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Access to Some Angular Aminochromeno[2,3-*c*]pyrazole Precursors by a Domino Knoevenagel–hetero-Diels–Alder Reaction

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A new, solvent-free tetrabutylammonium-hydrogensulfate-catalysed one-pot procedure to synthesise angular benzopyran-annulated pyrazoles, all of which incorporate a tertiary ring-junction carbon, has been demonstrated. A typical intermediate Knoevenagel heterodiene, formed by the reaction of 2-(alkenyloxy)- or 2-(alkynyloxy)acetophenones with pyrazolones smoothly underwent a subsequent hetero-Diels–Alder reaction to give chromeno-fused pyrazoles in a highly stereoselective reaction. When nitro-containing DKHDA products were treated further with Fe/HCl in tandem, they formed the corresponding amino frameworks in a reduction step, which highlights a new possibility for this cascade route to give aminopolyheterocycles. The stereochemistry of all new tertiary ring-junction carbon-containing polyheterocycles was confirmed by 2D NMR spectroscopy experiments, DQF-COSY and NOESY, and single crystal X-ray diffraction data. None of the products has had their biological profiled evaluated before, and they are expected to have heterosteroidal biological functions.

Introduction

Angularly fused polycyclic compounds are of interest due to their significant roles in biological systems, which ultimately make their various medicinal applications possible.[1,2] Compounds of interest from this family include naturally occurring cannabicyclol,[3a] mahanimbine,[3b] steroids[3c] and thyrsiferol.[1d] Analogues of thyrsiferol are known to show cytotoxic, antiviral, and antitumor activities. Similarly, heterosteroids,[4] analogues of steroids, containing a tertiary ring-junction carbon-like skeleton, have shown significantly improved biological functions. Thus, there is a great deal of research in this area, and more development of such scaffolds is not only desired, but also required.

The domino Knoevenagel–hetero-Diels–Alder (DKHDA) reaction has contributed to the development of polycyclic compounds, and it is still a vital part of the synthetic repertoire, allowing access to diverse complex molecules in modern synthetic organic chemistry.[5] To date, this reaction, in which an olefin-ether-tethered aldehyde reacts with a diketone, has been catalysed by Lewis acids,[6] EDDA (ethylenediammonium diacetate),[7] copper(I) iodide,[8] bismuth(III) chloride,[9] indium(III) chloride,[10] lithium perchlorate,[11] triphenylphosphonium perchlorate,[12] zinc oxide,[13] D-proline,[14] ionic liquids,[15] and pyridine,[16] and has been used for the preparation of polyheterocycles of pharmaceutical and photochromic interest.[17]

Tietze et al. have extensively studied this protocol.[18] Many aldehyde substrates were used in this pioneering work. By introducing tetrabutylammonium hydrogensulfate (TBA-HS) as an efficient catalyst, our group has recently extended this strategy further to cover some (aryldiazenyl)-salicylaldehydes.[19] Other improvements like shorter reaction times, highly regioselective and clean reactions, and finally the dispensability of a reaction solvent (as shown in the solvent-free green approach described in this paper), lead to a more economical and environmentally friendly reaction. Moreover, our use in this study of alkenyl- and alkynyl-ether-tethered ketones (instead of the more widely studied aldehydes) extends the substrate scope of this strategy. Work on activated ketones has been reported, but only in an intermolecular hetero-Diels–Alder reaction.[20] TBA-HS promoted a highly enantio- and regioselective catalytic inverse-electron-demand cycloaddition with a dienophile to form polyheterocyclic products, all incorporating a tertiary ring-junction carbon, starting from the corresponding *O*-allylated, prenylated, or propargylated 2-hydroxyacetophenones and pyrazolones. This hetero-Diels–Alder sequence could further be linked in tandem with another transformation i.e., reduction of nitro-substituted domino products, resulting in the formation of aminobenzopyran-annulated pyrazolones in one pot. In the literature, 6-aminochromenes are precursors to many bioactive compounds.[21] Moreover, their salts are suitable for pharmaceutical purposes and show drug activities. More interestingly, bridgehead methyl

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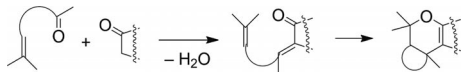
attached to a pyranyl ring-junction carbon in all new polyheterocycles may confer them with a new steroid-mimicking biological function (Scheme 1).[4a,22]



Scheme 1. Synthetic route to new angular polyheterocycles.

Results and Discussion

Compounds that contain an aldehyde functionality together with suitably placed alkene or alkyne moieties are widely studied substrates in the DKHDA protocol. Surprisingly, the corresponding compounds based on the ketone functionality have never been studied before. We therefore set about studying 2-(allyloxy)-, 2-(prenyloxy)-, and 2-(propargyloxy)acetophenones **2a**–**i** as a typical class of substrates. All are ketone-based substrates and all were formed in good yields by allylating, prenylating, or propargylating 2-hydroxyacetophenones using anhydrous potassium carbonate in DMF at room temperature (Scheme 2),[19] as reported elsewhere. All were isolated as oily products after extraction with ether.

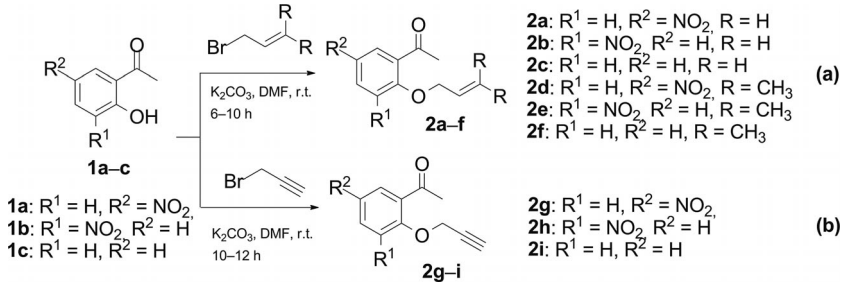
To optimise the DKHDA reaction conditions, we choose three model substrates to be coupled with pyrazolone **3a**. The *O*-allylated (**2a**), *O*-prenylated (**2d**), and *O*-propargylated 2-hydroxyacetophenones (**2g**) represent the three classes of dienophile substrates. The effect of different catalysts was examined, as summarised in Table 1. Ketone-based substrates **2a**, **2d**, and **2g** seemed completely unreactive at temperatures below that of refluxing toluene, and even the formation of Knoevenagel adducts was not observed.

We next heated an equimolar (0.3 mmol) mixture of **2a**, **2d** or **2g** with pyrazolone **3a** without catalyst in acetonitrile at reflux (Table 1, entry 1). Here, no products formed from any substrate even after prolonged heating (24 h). When the reactions were carried out in the presence of catalysts EDDA and TBA-HS (Table 1, entries 2–3), the formation of a trace of the Knoevenagel condensation product was observed by TLC. Despite extended heating, however, it never transformed into cyclised products. On the other hand, in refluxing toluene (Table 1, entries 4–6), a 6% yield of **4a** starting from allyl-based substrate **2a**, and an 8% yield of **4d** starting from prenyl-based substrate **2d**, could be achieved using 25 mol-% of catalyst TBA-HS (Table 1, entry 6). In the absence of catalyst (Table 1, entry 4), only traces of product **4d** were seen. Propargyl-based substrate **2g** showed no reactivity. Conventional heating, which took 24 h to yield ca. 6% of **4a** and 8% of **4d** was thus inadequate to run the protocol. Next, we attempted a catalyst- and solvent-free reaction at 160 °C (Table 1, entry 7), envisaging that the higher temperature would activate the substrate. Under these conditions, all substrates formed oily yellow Knoevenagel adducts with pyrazolone **3a**. On heating the reaction mass for 4–5 h, these adducts were transformed into cyclised products, except that derived from substrate **2g**. The Knoevenagel adduct derived from **2g** failed to give the final cyclised product (i.e., **4o**), which may be due to the low reactivity of the propargyl dienophile. Thus, increasing the reaction temperature to 160 °C for substrates **2a** and **2d** under catalyst- and solvent-free conditions, we noticed that the reaction time decreased from 24 h taken at reflux temperature to 5 h for allyl-based substrate **2a** (Table 1, entry 7), and to 4 h for prenyl-based substrate **2d** (Table 1, entry 7), yielding 60 and 61% of cyclised products **4a** and **4d**, respectively. No further improvement in the reaction was seen above 160 °C. To improve the yields, we then tried various amounts of the TBA-HS catalyst at this temperature. With 10 mol-% TBA-HS, **2a** gave **4a** in 58% yield, and **2d** gave **4d** in 62% yield after 4 h (Table 1, entry 8). Increasing the catalyst loading (Table 1, entries 9–11) cer-

Table 1. Optimizing the reaction conditions to assess model products **4a**, **4d** and **4o**.

Entry	Solvent (reflux)	Catalyst [mol-%]	Product **4a** Time [h]	Product **4a** Yield [%]	Product **4d** Time [h]	Product **4d** Yield [%]	Product **4o** Time [h]	Product **4o** Yield [%]
1	MeCN	–	24	–	24	–	24	–
2	MeCN	EDDA (25)	24	–	24	–	24	–
3	MeCN	TBA-HS (25)	24	–	24	–	24	–
4	toluene	–	24	–	24	trace	24	–
5	toluene	EDDA (25)	24	4	24	7	24	–
6	toluene	TBA-HS (25)	24	6	24	8	24	–
7	[a]	–	5.0	60	4.0	61	5.0	–
8	[a]	TBA-HS (10)	4.0	58	4.0	62	5.0	–
9	[a]	TBA-HS (15)	3.5	63	3.5	65	5.0	–
10	[a]	TBA-HS (25)	3.5	75	3.0	79	5.0	–
11	[a]	TBA-HS (35)	3.5	73	3.0	78	5.0	–

[a] Solvent-free at 160 °C.



Scheme 2. Synthesis of *O*-allylated, prenylated, and propargylated 2-hydroxyacetophenones **2a**–**i**: (a) allylation/prenylation, and (b) propargylation.

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tainly improved the yields and reaction times. This trend was continued up to 25 mol-% catalyst loading, after which no drastic changes were noted (Table 1, entries 9–11). The optimal yields of representative products **4a** and **4d** were 75 and 79%, respectively (Table 1, entry 10). Therefore, running the reaction in the presence of 25 mol-% TBA-HS and in the absence of solvent were the best conditions observed so far and even more meritorious than our refluxing xylene method reported elsewhere, which takes 12 h.[19] Other compounds **4b**–**n** were prepared under the optimised conditions of Table 1, entry 10. All Knoevenagel adducts were stable and isolable. Their structures were confirmed by IR and NMR spectroscopic data.

