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A novel and practical method for the synthesis of dinotefuran through Michael addition of nitromethane to diethyl maleate

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ABSTRACT

A novel and practical synthesis of dinotefuran **1**, featuring a new access to it from known key intermediate (tetrahydrofuran-3-yl)-methanamine **5**, has been achieved through Michael addition reaction of nitromethane to diethyl maleate in 6 steps with 45.5% total yield. This synthesis is scalable and hence has high potential for application to further synthetic elaboration on such new neonicotinoid insecticide dinotefuran **1**.

1. Introduction

Dinotefuran **1**, *N*-methyl-*N*′-nitro-*N*″-(tetrahydro-3-furylmethyl)guanidine, is the most recent synthesized third generation neonicotinoid insecticide.[1–6] It is developed by Mitsui Chemicals (Tokyo, Japan) and first registered in Japan in 2002, and is now increasingly utilized in more than 20 countries.[7–10] The structure of the dinotefuran **1** and its analogs (Fig. 1, **2**–**4**) are very different from the existing nicotine insecticides.[3,8,11] They have a characteristic tetrahydro-3-furylmethyl moiety instead of chloro thiazole (Fig. 1, Second generation neonicotinoids, such as clothianidin **6** and thiamethoxam **7**) and chlorinated pyridine (Fig. 1, First generation neonicotinoids, such as nitenpyram **8**, imidacloprid **9**, acetamiprid **10** and thiacloprid **11**) group of other neonicotinoids, that was previously considered indispensable for insecticidal activity of neonicotinoids.[3,6–9,11–13] At the same time, the properties of dinotefuran are different from nicotine, therefore, it will be known as the "furanicotine".[14]

Dinotefuran is a useful candidate in public health because it shows low mammalian toxicity and broad spectrum quick-kill insecticide which is effective on a wide variety of insect pests such as aphids, shiteflies, leafhoppers, leafminers, sawflies, mole crickets, mealybugs, sawfly larvae and cockroaches.[2–5,10,15,16]

As far as we know, (tetrahydrofuran-3-yl)-methanol and (tetrahydrofuran-3-yl)-methanamine **5** (Fig. 1) are the two important key intermediates in the synthesis of dinotefuran **1**.[9,16] Over the past more than ten years, many studies were performed to synthesize the methanamine **5**. Early synthesis of the methanamine **5** were mainly prepared from mesylated (tetrahydrofuran-3-yl)-methanol.[11,17,18] Among which, the production technique of dinotefuran **1** from (tetrahydrofuran-3-yl)-methanol through alkylation of diethyl malonate and ethyl chloroacetate under alkaline condition has been industrialized, but the route was complicated and hard to operate, the yield was low, and the cost was very high. Liu et al. reported an access to the methanamine **5** in a total yield of 41.1% in 5 steps, with 2, 3-dihydronfuran and trichloroacetyl chloride as starting materials.[19] Chen and Sharpe developed a method to synthesize the methanamine **5**, utilizing Ru/C catalytic hydrogenation, dehydration-cyclization, chlorination, nucleophilic substitution and Raney Ni catalytic hydrogenation from malic acid in an overall yield of 54.7%.[20] Very recently, Zhou et al. described the synthesis of the methanamine **5** through 5 steps starting from 4, 5-dihydrofuran-3-carboxylic acid with 38.0% yield by Pd/C catalytic hydrogenation, chlorination, aminolysis, dehydration and hydrogenation.[21] However, the above methods need long steps, and the application of strongly corrosive, highly toxic and hazardous chemicals would also cause environmental problems. Furthermore, much noble metal catalysts were used and

