Res Chem Intermed (2011) 37:859–868
DOI 10.1007/s11164-011-0293-z

# Cycloalkyl substituted *N*-nitrourea derivatives: a convenient synthesis and biological evaluation

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Received: 28 December 2010 / Accepted: 20 January 2011 / Published online: 15 February 2011


**Abstract** A series of *N*-nitrourea derivatives bearing various cycloalkyl were conveniently obtained via three steps including nitration, carbamic chlorination, and aminolysis reactions. The structures of all newly synthesized compounds were elucidated and confirmed by IR, $^{1}$H NMR, $^{13}$C NMR, and elemental analysis. The preliminary bioassay indicated that the target compounds exhibited moderate herbicidal activity against *Amaranthus albus* and *Sorghum sudanense*. However, some of the title compounds presented high plant growth regulating activity against rice.

**Keywords** *N*-nitrourea · Synthesis · Herbicidal activity · Plant growth regulating activity

## Introduction

Urea derivatives are well-known scaffolds for a significantly broad range of biological activities such as herbicidal activities [1, 2], antimicrobial, bactericidal, anti-HIV [3–6], and so on, which have occupied a pivotal position in medicine and pesticide chemistry due to their structural and bioactivity diversity. Up to now, many structural optimization studies on both sides of carbamide bridge's amines have been investigated. On the other hand, *N*-nitro substituted anilines have also been demonstrated to exhibit diversely biological activities, including herbicidal properties [7], antifungal effects [8], and plant growth regulating activities [9].

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In view of these observations, we attempt to synthesize *N*-nitro substituted anilines incorporating NH–CO–NH bridge units and search novel potential agrochemical agents with broad bioactivities.

Earlier work [10, 11] in our laboratory involved some aromatic ring and heterocyclic derivatives with moderate herbicidal and plant growth regulating activities. As a continuation of our ongoing project aim, we designed and synthesized a series of new *N*-nitro urea derivatives with various cycloalkyl substituents (Scheme 1). Preliminary bioassay showed that some of the target compounds had good herbicidal and plant growth regulating activities.

## Results and discussion

### Synthesis for cycloalkyl substituted *N*-nitrourea derivatives **4a–t**

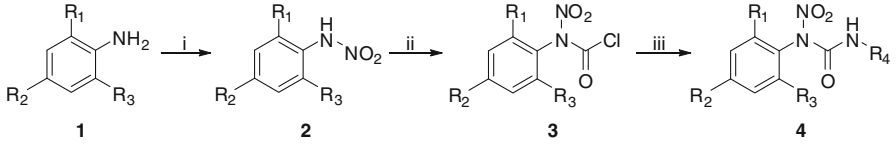
The target compounds *N*-nitro-*N*-2,4,6-trisubstituted phenyl-*N*′-cycloalkyl urea derivatives **4a–t** were conveniently synthesized according to Scheme 1.

Traditionally, trisubstituted phenylnitramines are prepared by reaction with nitric acid in the presence of acetic anhydride [9]. However, the aforementioned method always involves a large amount of organic solvent as well as having low yields. In order to overcome some of these problems, our team developed a convenient and efficient method for preparation of *N*-nitro-2,4,6-trichloroaniline in 90% yield [12]. As a continuation of our studies and to extend the range of substrates, we conveniently constructed a series of trisubstituted phenylnitramine **2** with 47–81% yields (Table 1).

Then the key intermediates **2a–h** were treated with the BTC (triphosgene) in the presence of toluene solution to obtain various *N*-nitro-2,4,6-trisubstituted phenyl carbamic chloride **3**. Further purification of intermediates **3** could not be achieved because of their air and water sensitivity. Hence, they were directly reacted with various cycloalkyl amines in toluene in the presence of DMAP to afford target compounds in 50–86% yields.

