesis of various 1,2,4-triazino[2,3-*b*]indazoles and 3*H*-1,4-benzodiazepines, which are of considerable interest as biologically active compounds or pharmaceuticals.

Experimental Section

General: All reactions were performed in round-bottom flasks. Column chromatography purifications were performed under "flash" conditions using 400–630 mesh silica gel, except where otherwise noted. Analytical thin-layer chromatography (TLC) was carried out on silica gel 60 F_{254} plates, which were visualized by exposure to ultraviolet light.

Instrumentation: Melting points were determined with an X-4 model apparatus (Beijing Taike Company, Beijing, People's Republic of China). IR spectra were recorded with a PE-983 infrared spectrometer (Perkin–Elmer) as KBr pellets with absorption in cm^{-1}. MS were measured with a Finnigan Trace MS spectrometer (Thermo Fisher Scientific Company). ^1H NMR spectra were recorded in $CDCl_3$ with a Varian Mercury Plus 600 (600 MHz) spectrometer and chemical shifts (δ) are reported in ppm using $(CH_3)_4Si$ as an internal reference (δ = 0 ppm). Elemental analyses were obtained with a Vario EL III elementary analysis instrument.

General Procedure for Preparation of Azides 8: To a well-stirred solution of azide **6** (4 mmol) in absolute ethanol (15 mL) was added methyldiphenylphosphane (0.80 g, 4 mmol) in ethanol (5 mL) at room temp. After the mixture was stirred for 3 h, 2-azidobenzaldehyde (0.59 g, 4 mmol) was added and the mixture was stirred at 50 °C for 4–8 h. The solvent was partly removed under reduced pressure and the yellow precipitated solid was collected by filtration and recrystallized from CH_2Cl_2/ethanol to give azide **8**.

2-(Azidobenzylideneamino)-1,3-diphenylprop-2-en-1-one (8a): Yellow crystals (1.27 g, 90%), m.p. 84–85 °C. IR (KBr): $\tilde{\nu}$ = 3069, 2134, 1652, 1592, 1448, 1251, 1126 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.82 (s, 1 H, N=CH), 8.28–7.23 (m, 14 H, Ar-H), 6.71 (s, 1 H, =CH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 193.8, 158.9, 145.2, 140.9, 137.5, 134.6, 132.7, 132.3, 131.3, 131.2, 129.8, 129.7, 129.3, 128.7, 128.3, 128.2, 127.7, 127.6, 127.1, 124.8, 118.5 ppm. $C_{22}H_{16}N_4O$ (352.39): calcd. C 74.98, H 4.58, N 15.90; found C 75.19, H 4.88, N 16.12.

2-(Azidobenzylideneamino)-3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (8b): Yellow crystals (1.42 g, 92%), m.p. 148–149 °C. IR (KBr): $\tilde{\nu}$ = 3095, 2133, 1651, 1448, 1250, 1069 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.81 (s, 1 H, N=CH), 8.23–7.22 (m, 13 H, Ar-H), 6.64 (s, 1 H, =CH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 193.8, 159.2, 159.1, 145.5, 141.1, 137.4, 134.6, 133.2, 132.9, 132.5, 129.9, 129.8, 128.6, 128.4, 128.0, 127.8, 127.7, 127.1, 124.9,

118.6 ppm. $C_{22}H_{15}ClN_4O$ (386.84): calcd. C 68.31, H 3.91, N 14.48; found C 68.52, H 4.08, N 14.22.

2-(Azidobenzylideneamino)-3-(4-fluorophenyl)-1-phenylprop-2-en-1-one (8c): Yellow crystals (1.11 g, 75%), m.p. 112–114 °C. IR (KBr): $\tilde{\nu}$ = 3072, 2133, 1655, 1594, 1450, 1296, 1127, 1069 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.83 (s, 1 H, N=CH), 8.24–7.03 (m, 13 H, Ar-H), 6.67 (s, 1 H, =CH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 193.7, 163.5, 161.8, 159.0, 144.6, 140.8, 137.4, 133.2, 132.7, 132.3, 130.8, 129.7, 128.4, 128.2, 127.5, 126.9, 124.8, 118.5, 115.4, 115.2 ppm. $C_{22}H_{15}FN_4O$ (370.38): calcd. C 71.34, H 4.08, N 15.13; found C 71.19, H 4.28, N 15.22.