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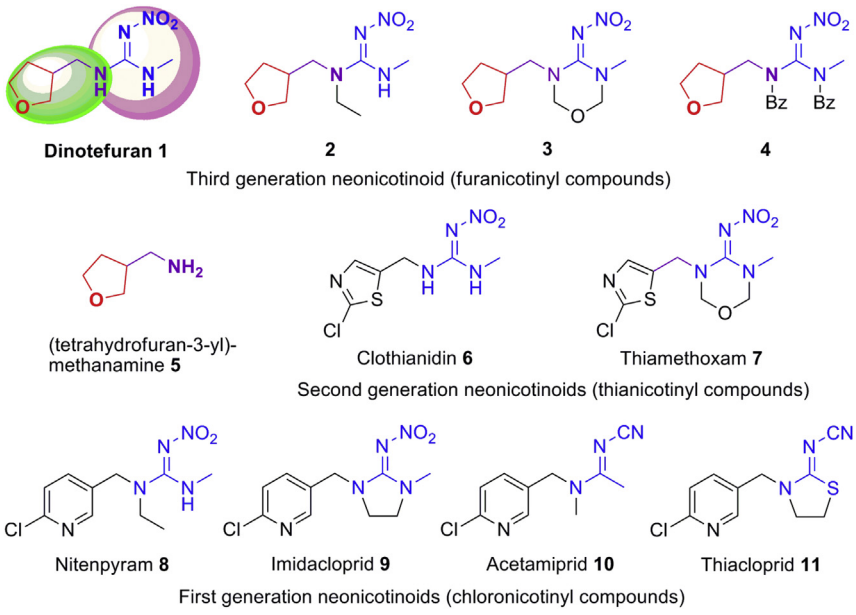
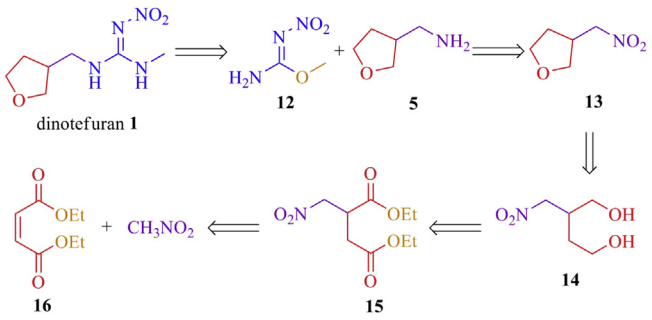


Fig. 1. Structures of dinotefuran **1**, (tetrahydrofuran-3-yl)-methanamine **5**, and other neonicotinoid insecticides **2**–**4** and **6**–**11**.

therefore the cost was high. Thus, it is still imperative to exploit more practical and scalable method to synthesize this methanamine **5**, which has a tetrahydro-3-furylmethyl moiety of dinotefuran **1** and its analogs (Fig. 1, **2**–**4**).

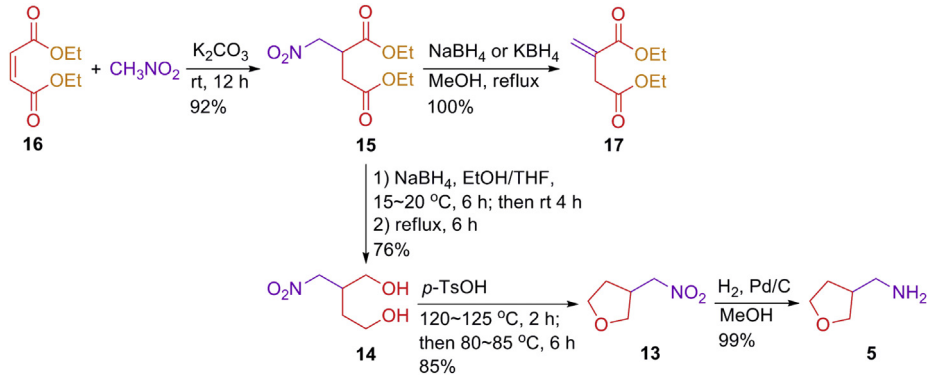
In the present work, our interest has been focused on a novel, practical and scalable method for the synthesis of dinotefuran **1** from (tetrahydrofuran-3-yl)-methanamine **5**, which was synthesized through Michael addition reaction of nitromethane to diethyl maleate.



Scheme 1. Retrosynthetic analysis of dinotefuran **1**.