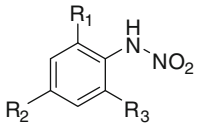
### Biological activity evaluation

The herbicidal activities of the title compound **4a–t** against *Amaranthus albus* and *Sorghum sudanense* have been investigated at the dosages of 50 mg/l compared to




**Scheme 1** General synthetic route for cycloalkyl substituted *N*-nitrourea derivatives **4**. Reagents and conditions: (*i*) $CH_3COONO_2$, $CH_3COOH$, $Ac_2O$, 16–20 °C, 1–1.5 h, (*ii*) BTC, triethylamine, toluene, 0–5 °C, 1 h; then 50 °C, 2–3 h. (*iii*) Cycloalkyl amines, DMAP, triethylamine, toluene, 0–5 °C; then 60 °C, 2–3 h

**Table 1** Preparation of 2,4,6-trisubstituted phenylnitramine **2a–h**

| | Compound | $R_{1,2,3}$ | Yield (%) | Compound | $R_{1,2,3}$ | Yield (%) |
|---|---|---|---|---|---|---|
|  **2** | **2a** | 2,4,6-tri-Cl | 71 | **2e** | 2,6-di-Br; 4-Cl | 70 |
| | **2b** | 2,4,6-tri-Br | 67 | **2f** | 2,4-di-Br; 6-Cl | 61 |
| | **2c** | 2,6-di-Br; 4-CH3 | 81 | **2g** | 2,6-di-Br; 4-F | 59 |
| | **2d** | 2,4-di-Br; 6-CH3 | 77 | **2h** | 2,4-di-Br; 6-CF3 | 47 |

distilled water and the commercially available herbicide Diuron according to the method described in the experimental section. The preliminary results of bioassay (Table 2) showed that the target compounds possessed higher herbicidal activity against root than that of hypocotyl. Especially, compounds **4a** and **4r** exhibited considerable herbicidal activity to Diuron. These data show that the presence of the electron-withdrawing group at the phenyl ring, such as fluorine, trifluoromethyl may decrease their herbicidal activity.

The plant growth regulatory activity of title compounds against rice was also evaluated at the concentration of 10 mg/l, and the results are shown in Table 2. From Table 2, we can find that the compounds **4d**, **4e**, **4f**, **4i**, **4n**, **4r** exhibited higher plant growth regulating activity than the other. This suggests that cyclopropane may cause an increase of their plant growth regulatory activity.

## Conclusions

In summary, we have conveniently constructed a novel series of cycloalkyl substituted *N*-nitrourea derivatives **4a–t**. The results of the preliminary bioassay indicated that some of the title compounds possessed moderate herbicidal and plant growth regulatory activities. Especially, compound **4r** displayed high herbicidal activity and excellent plant growth regulating activity, which may be used as a potential lead compound for further optimization.

## Experimental

### Instrumentation and chemicals

All reagents were commercially available and all solvents and liquid reagents were dried by standard methods and distilled before use. Melting points were determined with a digital melting point apparatus and are uncorrected. IR spectra were recorded on a Thermo Nicolet FT-IR Avatar 330 instrument. $^{1}$H NMR and $^{13}$C NMR spectra were measured on a Bruker AM spectrometer with tetramethylsilane (TMS) as internal standard and $CDCl_3$ or DMSO-$d_6$ as solvent. Elemental analysis was