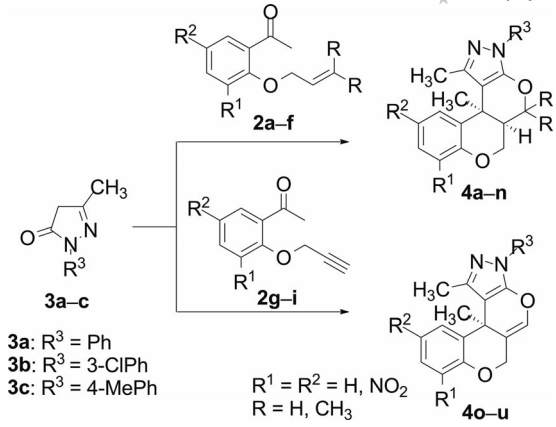
To our surprise, none of the catalysts tested was effective for the transformation of unreactive propargyl-based substrate **2g** into product **4o**, except for ZnO, which resulted in the formation of traces of products. Therefore, we worked further with this result, and combined 25 mol-% ZnO with varying amounts of TBA-HS Table 2. The yields of **4o** were improved when we performed the solvent-free reaction in the presence of catalytic mixture containing 25 mol-% ZnO and 25 mol-% TBA-HS (Table 2, entry 10). These optimised conditions were used for the preparation of other heterocycles **4o**–**u** (Scheme 3). The yields of the products (Table 3) were in the 65–73% range. The search to optimise the efficiency of this method is ongoing.

Table 2. Optimizing the reaction conditions to access **4o**.

Entry	Solvent	Catalytic mixture ZnO [mol-%]	TBA-HS [mol-%]	Time [h]	Yield [%]
1	xylene	–	–	24	–
2	toluene	25	–	24	–
3	xylene	25	–	24	8
4	toluene	25	25	24	trace
5	xylene	25	25	24	11
6	[a]	15	–	10	34
7	[a]	25	–	7.5	57
8	[a]	35	–	7.5	59
9	[a]	25	15	6	59
10	[a]	25	25	5	65
11	[a]	25	35	5	67

[a] Solvent-free at 160 °C.

Table 3 represents all the products formed using the optimised reaction conditions (i.e., those given in Table 1, entry 10 for **4a**–**h**, and those given in Table 2, entry 10 for **4o**–**u**). As expected, prenyl-based substrates generally require less time than unreactive allyl-based ones. Substitution on the phenyl ring attached to the 5-pyrazolone nitrogen N^1 was also found to affect the reaction time. Methyl substituents in comparison with others reduced the reaction time in case of prenyl-based substrates (Table 3, entries 4–6, 10–12), which may be due to a decrease in the HOMO–LUMO energy gap. The same trend however, could not be clearly observed for the analogous *O*-allylated 2-hydroxyacetophenone derivatives (Table 3, entries 1–3, 7–9). Finally, the presence of electron-withdrawing nitro groups has affected the reaction time in case of *O*-propargylated acetophenone substrates, taking 5 h compared to 3.5 h in case of others, to react with pyrazolones. It is important to note that no



Scheme 3. Synthesis of tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano-[2,3-*c*]pyrazoles **4a**–**n**, and dihydro-6*H*-chromeno[4′,3′:4,5]pyrano-[2,3-*c*] pyrazoles **4o**–**u**.

Table 3. Synthesis of tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazoles **4a**–**n**, and dihydro-6*H*-chromeno [4′,3′:4,5]pyrano[2,3-*c*] pyrazole **4o**–**u**.

Entry	Product	R	R^1	R^2	R^3	M.p. [°C]	Time [h]	Yield [%]
1	**4a**	H	H	NO_2	Ph	172–174	3.5	75
2	**4b**	H	H	NO_2	3-ClC_6H_4	196–198	3.5	79
3	**4c**	H	H	NO_2	4-MeC_6H_4	208–210	3.5	76
4	**4d**	CH_3	H	NO_2	Ph	232–234	3.0	79
5	**4e**	CH_3	H	NO_2	3-ClC_6H_4	208–210	2.5	72
6	**4f**	CH_3	H	NO_2	4-MeC_6H_4	238–240	2.0	78
7	**4g**	H	NO_2	H	Ph	162–164	3.0	81
8	**4h**	H	NO_2	H	3-ClC_6H_4	218–220	3.5	78
9	**4i**	H	NO_2	H	4-MeC_6H_4	224–226	3.0	80
10	**4j**	CH_3	NO_2	H	Ph	220–222	2.5	78
11	**4k**	CH_3	NO_2	H	3-ClC_6H_4	224–226	2.5	74
12	**4l**	CH_3	NO_2	H	4-MeC_6H_4	218–220	2.0	71
13	**4m**	H	H	H	Ph	152–154	2.5	78
14	**4n**	CH_3	H	H	Ph	170–172	2.0	76
15	**4o**	–	H	NO_2	Ph	170–173	5.0	65
16	**4p**	–	H	NO_2	3-ClC_6H_4	218–220	5.5	71
17	**4q**	–	H	NO_2	4-MeC_6H_4	203–205	5.0	73
18	**4r**	–	NO_2	H	Ph	182–184	5.5	67
19	**4s**	–	NO_2	H	3-ClC_6H_4	206–208	6.0	65
20	**4t**	–	NO_2	H	4-MeC_6H_4	196–197	5.0	70
21	**4u**	–	H	H	Ph	156–158	4.0	72

sigmatropic rearrangement of the allylic ethers was detected at higher temperature (160 °C), indicating that all of the acetophenones are stable, and that all retained their original carbonyl–dienophile skeleton to allow the DKHDA approach.

A plausible mechanism is proposed in Scheme 4. The reaction proceeds via a Knoevenagel adduct, the formation of which was confirmed by ^1H and ^{13}C NMR and DEPT-135 spectroscopy. Because of angle strain, the formation of either *endo-Z-anti* or *exo-E-anti* geometries must be ruled out. Only less steric interaction between an *ortho* substituent and the carbonyl group favours the *endo-E-syn* transition state. This was also supported by the X-ray crystal structure, in which the fused pyranyl ring-junction methyl and hydrogen are orientated *cis* to each other. Thus it is inferred that *endo-E-syn* transition state favoured the ex-

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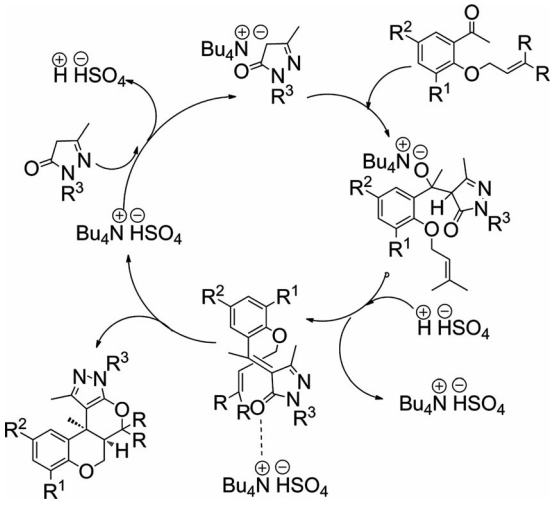
clusive formation of *cis* products, even though two pathways are possible. Both allyl- and prenyl-based substrates smoothly underwent a DKHDA reaction in the presence of TBA-HS. This was not observed for the unreactive propargyl-based substrate, which additionally required ZnO to promote the DKHDA reaction to form **4o**–**u**.



Scheme 4. Mechanism of TBA-HS catalysed DKHDA reaction **4a**–**n**.

The structures of all new polyheterocycles were deduced from their spectroscopic data. The ^{1}H NMR spectra of allyl- and propargyl-based products showed a singlet around 1.8 ppm, which was assigned to the bridgehead methyl protons attached to the ring-junction tertiary carbon. The corresponding protons in prenyl-based products could be seen as a singlet at around 1.0 ppm. This upfield shift may be due to the methyl group. From the ^{13}C NMR spectrum, it could also be observed that the methyl carbon that appeared at ca. 28 ppm in allyl- and propargyl-based products had shifted to ca. 22 ppm in prenyl-based products. The ring-junction CH protons appeared as multiplets in allyl-derived products and doublets (J = 4.0 Hz) in prenyl-derived products in the 2.0–2.2 ppm range. In all products, a ring-junction tertiary carbon appeared as a clear peak in the ^{13}C NMR spectrum in the 34–38 ppm range. To establish the stereochemistry of all new nitro-containing products, 2D NMR experiments were used. The nuclear Overhauser effect spectroscopy (NOESY) and double quantum filtered correlation spectroscopy (DQF-COSY) data of nitro derivative **4a** support its proposed structure (Figure 1). The NOESY data provided clear evidence for the vicinity of the methyl group attached to the ring-junction carbon with the pyrazolyl methyl protons, and also with the bridgehead CH, and with the aromatic ring. For the aminobenzopyrans, one more correlation could be added to these: the amine protons correlated with the neighbouring *ortho* aromatic CH proton (Figure 2).

The structure was finally ascertained by single-crystal X-ray diffraction data. Compound, **4m**, crystallised in the monoclinic space group $P2_1/c$ with the following unit-cell parameters: a = 9.7115(5), b = 12.6094(6), c = 13.8066(8) Å, β = 94.838(5)°, Z = 4. The crystal structure was solved by direct methods[23] using single-crystal X-ray diffraction data collected at room temperature, and refined by full-matrix least-squares procedures to a final R value of 0.0651 for 1941 observed reflections. An ORTEP view with atomic labelling is shown in Figure 3.[24]

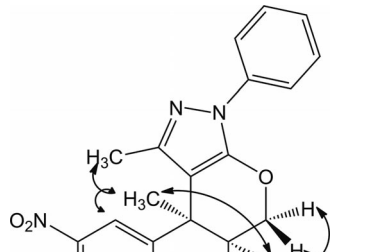


Figure 1. Characteristic nOe's of **4a**.

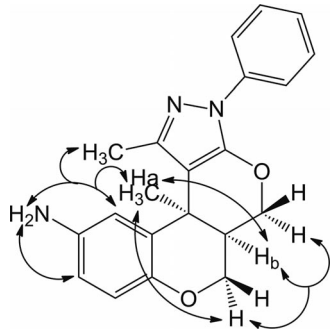


Figure 2. Characteristic nOe's of **5a**.

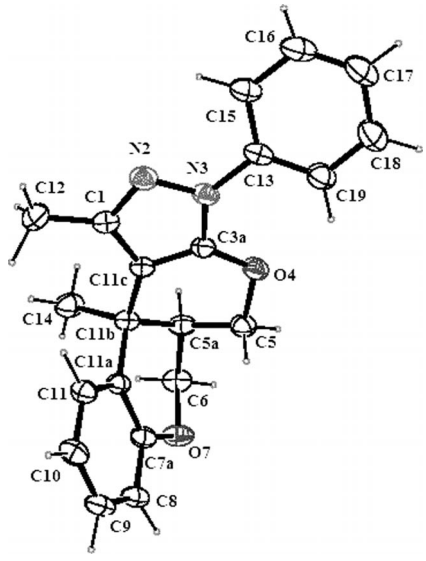


Figure 3. ORTEP view of compound **4m**.

The geometry of the molecule was calculated using the WinGX28 and PARST29 software packages.[25] The crystal-packing diagram is shown in Figure 4.

