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ORIGINAL PAPER

Triethylammonium acetate-mediated domino-Knoevenagel-hetero-Diels–Alder reaction: synthesis of some angular polyheterocycles

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Abstract A solvent-cum catalyst, ionic liquid triethylammonium acetate-mediated one-pot procedure for the synthesis of some new angular benzopyrano[3,4-*c*]pyrano-fused pyrazoles, all of which incorporate a tertiary ring junction carbon, has been developed. The stereochemistry of the products has been confirmed by single-crystal X-ray diffraction data.

Keywords Angular polyheterocycles · Green chemistry · Ketones · Lewis acids · One-pot synthesis · Pericyclic reactions

Introduction

Construction of angularly fused polycyclic compounds is of special interest because they possess significant biological properties that provide biologists with useful applications in medicinal chemistry [1–10]. Potential candidates of this class include naturally occurring cannabicyclol [11], mahanimbine [12], steroids [13], and thyrsiferol [4]. Analogs of thyrsiferol particularly are known to exhibit cytotoxic, antiviral, and antitumor activities. In addition, bioactive heterosteroids [14–16] possessing this skeleton have significantly improved the biological function. In this context, it is of interest to develop these polycyclic compounds.

The domino reaction continues to be a powerful tool to access a large number of polyheterocycles. Specifically, the one that assembles α,β-unsaturated carbonyl compounds derived from a suitable aldehyde substrate with an active methylene unit has been widely exploited [17–27]; it can be carried out in tandem with many fundamental reactions, such as the domino-Knoevenagel-hetero-Diels–Alder (DKHDA) reaction, Michael addition, ene reaction, and/or sigmatropic rearrangement [28–36]. Covering Tietze's pioneering work [34, 37–45] and others in this area, there seem to be extensive literature reports concerning the use of aldehyde substrates. To the best of our knowledge, no reports exist on ketone-based substrates, although the Knoevenagel adduct is known. So, the hetero-Diels–Alder cyclization in tandem with this ketone-based but sterically rigid typical Knoevenagel intermediate is an interesting area for accessing new angular polyheterocycles. As part of our ongoing interest, we have recently developed a new family of aminobenzopyran-annulated pyrano-fused pyrazoles [46–48]. To extend the scope and generality of this strategy further on typical ketone-based substrates, we therefore find it worthwhile to report an interesting reaction mode of acetophenones and their analogs, termed the DKHDA strategy.

Results and discussion

The typical intermediate oxabutadiene formed in situ was cyclized in a subsequent hetero-Diels–Alder step without changing any reagent or reaction conditions (Scheme 1). Because they incorporate a tertiary ring junction carbon, all

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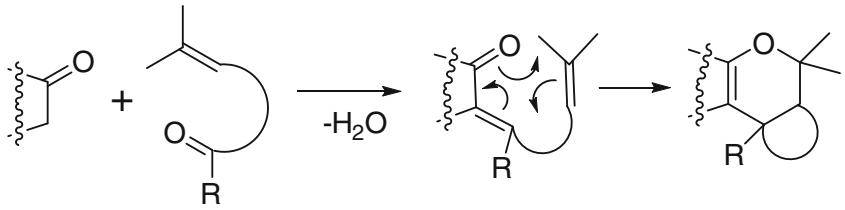
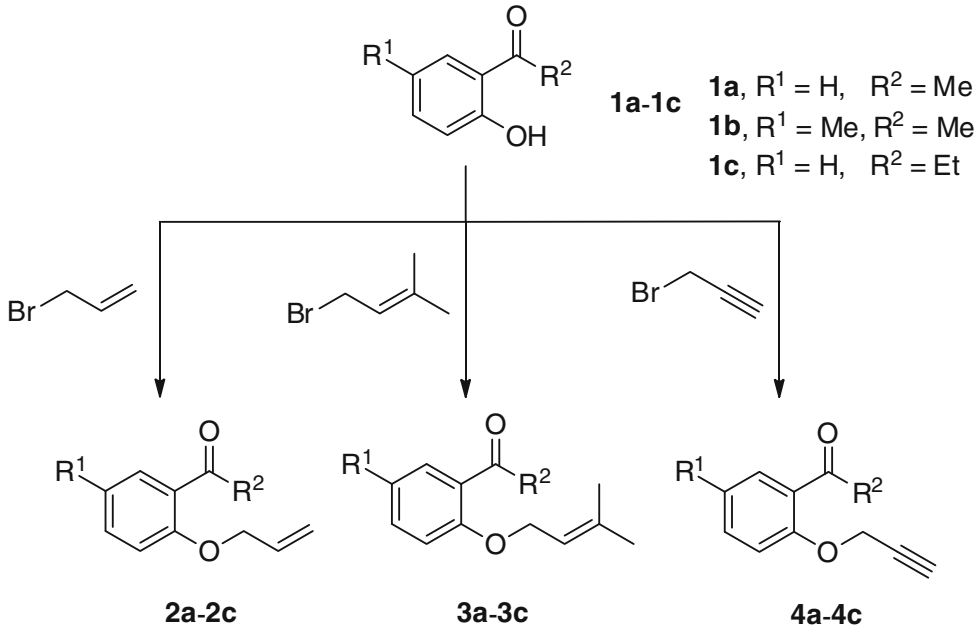
Scheme 1



Scheme 2



new angular polyheterocycles are expected to display a steroidal mimicking biological function [49–51].

Corresponding *O*-allylated/prenylated/propargylated acetophenones **2a**, **2b**, **3a**, **3b**, **4a**, and **4b** and propiophenones **2c**, **3c**, and **4c** were obtained in high yields with excellent purity, prepared by the method reported elsewhere (Scheme 2) [46–48].

To optimize the reaction conditions, we examined first triethylamine (TEA), *p*-toluenesulfonic acid (*p*-TSA), ethylene diammonium diacetate (EDDA), or zinc oxide (ZnO) in refluxing ethanol or acetonitrile as reported elsewhere [42–48, 52–55]. None of the catalysts except ZnO (Table 1, entry 3) was effective for promoting the reaction. Even ZnO in acetonitrile gave traces of product **9a** (entry 3). So, we tried conventional catalyst-free methods (entries 1, 4, and 7) and the catalyzed ones (entries 2, 5, and 8). There were no desired yields in acetonitrile (entries 1 and 2), but at least some yield in other solvents was obtained (entries 4–9). A maximum 28 % of cyclized product **9a** and 24 % of **6a** could be obtained from respective allyl-based **2a** and prenyl-based **3a** substrates in the presence of 25 mol% EDDA in refluxing xylene after 24 h (entry 8). Throughout the study, pyrazolone **5a** was reacted to three different ketone-based model substrates, **2a**, **3a**, and **4a**.

Conventional results thus revealed that prenyl-based ketone **3a** seemed more amenable to the reaction than the allyl-based ketone substrate **2a**, as it gave at least minor yields. However, the conventional method was inadequate to design an efficient synthetic methodology because of these lower yields.