**Table 2** Herbicidal and plant growth regulating activities of targeted compounds **4a–t**

| Compound | $R_{1,2,3}$ | $R_4$ | Relative inhibition at 50 mg/l (root %/hypocotyl %) | | Active grade[a] of formation-promoting against rice hypocotyl |
|---|---|---|---|---|---|
| | | | *A. albus* | *S. sudanense* | |
| **4a** | 2,4,6-tri-Cl | Cyclopropane | 85.2/57.3 | 57.9/39.0 | C |
| **4b** | 2,6-di-Br; 4-$CH_3$ | Cyclopropane | 76.9/72.1 | 47.9/55.7 | B |
| **4c** | 2,4-di-Br; 6-$CH_3$ | Cyclopropane | 34.4/57.3 | 45.3/25.1 | B |
| **4d** | 2,6-di-Br; 4-Cl | Cyclopropane | 54.4/42.4 | 73.1/57.5 | A |
| **4e** | 2,4-di-Br; 6-Cl | Cyclopropane | 69.7/51.1 | 55.6/40.3 | A |
| **4f** | 2,4-di-Br; 6-$CF_3$ | Cyclopropane | 46.9/53.8 | 52.0/54.0 | A |
| **4g** | 2,6-di-Br; 4-$CH_3$ | Cyclopentane | 61.6/52.9 | 50.2/41.0 | B |
| **4h** | 2,6-di-Br; 4-Cl | Cyclopentane | 51.6/51.2 | 43.3/29.8 | C |
| **4i** | 2,6-di-Br; 4-F | Cyclopentane | 44.4/46.8 | 54.2/37.2 | A |
| **4j** | 2,4,6-tri-Cl | Cyclohexane | 63.4/53.8 | 17.6.19.2 | D |
| **4k** | 2,4-di-Br; 6-$CH_3$ | Cyclohexane | 59.4/64.0 | 70.2/46.9 | D |
| **4l** | 2,4-di-Br; 6-Cl | Cyclohexane | 59.4/48.5 | 42.6/40.7 | D |
| **4m** | 2,6-di-Br; 4-F | Cyclohexane | 13.4/24.0 | 69.6/43.3 | D |
| **4n** | 2,4-di-Br; 6-$CF_3$ | Cyclohexane | 50.0/45.9 | 54.8/46.8 | A |
| **4o** | 2,4,6-tri-Br | Cycloheptane | 61.6/57.2 | 63.1/47.8 | C |
| **4p** | 2,4-di-Br; 6-$CH_3$ | Cycloheptane | 58.8/56.4 | 47.4/54.4 | C |
| **4q** | 2,6-di-Br; 4-Cl | Cycloheptane | 50.0/50.2 | 40.9/41.1 | C |
| **4r** | 2,4-di-Br; 6-Cl | Cycloheptane | 79.7/74.1 | 51.1/57.4 | A |
| **4s** | 2,6-di-Br; 4-F | Cycloheptane | 49.1/52.9 | 55.1/71.2 | C |
| **4t** | 2,4-di-Br; 6-$CF_3$ | Cycloheptane | 48.4/48.5 | 44.4/46.1 | C |
| Diuron | – | – | 88.4/63.1 | 87.0/57.6 | – |

[a] Active grade: A > 70%, B > 50%, C > 30%, D < 30% at the concentration of 10 mg/l

performed on a Vario EL III Elemental analysis instrument. The progress of the reactions was monitored by TLC on silica gel plates visualized with UV light.

General synthetic procedures for 2,4,6-trisubstituted phenylnitramine **2a–h**

Fuming nitric acid (1.01 ml, 24 mmol) was slowly added dropwise to the stirred acetic anhydride (2.27 ml, 24 mmol) at 10–12 °C. After the addition, the temperature of the reaction mixture was maintained between 10 and 12 °C for 40 min. Then a crude product of acetyl nitrate was obtained and was used directly for the next step. The obtained acetyl nitrate was added dropwise to a solution of 2,4,6-trisubstituted aniline **1** (20 mmol) in dry acetic acid (20 ml) and acetic anhydride (2 ml) at 16–20 °C. The reaction mixture was stirred for a further 45–90 min. The resulting purple solution was then poured into 60 ml of ice water, and the resulting precipitate was filtered, washed with water (1 l), and dissolved in aqueous 10% sodium carbonate. The solution was heated to boil for 10 min with a small amount of activated carbon so as to decolorize the products and was then

filtered off immediately. Filtrate was cooled to room temperature and acidified with ice-cold 2N hydrochloric acid to precipitate the phenylnitramine product **2**. The nitramine was filtered, washed with cold water, dried in vacuo, and recrystallized from hexane or cyclohexane. The physico-chemical spectral data and melting point of compounds **2a–h** were in agreement with the data reported in the literature [8, 9, 13, 14].