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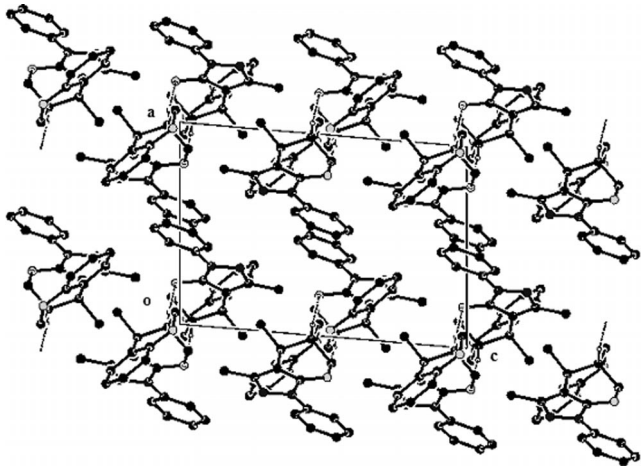


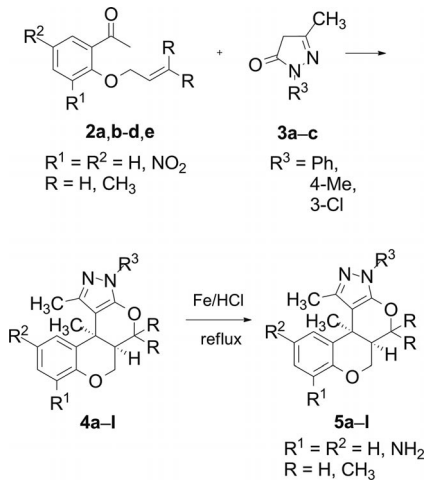
Figure 4. Crystal-packing diagram of **4m**.

To derive potentially bioactive aminochromene-annulated scaffolds, we treated all of the DKHDA nitro-containing products with various reducing agents under different reaction conditions. These included: treatment with sodium hydrogen sulfate in refluxing methanol or water; treatment with Fe/HCl in refluxing methanol or in an ethanol/water mixture; and treatment with $SnCl_2$ in water at room temperature and at reflux (Table 4). None of the methods gave good results except for Fe/HCl in a refluxing mixture of ethanol and water. A highest yield of 82% of model amino product **5a** was obtained under these conditions (Table 4, entry 4). Other aminochromene-fused heterocycles **5a**–**f** and **5g**–**l** were prepared by the same method (Scheme 5, Table 5). The structures of the reduced aminobenzopyran derivatives were also confirmed by 2D NMR experiments, which were consistent with the proposed structure shown in Figure 2.

Table 4. Optimizing the reaction conditions to afford model amino products **5a**.

Entry	Refluxing medium	Catalyst	Yield [%]
1	MeOH[a]	$SnCl_2$/HCl	20
2	acetone	$SnCl_2 \cdot H_2O$	32
3	H_2O	$SnCl_2$/HCl	23
4	H_2O/EtOH	Fe/HCl	82
5	H_2O/MeOH	Fe/HCl	68
6	MeOH	NaSH/MeOH	23

[a] Room temperature.



Scheme 5. Synthesis of tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano-[2,3-*c*]pyrazol-10-amines **5a**–**f** and tetrahydro-5*H*-chromeno-[4′,3′:4,5]pyrano[2,3-*c*]pyrazol-8-amines **5g**–**l**.

Table 5. Synthesis of tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazol-10-amines **5a**–**f** and tetrahydro-5*H*-chromeno[4′,3′:4,5]-pyrano[2,3-*c*]pyrazol-8-amines **5g**–**l**.

Entry	Product	R	R^1	R^2	R^3	M.p. [°C]	Yield [%]
1	**5a**	H	H	NH_2	Ph	118–120	72
2	**5b**	H	H	NH_2	3-ClC_6H_4	110–112	86
3	**5c**	H	H	NH_2	4-MeC_6H_4	98–100	75
4	**5d**	CH_3	H	NH_2	Ph	162–164	89
5	**5e**	CH_3	H	NH_2	3-ClC_6H_4	132–134	71
6	**5f**	CH_3	H	NH_2	4-MeC_6H_4	143–145	73
7	**5g**	H	NH_2	H	Ph	116–118	74
8	**5h**	H	NH_2	H	3-ClC_6H_4	138–140	82
9	**5i**	H	NH_2	H	4-MeC_6H_4	147–149	85
10	**5j**	CH_3	NH_2	H	Ph	115–117	73
11	**5k**	CH_3	NH_2	H	3-ClC_6H_4	152–154	70
12	**5l**	CH_3	NH_2	H	4-MeC_6H_4	126–128	83

Conclusions

In summary, we have described an intramolecular DKHDA approach to assess some new tertiary carbon containing polyheterocycles from three typical ketone-based substrates *O*-allylated, *O*-prenylated, and *O*-propargylated 2-hydroxyacetophenones and pyrazolones by carrying out the reaction in the presence of TBA-HS under solvent-free conditions at high temperature. The reaction proceeded efficiently for all substrates except for the *O*-propargyl-based substrate, which required the presence of ZnO as an additional catalyst to proceed moderately. When the crude DKHDA reaction products containing nitro groups were treated further with Fe/HCl in tandem, they gave the corresponding amino compounds in one pot. The compounds are potential candidates for biological and photochromic applications.

Experimental Section

General: All solvents and reagents were purified by standard techniques or used as supplied from commercial sources as appropriate. IR spectra were recorded using the KBr method with a Shimadzu FTIR 8300 spectrometer, and are reported in wavenumbers (cm^{-1}). ^1H and ^{13}C NMR spectra were recorded with a Bruker Avance 400 spectrometer operating at 400 MHz for ^1H NMR and 100 MHz for ^{13}C NMR as solutions in $CDCl_3$ or DMSO, unless otherwise indicated. Chemical shifts are reported as parts per million (ppm, δ) and are referenced to the residual protic solvent. Coupling constants are reported in Hertz (Hz). Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; br, broad; m, multiplet; comp, complex multiplet. The degree of substitution (C, CH, CH_2, and CH_3) was determined by the DEPT-135 method. Elemental

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analysis was carried out with a Perkin–Elmer 2400 Series-II elemental analyser. The ESI mass spectra were measured with a Shimadzu LCMS-2010 spectrometer. TLC was performed on Merck 60 F254 pre-coated silica plates, and spots were detected either by UV (254 nm, 366 nm) or by dipping into permanganate [$KMnO_4$ (3 g), K_2CO_3 (20 g), NaOH (5 mL, 5% in H_2O), H_2O (300 mL)] or (2,4-dinitrophenyl)hydrazine [2,4-DNP (12 g), conc. H_2SO_4 (6 mL), water (8 mL), EtOH (20 mL)] solutions followed by heating. Single crystal X-ray data were collected with a Bruker CCD area-detector diffractometer equipped with graphite monochromated Mo-K_α radiation (λ = 0.71073 Å). The structure was solved by direct methods using SHELXS97.[23] All non-hydrogen atoms of the molecule were located in the best E-map.

CCDC-840897 contains the supplementary crystallographic data for this paper.

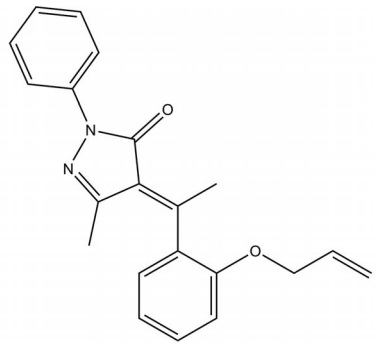
General Procedure for the Synthesis of *O*-Allylated, Prenylated, and Propargylated Acetophenones 2a–i: A solution of allyl or prenyl or propargyl bromide (0.013 mol) in DMF (2 mL) was added dropwise to a stirred suspension of a 2-hydroxyacetophenone derivative **1a**–**c** (0.01 mol) and anhydrous potassium carbonate (0.015 mol) in DMF (10 mL). The resulting mixture was stirred at room temperature until completion of reaction as confirmed by the TLC (6–12 h). It was then poured into ice (100 g) with constant stirring. Solid products were filtered, washed with cold water (3 × 10 mL), and then dried at room temperature. Oily products were extracted with diethyl ether (3 × 25 mL). The combined ether extracts were then dried with anhydrous sodium sulfate and evaporated to give the pure products as colourless oils. The products were obtained in 93–97% of yields.

General Procedure for the Synthesis of 4a–n: A mixture of an *O*-allylated/prenylated acetophenone **2a**–**f** (3.0 mmol) and a 5-pyrazolone derivative **3a**–**c** (3.0 mmol) was heated with catalyst TBA-HS (0.75 mmol, 25 mol-%) in a round-bottomed flask at 160 °C until the reaction was complete, as monitored by TLC. The crude products obtained were purified by column chromatography to give the products in good yields.

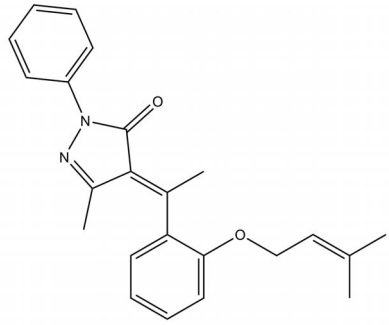
General Procedure for the Synthesis of 4o–u: An *O*-propargylated acetophenone **2g**–**i** (3.0 mmol), a 5-pyrazolone **3a**–**c** (3.0 mmol), and a catalytic mixture containing TBA-HS (0.75 mmol, 25 mol-%) and zinc oxide (0.75 mmol, 25 mol-%) were heated in a round-bottomed flask at 160 °C until the reaction was complete, as monitored by TLC. The crude products obtained were purified by column chromatography to give the products in good yields.

General Procedure for the Synthesis of 5a–l (Reduction of Nitro Compounds): Water (10 mL) and concentrated hydrochloric acid (1–2 drops) were added to the crude nitro compound **4a**–**l** (1 equiv.) that was formed in the DKHDA reaction as confirmed by TLC. This was followed by the addition of Fe powder (6 equiv.) in ethanol. The mixture was then heated for 1–2 hat reflux. The progress of the reaction was monitored by TLC, which indicated that resulted amine products had formed cleanly in all cases. The crude product was then obtained by chloroform extraction. The extracts were dried with anhydrous $MgSO_4$ and concentrated under reduced pressure to give a solid residue. The residue was further purified by column chromatography using hexane/ethyl acetate (6:4) as an eluent.

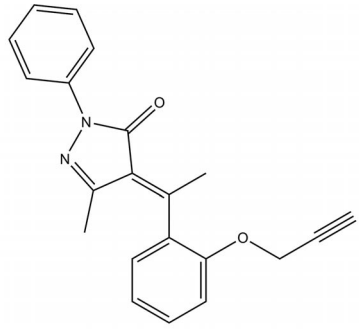
Spectroscopic data of typical Knoevenagel alkene intermediates **I**, **II** and **III**.