2. Results and discussion

Our study was mainly focused on the issue of access to the key intermediate (tetrahydrofuran-3-yl)methanamine **5**, which was previously prepared through two steps from another useful intermediate, (tetrahydrofuran-3-yl)methanol, for the synthesis of dinotefuran **1**. In fact, the synthesis of the methanamine **5** not only gave the key intermediate of the third generation neonicotinoid insecticide dinotefuran **1**, but also provided a novel efficient synthesis strategy for the neonicotinoid insecticides which have a characteristic tetrahydro-3-furylmethyl moiety instead of an aromatic heterocyclic ring. As our retrosynthetic analysis outlined in Scheme 1, dinotefuran **1** could be synthesized from *O*-methyl-*N*-nitroisourea **12** and methanamine **5**. The methanamine **5** could be conceived by catalytic hydrogenation of nitrocompound **13**. Next, in a key step, it was thought that nitrocompound **13** could be provided by acid-catalyzed dehydrative cyclization of diol **14**. Diol **14** could be achieved from the nitroester **15** by $NaBH_4$ reduction. We envisioned that nitroester **15** may be obtained from Michael addition reaction of the commercially available nitromethane to diethyl



Scheme 2. Synthesis of the key intermediate (tetrahydrofuran-3-yl)-methanamine **5**.

maleate **16** in the presence of K_2CO_3. The overall synthetic strategy would allow very concise syntheses of dinotefuran **1**.

Our synthesis commenced with the preparation of (tetrahydrofuran-3-yl)-methanamine **5** (Scheme 2). The Michael addition reaction, which benefits from mild reaction conditions and high functional group tolerance as well as high conversions and favorable reaction rates, is a facile and versatile synthetic methodology for the efficient coupling of nucleophiles with electron poor olefins in organic synthesis. Additionally, the Michael addition is one of the most useful methods for the mild formation of C–C bonds. According to the above synthetic consideration, as shown in Scheme 2, our synthesis relying on a Michael addition of commercially available nitromethane to diethyl maleate **16** in the presence of K_2CO_3 afforded nitroester **15** in an excellent yield (92%) after 12 h at room temperature. With the required nitroester **15** in hand, the key ester reduction was then performed in the presence of $NaBH_4$ or KBH_4. To our great surprise, it is not anticipated that nitroester **15** would be impossibly converted into the key intermediate, diol **14**, as a precursor of nitrocompound **13**, but converted to the nitro elimination compound diethyl methylenesuccinate **17** in 100% yield when we first tried to treat the nitroester **15** with $NaBH_4$ or KBH_4 in methanol at reflux temperature. The formation of **17** can be explained by the fact that the nitro group at the β-position of the electron-withdrawing nitroester **15** was eliminated to give α, β-unsaturated ester **17** on treated with $NaBH_4$ or KBH_4 which played a role as base in protic solvent. And we found that the nitro group can be easily removed from the β-position of the nitroester **15**. We next tried to carry out the reduction by adding the solution of nitroester **15** in EtOH dropwise to the suspension of $NaBH_4$ in THF at 15–20 °C, and then the reaction mixture was stirred at room temperature for 4 h and refluxed at 63 °C for 6 h until there were no H_2 bubbles released. Fortunately, the desired diol **14** was obtained in 76% yield.

The resulted reduction compound diol **14** was converted into nitrocompound **13** in 85% yield by acid catalyzed dehydration-cyclization. At first, the reaction mixture was heated in the presence of *p*-TsOH at 120–125 °C for 2 h. Then the reaction was cooled to 80–85 °C and the formed water was removed by distillation for about 4 h without the use of any organic solvent. Subsequent the direct hydrogenation of the nitrocompound **13** catalyzed by 10% Pd/C afforded methanamine **5** in 99% yield.

We further tried to explore the improved protocol to synthesize the universal precursor **18** of dinotefuran **1** by *O*-methyl-*N*-nitroisourea **12** and methanamine **5** (Scheme 3). According to the previous reports, the carbamimidate **18** was synthesized by treating the methanamine **5** with 36% HCl in distilled water, and then NaCl and *O*-methyl-*N*-nitroisourea **12** were added in subsequent order, after that, 0.1 N HCl or 0.1 N NaOH was added to adjust the pH of the reaction to 7.[22,23] However, it is noteworthy that the acidity of the solution is very strong when 1.0 equivalent of 36% HCl was added to the solution of methanamine **5**. Therefore, it was not reasonable to add 0.1 N HCl or 0.1 N NaOH to adjust the pH to 7 in the reaction. We thought that 1.0 N NaOH should be added to adjust the pH of the reaction to 7 when NaCl and *O*-methyl-*N*-nitroisourea **12** were added to the methanamine **5** aqueous solution, which was treated with 36% HCl. After that, the reaction was stirred at room temperature until the reaction was finished, in which 0.1 N NaOH was added to maintain the pH of the reaction at 7.