General procedure for the preparation of *N*-nitro-*N*-2,4,6-trisubstituted phenyl-*N*′-cycloalkyl urea **4a–t**

A solution of 2,4,6-trisubstituted phenylnitramine **2** (10 mmol) in 50 ml of anhydrous toluene with 2 ml triethylamine was added dropwise to a cold solution (0–5 °C) of BTC (3.6 mmol) in dry toluene (20 ml). After the addition, the temperature of the reaction mixture was maintained between 0 and 5 °C for 1 h and then heated to 50 °C for a further 2–3 h. The intermediate **3** was formed and used without further isolation. After quenching the unreacted phosgene with dry nitrogen, the mixture was cooled to 0–5 °C and treated dropwise with a solution of cycloalkyl amines (10 mmol) in anhydrous toluene (10 ml) with 2 ml of triethylamine in the presence of DMAP (0.5 mmol). The reaction was carried out at 60 °C for 2 h with vigorous stirring and then the mixture was cooled to 0 °C for 2–3 h. The respective urea **4a–t** were precipitated, filtered, and washed with excess water and acetone. Crude products were further purified by recrystallization (DMF/acetone).

*N-Nitro-N-(2,4,6-trichlorophenyl)-N′-cyclopropane urea (**4a**)*

White needle crystal, yield 66%, m.p. 245–246 °C. IR (KBr, $cm^{-1}$): *v* 3320 (NH), 3083 (ArH), 1649 (CO); $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 0.43 (s, 2H, $CH_2$, cyclopropane), 0.62 (d, 2H, $J = 5.4$ Hz, $CH_2$, cyclopropane), 3.86 (m, 1H, CH, cyclopropane), 6.67 (s, 1H, NH), 7.68 (s, 2H, ArH). $^{13}$C NMR (150 MHz, DMSO-$d_6$), $\delta_C$ 6.5, 22.6, 128.5, 131.1, 133.5, 134.8, 155.6. Anal. Calcd for $C_{10}H_8Cl_3N_3O_3$: C, 37.01; H, 2.48; N, 12.95. Found: C, 37.11; H, 2.53; N, 12.86.

*N-Nitro-N-(2,6-dibromo-4-methylphenyl)-N′-cyclopropane urea (**4b**)*

White needle crystal, yield 54%, m.p. 308–309 °C. IR (KBr, $cm^{-1}$): *v* 3300 (NH), 1638 (CO); $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 0.44 (s, 2H, $CH_2$, cyclopropane), 0.62 (d, 2H, $J = 5.4$ Hz, $CH_2$, cyclopropane), 2.28 (s, 3H, $CH_3$), 3.88 (q, 1H, $J = 20.4$ Hz, CH, cyclopropane), 6.51 (s, 1H, NH), 7.50 (s, 2H, ArH). Anal. Calcd for $C_{11}H_{11}Br_2N_3O_3$: C, 33.62; H, 2.82; N, 10.69. Found: C, 33.70; H, 2.91; N, 10.53.

*N-Nitro-N-(2,4-dibromo-6-methylphenyl)-N′-cyclopropane urea (**4c**)*

White needle crystal, yield 66%, m.p. 316–317 °C. IR (KBr, $cm^{-1}$): *v* 3300 (NH), 1638 (CO); $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 0.43 (s, 2H, $CH_2$, cyclopropane), 0.63 (q, 2H, $J = 18.0$ Hz, $CH_2$, cyclopropane), 2.20 (s, 3H, $CH_3$), 3.88 (m, 1H, CH,

cyclopropane), 6.58 (s, 1H, NH), 7.48 (d, 1H, $J = 1.2$ Hz, ArH), 7.69 (d, 1H, $J = 1.8$ Hz, ArH). Anal. Calcd for $C_{11}H_{11}Br_2N_3O_3$: C, 33.62; H, 2.82; N, 10.69. Found: C, 33.68; H, 2.89; N, 10.57.

*N-Nitro-N-(2,6-dibromo-4-chlorophenyl)-N′-cyclopropane urea (**4d**)*

White needle crystal, yield 80%, m.p. >330 °C. IR (KBr, $cm^{-1}$): *v* 3307 (NH), 1644 (CO); $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 0.44 (s, 2H, $CH_2$, cyclopropane), 0.63 (d, 2H, $J = 4.8$ Hz, $CH_2$, cyclopropane), 3.88 (q, 1H, $J = 20.4$ Hz, CH, cyclopropane), 6.63 (s, 1H, NH), 7.84 (s, 2H, ArH). Anal. Calcd for $C_{10}H_8Br_2ClN_3O_3$: C, 29.05; H, 1.95; N, 10.16. Found: C, 29.13; H, 2.01; N, 10.01.