Second, we examined catalyst- and solvent-free thermal procedures (entries 10, 11). The results showed 23 % of the only product **9a** at 130 °C (entry 10) from prenyl-based substrate **3a**. Other substrates **2a** and **4a** were unreactive and gave no desired products, which may be due to unactivated dienophile allyl and propargyl moieties in the substrates. At 160 °C, however, substrate **2a** gave 68 % of product **6a**, but no desired product **12a** from substrate **4a** was found. A maximum 65 % of **9a** was achieved from substrate **3a** (entry 11). However, decomposed impurities associated with the products made the product isolation step tedious. The same was observed in the solvent-free EDDA-mediated reaction despite the good yields achieved at 150 °C (entry 13). To avoid this, we envisaged the reaction in ionic liquid triethylammonium acetate (TEAA, entries 14–18). Surprisingly, no contamination and easy product isolation were achieved to get the desired products. In addition, it improved the reaction in temperature and

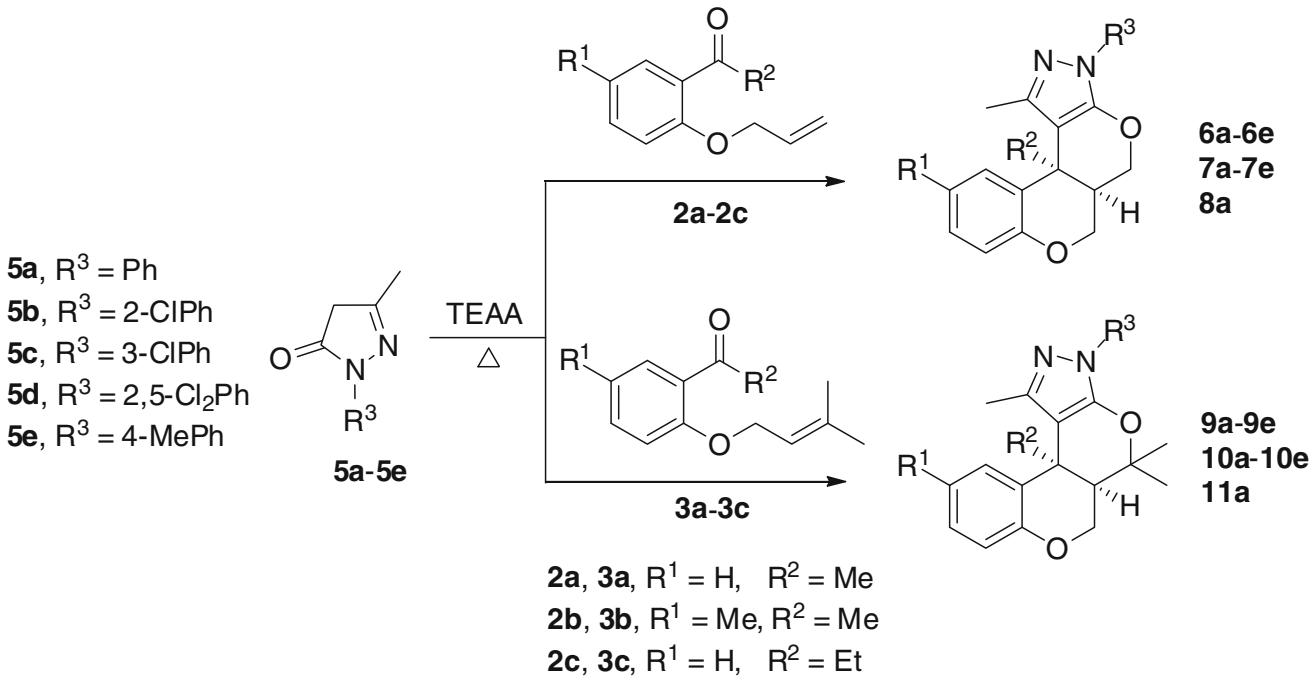
time for both substates **2a** and **3a** at 150 °C. At 100 °C, however, no effective conversion of unactivated dienophile allyl-based substrate was observed (entry 14), and also lower yields of the products resulted from the prenyl-based substrate (entries 15, 18). It gave a maximum of 71 % of **9a** at 140 °C and 67 % of **6a** at 150 °C (entries 17 and 18). Other compounds, **6a–6e**, **7a–7e**, **8a**, **9a–9e**, **10a–10e**, and **11a** (Scheme 3), were then prepared following the optimized reaction conditions. The yields were in the range 58–71 % (Table 2).

Table 1 Optimization of the conditions to yield domino products **6a** and **9a**

Entry	Solvent	Catalyst (25 mol%)	Temp/°C	Time/h	Yield/% **6a/9a**
1	MeCN	–	Reflux	24/24	–/–
2	MeCN	EDDA	Reflux	24/24	–/–
3	MeCN	ZnO	Reflux	24/24	–/Traces
4	Toluene	–	Reflux	24/24	7/12
5	Toluene	EDDA	Reflux	24/24	11/21
6	Toluene	ZnO	Reflux	24/24	12/23
7	Xylene	–	Reflux	24/24	18/27
8	Xylene	EDDA	Reflux	24/24	24/28
9	Xylene	ZnO	Reflux	24/24	22/30
10	–	–	130	5.0/5.0	–/23
11	–	–	160	3.5/2.5	68/65
12	–	EDDA	130	5.0/3.5	–/67
13	–	EDDA	150	4.0/2.5	64/63
14	–	TEAA	100	5.0/5.0	–/–
15	–	TEAA	120	5.0/5.0	–/28
16	–	TEAA	130	5.0/3.5	–/70
17	–	TEAA	140	5.0/3.0	20/71
18	–	TEAA	150	3.5/2.0	67/64

ZnO is effective in many useful transformations [54]. Its catalytic effect was therefore examined for substrate **4a** (Table 3). We studied first the catalyst-free and ZnO catalyzed reactions in refluxing acetonitrile, toluene, and xylene (Table 3, entries 1–6). While only 16 % of product **12a** resulted in refluxing xylene after prolong heating, no product was obtained in other solvents, making the conventional heating method inadequate. Next, we employed the catalyst- and solvent-free methods. No products, even after prolonged heating, could be achieved at 160 °C. So, we employed ZnO, and it not only yielded the products, but reduced the reaction time, too. A maximum 58 % of desired product **12a** could be achieved in 25 mol% ZnO (entry 9). To improve the yields further, we envisaged the reaction in ionic liquid TEAA (entry 12–14). Good results, however, were achieved in the presence of 25 mol% ZnO at 150 °C (entry 13), taking only 6 h to afford products. The work is still being continued to improve the yields. This optimized condition was employed for other heterocycles: **12a–12e**, **13a–13e**, and **14a** (Scheme 4; Table 4).

Besides pyrazolones, other analogous active methylene units such as hydroxycoumarin, cyclohexanedione, and phenyloxazolone were also tried with *O*-allylated,



Scheme 3

Table 2 Synthesis of novel tetrahydro-5*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazoles

Entry	2[a]/3[b]	5	Product	R^1	R^2	R^3	Time/h	Yield[c]/%
1	**2a/3a**	**5a**	**6a/9a**	H	Me	Ph	3.5/3.5	67/70
2	**2a/3a**	**5b**	**6b/9b**	H	Me	2-ClPh	4.5/4.0	61/58
3	**2a/3a**	**5c**	**6c/9c**	H	Me	3-ClPh	3.5/3.5	63/68
4	**2a/3a**	**5d**	**6d/9d**	H	Me	2,5-Cl_2Ph	3.0/3.5	61/65
5	**2a/3a**	**5e**	**6e/9e**	H	Me	4-MePh	3.0/3.0	69/68
6	**2b/3b**	**5a**	**7a/10a**	Me	Me	Ph	4.0/3.5	70/71
7	**2b/3b**	**5b**	**7b/10b**	Me	Me	2-ClPh	4.0/4.0	66/62
8	**2b/3b**	**5c**	**7c/10c**	Me	Me	3-ClPh	3.5/4.0	63/67
9	**2b/3b**	**5d**	**7d/10d**	Me	Me	2,5-Cl_2Ph	4.0/3.5	67/63
10	**2b/3b**	**5e**	**7e/10e**	Me	Me	4-MePh	3.5/3.0	65/70
11	**2c/3c**	**5a**	**8a/11a**	H	Et	Ph	4.5/3.5	39/46