2-(Azidobenzylideneamino)-1-phenyl-3-(*p*-tolyl)prop-2-en-1-one (8d): Yellow crystals (1.29 g, 88%), m.p. 134–136 °C. IR (KBr): $\tilde{\nu}$ = 3124, 2132, 1653, 1575, 1449, 1123, 1069 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.82 (s, 1 H, N=CH), 8.28–7.16 (m, 13 H, Ar-H), 6.71 (s, 1 H, =CH), 2.35 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 193.8; 158.8, 144.5, 140.9, 139.1, 137.8, 132.6, 132.2, 131.8, 131.4, 130.1, 129.7, 129.1, 128.2, 127.7, 127.2, 124.9, 118.5, 21.4, 21.2 ppm. $C_{23}H_{18}N_4O$ (366.42): calcd. C 75.39, H 4.95, N 15.29; found C 75.49, H 4.88, N 15.42.

2-(Azidobenzylideneamino)-1-(4-chlorophenyl)-3-phenylprop-2-en-1-one (8e): Yellow crystals (1.33 g, 86%), m.p. 90–92 °C. IR (KBr): $\tilde{\nu}$ = 3128, 2126, 1649, 1583, 1278, 1070 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.78 (s, 1 H, N=CH), 8.26–7.22 (m, 13 H, Ar-H), 6.68 (s, 1 H, =CH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 192.6, 159.0, 145.1, 141.0, 138.7, 135.8, 134.4, 132.8, 131.3, 131.2, 129.3, 128.9, 128.6, 128.4, 127.7, 127.0, 124.9, 118.6 ppm. $C_{22}H_{15}ClN_4O$ (386.84): calcd. C 68.31, H 3.91, N 14.48; found C 68.59, H 3.99, N 14.22.

2-(Azidobenzylideneamino)-1,3-bis(4-chlorophenyl)prop-2-en-1-one (8f): Yellow crystals (1.41 g, 84%), m.p. 169–170 °C. IR (KBr): $\tilde{\nu}$ = 3126, 2126, 1648, 1583, 1483, 1281, 1084 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.77 (s, 1 H, N=CH), 8.22–7.22 (m, 12 H, Ar-H), 6.62 (s, 1 H, =CH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 192.6, 159.3, 145.4, 141.1, 139.0, 135.5, 134.8, 133.1, 132.5, 131.3, 128.7, 128.6, 127.9, 127.7, 126.9, 125.0, 118.7 ppm. $C_{22}H_{14}Cl_2N_4O$ (421.28): calcd. C 62.72, H 3.35, N 13.30; found C 62.59, H 3.49, N 13.12.

2-(Azidobenzylideneamino)-1-(4-chlorophenyl)-3-(4-fluorophenyl)-prop-2-en-1-one (8g): Yellow crystals (1.34 g, 83%), m.p. 142–144 °C. IR (KBr): $\tilde{\nu}$ = 3130, 2131, 1648, 1584, 1247, 1129, 1070 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.79 (s, 1 H, N=CH), 8.23–7.04 (m, 12 H, Ar-H), 6.66 (s, 1 H, =CH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 192.7,163.7, 162.0, 159.3, 144.6, 141.1, 138.8, 135.7, 133.3, 133.0, 131.2, 130.8, 128.7, 128.4, 127.6, 126.9, 125.0, 118.7, 115.6, 115.4 ppm. $C_{22}H_{14}ClFN_4O$ (404.83): calcd. C 65.27, H 3.49, N 13.84; found C 65.43, H 3.58, N 13.92.

2-(Azidobenzylideneamino)-1-(4-chlorophenyl)-3-(*p*-tolyl)prop-2-en-1-one (8h): Yellow crystals (1.44 g, 90%), m.p. 130–132 °C, IR (KBr): $\tilde{\nu}$ = 3128, 2124, 1646, 1602, 1505, 1247, 1069 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.79 (s, 1 H, N=CH), 8.26–7.16 (m, 12 H, Ar-H), 6.68 (s, 1 H, =CH), 2.35 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 192.6, 158.9, 144.4, 140.9, 139.3, 138.6, 136.0, 132.7, 131.7, 131.4, 131.2, 130.0, 129.2, 128.6, 127.7, 127.1, 124.9, 118.6, 21.4 ppm. $C_{23}H_{17}ClN_4O$ (400.87): calcd. C 68.91, H 4.27, N 13.98; found C 69.14, H 4.16, N 14.11.