*N-Nitro-N-(2,4-dibromo-6-chlorophenyl)-N′-cyclopropane urea (**4e**)*

White needle crystal, yield 78%, m.p. 313–314 °C. IR (KBr, $cm^{-1}$): *v* 3307 (NH), 1646 (CO); $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 0.43 (s, 2H, $CH_2$, cyclopropane), 0.62 (d, 2H, $J = 5.4$ Hz, $CH_2$, cyclopropane), 3.88 (m, 1H, CH, cyclopropane), 6.68 (s, 1H, NH), 7.78 (s, 1H, ArH), 7.90 (s, 1H, ArH). Anal. Calcd for $C_{10}H_8Br_2ClN_3O_3$: C, 29.05; H, 1.95; N, 10.16. Found: C, 29.17; H, 2.06; N, 10.02.

*N-Nitro-N-[2,4-dibromo-6-(trifluoromethyl)phenyl]-N′-cyclopropane urea (**4f**)*

White needle crystal, yield 52%, m.p. 296–297 °C. IR (KBr, $cm^{-1}$): *v* 3317 (NH), 1637 (CO); $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 0.46 (q, 2H, $CH_2$, $J = 20.8$ Hz, cyclopropane), 0.62 (q, 2H, $J = 22.6$ Hz, $CH_2$, cyclopropane), 3.88 (q, 1H, $J = 14.4$ Hz, CH, cyclopropane), 6.36 (s, 1H, NH), 7.91 (d, 1H, $J = 1.8$ Hz, ArH), 8.27 (d, 1H, $J = 2.4$ Hz, ArH). Anal. Calcd for $C_{11}H_8Br_2F_3N_3O_3$: C, 29.56; H, 1.80; N, 9.40. Found: C, 29.65; H, 1.87; N, 9.31.

*N-Nitro-N-(2,6-dibromo-4-methylphenyl)-N′-cyclopentane urea (**4g**)*

White needle crystal, yield 70%, m.p. 298–299 °C. IR (KBr, $cm^{-1}$): *v* 3301 (NH), 2922, 2851 (CH), 1637 (CO); $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 1.36 (m, 2H, $CH_2$, cyclopentane), 1.47 (m, 2H, $CH_2$, cyclopentane), 1.59 (m, 2H, $CH_2$, cyclopentane), 1.79 (m, 2H, $CH_2$, cyclopentane), 2.28 (s, 3H, $CH_3$), 3.87 (q, 1H, $J = 20.4$ Hz, CH, cyclopropane), 6.23 (d, 1H, $J = 7.2$ Hz, NH), 7.45 (s, 2H, ArH). Anal. Calcd for $C_{13}H_{15}Br_2N_3O_3$: C, 37.08; H, 3.59; N, 9.98. Found: C, 37.12; H, 3.66; N, 9.90.

*N-Nitro-N-(2,6-dibromo-4-chlorophenyl)-N′-cyclopentane urea (**4h**)*

White needle crystal, yield 86%, m.p. 297–298 °C. IR (KBr, $cm^{-1}$): *v* 3301 (NH), 2922, 2850 (CH), 1637 (CO); $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 1.37 (m, 2H, $CH_2$, cyclopentane), 1.50 (m, 2H, $CH_2$, cyclopentane), 1.62(m, 2H, $CH_2$, cyclopentane), 1.79 (m, 2H, $CH_2$, cyclopentane), 3.87 (q, 1H, $J = 20.4$ Hz, CH, cyclopropane), 6.35 (d, 1H, $J = 7.2$ Hz, NH), 7.79 (s, 2H, ArH). $^{13}$C NMR

(150 MHz, DMSO-$d_6$), $\delta_C$ 23.2, 32.7, 51.2, 128.0, 130.7, 133.6, 134.4, 154.2. Anal. Calcd for $C_{12}H_{12}Cl_3N_3O_3$: C, 40.88; H, 3.43; N, 11.92. Found: C, 40.93; H, 3.47; N, 11.84.