I



II



III

(*E*)-4-{1-[2-(Allyloxy)phenyl]ethylidene}-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (Intermediate I): Yellow oil, IR (KBr): $\tilde{\nu}$ = 2967, 2926, 1689, 1629, 1500, 1232, 1119, 1048, 818, 755, 690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.61 (s, 3 H, CH_3), 2.84 (s, 3 H, pyrazolone CH_3), 4.60 (d, J = 4.0 Hz, 2 H, CH_2), 5.28 (dd, J = 10.4, J = 1.2 Hz, 1 H, one methylene proton), 5.37 (dd, J = 17.2, J = 1.6 Hz, 1 H, the other methylene proton), 5.99 (m, 1 H, CH), 6.98–7.99 (m, 9 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.62 (pyrazolone CH_3), 22.21 (CH_3), 69.00 (CH_2), 112.46 (CH), 117.76 (methylene), 118.74, 118.80, 118.90, 120.76, 124.62, 126.66, 128.20, 128.74, 128.93, 130.41, 132.60, 138.46, 148.83, 154.17, 163.76 (C=N), 163.90 (C=O) (Ar-C) ppm. MS (ESI): m/z = 333.1 $[M + H]^+$.

(E)-4-{1-[2-(Prenyloxy)phenyl]ethylidene}-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (Intermediate II): Yellow oil, IR (KBr): $\tilde{\nu}$ = 2972, 2927, 1692, 1609, 1528, 1496, 1231, 1107, 1041, 823, 757, 688 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.62 (s, 3 H, acetyl CH_3), 1.68 (s, 3 H, one prenyl CH_3), 1.74 (s, 3 H, the other prenyl CH_3), 2.85 (s, 3 H, pyrazolone CH_3), 4.60 (d, J = 5.6 Hz, 2 H, CH_2), 5.62 (t, J = 6.7 Hz, 1 H, CH=), 7.00–7.96 (m, 9 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.11 (pyrazolone CH_3), 23.08 (acetyl

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CH_3), 27.23 (one prenyl CH_3), 31.30 (the other prenyl CH_3), 68.67 (CH_2), 114.64 (CH=), 117.76, 118.64, 118.87, 119.12, 121.03, 124.85, 127.21, 128.36, 128.78, 129.21, 130.53, 132.71, 138.68, 148.56, 153.58, 164.14 (C=N), 165.63 (C=O) (Ar-C) ppm. MS (ESI): *m*/*z* = 361.2 $[M + H]^+$.

(E)-4-{1-[2-(Propargyloxy)phenyl]ethylidene}-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (Intermediate III): Yellow oil, IR (KBr): $\tilde{\nu}$ = 2966, 2932, 2158, 1695, 1612, 1513, 1494, 1236, 1113, 1038, 815, 754, 691 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.62 (s, 3 H, acetyl CH_3), 1.68 (s, 3 H, one prenyl CH_3), 2.43 (s, 1 H, CH), 4.90 (s, 2 H, CH_2), 7.08–7.98 (m, 9 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.11 (pyrazolone CH_3), 23.08 (acetyl CH_3), 58.34 (CH_2), 74.34 (CH), 79.02 (CCH), 116.22, 118.32, 118.68, 118.97, 120.85, 124.73, 127.46, 128.53, 128.65, 129.64, 130.35, 132.68, 138.46, 148.61, 154.12, 164.02 (C=N), 165.42 (C=O) (Ar-C) ppm. MS (ESI): *m*/*z* = 331.0 $[M + H]^+$.

Spectroscopic Data for Compounds 4a–u, and 5a–l

(5a*R*,11b*S*)-1,11b-Dimethyl-10-nitro-3-phenyl-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4a): Isolated yield (0.683 g, 75%) as white crystals, m.p. 172–174 °C. IR (KBr): $\tilde{\nu}$ = 2983, 2928, 1597, 1518, 1488, 1444, 1341, 1242, 1089, 1045, 831, 757, 695 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.83 (s, 3 H, angular CH_3), 2.26 (m, 1 H, 5a-H), 2.66 (s, 3 H, pyrazolone CH_3), 4.21 (t, *J* = 10.4 Hz, 1 H, 6-H), 4.38 (dd, *J* = 12.0, *J* = 3.6 Hz, 1 H, 5-H), 4.56 (dd, *J* = 11.2, *J* = 3.2 Hz, 1 H, 6′-H), 4.63 (dd, *J* = 12.0, *J* = 3.2 Hz, 1 H, 5′-H), 6.88–8.48 (m, 8 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.34 (pyrazolone CH_3), 29.38 (angular CH_3), 34.26 (C-11b), 37.18 (C-5a), 62.78 (C-5), 68.49 (C-6), 101.93, 117.87, 120.77, 123.77, 125.95, 126.36, 128.93, 129.51, 138.19, 141.73, 146.19, 148.29, 156.78 (Ar-C) ppm. MS (ESI): *m*/*z* = 378.2 $[M + H]^+$. $C_{21}H_{19}N_3O_4$ (378.1): calcd. C 66.83, H 5.07, N 11.13; found C 66.68, H 5.19, N 11.01.

(5a*R*,11b*S*)-3-(3-Chlorophenyl)-1,11b-dimethyl-10-nitro-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4b): Isolated yield (0.785 g, 79%) as white crystals, m.p. 196–198 °C. IR (KBr): $\tilde{\nu}$ = 2978, 2923, 1594, 1518, 1482, 1432, 1339, 1240, 1089, 1048, 849, 783, 742, 676 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.81 (s, 3 H, angular CH_3), 2.24 (m, 1 H, 5a-H), 2.65 (s, 3 H, pyrazolone CH_3), 4.22 (t, *J* = 11.2 Hz, 1 H, 6-H), 4.38 (dd, *J* = 12.4, *J* = 3.6 Hz, 1 H, 5-H), 4.55 (dd, *J* = 12.0, *J* = 3.2 Hz, 1 H, 6′-H), 4.63 (dd, *J* = 12.0, *J* = 3.6 Hz, 1 H, 5′-H), 6.75–8.42 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.10 (pyrazolone CH_3), 29.07 (angular CH_3), 34.68 (C-11b), 37.86 (C-5a), 62.78 (C-5), 69.13 (C-6), 101.65, 116.78, 121.43, 124.02, 128.05, 129.21, 129.54, 129.79, 130.32, 131.54, 135.84, 141.13, 147.34, 149.43, 155.87 ppm. MS (ESI): *m*/*z* = 412.80 $[M + H]^+$. $C_{21}H_{18}ClN_3O_4$ (411.10): calcd. C 61.24, H 4.41, N 10.20; found C 61.38, H 4.52, N 10.08.

(5a*R*,11b*S*)-1,11b-Dimethyl-3-(4-methylphenyl)-10-nitro-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4c): Isolated yield (0.717 g, 76%) as white crystals, m.p. 208–210 °C. IR (KBr): $\tilde{\nu}$ = 2985, 2930, 1589, 1516, 1487, 1434, 1342, 1232, 1079, 1038, 864, 757, 682 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.81 (s, 3 H, angular CH_3), 2.25 (m, 1 H, 5a-H), 2.39 (s, 3 H, CH_3 of phenyl ring), 2.66 (s, 3 H, pyrazolone CH_3), 4.24 (t, *J* = 9.8 Hz, 1 H, 6-H), 4.39 (dd, *J* = 12.2, *J* = 3.6 Hz, 1 H, 5-H), 4.53 (dd, *J* = 11.2, *J* = 3.2 Hz, 1 H, 6′-H), 4.61 (dd, *J* = 12.4, *J* = 3.2 Hz, 1 H, 5′-H), 6.78–8.46 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.43 (pyrazolone CH_3), 21.11 (CH_3 of phenyl ring), 29.46 (angular CH_3), 34.92 (C-11b), 37.54 (C-5a), 63.08 (C-5), 69.02 (C-6), 102.14, 117.32, 120.75, 123.67, 127.34, 129.43, 129.63, 135.21, 135.96, 141.52, 146.32, 148.64, 156.54 ppm. MS (ESI): *m*/*z* = 392.12 $[M + H]^+$. $C_{22}H_{21}N_3O_4$ (391.2): calcd. C 67.51, H 5.41, N 10.74; found C 67.68, H 5.26, N 10.51.

(5a*R*,11b*S*)-1,5,5,11b-Tetramethyl-10-nitro-3-phenyl-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4d): Isolated yield (0.680 g, 79%) as white crystals, m.p. 232–234 °C. IR (KBr): $\tilde{\nu}$ = 2981, 2929, 1598, 1512, 1444, 1339, 1250, 1089, 1041, 832, 756, 694 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.08 (s, 3 H, angular CH_3), 1.67 (s, 3 H, 5-CH_3), 1.79 (s, 3 H, 5′-CH_3′), 2.05 (d, *J* = 4.0, 1 H, 5a-H), 2.79 (s, 3 H, pyrazolone CH_3), 4.58 (d, *J* = 13.2 Hz, 1 H, 6-H), 4.78 (dd, *J* = 13.0, *J* = 4.4 Hz, 1 H, 6′-H), 6.84–8.49 (m, 8 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.73 (pyrazolone CH_3), 22.71 (angular CH_3), 29.12 (CH_3-5), 32.03 (CH_3-5′), 33.77 (C-11b), 46.31 (C-5a), 62.75 (C-6), 82.21 (C-5), 99.99, 116.94, 120.79, 123.74, 124.24, 125.71, 128.88, 129.88, 138.50, 141.73, 146.36, 148.00, 158.04 ppm. MS (ESI): *m*/*z* = 406.15 $[M + H]^+$. $C_{23}H_{23}N_3O_4$ (405.10): calcd. C 68.13, H 5.72, N 10.36; found C 68.41, H 5.40, N 10.42.

(5a*R*,11b*S*)-3-(3-Chlorophenyl)-1,5,5,11b-tetramethyl-10-nitro-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4e): Isolated yield (0.673 g, 72%) as white crystals, m.p. 208–210 °C. IR (KBr): $\tilde{\nu}$ = 2972, 2931, 1604, 1516, 1498, 1437, 1336, 1233, 1091, 1039, 853, 764, 683 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.09 (s, 3 H, angular CH_3), 1.67 (s, 3 H, 5-CH_3), 1.78 (s, 3 H, 5′-CH_3), 2.01 (d, *J* = 4.0, 1 H, 5a-H), 2.76 (s, 3 H, pyrazolone CH_3), 4.57 (d, *J* = 13.2 Hz, 1 H, 6-H), 4.78 (dd, *J* = 13.0, *J* = 4.4 Hz, 1 H, 6′-H), 6.78–8.46 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.13 (pyrazolone CH_3), 22.56 (angular CH_3), 29.72 (CH_3-5), 32.73 (CH_3-5′), 33.76 (C-11b), 46.62 (C-5a), 63.31 (C-6), 82.29 (C-5), 100.55, 117.13, 120.43, 123.87, 128.65, 129.28, 129.64, 129.81, 130.54, 131.73, 136.24, 141.26, 148.01, 149.77, 156.6 ppm. MS (ESI): *m*/*z* = 440.83 $[M + H]^+$. $C_{23}H_{22}ClN_3O_4$ (439.12): calcd. C 62.80, H 5.04, N 9.55; found C 62.59, H 5.16, N 9.49.