Finally, the methylamination of carbamimidate **18** with 40% CH_3NH_2 solution in distilled water at room temperature for 3 h successfully afforded the target dinotefuran **1** in 90% yield. The melting point (100–101 °C) was in good agreement with the data reported for the new neonicotinoid insecticide (99.5–100.7 °C) and the spectral data (^1H and ^{13}C NMR) were also in good agreement with the reported values of the new neonicotinoid insecticide.[22–24]

3. Conclusion

In summary, we have developed a novel and practical method to synthesize dinotefuran **1** based on the synthesis of the known key intermediate (tetrahydrofuran-3-yl)-methanamine **5** using Michael additions reaction, $NaBH_4$ reduction, dehydration cyclization and catalytic hydrogenation as the key steps. Notably, the current synthesis gave a 45.5% overall yield in 6 steps and resulted in an efficient, practical, and scalable synthesis of dinotefuran **1** from easily accessible starting materials. More importantly, this work provided a new strategy to accomplish other structurally relevant neonicotinoid insecticides which has a characteristic tetrahydro-3-furylmethyl moiety.

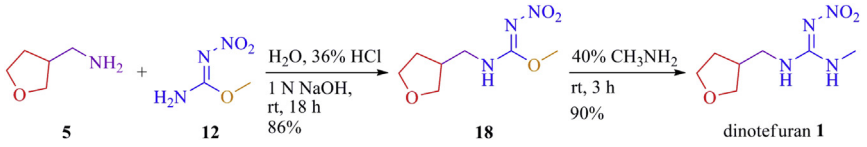
4. Experimental section

4.1. General

All reagents and solvents purchased from commercial suppliers were used without further purification unless otherwise specified. Reactions were monitored by thin layer chromatography (TLC) on glass plates precoated with silica gel with a fluorescent indicator. Flash chromatography was performed on silica gel (200–300 mesh) purchased from Qingdao Haiyang Chemical Co. Ltd. ^1H NMR and ^{13}C NMR spectra were collected on a Bruker AVANCE 400 MHz spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) from tetramethylsilane (TMS) using the residual solvent resonance. Multiplicities are abbreviated as s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). High resolution mass spectra (HRMS) were recorded on a Bulker microTOF-QII mass spectrometer. Fourier transform infrared (FTIR) analysis was performed using the Nicolet iS10 FTIR. All the samples were scanned in the range from 4000 to 400 cm^{-1} and 32 scans per sample were collected by using the KBr pellet technique. Melting-point of solid samples was measured by X-4 digital melting-point apparatus with microscope (Beijing Tech Instrument Co. Ltd. is located in Beijing, China.).

4.2. Synthesis of diethyl 2-(nitromethyl)succinate (**15**)

A suspension of K_2CO_3 (10.4 g, 0.075 mol, 0.3 equiv) in CH_3NO_2 (100 mL) was stirred at room temperature for 30 min, and then diethyl maleate (**16**) (43.0 g, 0.25 mmol, 1.0 equiv) was added. The reaction mixture was stirred for 12 h at room temperature. The mixture was filtered through a pad of Celite to remove K_2CO_3, and the filter cake was washed with CH_2Cl_2 (50 mL × 2). The solvent, including excess CH_3NO_2, was evaporated to give an orange liquid.



Scheme 3. Synthesis of dinotefuran **1** from (tetrahydrofuran-3-yl)-methanamine **5**.