*N-Nitro-N-(2,6-dibromo-4-fluorophenyl)-N′-cyclopentane urea (**4i**)*

White needle crystal, yield 56%, m.p. 300–301 °C. IR (KBr, $cm^{-1}$): *v* 3305 (NH), 2929, 2853 (CH), 1635 (CO); $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 1.37 (m, 2H, $CH_2$, cyclopentane), 1.50 (m, 2H, $CH_2$, cyclopentane), 1.60(m, 2H, $CH_2$, cyclopentane), 1.79 (m, 2H, $CH_2$, cyclopentane), 3.87 (q, 1H, $J = 20.4$ Hz, CH, cyclopropane), 6.30 (d, 1H, $J = 6.0$ Hz, NH), 7.68 (d, 2H, $J = 7.8$ Hz, ArH). Anal. Calcd for $C_{12}H_{12}Br_2FN_3O_3$: C, 33.91; H, 2.85; N, 9.89; Found: C, 33.95; H, 2.89; N, 9.80.

*N-Nitro-N-(2,4,6-trichlorophenyl)-N′-cyclohexane urea (**4j**)*

White needle crystal, yield 62%, m.p. 268–269 °C. IR (KBr, $cm^{-1}$): *v* 3304 (NH), 2920, 2850 (CH), 1638 (CO); $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 1.15–1.78 (m, 10H, $C_5H_{10}$, cyclohexane), 3.38 (s, 1H, CH, cyclohexane), 6.30 (d, 1H, $J = 6.6$ Hz, NH), 7.66 (s, 2H, ArH). Anal. Calcd for $C_{13}H_{14}Cl_3N_3O_3$: C, 42.59; H, 3.85; N, 11.46. Found: C, 42.51; H, 3.89; N, 11.49.

*N-Nitro-N-(2,4-dibromo-6-methylphenyl)-N′-cyclohexane urea (**4k**)*

White needle crystal, yield 50%, m.p. 310–311 °C. IR (KBr, $cm^{-1}$): *v* 3300 (NH), 2922, 2852 (CH), 1635 (CO); $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 1.14–1.80 (m, 10H, $C_5H_{10}$, cyclohexane), 2.19 (s, 3H, $CH_3$), 3.39 (t, 1H, $J = 7.8$ Hz, CH, cyclohexane), 6.23 (d, 1H, $J = 7.8$ Hz, NH), 7.47 (s, 1H, ArH), 7.57 (s, 1H, ArH). Anal. Calcd for $C_{14}H_{17}Br_2N_3O_3$: C, 38.65; H, 3.94; N, 9.66. Found: C, 38.67; H, 3.96; N, 9.62.

*N-Nitro-N-(2,6-dibromo-4-chlorophenyl)-N′-cyclohexane urea (**4l**)*

White needle crystal, yield 76%, m.p. 311–312 °C,. IR (KBr, $cm^{-1}$): *v* 3301 (NH), 2922, 2850 (CH), 1637 (CO); $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 1.16–1.81 (m, 10H, $C_5H_{10}$, cyclohexane), 3.40 (d, 1H, $J = 5.4$ Hz, CH, cyclohexane), 6.25 (d, 1H, $J = 6.2$ Hz, NH), 7.83 (s, 2H, ArH). $^{13}$C NMR (150 MHz, DMSO-$d_6$), $\delta_C$ 24.4, 25.2, 33.0, 48.1, 125.1, 131.4, 131.5, 136.1, 153.9. Anal. Calcd for $C_{13}H_{14}Br_2ClN_3O_3$: C, 34.28; H, 3.10; N, 9.22. Found: C, 34.27; H, 3.16; N, 9.20.