[a] *O*-allylated substrates

[b] *O*-prenylated substrates

[c] Optimized conditions: 25 mol% TEAA, 150 °C for 2 and 130 °C for 3

Table 3 Optimization of the conditions to afford **12a**

Entry	Solvent	Catalyst	Temp/°C	Time/h	Yield/%
1	MeCN	–	Reflux	24	–
2	Toluene	–	Reflux	24	–
3	Xylene	–	Reflux	24	–
4	MeCN	ZnO (25 %)	Reflux	24	–
5	Toluene	ZnO (25 %)	Reflux	24	Trace
6	Xylene	ZnO (25 %)	Reflux	24	16
7	–	–	160	10	–
8	–	ZnO (15 %)	160	10	33
9	–	ZnO (25 %)	160	6	58
10	–	ZnO (35 %)	160	6	56
11	–	TEAA (25 %)	160	10	–
12	–	TEAA (25 %)[a]	130	6	–
13	–	TEAA (25 %)[a]	150	6	62
14	–	TEAA (25 %)[a]	160	6	57

[a] As a mixture with ZnO (25 mol%)

O-prenylated, and *O*-propargylated acetophenones, using the optimized condition (Table 3, entry 13). Also, other ketone-based substrates derived from 2-hydroxybenzophenone were tested. But they failed to give subsequent cyclized products after forming the Knoevenagel adduct. Work in this area is ongoing.

The formation of the Knoevenagel intermediate [52–55] was confirmed by ^{1}H NMR, ^{13}C NMR, and DEPT-135 studies. From single-crystal X-ray data of **9a**, a *cis* orientation of the bridge head methyl and hydrogen at the pyranyl ring junction was evident, indicative of a less sterically hindered *endo-E-syn* transition state.

A plausible mechanism is proposed in Scheme 5. The reaction proceeds via formation of Knoevenagel intermediate IV [52–55]. Triethylammonium pyrazolonate I, obtained from pyrazolone in the presence of TEAA, forms unstable enolate intermediate III with dienophile-ether-tethered ketone substrate II via nucleophilic attack of pyrazolonate on carbonyl carbon of II, which forms Knoevenagel alkene intermediate IV and releases ionic liquid. The intermediate IV was isolated and its structure was also confirmed by ^{1}H NMR, ^{13}C NMR, and DEPT-135. Finally, under the influence of TEAA, IV undergoes the hetero-Diels–Alder reaction to form the cyclized product.

Four transition states are possible when the dienophile approaches toward the alkene intramolecularly in the Knoevenagel intermediate. Formation of either *endo-Z-anti* or *exo-E-anti* geometries are ruled out because of angle strain. Thus, fewer steric interactions of *the ortho* substituent with an alkyl attached to Knoevenagel alkene favors the *endo-E-syn* transition state. The same can also be inferred from the single crystal X-ray analysis, which showed both the pyranyl bridge methyl and hydrogen in *cis* position to each other. It was therefore concluded that the reaction proceeds via *endo-E-syn* transition states even though two pathways are possible.

^{1}H NMR spectra featured a singlet at around $\delta = 1.0$–1.9 ppm attributable to a methyl proton attached to the ring junction carbon and which in turn showed a ^{13}C NMR peak in the range $\delta = 22$–30 ppm, except the compounds derived from propiophenones. In polyheterocycles derived from propiophenones, two bridge head methylene protons showed multiplets in the 2.03–2.39 ppm range and a carbon signal at around $\delta = 33$ ppm. Further structural conformation could also be ascertained by the single crystal X-ray diffraction data of representatives **9a** and **12a** (Figs. 1, 2) [56–59].The data fully agreed with the proposed structure.

Conclusion

Thus, we have described a new ionic liquid TEAA-mediated one-pot method for the synthesis of a new family of angularly fused polyheterocycles via a domino intermolecular Knoevenagel intramolecular hetero-Diels–alder route. Besides providing efficient and improved reaction conditions for unactivated dienophile propargyl, needing no additional catalyst required for allyl- and prenyl-based substrates is another advantage of this method. Since the bridge head alkyl group is present in all the polycyclic heterocycles, they are expected to display some new bioprofiles.

Experimental

Solvents were dried by standard procedures. ^{1}H and ^{13}C NMR spectra were determined in $CDCl_3$ on a Bruker

Scheme 4

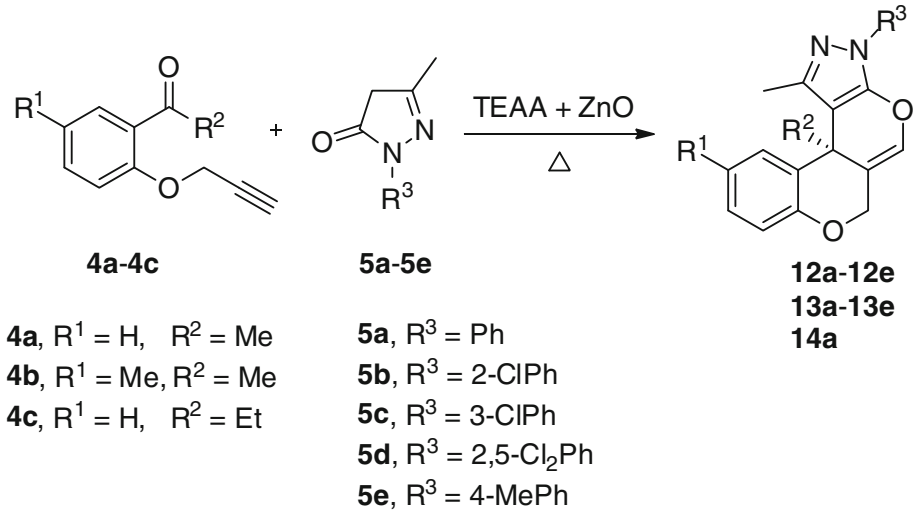


Table 4 Synthesis of novel dihydro-6*H*-chromeno[4′,3′:4,5]pyrano[2,3-*c*]pyrazoles **12a–12e**, **13a–13e**, **14a**

Entry	4[a]	5	Product	R^1	R^2	R^3	Time/h	Yield[b]/%
1	**4a/4b**	**5a**	**12a/13a**	H/Me	Me	Ph	6.0/6.5	62/68
2	**4a/4b**	**5b**	**12b/13b**	H/Me	Me	2-ClPh	7.5/8.0	60/57
3	**4a/4b**	**5c**	**12c/13c**	H/Me	Me	3-ClPh	8.0/7.5	64/64
4	**4a/4b**	**5d**	**12d/13d**	H/Me	Me	2,5-Cl_2Ph	7.0/7.0	61/56
5	**4a/4b**	**5e**	**12e/13e**	H/Me	Me	4-MePh	6.5/7.0	67/69
6	**4c**	**5a**	**14a**	H	Et	Ph	7.0	32

[a] Propargylated substrates

[b] Optimized condition: equal amount (25 mol%) of TEAA and ZnO, 150 °C

Avance (^{1}H 400 MHz, ^{13}C 100 MHz) using the $CDCl_3$ peak as a reference peak. IR spectra were obtained on a Shimadzu FT-IR 8300 spectrophotometer using the KBr disc. Mass spectra were taken on a Shimadzu LCMS 2010 instrument. Elemental analysis (C, H, N) was carried out by a Perkin-Elmer 2400 series-II elemental analyzer (Perkin-Elmer, USA). The reactions were monitored by silica gel 60 F254 thin-layer chromatographic (TLC) plates of Merck. Melting points were determined in an open capillary tube on a TEMPO melting point apparatus. Ionic liquid-cum-catalyst TEAA was prepared by reported literature methods [60].