The liquid was purified by silica gel column chromatography using EtOAc/PE (1:8, v/v) as eluent. Diethyl 2-(nitromethyl)succinate (**15**) was obtained as a colorless oil (53.6 g, 92% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.82–4.77 (dd, J = 8.0, 4.0 Hz, 1H), 4.71–4.66 (dd, J = 8.0, 4.0 Hz, 1H), 4.21–4.17 (q, J = 4.0 Hz, 2H), 4.16–4.12 (q, J = 4.0 Hz, 2H), 3.55–3.49 (m, 1H), 2.84–2.79 (dd, J = 4.0, 4.0 Hz, 1H), 2.71–2.65 (dd, J = 8.0, 8.0 Hz, 1H), 1.26–1.22 (t, J = 8.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.49, 170.23, 74.41, 61.84, 61.16, 39.05, 32.87, 14.02, 13.88; IR (KBr) ν_{max} 2985, 2940, 1736, 1558, 1379, 1216, 1097, 1065, 1028, 858 cm^{-1}; HRMS (ESI) m/z calcd for $C_9H_{15}NNaO_6$ $[M + Na]^+$ 256.0804, found 256.0792.

4.3. Synthesis of diethyl 2-methylenesuccinate (*17*)

A solution of nitroester (**15**) (23.3 g, 0.1 mol) in MeOH (20 mL) was heated to reflux, and then $NaBH_4$ (6.8 g, 0.18 mol) or KBH_4 (9.7 g, 0.18 mol) was portionwise added. Progress of the reaction was monitored by TLC, and when finished, it was quenched by addition of saturated aqueous NaCl and extracted with EtOAc. The combined organic extracts were dried over Na_2SO_4, filtered, and evaporated to give diethyl 2-methylenesuccinate (**17**) as an orange oil (18.6 g, 100% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.26 (s, 1H), 5.67–5.66 (d, J = 4.0 Hz, 1H), 4.23–4.16 (m, 2H), 4.15–4.10 (q, J = 8.0 Hz, 2H), 3.30 (s, 2H), 1.28–1.21 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.63, 166.10, 134.11, 127.95, 60.90, 60.76, 37.74, 14.05, 13.93; IR (KBr) ν_{max} 2984, 2939, 1739, 1720, 1640, 1369, 1317, 1194, 1148, 1033, 947, 819 cm^{-1}; HRMS (ESI) m/z calcd for $C_9H_{14}NaO_4$ $[M + Na]^+$ 209.0787, found 209.0784.

4.4. Synthesis of 2-(nitromethyl)butane-1,4-diol (*14*)

A suspension of $NaBH_4$ (14.4 g, 0.38 mol, 1.8 equiv) in THF (200 mL) was cooled to 15–20 °C with ice water. Nitroester (**15**) (49.0 g, 0.21 mol) was dissolved in 55 mL of ethanol and added dropwise to this suspension over 6 h. Once addition was completed, the reaction mixture was naturally warmed up to room temperature and stirred for 4 h until there were no H_2 bubbles released. The resulting slurry was then heated under reflux at 63 °C for 6 h as the slurry thickened. The slurry was cooled to 15–20 °C again with ice water and 32 mL of 36% HCl was added dropwised to adjust the pH to 7, and then a large amount of white solid was precipitated from the reaction mixture. The precipitate was filtered, and the filter cake was washed with THF (50 mL × 3). The combined filtrates were evaporated to remove the solvent and then repeated the filtration again. The filtrate was concentrated in vacuum to dryness and the resulting residue was then dissolved in 20 mL of MeOH and concentrated in vacuum to dryness again. The yellow oil residue was purified by silica gel column chromatography using EtOAc/PE (3:1, v/v) as eluent. 2-(nitromethyl)butane-1,4-diol (**14**) was obtained as a colorless oil (23.8 g, 76% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 4.62–4.57 (dd, J = 8.0, 8.0 Hz, 1H), 4.57–4.50 (dd, J = 8.0, 8.0 Hz, 1H), 3.67–3.60 (m, 3H), 3.58–3.53 (dd, J = 8.0, 8.0 Hz, 1H), 2.54–2.46 (m, 1H), 1.72–1.62 (m, 1H), 1.60–1.53 (m, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 77.79, 62.53, 59.94, 38.33, 32.18; IR (KBr) ν_{max} 3373, 2941, 1552, 1435, 1385, 1055 cm^{-1}; HRMS (ESI) m/z calcd for $C_5H_{11}NNaO_4$ $[M + Na]^+$ 172.0581, found 172.0580.