*N-Nitro-N-(2,6-dibromo-4-fluorophenyl)-N′-cyclohexane urea (**4m**)*

White needle crystal, yield 54%, m.p. 298–299 °C. IR (KBr, $cm^{-1}$): *v* 3305 (NH), 2929, 2853 (CH), 1635 (CO); $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 1.16–1.81 (m, 10H, $C_5H_{10}$, cyclohexane), 3.39 (d, 1H, CH, $J = 7.8$ Hz, cyclohexane), 6.21 (d, 1H, $J = 3.6$ Hz, NH), 7.69 (s, 2H, ArH). Anal. Calcd for $C_{13}H_{14}Br_2FN_3O_3$: C, 35.56; H, 3.21; N, 9.57. Found: C, 35.54; H, 3.33; N, 9.60.

*N-Nitro-N-[2,4-dibromo-6-(trifluoromethyl)phenyl]-N′-cyclohexane urea (**4n**)*

White needle crystal, yield 51%, m.p. 289–290 °C. IR (KBr, $cm^{-1}$): *v* 3315 (NH), 2928, 2853 (CH), 1637 (CO); $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 1.15–1.78 (m, 10H, $C_5H_{10,}$ cyclohexane), 3.39 (t, 1H, $J = 7.8$ Hz, CH, cyclohexane), 6.27 (d, 1H, $J = 27$ Hz, NH), 7.92 (s, 1H, ArH), 8.27 (s, 1H, ArH). Anal. Calcd for $C_{14}H_{15}Br_2F_3N_3O_3$: C, 33.03; H, 2.97; N, 8.43. Found: C, 33.08; H, 2.39; N, 8.38.

*N-Nitro-N-(2,4,6-tribromophenyl)-N′-cycloheptane urea (**4o**)*

White needle crystal, yield 78%, m.p. 298–299 °C. IR (KBr, $cm^{-1}$): *v* 3322 (NH), 2931, 2855 (CH), 1645 (CO); $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 1.39–1.83 (m, 12H, $C_6H_{12,}$ Cycloheptane), 3.58 (m, 1H, CH, Cycloheptane), 6.30 (d, 1H, $J = 8.4$ Hz, NH), 7.93 (s, 2H, ArH). $^{13}$C NMR (150 MHz, DMSO-$d_6$), $\delta_C$ 23.5, 27.6, 34.9, 50.3, 119.4, 125.5, 134.0, 136.5, 153.7. Anal. Calcd for $C_{14}H_{16}Br_3N_3O_3$: C, 32.71; H, 3.14; N, 8.18. Found: C, 32.66; H, 3.17; N, 8.12.

*N-Nitro-N-(2,4-dibromo-6-methylphenyl)-N′-cycloheptane urea (**4p**)*

White needle crystal, yield 53%, m.p. 292–293 °C. IR (KBr, $cm^{-1}$): *v* 3318 (NH), 2928, 2856 (CH), 1638 (CO). $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 1.40–1.83 (m, 12H, $C_6H_{12,}$ Cycloheptane), 2.19 (s, 3H, $CH_3$), 3.60 (m, 1H, CH, Cycloheptane), 6.27 (d, 1H, $J = 7.8$ Hz, NH), 7.47 (s, 1H, ArH), 7.55 (s, 1H, ArH). Anal. Calcd for $C_{15}H_{19}Br_2N_3O_3$: C, 40.11; H, 4.26; N, 9.36. Found: C, 40.20; H, 4.18; N, 9.33.

*N-Nitro-N-(2,6-dibromo-4-chlorophenyl)-N′-cycloheptane urea (**4q**)*

White needle crystal, yield 69%, m.p. 296–297 °C. IR (KBr, $cm^{-1}$): *v* 3330 (NH), 2927, 2853 (CH), 1638 (CO). $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 1.40–1.83 (m, 12H, $C_6H_{12,}$ Cycloheptane), 3.58 (m, 1H, CH, Cycloheptane), 6.29 (d, 1H, $J = 7.8$ Hz, NH), 7.83 (s, 1H, ArH). Anal. Calcd for $C_{14}H_{16}Br_2ClN_3O_3$: C, 35.81; H, 3.43; N, 8.95. Found: C, 35.87; H, 3.46; N, 8.95.