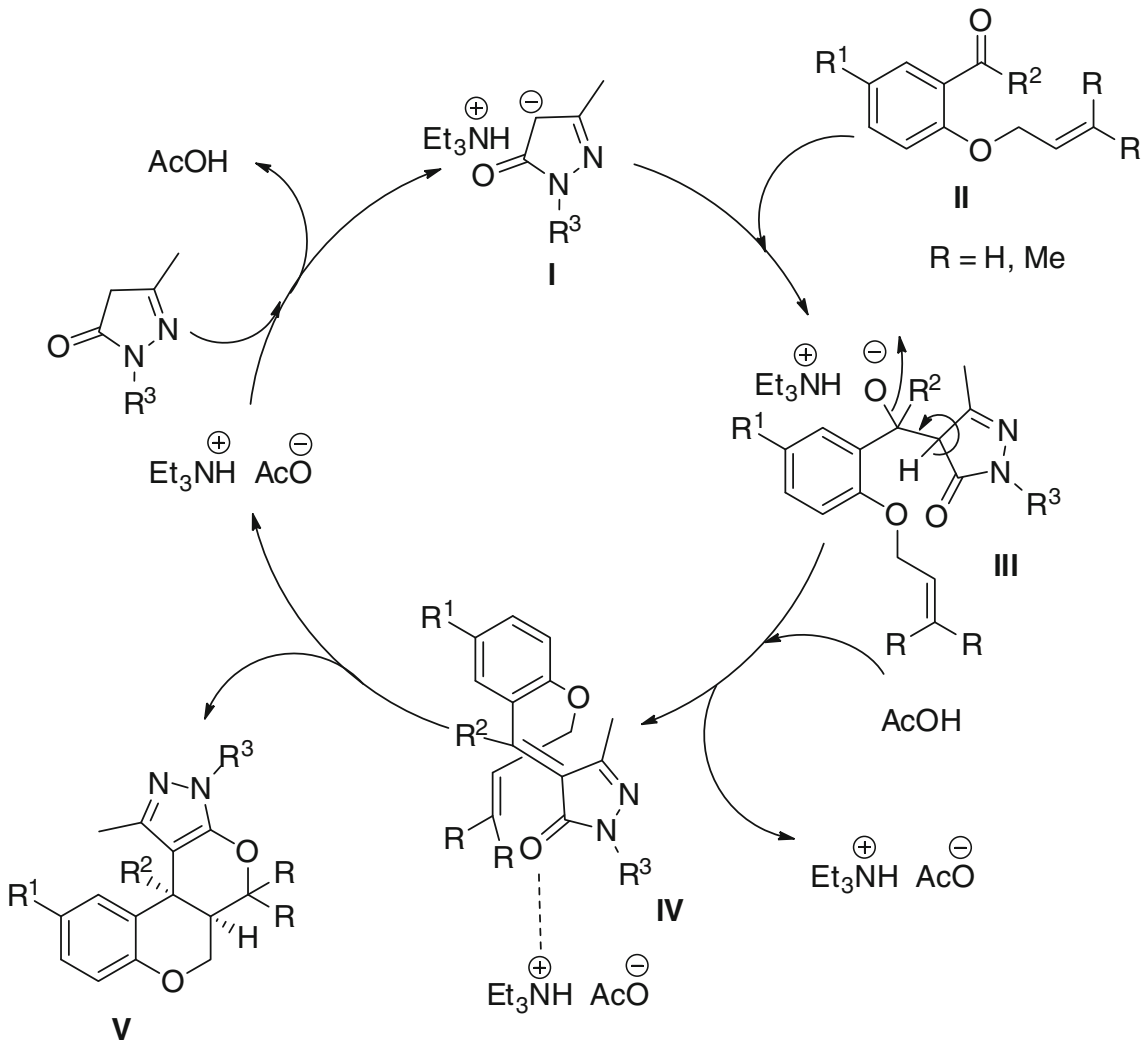
Single crystal X-ray diffraction data were collected on a Bruker CCD area-detector diffractometer equipped with a graphite monochromatic MoKα radiation ($\lambda = 0.71073$ Å). The structure was solved by direct methods using SHELXS 97 [56]. All non-hydrogen atoms in the molecule were located in the best E-map. The title compound **9a** crystallizes in the monoclinic space group *P*21/n with the following unit-cell parameters: $a = 13.4695(4)$, $b = 10.3715(3)$, $c = 13.8111(4)$ Å, $\beta = 95.724(3)°$, and $Z = 4$. Compound **12a** crystallizes in the monoclinic space group *P*21/c with the following unit-cell parameters: $a = 10.2068(3)$, $b = 11.2849(5)$, $c = 14.3720(5)$ Å, $\beta = 91.778(3)$ °, and $Z = 4$. The crystal structures of **9a** and **12a** were solved by direct methods and refined by full-matrix least-squares procedures to a final *R* value of 0.0424 for 2,605 and 0.0431 for 2,473 observed reflections, respectively.

*General procedure for the synthesis of **6a–6e**, **7a–7e**, and **8a***

A mixture of *O*-allylated acetophenones/propiophenone **2a–2c** (3.0 mmol) and corresponding 5-pyrazolone **5a–5e** (3.0 mmol) in TEAA (0.75 mmol, 25 mol%) was heated at 150 °C until the reaction was completed as monitored by TLC. Crude cycloadducts thus received in good yields were purified further by column chromatography.

(5aR,11bS)-3,5a,6,11b-Tetrahydro-1,11b-dimethyl-3-phenyl-5H-chromeno[4′,3′:4,5]pyrano[2,3-c]pyrazole (**6a**, $C_{21}H_{20}N_2O_2$)

White powder; yield 631 mg (67 %); m.p.: 152–154 °C; $R_f = 0.42$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}957$, 2,927, 1,595, 1,516, 1,485, 1,442, 1,227, 1,093, 1,048, 840, 756, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.81$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.16 (m, 1H, H_{5a}), 2.64 (s, 3H, CH_3 of pyrazolone), 4.27 (m, 2H, H_5 and H_6), 4.53 (dd, $J = 11.2$, 3.6 Hz, 1H, $H_{6'}$), 4.58 (dd, $J = 12.0$, 2.8 Hz, 1H, $H_{5'}$), 6.80–7.73



Scheme 5

(m, 9H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.47$ (CH_3 of pyrazolone), 29.64 (CH_3 attached to 3° ring junction carbon), 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 (Ar–C) ppm; MS: $m/z = 333.1$ [M+H$^+$].