(5a*R*,11b*S*)-1,5,5,11b-Tetramethyl-3-(4-methylphenyl)-10-nitro-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4f): Isolated yield (0.695 g, 78%) as white crystals, m.p. 238–240 °C. IR (KBr): $\tilde{\nu}$ = 2977, 2930, 1597, 1518, 1496, 1445, 1341, 1242, 1086, 1041, 863, 758, 688 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.09 (s, 3 H, angular CH_3), 1.68 (s, 3 H, 5-CH_3), 1.78 (s, 3 H, 5′-CH_3), 1.99 (d, *J* = 3.6, 1 H, 5a-H), 2.37 (s, 3 H, CH_3 of phenyl ring), 2.78 (s, 3 H, pyrazolone CH_3), 4.56 (d, *J* = 12.8 Hz, 1 H, 6-H), 4.78 (dd, *J* = 12.4, *J* = 4.0 Hz, 1 H, 6′-H), 6.79–8.47 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.67 (pyrazolone CH_3), 20.01 (CH_3 of phenyl ring), 22.75 (angular CH_3), 29.65 (CH_3-5), 32.87 (CH_3-5′), 33.68 (C-11b), 47.34 (C-5a), 62.24 (C-6), 82.07 (C-5), 102.13, 116.35, 120.57, 123.61, 128.12, 129.72, 130.01, 135.64, 136.23, 141.86, 146.63, 149.20, 157.14 ppm. MS (ESI): *m*/*z* = 420.47 $[M + H]^+$. $C_{24}H_{25}N_3O_4$ (419.20): calcd. C 68.72, H 6.01, N 10.02; found C 68.55, H 6.10, N 10.19.

(5a*R*,11b*S*)-1,11b-Dimethyl-8-nitro-3-phenyl-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4g): Isolated yield (0.738 g, 81%) as white crystals, m.p. 162–164 °C. IR (KBr): $\tilde{\nu}$ = 2983, 2928, 1597, 1518, 1488, 1444, 1340, 1242, 1089, 1045, 831, 757, 695 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.82 (s, 3 H, angular CH_3), 2.28 (m, 1 H, 5a-H), 2.60 (s, 3 H, pyrazolone CH_3), 4.26 (t, *J* = 11.2 Hz, 1 H, 6-H), 4.44 (dd, *J* = 12.4, *J* = 3.2 Hz, 1 H, 5-H), 4.57 (dd, *J* = 11.6, *J* = 3.6 Hz, 1 H, 6′-H), 4.70 (dd, *J* = 12.0, *J* = 3.2 Hz, 1 H, 5′-H), 6.98–7.71 (m, 8 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.40 (pyrazolone CH_3), 29.30 (angular CH_3), 34.38 (C-11b), 37.00 (C-5a), 63.77 (C-5), 68.64 (C-6), 102.05, 120.09, 120.77, 123.96, 125.98, 128.96, 132.09, 134.21, 138.17, 139.44, 145.22, 146.10, 148.45 ppm. MS (ESI): *m*/*z* =

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378.39 [M + H]$^+$. $C_{21}H_{19}N_3O_4$ (377.16): calcd. C 66.83, H 5.07, N 11.13; found C 66.68, H 5.19, N 11.01.

(5a*R*,11b*S*)-3-(3-Chlorophenyl)-1,11b-dimethyl-8-nitro-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4h): Isolated yield (0.775 g, 78%) as white crystals, m.p. 218–220 °C. IR (KBr): $\tilde{\nu}$ = 2967, 2931, 1594, 1516, 1493, 1438, 1338, 1234, 1092, 1041, 864, 756, 685 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.84 (s, 3 H, angular CH_3), 2.29 (m, 1 H, 5a-H), 2.63 (s, 3 H, pyrazolone CH_3), 4.28 (t, J = 11.6 Hz, 1 H, 6-H), 4.46 (dd, J = 12.0, J = 3.2 Hz, 1 H, 5-H), 4.59 (dd, J = 11.2, J = 3.2 Hz, 1 H, 6′-H), 4.73 (dd, J = 12.0, J = 3.6 Hz, 1 H, 5′-H), 6.82–7.76 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.92 (pyrazolone CH_3), 29.16 (angular CH_3), 34.63 (C-11b), 37.45 (C-5a), 63.41 (C-5), 69.24 (C-6), 101.28, 120.15, 120.84, 121.65, 123.87, 125.41, 127.69, 129.52, 133.36, 134.97, 138.75, 139.44, 145.67, 146.76, 148.13 ppm. MS (ESI): m/z = 412.24 [M + H]$^+$. $C_{21}H_{18}ClN_3O_4$ (411.10): calcd. C 61.24, H 4.41, N 10.20; found C 62.08, H 4.32, N 10.26.

(5a*R*,11b*S*)-1,11b-Dimethyl-3-(4-methylphenyl)-8-nitro-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4i): Isolated yield (0.755 g, 80%) as white crystals, m.p. 224–226 °C. IR (KBr): $\tilde{\nu}$ = 2976, 2927, 1589, 1519, 1486, 1440, 1338, 1241, 1089, 1032, 852, 758, 667 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.81 (s, 3 H, angular CH_3), 2.29 (m, 1 H, 5a-H), 2.37 (s, 3 H, CH_3 of phenyl ring), 2.64 (s, 3 H, pyrazolone CH_3), 4.30 (t, J = 10.8 Hz, 1 H, 6-H), 4.44 (dd, J = 12.4, J = 3.6 Hz, 1 H, 5-H), 4.56 (dd, J = 11.6, J = 3.2 Hz, 1 H, 6′-H), 4.74 (dd, J = 11.6, J = 3.2 Hz, 1 H, 5′-H), 6.89–7.79 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.72 (pyrazolone CH_3), 21.53 (CH_3 of phenyl ring), 29.35 (angular CH_3), 34.56 (C-11b), 37.86 (C-5a), 63.18 (C-5), 69.75 (C-6), 101.90, 120.43, 120.85, 121.07, 123.46, 132.19, 134.27, 135.47, 135.96, 139.64, 145.46, 146.14, 148.34 ppm. MS (ESI): m/z = 392.42 [M + H]$^+$. $C_{22}H_{21}N_3O_4$ (391.12): calcd. C 67.51, H 5.41, N 10.74; found C 67.68, H 5.46, N 10.31.

(5a*R*,11b*S*)-1,5,5,11b-Tetramethyl-8-nitro-3-phenyl-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4j): Isolated yield (0.672 g, 78%) as white crystals, m.p. 220–222 °C. IR (KBr): $\tilde{\nu}$ = 2976, 2931, 1586, 1515, 1436, 1339, 1245, 1043, 1034, 848, 758, 668 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10 (s, 3 H, angular CH_3), 1.66 (s, 3 H, 5-CH_3), 1.78 (s, 3 H, 5′-CH_3), 2.02 (d, J = 3.6, 1 H, 5a-H), 2.76 (s, 3 H, pyrazolone CH_3), 4.56 (d, J = 11.6 Hz, 1 H, 6-H), 4.77 (dd, J = 12.8, J = 4.0 Hz, 1 H, 6′-H), 6.72–7.78 (m, 8 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.24 (pyrazolone CH_3), 22.13 (angular CH_3), 28.88 (CH_3-5), 32.43 (CH_3-5′), 34.06 (C-11b), 46.43 (C-5a), 62.65 (C-6), 82.64 (C-5), 101.56, 120.26, 120.85, 123.67, 125.79, 128.36, 131.94, 134.46, 138.33, 139.87, 145.46, 146.57, 148.94 ppm. MS (ESI): m/z = 406.14 [M + H]$^+$. $C_{23}H_{23}N_3O_4$ (405.19): calcd. C 68.13, H 5.72, N 10.36; found C 68.51, H 5.46, N 10.12.

(5a*R*,11b*S*)-3-(3-Chlorophenyl)-1,5,5,11b-tetramethyl-8-nitro-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4k): Isolated yield (0.692 g, 74%) as white crystals, m.p. 224–226 °C. IR (KBr): $\tilde{\nu}$ = 2983, 2933, 1593, 1517, 1443, 1342, 1239, 1084, 1037, 858, 757, 679 cm^{-1}. ^{1}H NMR(400 MHz, $CDCl_3$): δ = 1.09 (s, 3 H, angular CH_3), 1.66 (s, 3 H, 5-CH_3), 1.79 (s, 3 H, 5′-CH_3), 1.99 (d, J = 3.6, 1 H, 5a-H), 2.78 (s, 3 H, pyrazolone CH_3), 4.58 (d, J = 10.8 Hz, 1 H, 6-H), 4.79 (dd, J = 12.4, J = 4.0 Hz, 1 H, 6′-H), 6.71–7.83 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.69 (pyrazolone CH_3), 22.86 (angular CH_3), 29.45 (CH_3-5), 32.64 (CH_3-5′), 33.28 (C-11b), 46.83 (C-5a), 63.15 (C-6), 82.58 (C-5), 100.79, 120.54, 121.68, 121.98, 123.75, 125.69, 127.88, 129.62, 133.46, 134.76, 137.60, 139.16, 145.74, 146.93, 149.24 ppm. MS (ESI): m/z = 440.89 [M + H]$^+$. $C_{23}H_{22}ClN_3O_4$ (439.15): calcd. C 62.80, H 5.04, N 9.55; found C 62.67, H 5.16, N 9.29.

(5a*R*,11b*S*)-1,5,5,11b-Tetramethyl-3-(4-methylphenyl)-8-nitro-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4l): Isolated yield (0.633 g, 71%) as white crystals, m.p. 218–220 °C. IR (KBr): $\tilde{\nu}$ = 2978, 2928, 1585, 1516, 1438, 1337, 1242, 1091, 1041, 864, 756, 686 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.07 (s, 3 H, angular CH_3), 1.66 (s, 3 H, 5-CH_3), 1.79 (s, 3 H, 5′-CH_3), 2.00 (d, J = 3.6, 1 H, 5a-H), 2.39 (s, 3 H, CH_3 of phenyl ring), 2.80 (s, 3 H, pyrazolone CH_3), 4.59 (d, J = 10.8 Hz, 1 H, 6-H), 4.76 (dd, J = 12.0, J = 3.2 Hz, 1 H, 6′-H), 6.78–7.87 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.46 (pyrazolone CH_3), 20.83 (CH_3 of phenyl ring), 23.14 (angular CH_3), 29.65 (CH_3-5), 32.48 (CH_3-5′), 33.42 (C-11b), 46.59 (C-5a), 61.94 (C-6), 81.76 (C-5), 101.48, 120.56, 121.17, 121.61, 123.73, 132.53, 134.42, 135.53, 135.91, 139.21, 145.32, 145.49, 148.75 ppm. MS (ESI): m/z = 420.27 [M + H]$^+$. $C_{24}H_{25}N_3O_4$ (419.18): calcd. C 68.72, H 6.01, N 10.02; found C 68.51, H 6.26, N 10.13.