2-(Azidobenzylideneamino)-1-(4-chlorophenyl)-3-(4-methoxyphenyl)-prop-2-en-1-one (8i): Yellow crystals (1.43 g, 86%), m.p. 112–113 °C. IR (KBr): $\tilde{\nu}$ = 3130, 2126, 1647, 1582, 1279, 1069 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.81 (s, 1 H, N=CH), 8.27–6.89 (m, 12 H, Ar-H), 6.70 (s, 1 H, =CH), 3.82 (s, 3 H, OCH_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 192.6, 160.3, 158.9, 143.3, 140.9, 138.4, 136.3, 133.3, 132.7, 131.1, 130.6, 128.5, 127.6, 127.3, 127.2, 124.9, 118.6, 114.0, 55.2 ppm. $C_{23}H_{17}ClN_4O_2$ (416.87): calcd. C 66.27, H 4.11, N 13.44; found C 66.39, H 4.28, N 13.66.

2-(Azidobenzylideneamino)-1-(4-chlorophenyl)-3-[4-(trifluoromethyl)phenyl]prop-2-en-1-one (8j): Yellow crystals (1.49 g, 82%), m.p. 174–176 °C. IR (KBr): $\tilde{\nu}$ = 3116, 2125, 1647, 1585, 1328, 1278, 1069 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.77 (s, 1 H, N=CH), 8.22–7.22 (m, 12 H, Ar-H), 6.64 (s, 1 H, =CH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 192.6, 159.5, 146.8, 141.3, 139.3, 137.9, 135.2, 133.3, 131.4, 131.2, 129.9, 128.8, 127.7, 126.7, 126.4, 125.2, 125.1, 125.0, 124.9, 118.8, 118.7 ppm. $C_{23}H_{14}ClF_3N_4O$ (454.84): calcd. C 60.74, H 3.10, N 12.32; found C 60.49, H 3.28, N 12.47.

General Procedure for Preparation of 1,2,4-Triazino[2,3-*b*]indazoles 12: A solution of triphenylphosphane (1.5 mmol, 0.39 g) in dry CH_2Cl_2 (10 mL) was added dropwise under nitrogen to a well-stirred solution of azides **8** (1.5 mmol) in CH_2Cl_2 (10 mL) at 0 °C. After the stirring was continued for 2 h, the mixture was slowly warmed to room temp. while the stirring was continued for 2 h. The solvent was evaporated under reduced pressure, and the residue was chromatographed on a silica gel column using petroleum ether and ether (10:1) as eluent to give 1,2,4-triazino[2,3-*b*]indazoles **12** as yellow solids.

2-Benzyl-3-phenyl-1,2,4-triazino[2,3-*b*]indazole (12a): Yellow crystals (0.46 g, 91%); m.p.168–169 °C. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.37–7.02 (m, 14 H, Ar-H), 4.40 (s, 2 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.9, 148.9, 147.4, 137.1, 135.8, 134.3, 130.0, 129.8, 129.4, 128.7, 126.5, 128.4, 128.3, 126.7, 122.5, 120.6, 117.3, 112.3, 41.3 ppm. MS: *m*/*z* (%) = 336 (100) [M^+], 204 (39), 102 (26), 91 (32), 77 (18). $C_{22}H_{16}N_4$ (336.40): calcd. C 78.55, H 4.79, N 16.66; found C 78.64, H 4.68, N 16.69.

2-(4-Chlorobenzyl)-3-phenyl-1,2,4-triazino[2,3-*b*]indazole (12b): Yellow crystals (0.49 g, 90%); m.p. 141–142 °C. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.34–6.94 (m, 13 H, Ar-H), 4.35 (s, 2 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.7, 148.9, 146.7, 135.7, 135.6, 134.2, 132.6, 130.1, 129.9, 129.3, 128.6, 125.5, 122.6, 120.6, 117.3, 112.3, 40.6 ppm. MS: *m*/*z* (%) = 370 (100) [M^+], 204 (36), 125 (45), 102 (32), 88 (17). $C_{22}H_{15}ClN_4$ (370.84): calcd. C 71.25, H 4.08, N 15.11; found C 71.54, H 3.94, N 15.23.