(5aR,11bS)-3-(2-Chlorophenyl)-3,5a,6,11b-tetrahydro-1,11b-dimethyl-5H-chromeno[4′,3′:4,5]pyrano[2,3-c]-pyrazole (**6b**, $C_{21}H_{19}ClN_2O_2$)

White powder; yield 634 mg (61 %); m.p.: 154–156 °C; $R_f = 0.24$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}965$, 2,929, 1,590, 1,517, 1,479, 1,443, 1,228, 1,094, 1,043, 841, 757, 683 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.81$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.17 (m, 1H, H_{5a}), 2.62 (s, 3H, CH_3 of pyrazolone), 4.27 (m, 2H, H_5 and C-H_6), 4.52 (dd, $J = 11.2$, 3.6 Hz, 1H, $H_{6'}$), 4.58 (dd, $J = 12.0$, 2.8 Hz, 1H, $H_{5'}$), 6.79–7.71 (m, 8H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.47$ (CH_3 of pyrazolone), 29.64 (CH_3 attached to 3° ring junction carbon), 34.07 (C-11b), 37.85 (C-5a), 62.86 (C-5), 69.07 (C-6), 101.39, 116.37, 120.72 127.59, 128.22, 129.31, 129.68, 129.87, 130.25, 130.92, 131.35, 135.69, 147.36, 149.35, 150.94 (Ar–C) ppm; MS: $m/z = 367.2$ [M+H$^+$].

(5aR,11bS)-3-(3-Chlorophenyl-3,5a,6,11b-tetrahydro)-1,11b-dimethyl-5H-chromeno[4′,3′:4,5]pyrano[2,3-c]-pyrazole (**6c**, $C_{21}H_{19}ClN_2O_2$)

White powder; yield 655 mg (63 %); m.p.: 146–148 °C; $R_f = 0.47$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}968$, 2,926, 1,591, 1,517, 1,477, 1,440, 1,226, 1,090, 1,039, 844, 821, 755, 673 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.80$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.16 (m, 1H, H_{5a}), 2.62 (s, 3H, CH_3 of pyrazolone), 4.28 (m, 2H, H_5 and H_6), 4.52 (dd,

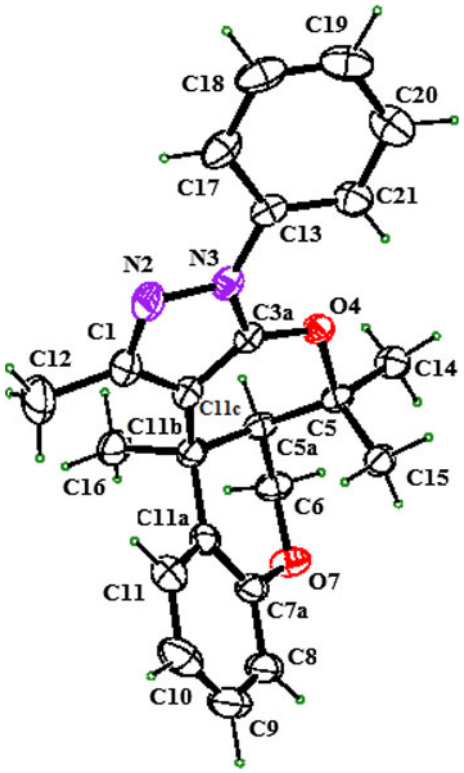


Fig. 1 ORTEP view of compound **9a**

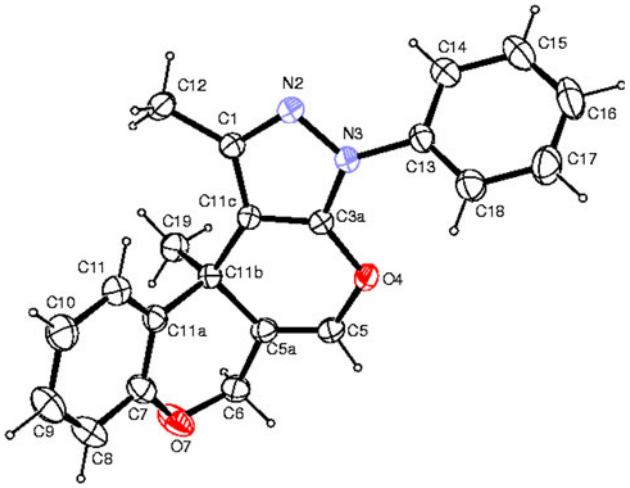


Fig. 2 ORTEP view of compound **12a**

$J = 11.2$, 3.6 Hz, 1H, $H_{6'}$), 4.57 (dd, $J = 12.0$, 2.8 Hz, 1H, $H_{5'}$), 6.80–7.72 (m, 8H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.47$ (CH_3 of pyrazolone), 29.64 (CH_3 attached to 3° ring junction carbon), 34.07 (C-11b), 37.85 (C-5a), 62.86 (C-5), 69.07 (C-6), 101.57, 116.64, 120.92, 128.05, 128.62, 129.21, 129.43, 129.72, 130.09, 130.36, 131.65, 135.74, 147.53, 149.65, 150.87 (Ar–C) ppm; MS: $m/z = 367.2$ [M+H$^+$].

(5aR,11bS)-3-(2,5-Dichlorophenyl)-3,5a,6,11b-tetrahydro-1,11b-dimethyl-5H-chromeno[4′,3′:4,5]pyrano[2,3-c]-pyrazole (**6d**, $C_{21}H_{18}Cl_2N_2O_2$)

White powder; yield 693 mg (61 %); m.p.: 204–206 °C; $R_f = 0.43$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}972$, 2,923, 1,594, 1,518, 1,482, 1,432, 1,240, 1,089, 1,048, 849, 822, 783, 677 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.81$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.17 (m, 1H, H_{5a}), 2.59 (s, 3H, CH_3 of pyrazolone), 4.26 (m, 2H, H_5 and H_6), 4.47 (dd, $J = 11.2$, 3.6 Hz, 1H, $H_{6'}$), 4.55 (dd, $J = 12.0$, 2.8 Hz, 1H, $H_{5'}$), 6.80–7.52 (m, 7H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.40$ (CH_3 of pyrazolone), 29.62 (CH_3 attached to 3° ring junction carbon), 34.09 (C-11b), 38.04 (C-5a), 62.98 (C-5), 69.06 (C-6), 102.11, 117.10, 121.04, 127.90, 128.78, 129.48, 129.60, 129.68, 129.98, 130.98, 132.86, 136.24, 147.75, 149.40, 151.29 (Ar–C) ppm; MS: $m/z = 401.1$ [M+H$^+$].

(5aR,11bS)-3,5a,6,11b-Tetrahydro-1,11b-dimethyl-3-(4-methylphenyl)-5H-chromeno[4′,3′:4,5]pyrano[2,3-c]-pyrazole (**6e**, $C_{22}H_{22}N_2O_2$)

White powder; yield 677 mg (69 %); m.p.: 150–152 °C; $R_f = 0.45$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}980$, 2,928, 1,591, 1,523, 1,484, 1,444, 1,232, 1,097, 1,045, 820, 754, 673 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.81$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.17 (m, 1H, H_{5a}), 2.37 (s, 3H, CH_3 of phenyl), 2.63 (s, 3H, CH_3 of pyrazolone), 4.27 (m, 2H, H_5 and H_6), 4.52 (dd, $J = 11.0$, 3.2 Hz, 1H, $H_{6'}$), 4.58 (dd, $J = 11.6$, 2.4 Hz, 1H, $H_{5'}$), 6.79–7.58 (m, 8H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.43$ (CH_3 of pyrazolone), 20.95 (CH_3 attached to 3° ring junction carbon), 29.66 (CH_3 of pyrazolone), 34.07 (C-11b), 37.90 (C-5a), 62.90 (C-5), 69.02 (C-6), 102.90, 117.04, 120.85, 121.07, 127.83, 129.15, 129.43, 129.63, 135.47, 135.96, 146.14, 148.34, 151.14 (Ar–C) ppm; MS: $m/z = 347.1$ [M+H$^+$].