(5a*R*,11b*S*)-1,11b-Dimethyl-3-phenyl-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4m): Isolated yield (0.735 g, 78%) as white crystals, m.p. 152–154 °C. IR (KBr): $\tilde{\nu}$ = 2957, 2927, 1595, 1516, 1485, 1442, 1227, 1093, 1048, 840, 756, 692 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.81 (s, 3 H, angular CH_3), 2.16 (m, 1 H, 5a-H), 2.64 (s, 3 H, pyrazolone CH_3), 4.27 (m, 2 H, 5-H and 6-H), 4.53 (dd, J = 11.2, J = 3.6 Hz, 1 H, 6′-H), 4.58 (dd, J = 12.0, J = 2.8 Hz, 1 H, 5′-H), 6.80–7.73 (m, 9 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.47 (pyrazolone CH_3), 29.64 (angular CH_3), 34.07 (C-11b), 37.85 (C-5a), 62.86 (C-5), 69.07 (C-6), 103.15, 117.09, 120.71, 121.10, 125.68, 127.87, 128.89, 129.09, 129.60, 138.45, 146.50, 148.51, 151.16 ppm. MS (ESI): m/z = 333.20 [M + H]$^+$. $C_{21}H_{20}N_2O_2$ (332.19): calcd. C 75.88, H 6.06, N 8.43; found C 75.62, H 6.21, N 8.67.

(5a*R*,11b*S*)-1,5,5,11b-Tetramethyl-3-phenyl-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4n): Isolated yield (0.670 g, 76%) as white crystals, m.p. 170–172 °C. IR (KBr): $\tilde{\nu}$ = 2981, 2929, 1597, 1511, 1491, 1443, 1230, 1084, 1043, 838, 757, 673 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.09 (s, 3 H, angular CH_3), 1.64 (s, 3 H, 5-CH_3), 1.77 (s, 3 H, 5′-CH_3), 1.98 (d, J = 3.2, 1 H, 5a-H), 2.71 (s, 3 H, pyrazolone CH_3), 4.43 (td, J = 12.8, J = 1.2 Hz, 1 H, 6-H), 4.72 (ddd, J = 12.6, J = 4.4, J = 2.0 Hz, 1 H, 6′-H), 6.76–7.78 (m, 9 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.78 (pyrazolone CH_3), 22.75 (angular CH_3), 29.21 (CH_3-5), 32.07 (CH_3-5′), 33.64 (C-11b), 47.11 (C-5a), 61.95 (C-6), 82.72 (C-5), 101.20, 116.29, 120.65, 120.99, 125.41, 127.50, 127.69, 128.83, 129.22, 138.75, 146.76, 148.13, 152.67 ppm. MS (ESI): m/z = 361.24 [M + H]$^+$. $C_{23}H_{24}N_2O_2$ (360.18): calcd. C 76.64, H 6.71, N 7.77; found C 76.41, H 6.59, N 7.91.

(11b*S*)-1,11b-Dimethyl-10-nitro-3-phenyl-3,11b-dihydro-6*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4o): Isolated yield (0.561 g, 65%) as white crystals, m.p. 170–173 °C. IR (KBr): $\tilde{\nu}$ = 2972, 2927, 1686, 1518, 1476, 1443, 1339, 1231, 1096, 1039, 856, 757, 683 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.85 (s, 3 H, angular CH_3), 2.64 (s, 3 H, pyrazolone CH_3), 4.64 (d, J = 12.0 Hz, 1 H, 6-H), 5.14 (dd, J = 11.6, J = 1.2 Hz, 1 H, 6′-H), 6.55 (d, J = 1.2 Hz, 1 H, 5-H), 6.75–8.73 (m, 8 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.75 (pyrazolone CH_3), 27.56 (angular CH_3), 35.87 (C-11b), 65.89 (C-6), 101.23, 115.45, 117.54, 120.46, 123.34, 125.05, 126.43, 129.86, 131.42, 134.77, 138.85, 141.43, 146.42, 148.46, 158.53 ppm. MS (ESI): m/z = 376.23 [M + H]$^+$. $C_{21}H_{17}N_3O_4$ (375.12): calcd. C 67.19, H 4.56, N 11.19; found C 66.92, H 4.78, N 11.01.

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11b*S*)-3-(3-Chlorophenyl)-1,11b-dimethyl-10-nitro-3,11b-dihydro-6*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4p): Isolated yield (0.669 g, 71%) as white crystals, m.p. 218–220 °C. IR (KBr): $\tilde{\nu}$ = 2971, 2928, 1691, 1520, 1478, 1427, 1336, 1242, 1094, 1046, 868, 767, 691 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.86 (s, 3 H, angular CH_3), 2.66 (s, 3 H, pyrazolone CH_3), 4.65 (d, J = 12.0 Hz, 1 H, 6-H), 5.17 (dd, J = 11.2, J = 1.2 Hz, 1 H, 6′-H), 6.57 (d, J = 0.8 Hz, 1 H, 5-H), 6.79–8.48 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.75 (pyrazolone CH_3), 27.23 (angular CH_3), 36.42 (C-11b), 64.74 (C-6), 100.23, 115.68, 117.16, 120.43, 123.69, 128.71, 129.67, 129.93, 130.43, 130.92, 132.68, 134.35, 136.59, 142.12, 146.85, 149.56, 157.49 ppm. MS (ESI): m/z = 410.82 [M + H]$^+$. $C_{21}H_{16}ClN_3O_4$ (409.1): calcd. C 61.54, H 3.94, N, 10.25; found C 61.28, H, 4.17, N 10.02.

(11b*S*)-1,11b-Dimethyl-3-(4-methylphenyl)-10-nitro-3,11b-dihydro-6*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4q): Isolated yield (0.654 g, 73%) as white crystals, m.p. 203–205 °C. IR (KBr): $\tilde{\nu}$ = 2968, 2927, 1681, 1517, 1473, 1433, 1339, 1229, 1084, 1039, 871, 758, 682 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.86 (s, 3 H, angular CH_3), 2.36 (s, 3 H, CH_3 of phenyl ring), 2.66 (s, 3 H, pyrazolone CH_3), 4.67 (d, J = 12.4 Hz, 1 H, 6′-H), 5.18 (dd, J = 12.8, J = 1.6 Hz, 1 H, 6-H), 6.62 (d, J = 1.2 Hz, 1 H, 5-H), 6.76–8.49 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.43 (pyrazolone CH_3), 20.64 (CH_3 of phenyl ring), 27.42 (angular CH_3), 36.37 (C-11b), 64.59 (C-6), 101.12, 115.63, 117.56, 120.46, 124.65, 127.86, 129.87, 130.48, 134.73, 136.47, 137.24, 141.38, 146.79, 148.68, 157.82 ppm. MS (ESI): m/z = 390.20 [M + H]$^+$. $C_{22}H_{19}N_3O_4$ (389.12): calcd. C 67.86, H 4.92, N 10.79; found C 67.49, H 4.67, N 11.06.

(11b*S*)-1,11b-Dimethyl-8-nitro-3-phenyl-3,11b-dihydro-6*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4r): Isolated yield (0.579 g, 67%) as white crystals, m.p. 182–184 °C. IR (KBr): $\tilde{\nu}$ = 2969, 2928, 1689, 1516, 1481, 1436, 1231, 1086, 1041, 856, 759, 690 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.85 (s, 3 H, angular CH_3), 2.65 (s, 3 H, pyrazolone CH_3), 4.63 (d, J = 12.0 Hz, 1 H, 6′-H), 5.16 (dd, J = 12.4, J = 1.2 Hz, 1 H, 6-H), 6.57 (d, J = 1.2 Hz, 1 H, 5-H), 6.75–7.83 (m, 8 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.72 (pyrazolone CH_3), 27.33 (angular CH_3), 36.42 (C-11b), 65.67 (C-6), 101.67, 115.42, 120.32, 120.94, 124.63, 125.87, 129.32, 132.16, 134.21, 135.36, 138.74, 140.23, 145.63, 146.46, 148.45 ppm. MS (ESI): m/z = 376.38 [M + H]$^+$. $C_{21}H_{17}N_3O_4$ (375.18): calcd. C 67.19, H 4.56, N 11.19; found C 67.42, H 4.91, N 11.41.

(11b*S*)-3-(3-Chlorophenyl)-1,11b-dimethyl-8-nitro-3,11b-dihydro-6*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4s): Isolated yield (0.613 g, 65%) as white crystals, m.p. 206–208 °C. IR (KBr): $\tilde{\nu}$ = 2967, 2925, 1691, 1517, 1483, 1428, 1231, 1075, 1037, 876, 767, 692 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.87 (s, 3 H, angular CH_3), 2.66 (s, 3 H, pyrazolone CH_3), 4.62 (d, J = 12.0 Hz, 1 H, 6′-H), 5.18 (dd, J = 12.4, J = 1.2 Hz, 1 H, 6-H), 6.56 (d, J = 1.2 Hz, 1 H, 5-H), 6.74–7.78 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.34 (pyrazolone CH_3), 28.03 (angular CH_3), 37.02 (C-11b), 65.39 (C-6), 101.43, 115.76, 120.46, 121.67, 122.43, 124.07, 125.49, 127.66, 129.64, 133.23, 134.52, 135.16, 138.48, 139.57, 145.73, 146.89, 148.46 ppm. MS (ESI): m/z = 410.22 [M + H]$^+$. $C_{21}H_{16}ClN_3O_4$ (409.13): calcd. C 61.54, H 3.94, N 10.25; found C 61.87, H 3.57, N 10.53.

(11b*S*)-1,11b-Dimethyl-3-(4-methylphenyl)-8-nitro-3,11b-dihydro-6*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4t): Isolated yield (0.627 g, 70%) as white crystals, m.p. 196–197 °C. IR (KBr): $\tilde{\nu}$ = 2969, 2925, 1681, 1517, 1475, 1428, 1338, 1229, 1101, 1042, 870, 759, 682 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.85 (s, 3 H, angular CH_3), 2.34 (s, 3 H, CH_3 of phenyl ring), 2.64 (s, 3 H, pyrazolone CH_3), 4.66 (d, J = 12.4 Hz, 1 H, 6-H), 5.20 (dd, J = 12.0, J = 1.2 Hz, 1 H, 6′-H), 6.58 (d, J = 1.2 Hz, 1 H, 5-H), 6.87–7.78 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.18 (pyrazolone CH_3), 20.23 (CH_3 of phenyl ring), 27.64 (angular CH_3), 36.68 (C-11b), 64.35 (C-6), 101.26, 115.16, 120.54, 121.34, 122.03, 123.46, 132.17, 134.56, 134.89, 135.64, 137.12, 139.65, 145.37, 146.87, 148.54 ppm. MS (ESI): m/z = 390.29 [M + H]$^+$. $C_{22}H_{19}N_3O_4$ (389.20): calcd. C 67.86, H 4.92, N 10.79; found C 67.44, H 5.17, N 11.03.