*N-Nitro-N-(2,4-dibromo-6-chlorophenyl)-N′-cycloheptane urea (**4r**)*

White needle crystal, yield 69%, m.p. 294–295 °C. IR (KBr, $cm^{-1}$): *v* 3322 (NH), 2922, 2850 (CH), 1638 (CO). $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 1.41–1.88 (m, 12H, $C_6H_{12,}$ Cycloheptane), 3.60 (m, 1H, Hz, CH, Cycloheptane), 6.27 (d, 1H, $J = 7.8$ Hz, NH), 7.49 (s, 1H, ArH), 7.65 (s, 1H, ArH). Anal. Calcd for $C_{14}H_{16}Br_2ClN_3O_3$: C, 35.81; H, 3.43; N, 8.95. Found: C, 35.78; H, 3.47; N, 8.90.

*N-Nitro-N-(2,6-dibromo-4-fluorophenyl)-N′-cycloheptane urea (**4s**)*

White needle crystal, yield 53%, m.p. 289–290 °C. IR (KBr, $cm^{-1}$): *v* 3317 (NH), 2929, 2853 (CH), 1635 (CO); $^1$H NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 1.40–1.83 (m, 12H, $C_6H_{12,}$ Cycloheptane), 3.58 (m, 1H, CH, Cycloheptane), 6.27 (d, 1H,

$J = 7.8$ Hz, NH), 7.88 (s, 1H, ArH). Anal. Calcd for $C_{14}H_{16}Br_2FN_3O_3$: C, 37.11; H, 3.56; N, 9.27. Found: C, 37.14; H, 3.53; N, 9.20.

*N-Nitro-N-[2,4-dibromo-6-(trifluoromethyl)phenyl]-N′-cycloheptane urea (**4t**)*

White needle crystal, yield 55%, m.p. 285–286 °C. IR (KBr, $cm^{-1}$): *v* 3322 (NH), 2928, 2858 (CH), 1637 (CO). $^1H$ NMR (600 MHz, DMSO-$d_6$), $\delta_H$ 1.42–1.89 (m, 12H, $C_6H_{12}$, Cycloheptane), 3.60 (m, 1H, CH, Cycloheptane), 6.28 (d, 1H, $J = 7.8$ Hz, NH), 7.47 (s, 1H, ArH), 7.57 (s, 1H, ArH). Anal. Calcd for $C_{15}H_{16}Br_2F_3N_3O_3$: C, 35.81; H, 3.21; N, 8.35. Found: C, 35.88; H, 2.27; N, 8.38.

Herbicidal activity testing

Herbicidal testing of the title compound was carried out in a greenhouse, with temperature 25 ± 1 °C, relative humidity (RH) 60 ± 5%, light intensity 10 Klux, photoperiod 8 h/day. Twenty seeds of each weed species including *Amaranthus albus* and *Sorghum sudanense* were chosen for testing. Seedlings were grown in a test plate of 9-cm diameter containing two pieces of filter paper and 9 ml of solution of tested compound (50 mg/l). Distilled water and *Diuron* were used as the comparison compounds. The herbicidal activity was assessed as the inhibitory rate in comparison to the distilled water. The lengths of roots and hypocotyl are measured and the means were calculated. The percentage inhibition was used to describe the control efficiency of the compounds. For the entire bioassay test, each treatment was repeated twice. The herbicidal activity is summarized in Table 2.

Plant growth regulating activity testing

A solution of title compounds in a small amount of dimethyl sulfoxide (DMSO) was diluted with distilled water that contained 0.1% Tween 80 to the concentration of 10 mg/l. Twenty seeds of rice were placed into a 9-cm-diameter plate containing two pieces of filter paper and a 9-ml solution of tested compound. The plate was placed in a greenhouse and allowed to germinate for 96 h at a temperature of 25 ± 1 °C. The mixture of the same amount of water, DMSO, and Tween 80 was used as the control. Weeds treated with water were the blank test. Each treatment was repeated twice and the lengths of hypocotyl of seedlings in each plate were measured. The hypocotyl formation-promoting activity was calculated by the method of (test−control)/blank (Table 2).

**Acknowledgments** The author gratefully acknowledge the financial support from the Academic Discipline-Crossed Project (2010JC001) and the Research Initiation Funds (2009BQ027) of the Huazhong Agricultural University.

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