(5aR,11bS)-3,5a,6,11b-Tetrahydro-1,10,11b-trimethyl-3-phenyl-5H-chromeno[4′,3′:4,5]pyrano[2,3-c]pyrazole (**7a**, $C_{22}H_{22}N_2O_2$)

White powder; yield 637 mg (70 %); m.p.: 138–140 °C; $R_f = 0.47$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}963$, 2,936, 1,586, 1,519, 1,489, 1,450, 1,232, 1,085, 1,049, 846, 756, 671 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.80$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.17 (m, 1H, H_{5a}), 2.31 (s, 3H, CH_3-10), 2.71 (s, 3H, CH_3 of pyrazolone), 4.30 (m, 2H, H_5 and H_6), 4.55 (dd, $J = 11.4$, 3.6 Hz, 1H, $H_{6'}$), 4.59 (dd, $J = 12.4$, 2.8 Hz, 1H, $H_{5'}$), 6.66–7.65 (m, 8H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.67$ (CH_3 of pyrazolone), 20.72 (CH_3-10) 29.92 (CH_3 attached to 3° ring junction carbon), 34.26 (C-11b), 37.65 (C-5a), 62.82 (C-5), 69.56 (C-6), 102.11, 118.01, 120.67, 125.64, 127.76, 128.25, 128.90, 129.29,

129.81, 138.52, 146.63, 148.62, 151.82 (Ar–C) ppm; MS: $m/z = 347.2$ [M+H$^+$].

(5aR,11bS)-3-(2-Chlorophenyl)-3,5a,6,11b-tetrahydro-1,10,11b-trimethyl-5H-chromeno[4′,3′:4,5]pyrano[2,3-c]-pyrazole (**7b**, $C_{22}H_{21}ClN_2O_2$)
White powder; yield 661 mg (66 %); m.p.: 164–166 °C; $R_f = 0.25$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}956$, 2,932, 1,589, 1,517, 1,494, 1,456, 1,230, 1,091, 1,052, 853, 758, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.82$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.18 (m, 1H, H_{5a}), 2.33 (s, 3H, CH_3-10), 2.69 (s, 3H, CH_3 of pyrazolone), 4.28 (m, 2H, H_5 and H_6), 4.52 (dd, $J = 12.0$, 3.2 Hz, 1H, $H_{6'}$), 4.58 (dd, $J = 12.6$, 2.4 Hz, 1H, $H_{5'}$), 6.67–7.70 (m, 7H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.82$ (CH_3 of pyrazolone), 20.81 (CH_3-10) 29.75 (CH_3 attached to 3° ring junction carbon), 34.02 (C-11b), 37.71 (C-5a), 63.03 (C-5), 69.42 (C-6), 100.59, 116.32, 127.36, 128.01, 128.33, 129.16, 129.52, 129.65, 130.11, 130.28, 131.56, 135.65, 147.26, 149.24, 150.62 (Ar–C) ppm; MS: $m/z = 381.1$ [M+H$^+$].

(5aR,11bS)-3-(3-Chlorophenyl)-3,5a,6,11b-tetrahydro-1,10,11b-trimethyl-5H-chromeno[4′,3′:4,5]pyrano[2,3-c]-pyrazole (**7c**, $C_{22}H_{21}ClN_2O_2$)
White powder; yield 630 mg (63 %); m.p.: 142–144 °C; $R_f = 0.55$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}960$, 2,927, 1,590, 1,518, 1,491, 1,445, 1,232, 1,093, 1,039, 848, 749, 676 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.81$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.16 (m, 1H, H_{5a}), 2.31 (s, 3H, CH_3-10), 2.68 (s, 3H, CH_3 of pyrazolone), 4.26 (m, 2H, H_5 and H_6), 4.53 (dd, $J = 12.2$, 3.2 Hz, 1H, $H_{6'}$), 4.59 (dd, $J = 12.4$, 2.4 Hz, 1H, $H_{5'}$), 6.68–7.71 (m, 7H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.63$ (CH_3 of pyrazolone), 20.68 (CH_3-10) 29.69 (CH_3 attached to 3° ring junction carbon), 33.86 (C-11b), 37.52 (C-5a), 62.74 (C-5), 69.56 (C-6), 101.12, 116.36, 127.36, 128.01, 128.33, 129.16, 129.52, 129.65, 130.11, 130.28, 131.56, 135.65, 147.26, 149.24, 150.62 (Ar–C) ppm; MS: $m/z = 381.1$ [M+H$^+$].

(5aR,11bS)-3-(2,5-Dichlorophenyl)-3,5a,6,11b-tetrahydro-1,10,11b-trimethyl-5H-chromeno[4′,3′:4,5]pyrano[2,3-c]-pyrazole (**7d**, $C_{22}H_{20}Cl_2N_2O_2$)
White powder; yield 730 mg (67 %); m.p.: 178–180 °C; $R_f = 0.44$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}962$, 2,930, 1,577, 1,515, 1,481, 1,441, 1,226, 1,085, 1,043, 862, 761, 658 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.82$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.17 (m, 1H, H_{5a}), 2.32 (s, 3H, CH_3-10), 2.68 (s, 3H, CH_3 of pyrazolone), 4.27 (m, 2H, H_5 and H_6), 4.52 (dd, $J = 12.2$, 3.2 Hz, 1H, $H_{6'}$), 4.59 (dd, $J = 12.4$, 2.4 Hz, 1H, $H_{5'}$), 6.64–7.69 (m, 6H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.71$ (CH_3 of pyrazolone), 20.76 (CH_3-10) 29.52 (CH_3 attached to 3° ring junction carbon), 33.81 (C-11b), 37.42 (C-5a), 62.56 (C-5), 69.39 (C-6), 101.87, 118.13, 127.32, 127.56, 127.88, 129.58, 129.82, 130.14, 130.68, 131.39, 132.76, 136.33, 147.52, 149.41, 151.67 (Ar–C) ppm; MS: $m/z = 415.0$ [M+H$^+$].

(5aR,11bS)-3,5a,6,11b-Tetrahydro-1,10,11b-trimethyl-3-(4-methylphenyl)-5H-chromeno[4′,3′:4,5]pyrano[2,3-c]-pyrazole (**7e**, $C_{23}H_{24}N_2O_2$)
White powder; yield 615 mg (65 %); m.p.: 132–134 °C; $R_f = 0.49$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}967$, 2,928, 1,583, 1,523, 1,489, 1,445, 1,231, 1,078, 1,038, 859, 758, 684 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.82$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.17 (m, 1H, H_{5a}), 2.28 (s, 3H, CH_3-10), 2.36 (s, 3H, CH_3 of phenyl), 2.63 (s, 3H, CH_3 of pyrazolone), 4.28 (m, 2H, H_5 and H_6), 4.53 (dd, $J = 11.6$, 3.2 Hz, 1H, $H_{6'}$), 4.59 (dd, $J = 12.0$, 2.4 Hz, 1H, $H_{5'}$), 6.66–7.68 (m, 7H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.75$ (CH_3 of pyrazolone), 20.66 (CH_3-10) 20.95 (CH_3 of phenyl), 29.89 (CH_3 attached to 3° ring junction carbon), 34.51 (C-11b), 37.85 (C-5a), 62.91 (C-5), 69.29 (C-6), 101.85, 116.92, 120.62, 127.98, 128.36, 128.90, 129.41, 130.53, 135.32, 136.41, 146.74, 148.15, 150.60 (Ar–C) ppm; MS: $m/z = 361.2$ [M+H$^+$].