4.5. Synthesis of 3-(nitromethyl)tetrahydrofuran (*13*)

Diol (**14**) (29.8 g, 0.2 mol) was heated at 120–125 °C for 2 h in the presence of *p*-TsOH (3.8 g, 0.02mol), then the reaction mixture was cooled to 80–85 °C and the formed water was removed by distillation for about 4 h. The reaction mixture was cooled to room temperature and dissolved in dichloromethane (80 mL). The organic layer was washed once with saturated $NaHCO_3$ (60 mL) and twice with water (60 mL × 3). The dichloromethane phase was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography using EtOAc/PE (1:2, v/v) as eluent. 3-(nitromethyl)tetrahydrofuran (**13**) was obtained as a colorless oil (22.3 g, 85% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.39–4.37 (d, J = 8.0 Hz, 2H), 3.91–3.86 (m, 2H), 3.78–3.72 (q, J = 8.0 Hz, 1H), 3.59–3.56 (q, J = 8.0 Hz, 1H), 3.05–2.94 (m, 1H), 2.19–2.11 (m, 1H), 1.69–1.60 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 77.67, 70.55, 67.36, 37.38, 29.41; IR (KBr) ν_{max} 2977, 2872, 1737, 1553, 1433, 1385, 1244, 1188, 1072, 911 cm^{-1}; HRMS (ESI) m/z calcd for $C_5H_9NNaO_3$ $[M + Na]^+$ 154.0477, found 154.0475.

4.6. Synthesis of (tetrahydrofuran-3-yl)methanamine (*5*)

3-(Nitromethyl)tetrahydrofuran (**13**) (26.2 g, 0.2 mol) and 10% Pd/C (2.6 g) in methanol (250 mL) were hydrogenated at 1 atm and room temperature for 6 h. Then, the mixture was filtered through a pad of Celite and the solid was washed by methanol (10 mL × 3). The filtrate was concentrated in rotary evaporator to give (tetrahydrofuran-3-yl)-methanamine (**5**) in 99% yield as a yellow oil .^{1}H NMR (400 MHz, CD_3OD) δ 3.87–3.82 (q, J = 8.0, 8.0 Hz, 2H), 3.75–3.70 (q, J = 4.0, 8.0 Hz, 1H), 3.51–3.48 (t, J = 8.0 Hz, 1H), 2.73–2.72 (d, J = 4.0, 2H), 2.40–2.34 (m, 1H), 2.09–2.06 (m, 1H), 1.66–1.58 (m, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 72.24, 68.71, 44.92, 42.02, 31.05; IR (KBr) ν_{max} 3420, 2868, 1567, 1395, 1062, 904, 819 cm^{-1}; HRMS (ESI) m/z calcd for $C_5H_{12}NO$ $[M + H]^+$ 102.0919, found 102.0913.

4.7. Synthesis of O-methyl-N-nitroisourea (*12*)

Dimethyl sulfate (63.1 g, 0.5 mol) was added to urea (30.0 g, 0.5 mol) at room temperature and the mixture was stirred in a few minutes. The mixture was then stirred at 80 °C for 24 h. After cooling to room temperature, 98% H_2SO_4 (109 mL, 2.0 mol) was added to the mixture. Then the mixture was further cooled to 5 °C and fuming nitric acid (97%, 64 mL, 1.5 mol) was added dropwise over 0.5 h while maintaining the internal temperature to below 10 °C. The ice bath was then removed and the temperature was gradually raised to room temperature. After stirring for total 2 h, the mixture was poured on crushed ice, neutralized by adding 30% NaOH and extracted with ethyl acetate (80 mL × 3). The combined ethyl acetate phase was dried over Na_2SO_4, filtered, and concentrated. The solid was washed with ethyl ether to obtain 32.2 g (54%) of *O*-methyl-*N*-nitroisourea (**12**) as a white crystal. Mp: 107–109 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.88 (2H, s), 3.75 (3H, S); ^{13}C NMR (101 MHz, DMSO-d_6) δ 163.31, 55.60; IR (KBr) ν_{max} 3458, 3347, 1619, 1498, 1446, 1383, 1268, 1112, 1072, 788 cm^{-1}; HRMS (ESI) m/z calcd for $C_2H_5N_3NaO_3$ $[M + Na]^+$ 142.0229, found 142.0237.