2-(4-Fluorobenzyl)-3-phenyl-1,2,4-triazino[2,3-*b*]indazole (12c): Yellow crystals (0.45 g, 84%); m.p. 141–142 °C. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.36–6.87 (m, 13 H, Ar-H), 4.36 (s, 2 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.4, 160.8, 150.7, 148.9, 147.1, 135.7, 134.2, 132.7, 130.3, 130.0, 129.8, 129.3, 128.6, 122.5, 120.5, 117.2, 115.3, 115.2, 112.3, 40.5 ppm. MS: *m*/*z* (%) = 354 (100) [M^+], 222 (40), 109 (52), 102 (21), 88 (9). $C_{22}H_{15}FN_4$ (354.39): calcd. C 74.56, H 4.27, N 15.81; found C 74.42, H 4.38, N 15.53.

2-(4-Methylbenzyl)-3-phenyl-1,2,4-triazino[2,3-*b*]indazole (12d): Yellow crystals (0.45 g, 86%); m.p. 175–177 °C. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.37–6.91 (m, 13 H, Ar-H), 4.35 (s, 2 H, CH_2), 2.28 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.9, 148.9, 147.7, 136.3, 135.9, 134.4, 134.1, 130.0, 129.7, 129.4, 129.2, 128.6, 128.5, 122.4, 120.7, 120.6, 119.5, 117.3, 117.2, 112.3, 40.8, 20.9 ppm. MS: *m*/*z* (%) = 350 (100) [M^+], 218 (11), 204 (17), 105 (18), 102 (9). $C_{23}H_{18}N_4$ (350.42): calcd. C 78.83, H 5.18, N 15.99; found C 78.91, H 5.08, N 15.63.

2-Benzyl-3-(4-chlorophenyl)-1,2,4-triazino[2,3-*b*]indazole (12e): Yellow crystals (0.49 g, 89%); m.p. 145–147 °C. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.37–7.03 (m, 13 H, Ar-H), 4.38 (s, 2 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.8, 149.0, 146.9, 137.0, 136.2, 135.8, 132.7, 130.7, 130.2, 128.7, 128.6, 126.8, 122.7, 120.6, 117.3,

112.3, 41.3 ppm. MS: *m*/*z* (%) = 370 (100) [M$^+$], 204 (58), 102 (60), 91 (89), 77 (30). $C_{22}H_{15}ClN_4$ (370.84): calcd. C 71.25, H 4.08, N 15.11; found C 71.32, H 4.03, N 15.39.

2-(4-Chlorobenzyl)-3-(4-chlorophenyl)-1,2,4-triazino[2,3-*b*]indazole (12f): Yellow crystals (0.52 g, 86%); m.p. 142–144 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.35–6.97 (m, 12 H, Ar-H), 4.34 (s, 2 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.5, 149.0, 146.2, 136.3, 135.8, 135.4, 132.7, 132.6, 130.6, 130.2, 130.0, 128.9, 128.7, 122.8, 120.6, 117.3, 112.2, 40.6 ppm. MS: *m*/*z* (%) = 404 (100) [M$^+$], 238 (19), 204 (32), 125 (64), 102 (57), 88 (19). $C_{22}H_{14}Cl_2N_4$ (405.29): calcd. C 65.20, H 3.48, N 13.82; found C 65.37, H 3.53, N 13.99.

3-(4-Chlorophenyl)-2-(4-fluorobenzyl)-1,2,4-triazino[2,3-*b*]indazole (12g): Yellow crystals (0.51 g, 88%); m.p. 177–178 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.36–6.90 (m, 12 H, Ar-H), 4.35 (s, 2 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.5, 160.8, 149.6, 149.0, 146.6, 136.2, 135.8, 132.6, 132.5, 130.6, 130.2, 128.9, 122.7, 120.6, 117.2, 115.5, 115.3, 112.2, 40.4 ppm. MS: *m*/*z* (%) = 388 (100) [M$^+$], 222 (30), 109 (43), 102 (11). $C_{22}H_{14}ClFN_4$ (388.83): calcd. C 67.96, H 3.63, N 14.41; found C 68.07, H 3.69, N 14.38.