(5aR,11bS)-11b-Ethyl-3,5a,6,11b-tetrahydro-1-methyl-3-phenyl-5H-chromeno[4′,3′:4,5]pyrano[2,3-c]pyrazole (**8a**, $C_{22}H_{22}N_2O_2$)
White powder; yield 0.355 mg (39 %); m.p.: 132–133 °C; $R_f = 0.36$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}967$, 2,929, 1,586, 1,509, 1,493, 1,440, 1,231, 1,085, 1,035, 989, 857, 759, 682 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.88$ (t, $J = 7.6$ Hz, 3H, CH_3 of ethyl), 2.11 (m, 1H, –CH_2CH_3), 2.35 (m, 1H, –CH_2CH_3), 2.43 (m, 1H, H_{5a}), 2.59 (s, 3H, CH_3 of pyrazolone), 4.27 (m, 2H, H_5 and H_6), 4.51 (m, 2H, $H_{5'}$ and $H_{6'}$), 6.78–7.73 (m, 9H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 8.10$ (CH_3 of ethyl), 16.20 (CH_3 of pyrazolone), 31.90 (C-5a), 32.08 (CH_2 of ethyl), 38.42 (C-11b), 62.46 (C-5), 69.02 (C-6), 100.47, 116.99, 120.58, 121.05, 125.63, 127.79, 128.89, 129.54, 129.66, 138.46, 146.36, 149.83, 151.19 (Ar–C) ppm; MS: $m/z = 347.1$[M+H$^+$].

*General procedure for the synthesis of **9a–9e**, **10a–10e**, and **11a***

A mixture of *O*-prenylated acetophenones/propiophenone **3a–3c** (3.0 mmol) and the corresponding 5-pyrazolone **5a–5e** (3.0 mmol) in TEAA (0.75 mmol, 25 mol%) was heated at 130 °C until the reaction was completed as monitored by TLC. Crude cycloadducts were received in good yields and purified further by column chromatography.

(5aR,11bS)-3,5a,6,11b-Tetrahydro-1,5,5,11b-tetramethyl-3-phenyl-5H-chromeno[4′,3′:4,5]pyrano[2,3-c]pyrazole (**9a**, $C_{23}H_{24}N_2O_2$)

White powder; yield 623 mg (70 %); m.p.: 170–172 °C; $R_f = 0.51$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}981$, 2,929, 1,597, 1,511, 1,491, 1,443, 1,230, 1,084, 1,043, 838, 757, 673 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.09$ (s, 3H, CH_3 attached to 3° ring junction carbon), 1.64 (s, 3H, CH_3-5), 1.77 (s, 3H, CH_3-5′), 1.98 (d, $J = 3.2$ Hz, 1H, H_{5a}), 2.71 (s, 3H, CH_3 of pyrazolone), 4.43 (td, $J = 12.8$, 1.2 Hz, 1H, H_6), 4.72 (ddd, $J = 12.6$, 4.4, 2.0 Hz, 1H, $H_{6'}$), 6.76–7.78 (m, 9H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.78$ (CH_3 of pyrazolone), 22.75 (CH_3 attached to 3° ring junction carbon), 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 (Ar–C) ppm; MS: $m/z = 361.1$ [M+H$^+$].

(5aR,11bS)-3-(2-Chlorophenyl)-3,5a,6,11b-tetrahydro-1,5,5,11b-tetramethyl-5H-chromeno[4′,3′:4,5]pyrano[2,3-c]-pyrazole (**9b**, $C_{23}H_{23}ClN_2O_2$)

White powder; yield 560 mg (58 %); m.p.: 135–137 °C; $R_f = 0.24$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}965$, 2,925, 1,587, 1,514, 1,482, 1,441, 1,229, 1,088, 1,038, 845, 758, 684 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.05$ (s, 3H, CH_3 attached to 3° ring junction carbon), 1.66 (s, 3H, CH_3-5), 1.79 (s, 3H, CH_3-5′), 1.99 (d, $J = 3.6$ Hz, 1H, H_{5a}), 2.69 (s, 3H, CH_3 of pyrazolone), 4.42 (td, $J = 12.4$, 1.6 Hz, 1H, H_6), 4.71 (ddd, $J = 12.4$, 4.2, 2.0 Hz, 1H, $H_{6'}$), 6.77–7.79 (m, 8H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.61$ (CH_3 of pyrazolone), 22.86 (CH_3 attached to 3° ring junction carbon), 29.39 (CH_3-5), 31.87 (CH_3-5′), 33.58 (C-11b), 46.93 (C-5a), 62.02 (C-6), 82.99 (C-5), 103.25, 117.18, 120.76, 121.31, 125.53, 127.77, 128.79, 129.02, 129.53, 138.58, 146.61, 148.49, 151.24 (Ar–C) ppm; MS: $m/z = 395.1$ [M+H$^+$].

(5aR,11bS)-3-(3-Chlorophenyl)-3,5a,6,11b-tetrahydro-1,5,5,11b-tetramethyl-5H-chromeno[4′,3′:4,5]pyrano-[2,3-c]pyrazole (**9c**, $C_{23}H_{23}ClN_2O_2$)

White powder; yield 656 mg (68 %); m.p.: 148–150 °C; $R_f = 0.55$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}968$, 2,927, 1,589, 1,559, 1,480, 1,440, 1,232, 1,091, 1,041, 849, 820, 755, 690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.09$ (s, 3H, CH_3 attached to 3° ring junction carbon), 1.63 (s, 3H, CH_3-5), 1.76 (s, 3H, CH_3-5′), 1.97 (d, $J = 3.2$ Hz, 1H, H_{5a}), 2.72 (s, 3H, CH_3 of pyrazolone), 4.43 (td, $J = 12.8$, 0.8 Hz, 1H, H_6), 4.71 (ddd, $J = 12.4$, 4.4, 2.0 Hz, 1H, $H_{6'}$), 6.71–7.79 (m, 8H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.48$ (CH_3 of pyrazolone), 22.65 (CH_3 attached to 3° ring junction carbon), 29.29 (CH_3-5), 31.85 (CH_3-5′), 33.85 (C-11b), 47.01 (C-5a), 62.02 (C-6), 82.63 (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 (Ar–C) ppm; MS: $m/z = 395.1$ [M+H$^+$].