(11b*S*)-1,11b-Dimethyl-3-phenyl-3,11b-dihydro-6*H*-chromeno-[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (4u): Isolated yield (0.683 g, 72%) as white crystals, m.p. 156–158 °C. IR (KBr): $\tilde{\nu}$ = 2969, 2927, 1672, 1595, 1518, 1488, 1451, 1227, 1109, 1039, 844, 753, 683 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.87 (s, 3 H, angular CH_3), 2.66 (s, 3 H, pyrazolone CH_3), 4.65 (d, J = 12.4 Hz, 1 H, 6-H), 5.17 (dd, J = 12.0, J = 1.6 Hz, 1 H, 6′-H), 6.56 (d, J = 1.2 Hz, 1 H, 5-H), 6.87–7.73 (m, 9 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.10 (pyrazolone CH_3), 27.67 (angular CH_3), 36.05 (C-11b), 65.02 (C-6), 100.05, 115.01, 117.59, 120.75, 121.10, 125.19, 126.32, 128.08, 129.07, 133.48, 134.02, 137.99, 145.55, 146.44, 152.78 ppm. MS (ESI): m/z = 331.38 [M + H]$^+$. $C_{21}H_{18}N_2O_2$ (330.20): calcd. C 76.34, H 5.49, N 8.48; found C 76.05, H 5.76, N 8.28.

(5a*R*,11b*S*)-1,11b-Dimethyl-3-phenyl-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazol-10-amine (5a): Isolated yield (0.565 g, 72%) as a pinkish white powder, m.p. 118–120 °C. IR (KBr): $\tilde{\nu}$ = 3454, 3336, 2971, 2925, 1632, 1594, 1578, 1521, 1497, 1443, 1227, 1095, 1049, 159, 681 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.78 (s, 3 H, angular CH_3), 2.12 (m, 1 H, 5a-H), 2.64 (s, 3 H, pyrazolone CH_3), 4.28 (t, J = 10.4 Hz, 1 H, 6-H), 4.26 (dd, J = 12.0, J = 3.6 Hz, 1 H, 5-H), 4.56 (dd, J = 11.2, J = 3.2 Hz, 1 H, 6′-H), 4.63 (dd, J = 12.0, J = 3.2 Hz, 1 H, 5′-H), 4.77 (s, 2 H, NH_2), 6.50–7.71 (m, 8 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.53 (pyrazolone CH_3), 29.44 (angular CH_3), 34.26 (C-11b), 38.03 (C-5a), 62.67 (C-5), 69.34 (C-6), 103.18, 115.84, 115.87, 117.66, 120.79, 125.72, 128.89, 129.89, 138.36, 139.95, 143.94, 146.41, 148.70 ppm. MS (ESI): m/z = 348.41 [M + H]$^+$. $C_{21}H_{21}N_3O_2$ (347.18): calcd. C 72.60, H 6.09, N 12.10; found C 72.45, H 6.54, N 11.16.

(5a*R*,11b*S*)-3-(3-Chlorophenyl)-1,11b-dimethyl-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazol-10-amine (5b): Isolated yield (0.741 g, 86%) as an off-white powder, m.p. 110–112 °C. IR (KBr): $\tilde{\nu}$ = 3387, 3336, 2971, 2924, 1615, 1593, 1526, 1497, 1443, 1395, 1228, 1097, 1044, 865, 759, 645 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.67 (s, 3 H, angular CH_3), 2.10 (m, 1 H, 5a-H), 2.53 (s, 3 H, pyrazolone CH_3), 4.02 (t, J = 10.4 Hz, 1 H, 6-H), 4.36 (dd, J = 12.0, J = 3.6 Hz, 1 H, 5-H), 4.58 (dd, J = 11.2, J = 3.2 Hz, 1 H, 6′-H), 4.62 (dd, J = 12.0, J = 3.2 Hz, 1 H, 5′-H), 4.94 (s, 2 H, NH_2), 6.35–7.54 (m, 8 H, Ar-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 16.59 (pyrazolone CH_3), 29.34 (angular CH_3), 34.31 (C-11b), 38.09 (C-5a), 62.70 (C-5), 69.39 (C-6), 103.21, 115.89, 115.92, 117.63, 120.76, 125.78, 128.86, 129.87, 138.38, 139.85, 143.91, 146.51, 148.76 ppm. MS (ESI): m/z = 382.86 [M + H]$^+$. $C_{21}H_{20}ClN_3O_2$ (381.20): calcd. C 66.05, H 5.28, N 11.00; found C 66.38, H 5.12, N 11.08.

(5a*R*,11b*S*)-1,11b-Dimethyl-3-(4-methylphenyl)-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazol-10-amine (5c): Isolated yield (0.613 g, 75%) as a white powder, m.p. 98–100 °C. IR (KBr): $\tilde{\nu}$ = 3431, 3206, 2986, 2926, 1604, 1521, 1489, 1446, 1363, 1246, 1091, 1046, 836, 753, 696 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 1.79 (s, 3 H, angular CH_3), 2.13 (m, 1 H, 5a-H), 2.65 (s, 3 H, pyrazolone CH_3), 4.26 (t, J = 10.4 Hz, 1 H, 6-H), 4.23 (dd,

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J = 12.0, J = 3.6 Hz, 1 H, 5-H), 4.57 (dd, J = 11.2, J = 3.2 Hz, 1 H, 6′-H), 4.64 (dd, J = 12.0, J = 3.2 Hz, 1 H, 5′-H), 4.76 (s, 2 H, NH_2), 6.51–7.72 (m, 8 H, Ar-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 16.56 (pyrazolone CH_3), 29.39 (angular CH_3), 34.36 (C-11b), 38.09 (C-5a), 62.68 (C-5), 69.33 (C-6), 103.20, 115.84, 115.87, 117.66, 120.79, 125.74, 128.89, 129.89, 138.34, 139.91, 143.94, 146.48, 148.73 ppm. MS (ESI): m/z = 362.49 [M + H]$^+$. $C_{22}H_{23}N_3O_2$ (361.18): calcd. C 73.11, H 6.41, N 11.63; found C 73.21, H 6.38, N 11.56.

(5aR,11bS)-1,5,5,11b-Tetramethyl-3-phenyl-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazol-10-amine (5d): Isolated yield (0.670 g, 89%) as a white powder, m.p. 162–164 °C. IR (KBr): $\tilde{\nu}$ = 3432, 3215, 2984, 2930, 1523, 1488, 1447, 1361, 1241, 1088, 1044, 839, 751, 693 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.09 (s, 3 H, angular CH_3), 1.68 (s, 3 H, 5-CH_3), 1.78 (s, 3 H, 5′-CH_3), 1.99 (d, J = 3.4, 1 H, 5a-H), 2.37 (s, 3 H, CH_3 of phenyl ring), 2.78 (s, 3 H, pyrazolone CH_3), 4.56 (d, J = 12.7 Hz, 1 H, 6-H), 4.78 (dd, J = 12.6, J = 4.0 Hz, 1 H, 6′-H), 4.80 (s, 2 H, NH_2), 6.79–8.47 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 16.67 (pyrazolone CH_3), 20.01 (CH_3 of phenyl ring), 22.75 (angular CH_3), 29.65 (CH_3-5), 32.87 (CH_3-5′), 33.68 (C-11b), 47.34 (C-5a), 62.24 (C-6), 82.07 (C-5), 102.13, 116.35, 120.57, 123.61, 128.12, 129.72, 130.01, 135.64, 136.23, 141.86, 146.63, 149.20, 157.14 ppm. MS (ESI): m/z = 376.49 [M + H]$^+$. $C_{23}H_{25}N_3O$ (375.15): calcd. C 73.57, H 6.71, N 11.19; found C 73.48, H 6.89, N 11.28.

(5a*R*,11b*S*)-3-(3-Chlorophenyl)-1,5,5,11b-tetramethyl-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazol-10-amine (5e): Isolated yield (0.583 g, 71%) as a yellow powder, m.p. 132–134 °C. IR (KBr): $\tilde{\nu}$ = 3430, 3204, 2986, 2930, 1521, 1485, 1443, 1362, 1243, 1085, 1036, 832, 732, 689 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.08 (s, 3 H, angular CH_3), 1.66 (s, 3 H, 5-CH_3), 1.76 (s, 3 H, 5′-CH_3), 1.96 (d, J = 3.8, 1 H, 5a-H), 2.36 (s, 3 H, CH_3 of phenyl ring), 2.75 (s, 3 H, pyrazolone CH_3), 4.53 (d, J = 12.7 Hz, 1 H, 6-H), 4.76 (dd, J = 12.6, J = 4.2 Hz, 1 H, 6′-H), 4.78 (s, 2 H, NH_2), 6.78–8.46 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 16.63 (pyrazolone CH_3), 20.08 (CH_3 of phenyl ring), 22.76 (angular CH_3), 29.66 (CH_3-5), 32.91 (CH_3-5′), 33.70 (C-11b), 47.36 (C-5a), 62.36 (C-6), 82.05 (C-5), 102.16, 116.30, 120.59, 123.59, 128.16, 129.80, 130.10, 135.70, 136.26, 141.89, 146.66, 149.28, 157.20 ppm. MS (ESI): m/z = 410.97 [M + H]$^+$. $C_{23}H_{24}ClN_3O_2$ (409.12): calcd. C 67.39, H 5.90, N 10.25; found C 67.86, H 6.01, N 10.32.

(5a*R*,11b*S*)-1,5,5,11b-Tetramethyl-3-(4-methylphenyl)-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazol-10-amine (5f): Isolated yield (0.571 g, 73%) as a white powder, m.p. 143–145 °C. IR (KBr): $\tilde{\nu}$ = 3436, 3209, 2986, 2930, 1521, 1485, 1443, 1362, 1243, 1085, 1036, 832, 732, 689 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.06 (s, 3 H, angular CH_3), 1.65 (s, 3 H, 5-CH_3), 1.76 (s, 3 H, 5′-CH_3), 1.98 (d, J = 3.6, 1 H, 5a-H), 2.38 (s, 3 H, CH_3 of phenyl ring), 2.76 (s, 3 H, pyrazolone CH_3), 4.58 (d, J = 12.8 Hz, 1 H, 6-H), 4.76 (dd, J = 12.4, J = 4.0 Hz, 1 H, 6′-H), 4.79 (s, 2 H, NH_2), 6.76–8.47 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 16.65 (pyrazolone CH_3), 20.20 (CH_3 of phenyl ring), 22.70 (angular CH_3), 29.63 (CH_3-5), 32.86 (CH_3-5′), 33.70 (C-11b), 47.30 (C-5a), 62.28 (C-6), 82.11 (C-5), 102.12, 116.39 120.60, 123.66, 128.19, 129.69, 130.06, 135.69, 136.29, 141.91, 146.69, 149.27, 157.16 ppm. MS (ESI): m/z = 390.49 [M + H]$^+$. $C_{24}H_{27}N_3O_2$ (389.23): calcd. C 74.01, H 6.99, N 10.79; found C 74.20, H 6.56, N 10.63.