3-(4-Chlorophenyl)-2-(4-methylbenzyl)-1,2,4-triazino[2,3-*b*]indazole (12h): Yellow crystals (0.50 g, 87%); m.p. 170–171 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.37–6.92 (m, 12 H, Ar-H), 4.33 (s, 2 H, CH_2), 2.29 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.7, 148.9, 147.1, 136.4, 136.1, 135.8, 133.9, 132.8, 130.7, 130.1, 129.3, 128.8, 128.5, 122.6, 120.6, 117.2, 112.2, 40.8, 20.9 ppm. MS: *m*/*z* (%) = 384 (100) [M$^+$], 218 (20), 105 (34), 102 (23). $C_{23}H_{17}ClN_4$ (384.87): calcd. C 71.78, H 4.45, N 14.56; found C 71.59, H 4.39, N 14.53.

3-(4-Chlorophenyl)-2-(4-methoxybenzyl)-1,2,4-triazino[2,3-*b*]-indazole (12i): Yellow crystals (0.53 g, 89%); m.p. 150–152 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.37–6.75 (m, 12 H, Ar-H), 4.31 (s, 2 H, CH_2), 3.76 (s, 3 H, OCH_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 158.4, 149.8, 149.0, 147.3, 136.1, 135.8, 132.8, 130.7, 130.1, 129.7, 128.9, 128.8, 122.6, 120.6, 117.2, 114.0, 112.3, 55.2, 40.4 ppm. MS: *m*/*z* (%) = 400 (100) [M$^+$], 121 (41), 102 (17), 96 (4). $C_{23}H_{17}ClN_4O$ (400.87): calcd. C 68.91, H 4.27, N 13.98; found C 68.74, H 4.12, N 14.24.

3-(4-Chlorophenyl)-2-[4-(trifluoromethyl)benzyl]-1,2,4-triazino-[2,3-*b*]indazole (12j): Yellow crystals (0.59 g, 90%); m.p. 176–177 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.33–7.18 (m, 12 H, Ar-H), 4.43 (s, 2 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.4. 148.9, 145.6, 141.0, 136.3, 135.7, 132.4, 130.6, 130.2, 129.1, 128.9, 128.7, 125.4, 124.8, 123.0, 122.7, 120.5, 117.1, 112.1, 40.9 ppm. MS: *m*/*z* (%) = 438 (100) [M$^+$], 272 (27), 159 (56), 102 (67), 88 (53), 75 (22). $C_{23}H_{14}ClF_3N_4$ (438.84): calcd. C 62.95, H 3.22, N 12.77; found C 63.02, H 3.34, N 12.59.

General Procedure for Preparation of 3*H*-1,4-Benzodiazepines 14: To a well-stirred solution of triphenylphosphane (0.39 g, 1.5 mmol) in dry toluene (10 mL) at 80 °C, was added dropwise a solution of azides **8** (1.5 mmol) in toluene (5 mL). After the stirring was continued for 8 h at 80 °C, the solvent was evaporated under reduced pressure. The obtained residue was chromatographed on a silica gel column using petroleum ether and ether (7:1) as eluent to give 3*H*-1,4-benzodiazepines **14** as yellow solids.

3-Benzylidene-2-phenyl-3*H*-1,4-benzodiazepine (14a): Yellow crystals (0.42 g, 91%), m.p. 170–172 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.55 (s, 1 H, N = CH), 8.24–7.20 (m, 14 H, Ar-H), 5.80 (s, 1 H, =CH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.0, 160.7, 160.6, 148.8, 140.2, 137.3, 135.3, 131.3, 131.2, 130.0, 129.9, 129.5, 128.8, 128.5, 128.2, 127.4, 127.2, 125.0, 118.0 ppm. MS: *m*/*z* (%) = 308 (100) [M$^+$], 231 (45), 192 (25), 165 (84), 89 (11). $C_{22}H_{16}N_2$ (308.38): calcd. C 85.69, H 5.23, N 9.08; found C 85.75, H 5.28, N 9.26.