4.8. Synthesis of O-methyl-N′-nitro-N″-[(tetrahydro-3-furanyl) methyl] carbamimidate (*18*)

A solution of (tetrahydrofuran-3-yl)-methanamine (**5**) (20.2 g, 0.2 mol) in distilled water (84 mL) was cooled to 0 °C with ice water, and then 36% HCl (17 mL, 0.2 mol) was added. After the addition was completed, NaCl (23.4 g, 0.4 mol) and *O*-methyl-*N*-nitroisourea (**12**) (23.8 g, 0.2 mol) was added and then the pH of the reaction mixture was adjusted to 7 with 1.0 N NaOH (140 mL, 0.14 mol). Then the reaction mixture was stirred at room temperature for 18 h. The pH of the reaction mixture was maintained at 7 with aliquots 0.1 N NaOH in the reaction. After completion of the reaction, the mixture was extracted with dichloromethane (80 mL × 3). The combined organic layer was washed with saturated $NaHCO_3$ (80 mL) and brine (80 mL), and then dried over Na_2SO_4. After

filtration of the mixture and concentrated, the crude product was recrystallized from EtOAc/Hex (1:1, v/v) to obtain carbamimidate (**18**) as a white crystal (34.9 g, 86% yield). Mp: 62–63 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (1H, s), 3.93 (3H, S), 3.92–3.86 (1H, m), 3.81–3.70 (2H, m), 3.56–3.52(1H, m), 3.39–3.34 (2H, m), 2.56–2.46 (1H, m), 2.10–2.06 (1H, m), 1.64–1.56 (1H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.01, 70.77, 67.49, 56.69, 44.27, 38.70, 29.62; IR (KBr) ν_{max} 3307, 2969, 2872, 1738, 1615, 1538, 1366, 1228, 1216, 910, 734 cm^{-1}; HRMS (ESI) for *m*/*z* calcd $C_7H_{13}N_3NaO_4$ $[M + Na]^+$ 226.0808, found 226.0798.

4.9. Synthesis of dinotefuran (*1*)

A solution of carbamimidate (**18**) (32.5 g, 0.16 mol) in distilled water (100 mL) was cooled to 0 °C with ice water. Then 40% CH_3NH_2 (24.8 g, 0.32 mol) was added. After the addition was completed, the reaction mixture was stirred at room temperature for additional 3 h. After completion of the reaction, the mixture was diluted with 0.1 N HCl to adjust pH to 6–7. Then the reaction mixture was poured into dichloromethane (100 mL). The organic layer was separated, and the aqueous layer was washed with dichloromethane (80 mL × 2) and separated. The combined organic layer was washed with saturated $NaHCO_3$ (100 mL) and brine solution (100 mL). It was dried over anhydrous sodium sulfate and concentrated to obtain a pale yellow crude solid, which was recrystallization from EtOAc/MeOH (50:1, v/v) to give dinotefuran (**1**) as a white solid (29.2 g; 90%). Mp: 100–101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.32 (1H, s), 5.97 (1H, s), 3.92–3.86 (1H, dd, J = 8.0, 8.0 Hz), 3.77–3.68 (2H, m), 3.63–3.60 (1H, m), 3.33–3.32 (2H, m), 2.95 (3H, d, J = 4.0 Hz), 2.61–2.60 (1H, m), 2.13–2.02 (1H, m),1.68–1.60 (1H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.48, 70.94, 67.56, 44.63, 38.25, 29.52, 28.14; IR (KBr) ν_{max} 3339, 3296, 2952, 2879, 1618, 1542, 1317, 1230, 1168, 891, 786 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_7H_{15}N_4O_3$ $[M + H]^+$ 203.1146, found 203.1139.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.tet.2017.12.002.

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