(5a*R*,11b*S*)-1,11b-Dimethyl-3-phenyl-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazol-8-amine (5g): Isolated yield (0.581 g, 74%) as a white powder, m.p. 116–118 °C. IR (KBr): $\tilde{\nu}$ = 3330, 3207, 2928, 1518, 1488, 1444, 1360, 1242, 1089, 1045, 831, 757, 695 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.83 (s, 3 H, angular CH_3), 2.28 (m, 1 H, 5a-H), 2.60 (s, 3 H, pyrazolone CH_3), 4.26 (t, J = 11.2 Hz, 1 H, 6-H), 4.44 (dd, J = 12.4, J = 3.2 Hz, 1 H, 5-H), 4.57 (dd, J = 11.6, J = 3.6 Hz, 1 H, 6′-H), 4.70 (dd, J = 12.0, J = 3.2 Hz, 1 H, 5′-H), 4.73 (s, 2 H, NH_2), 6.98–7.71 (m, 8 H, Ar-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 16.40 (pyrazolone CH_3), 29.30 (angular CH_3), 34.38 (C-11b), 37.00 (C-5a), 63.77 (C-5), 68.64 (C-6), 102.05, 120.09, 120.77, 123.96, 125.98, 128.96, 132.09, 134.21, 138.17, 139.44, 145.22, 146.10, 148.45 ppm. MS (ESI): m/z = 348.23 [M + H]$^+$. $C_{21}H_{21}N_3O_2$ (347.20): calcd. C 72.60, H 6.09, N 12.10; found C 72.68, H 5.99, N 12.19.

(5a*R*,11b*S*)-3-(3-Chlorophenyl)-1,11b-dimethyl-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazol-8-amine (5h): Isolated yield (0.706 g, 82%) as a pink powder, m.p. 138–140 °C. IR (KBr): $\tilde{\nu}$ = 3335, 3210, 2931, 1516, 1438, 1360, 1338, 1234, 1092, 1041, 864, 756, 685 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.84 (s, 3 H, angular CH_3), 2.26 (m, 1 H, 5a-H), 2.64 (s, 3 H, pyrazolone CH_3), 4.26 (t, J = 11.8 Hz, 1 H, 6-H), 4.46 (dd, J = 12.2, J = 3.1 Hz, 1 H, 5-H), 4.59 (dd, J = 11.2, J = 3.4 Hz, 1 H, 6′-H), 4.73 (dd, J = 12.1, J = 3.4 Hz, 1 H, 5′-H), 4.76 (s, 2 H, NH_2), 6.84–7.74 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 15.93 (pyrazolone CH_3), 29.21 (angular CH_3), 34.66 (C-11b), 37.49 (C-5a), 63.51 (C-5), 69.30 (C-6), 101.29, 120.17, 120.90, 121.70, 123.86, 125.50, 127.71, 129.53, 133.37, 134.99, 138.79, 139.51, 145.59, 146.78, 148.20 ppm. MS (ESI): m/z = 382.86 [M + H]$^+$. $C_{21}H_{20}ClN_3O_2$ (381.20): calcd. C 66.05, H 5.28, N 11.00; found C 66.39, H 5.77, N 11.25.

(5a*R*,11b*S*)-1,11b-Dimethyl-3-(4-methylphenyl)-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazol-8-amine (5i): Isolated yield (0.694 g, 85%) as a white powder, m.p. 147–149 °C; IR (KBr): $\tilde{\nu}$ = 3334, 3201, 2978, 2927, 1486, 1440, 1338, 1241, 1089, 1032, 852, 758, 667 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.82 (s, 3 H, angular CH_3), 2.28 (m, 1 H, 5a-H), 2.36 (s, 3 H, CH_3 of phenyl ring), 2.65 (s, 3 H, pyrazolone CH_3), 4.32 (t, J = 10.8 Hz, 1 H, 6-H), 4.46 (dd, J = 12.6, J = 3.4 Hz, 1 H, 5-H), 4.56 (dd, J = 11.4, J = 3.4 Hz, 1 H, 6′-H), 4.76 (dd, J = 11.6, J = 3.4 Hz, 1 H, 5′-H), 4.79 (s, 2 H, NH_2), 6.86–7.76 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 16.76 (pyrazolone CH_3), 21.60 (CH_3 of phenyl ring), 29.38 (angular CH_3), 34.58 (C-11b), 37.90 (C-5a), 63.19 (C-5), 69.79 (C-6), 101.96, 120.49, 120.86, 121.03, 123.66, 132.20, 134.26, 135.46, 135.99, 139.63, 145.49, 146.12, 148.40 ppm. MS (ESI): m/z = 362.34 [M + H]$^+$. $C_{22}H_{23}N_3O_2$ (361.20): calcd. C 73.11, H 6.41, N 11.63; found C 73.07, H 6.86, N 11.31.

(5a*R*,11b*S*)-1,5,5,11b-Tetramethyl-3-phenyl-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazol-8-amine (5j): Isolated yield (0.549 g, 73%) as a brown powder, m.p. 115–117 °C. IR (KBr): $\tilde{\nu}$ = 3328, 3211, 2973, 2926, 1486, 1440, 1338, 1241, 1089, 1032, 852, 758, 667 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.10 (s, 3 H, angular CH_3), 1.66 (s, 3 H, 5-CH_3), 1.78 (s, 3 H, 5′-CH_3), 2.02 (d, J = 3.6, 1 H, 5a-H), 2.76 (s, 3 H, pyrazolone CH_3), 4.56 (d, J = 11.6 Hz, 1 H, 6-H), 4.77 (dd, J = 12.8, J = 4.0 Hz, 1 H, 6′-H), 4.80 (s, 2 H, NH_2), 6.72–7.78 (m, 8 H, Ar-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 16.24 (pyrazolone CH_3), 22.13 (angular CH_3), 28.88 (CH_3-5), 32.43 (CH_3-5′), 34.06 (C-11b), 46.43 (C-5a), 62.65 (C-6), 82.64 (C-5), 101.56, 120.26, 120.85, 123.67, 125.79, 128.36, 131.94, 134.46, 138.33, 139.87, 145.46, 146.57, 148.94 ppm. MS (ESI): m/z = 376.46 [M + H]$^+$. $C_{23}H_{25}N_3O_2$ (375.21): calcd. C 73.57, H 6.71, N 11.19; found C 73.68, H 6.34, N 11.08.

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(5a*R*,11b*S*)-3-(3-Chlorophenyl)-1,5,5,11b-tetramethyl-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazol-8-amine (5k): Isolated yield (0.576 g, 70%) as a reddish powder, m.p. 152–154 °C. IR (KBr): $\tilde{\nu}$ = 3331, 3205, 2978, 2930, 1484, 1442, 1341, 1243, 1086, 1030, 859, 760, 681 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 1.08 (s, 3 H, angular CH_3), 1.68 (s, 3 H, 5-CH_3), 1.76 (s, 3 H, 5′-CH_3), 1.98 (d, J = 3.6, 1 H, 5a-H), 2.76 (s, 3 H, pyrazolone CH_3), 4.56 (d, J = 10.8 Hz, 1 H, 6-H), 4.76 (s, 2 H, NH_2), 4.79 (dd, J = 12.4, J = 4.0 Hz, 1 H, 6′-H), 6.72–7.84 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 16.70 (pyrazolone CH_3), 22.84 (angular CH_3), 29.49 (CH_3-5), 32.62 (CH_3-5′), 33.30 (C-11b), 46.88 (C-5a), 63.20 (C-6), 82.56 (C-5), 100.60, 120.60, 121.71, 121.89, 123.80, 125.71, 127.86, 129.68, 133.56, 134.80, 137.68, 139.20, 145.78, 146.98, 149.30 ppm. MS (ESI): m/z = 410.99 $[M + H]^+$. $C_{23}H_{24}ClN_3O_2$ (409.23): calcd. C 67.39, H 5.90, N 10.25; found C 67.46, H 5.58, N 10.67.

(5a*R*,11b*S*)-1,5,5,11b-Tetramethyl-3-(4-methylphenyl)-3,5a,6,11b-tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazol-8-amine (5l): Isolated yield (0.648 g, 83%) as a yellow powder, m.p. 126–128 °C. IR (KBr): $\tilde{\nu}$ = 3331, 3204, 2978, 2930, 1484, 1442, 1341, 1243, 1086, 1030, 859, 760, 681 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 1.07 (s, 3 H, angular CH_3), 1.66 (s, 3 H, 5-CH_3), 1.79 (s, 3 H, 5′-CH_3), 2.00 (d, J = 3.6, 1 H, 5a-H), 2.39 (s, 3 H, CH_3 of phenyl ring), 2.80 (s, 3 H, pyrazolone CH_3), 4.59 (d, J = 10.8 Hz, 1 H, 6-H), 4.76 (dd, J = 12.0, J = 3.2 Hz, 1 H, 6′-H), 4.78 (s, 2 H, NH_2), 6.78–7.87 (m, 7 H, Ar-H) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 17.46 (pyrazolone CH_3), 20.83 (CH_3 of phenyl ring), 23.14 (angular CH_3), 29.65 (CH_3-5), 32.48 (CH_3-5′), 33.42 (C-11b), 46.59 (C-5a), 61.94 (C-6), 81.76 (C-5), 101.48, 120.56, 121.17, 121.61, 123.73, 132.53, 134.42, 135.53, 135.91, 139.21, 145.32, 145.49, 148.75 ppm. MS (ESI): m/z = 390.50 $[M + H]^+$. $C_{24}H_{27}N_3O_2$ (389.23): calcd. C 74.01, H 6.99, N 10.79; found C 74.51, H 6.56, N 10.13.

Supporting Information (see footnote on the first page of this article): General information and experimental procedures, characterization of compounds, spectra.

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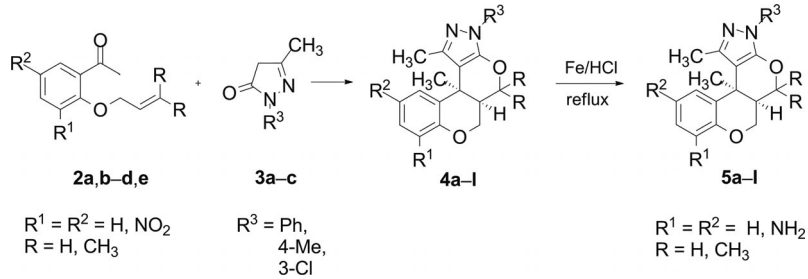

A solvent-free, tetrabutylammonium-hydrogensulfate-catalysed method to synthesise angular aminobenzopyrano[2,3-*c*]-pyrazole precursors by a domino Knoevenagel–hetero-Diels–Alder (DKHDA) reaction has been developed. When nitro-containing DKHDA products were treated further with Fe/HCl in tandem, they smoothly underwent a subsequent reduction, facilitating access to aminobenzopyran annulated products by this cascade route.

Keywords: Domino reactions / Oxygen heterocycles / Nitrogen heterocycles / Cyclization / One-pot reactions

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