3-(4-Chlorobenzylidene)-2-phenyl-3*H*-1,4-benzodiazepine (14b): Yellow crystals (0.46 g, 90%), m.p. 199–201 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.54 (s, 1 H, N=CH), 8.21–7.26 (m, 13 H, Ar-H), 5.75 (s, 1 H, =CH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.3, 160.5, 148.8, 139.6, 137.4, 137.1, 132.5, 131.2, 131.1, 129.9, 129.5, 129.0, 128.9, 128.7, 128.4, 127.5, 125.0, 124.9, 118.2, 118.1 ppm. MS: *m*/*z* (%) = 342 (75) [M$^+$], 231 (45), 192 (17), 165 (100), 89 (11). $C_{22}H_{15}ClN_2$ (342.83): calcd. C 77.08, H 4.41, N 8.17; found C 77.31, H 4.29, N 8.23.

3-(4-Fluorobenzylidene)-2-phenyl-3*H*-1,4-benzodiazepine (14c): Yellow crystals (0.41 g, 84%), m.p. 166–167 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.54 (s, 1 H, N=CH), 8.22–6.98 (m, 13 H, Ar-H), 5.77 (s, 1 H, =CH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.7, 161.9, 161.1, 160.9, 148.7, 139.8, 137.3, 131.4, 131.3, 131.2, 130.0, 129.8, 128.8, 128.5, 127.4, 125.1, 125.0, 117.0, 116.9, 115.2, 115.1 ppm. MS: *m*/*z* (%) = 326 (100) [M$^+$], 231 (42), 192 (29), 165 (95), 89 (13). $C_{22}H_{15}FN_2$ (326.37): calcd. C 80.96, H 4.63, N 8.58; found C 80.77, H 4.88, N 8.74.

3-(4-Methylbenzylidene)-2-phenyl-3*H*-1,4-benzodiazepine (14d): Yellow crystals (0.42 g, 86%), m.p. 136–138 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.54 (s, 1 H, N=CH), 8.23–7.11 (m, 13 H, Ar-H), 5.78 (s, 1 H, =CH), 2.32 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 162.2, 160.6, 160.5, 148.8, 139.6, 137.4, 137.0, 132.4, 131.2, 131.1, 129.9, 129.5, 128.9, 128.7, 128.4, 127.5, 124.9, 118.1, 21.2 ppm. MS: *m*/*z* (%) = 322 (100) [M$^+$], 231 (44), 192 (22), 165 (76), 130 (28), 89 (12). $C_{23}H_{18}N_2$ (322.41): calcd. C 85.68, H 5.63, N 8.69; found C 85.83, H 5.74, N 8.79.

3-Benzylidene-2-(4-chlorophenyl)-3*H*-1,4-benzodiazepine (14e): Yellow crystals (0.46 g, 89%), m.p. 146–148 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.55 (s, 1 H, N=CH), 8.18–7.21 (m, 13 H, Ar-H), 5.78 (s, 1 H, =CH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 160.8, 160.7, 148.6, 139.8, 137.4, 135.8, 135.1, 131.4, 131.2, 130.1, 129.6, 128.8, 128.7, 128.3, 127.5, 127.4, 125.3, 118.3, 118.2 ppm. MS: *m*/*z* (%) = 342 (100) [M$^+$], 265 (43), 199 (94), 152 (44), 89 (54). $C_{22}H_{15}ClN_2$ (342.83): calcd. C 77.08, H 4.41, N 8.17; found C 76.81, H 4.68, N 8.25.

3-(4-Chlorobenzylidene)-2-(4-chlorophenyl)-3*H*-1,4-benzodiazepine (14f): Yellow crystals (0.49 g, 86%), m.p. 180–181 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.54 (s, 1 H, N=CH), 8.15–7.26 (m, 12 H, Ar-H), 5.73 (s, 1 H, =CH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 160.9, 160.4, 148.5, 140.2, 137.5, 135.6, 133.6, 133.5, 133.1, 131.6, 131.1, 130.7, 130.1, 128.9, 128.8, 128.4, 127.3, 125.4, 117.0 ppm. MS: *m*/*z* (%) = 376 (100) [M$^+$], 265 (65), 199 (100), 152 (21), 89 (26). $C_{22}H_{14}Cl_2N_2$ (377.27): calcd. C 70.04, H 3.74, N 7.43; found C 69.89, H 3.88, N 7.64.

2-(4-Chlorophenyl)-3-(4-fluorobenzylidene)-3*H*-1,4-benzodiazepine (14g): Yellow crystals (0.48 g, 88%), m.p. 150–152 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.54 (s, 1 H, N=CH), 8.16–6.99 (m, 12 H, Ar-H), 5.75 (s, 1 H, =CH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.8, 161.2, 161.1, 161.0, 160.6, 148.5, 139.4, 137.5, 135.8, 131.5, 131.3, 131.2, 131.1, 130.1, 128.9, 128.7, 127.4, 125.3, 117.3, 115.3, 115.2 ppm. MS: *m*/*z* (%) = 360 (100) [M$^+$], 265 (44), 199 (78), 134 (13), 102 (6). $C_{22}H_{14}ClFN_2$ (360.82): calcd. C 73.23, H 3.91, N 7.76; found C 73.36, H 4.07, N 7.92.

2-(4-Chlorophenyl)-3-(4-methylbenzylidene)-3*H*-1,4-benzodiazepine (14h): Yellow crystals (0.46 g, 87%), m.p. 189–191 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.53 (s, 1 H, N=CH), 8.16–7.11 (m, 12 H, Ar-H), 5.76 (s, 1 H, =CH), 2.32 (s, 3 H, CH3) ppm. ^{13}C NMR

(150 MHz, $CDCl_3$): δ = 161.0, 160.7, 160.6, 148.6, 139.1, 137.3, 135.9, 132.3, 131.3, 131.1, 130.0, 129.5, 129.0, 128.8, 128.6, 127.5, 125.2, 118.4, 21.2 ppm. MS: *m/z* (%) = 356 (100) [M^+], 264 (43), 199 (54), 164 (17), 130 (62), 89 (18). $C_{23}H_{17}ClN_2$ (356.85): calcd. C 77.41, H 4.80, N 7.85; found C 77.69, H 4.98, N 7.93.

2-(4-Chlorophenyl)-3-(4-methoxybenzylidene)-3*H*-1,4-benzodiazepine (14i): Yellow crystals (0.46 g, 82%), m.p. 169–171 °C. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.52 (s, 1 H, N=CH), 6.85–8.16 (m, 12 H, Ar-H), 5.76 (s, 1 H, =CH), 3.79 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 161.3, 160.8, 159.0, 148.7, 138.3, 137.3, 136.1, 131.3, 131.1, 131.0, 130.0, 128.8, 128.6, 127.9, 127.6, 125.2, 118.4, 113.7, 55.2 ppm. MS: *m/z* (%) = 372 (69) [M^+], 265 (16), 146 (100), 91 (4). $C_{23}H_{17}ClN_2O$ (372.85): calcd. C 74.09, H 4.60, N 7.51; found C 74.31, H 4.77, N 7.46.

2-(4-Chlorophenyl)-3-[4-(trifluoromethyl)benzylidene]-3*H*-1,4-benzodiazepine (14j): Yellow crystals (0.55 g, 90%), m.p. 176–178 °C. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.56 (s, 1 H, N=CH), 8.17–7.26 (m, 12 H, Ar-H), 5.78 (s, 1 H, =CH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 161.0, 159.8, 148.4, 141.5, 138.6, 137.7, 135.4, 131.7, 131.1, 130.1, 129.6, 129.0, 128.8, 127.2, 125.5, 125.1, 116.4 ppm. MS: *m/z* (%) = 410 (58) [M^+], 265 (50), 199 (100), 164 (22), 89 (30). $C_{23}H_{14}ClF_3N_2$ (410.82): calcd. C 67.24, H 3.43, N 6.82; found C 67.53, H 3.56, N 6.98.

Crystallographic data for the structures of **12i** and **14j** reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-823549 (for **12i**) and CCDC-823179 (for **14j**). These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): Copies of ^1H and ^{13}C NMR spectra of **8a**–**j**, **12a**–**j**, and **14a**–**j**.

Acknowledgments

We gratefully acknowledge financial support of this work by the National Natural Science Foundation of China (NSFC) (grant number 21032001), the Program for Changjiang Scholars and Innovative Research Team in University (grant number IRT0953), and research funds from CCNU for basic research and operations of MOE (grant number 10020176).

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Received: May 20, 2011
Published Online: October 10, 2011