(5aR,11bS)-3-(2,5-Dichlorophenyl)-3,5a,6,11b-tetrahydro-1,5,5,11b-tetramethyl-5H-chromeno[4′,3′:4,5]pyrano-[2,3-c]pyrazole (**9d**, $C_{23}H_{22}Cl_2N_2O_2$)

White powder; yield 682 mg (65 %); m.p.: 130–132 °C; $R_f = 0.48$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}970$, 2,925, 1,590, 1,512, 1,481, 1,445, 1,228, 1,088, 1,039, 851, 759, 675 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.08$ (s, 3H, CH_3 attached to 3° ring junction carbon), 1.67 (s, 3H, CH_3-5), 1.78 (s, 3H, CH_3-5′), 1.96 (d, $J = 3.2$ Hz, 1H, H_{5a}), 2.70 (s, 3H, CH_3 of pyrazolone), 4.41 (td, $J = 12.4$, 1.6 Hz, 1H, H_6), 4.66 (ddd, $J = 12.6$, 4.2, 2.0 Hz, 1H, $H_{6'}$), 6.69–7.56 (m, 7H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.77$ (CH_3 of pyrazolone), 22.53 (CH_3 attached to 3° ring junction carbon), 29.65 (CH_3-5), 32.06 (CH_3-5′), 34.02 (C-11b), 46.65 (C-5a), 62.43 (C-6), 83.12 (C-5), 102.32, 117.43, 121.21, 127.97, 128.88, 129.15, 129.68, 129.93, 130.92, 131.16, 132.95, 136.54, 147.86, 149.67, 151.52 (Ar–C) ppm; MS: $m/z = 429.2$ [M+H$^+$].

(5aR,11bS)-3,5a,6,11b-Tetrahydro-1,5,5,11b-tetramethyl-3-(4-methylphenyl)-5H-chromeno[4′,3′:4,5]pyrano-[2,3-c]pyrazole (**9e**, $C_{24}H_{26}N_2O_2$)

White powder; yield 623 mg (68 %); m.p.: 178–180 °C; $R_f = 0.47$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}971$, 2,929, 1,591, 1,560, 1,478, 1,444, 1,226, 1,094, 1,045, 853, 760, 661 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.09$ (s, 3H, CH_3 attached to 3° ring junction carbon), 1.64 (s, 3H, CH_3-5), 1.79 (s, 3H, CH_3-5′), 1.99 (d, $J = 3.2$ Hz, 1H, H_{5a}), 2.39 (s, 3H, CH_3 of phenyl), 2.75 (s, 3H, CH_3 of pyrazolone), 4.48 (td, $J = 12.6$, 1.6 Hz, 1H, H_6), 4.74 (ddd, $J = 12.8$, 4.2, 2.0 Hz, 1H, $H_{6'}$), 6.70–7.79 (m, 8H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.76$ (CH_3 of pyrazolone), 20.92 (CH_3 of phenyl), 22.71 (CH_3 attached to 3° ring junction carbon), 29.14 (CH_3-5), 31.93 (CH_3-5′), 33.76 (C-11b), 46.73 (C-5a), 62.06 (C-6), 82.54 (C-5), 102.87, 117.01, 120.85, 121.05, 127.81, 129.14, 129.42, 129.59, 135.46, 135.92, 146.16, 148.37, 151.17 (Ar–C) ppm; MS (ESI): $m/z = 375.0$ [M+H$^+$].

(5aR,11bS)-3,5a,6,11b-Tetrahydro-1,5,5,10,11b-pentamethyl-3-phenyl-5H-chromeno[4′,3′:4,5]pyrano-[2,3-c]pyrazole (**10a**, $C_{24}H_{26}N_2O_2$)

White powder; yield 573 mg (71 %); m.p.: 212–214 °C; $R_f = 0.46$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}972$, 2,927, 1,594, 1,519, 1,472, 1,432, 1,238, 1,081, 1,039, 844, 748, 669 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.11$ (s, 3H, CH_3 attached to 3° ring junction carbon), 1.56 (s, 3H, CH_3-5), 1.78 (s, 3H, CH_3-5′), 1.93 (d, $J = 3.6$ Hz, 1H, H_{5a}), 2.32 (s, 3H, CH_3-10), 2.72 (s, 3H, CH_3 of pyrazolone), 4.41 (td, $J = 12.6$, 0.8 Hz, 1H, H_6),

4.70 (ddd, $J = 12.6$, 4.4, 1.6 Hz, 1H, $H_{6'}$), 6.65–7.55 (m, 8H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.89$ (CH_3 of pyrazolone), 20.88 (CH_3-10), 22.66 (CH_3 attached to 3° ring junction carbon), 28.92 (CH_3-5), 32.29 (CH_3-5′), 33.77 (C-11b), 47.42 (C-5a), 61.93 (C-6), 82.73 (C-5), 102.11, 116.90, 119.98, 125.72, 127.96, 128.89, 129.13, 129.72, 139.11, 146.56, 149.01, 151.76 (Ar–C) ppm; MS: $m/z = 375.2$ [M+H$^+$].

(5aR,11bS)-3-(2-Chlorophenyl)-3,5a,6,11b-tetrahydro-1,5,5,10,11b-pentamethyl-5H-chromeno[4′,3′:4,5]-pyrano[2,3-c]pyrazole (**10b**, $C_{24}H_{25}ClN_2O_2$)
White powder; yield 580 mg (62 %); m.p.: 168–170 °C; $R_f = 0.22$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}978$, 2,922, 1,592, 1,518, 1,443, 1,232, 1,095, 1,036, 845, 756, 655 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.10$ (s, 3H, CH_3 attached to 3° ring junction carbon), 1.51 (s, 3H, CH_3-5), 1.77 (s, 3H, CH_3-5′), 1.91 (d, $J = 4.0$ Hz, 1H, H_{5a}), 2.30 (s, 3H, CH_3-10), 2.71 (s, 3H, CH_3 of pyrazolone), 4.38 (td, $J = 12.8$, 1.2 Hz, 1H, H_6), 4.68 (ddd, $J = 12.4$, 4.4, 1.6 Hz, 1H, $H_{6'}$), 6.64–7.50 (m, 7H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.89$ (CH_3 of pyrazolone), 20.88 (CH_3-10), 22.66 (CH_3 attached to 3° ring junction carbon), 28.92 (CH_3-5), 32.29 (CH_3-5′), 33.77 (C-11b), 47.42 (C-5a), 61.93 (C-6), 82.73 (C-5), 100.00, 116.01, 127.26, 127.99, 128.23, 129.09, 129.48, 129.57, 130.04, 130.13, 131.69, 135.76, 147.32, 149.33, 150.40 (Ar–C) ppm; MS: $m/z = 409.0$ [M+H$^+$].

(5aR,11bS)-3-(3-Chlorophenyl)-3,5a,6,11b-tetrahydro-1,5,5,10,11b-pentamethyl-5H-chromeno[4′,3′:4,5]-pyrano[2,3-c]pyrazole (**10c**, $C_{24}H_{25}ClN_2O_2$)
White powder; yield 627 mg (67 %); m.p.: 168–170 °C; $R_f = 0.58$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}964$, 2,934, 1,585, 1,522, 1,436, 1,230, 1,086, 1,046, 861, 755, 668 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.11$ (s, 3H, CH_3 attached to 3° ring junction carbon), 1.53 (s, 3H, CH_3-5), 1.75 (s, 3H, CH_3-5′), 1.94 (d, $J = 4.0$ Hz, 1H, H_{5a}), 2.33 (s, 3H, CH_3-10), 2.75 (s, 3H, CH_3 of pyrazolone), 4.42 (td, $J = 12.4$, 1.2 Hz, 1H, H_6), 4.66 (ddd, $J = 12.6$, 4.4, 1.6 Hz, 1H, $H_{6'}$), 6.65–7.53 (m, 7H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.83$ (CH_3 of pyrazolone), 20.80 (CH_3-10), 22.68 (CH_3 attached to 3° ring junction carbon), 28.86 (CH_3-5), 32.38 (CH_3-5′), 33.92 (C-11b), 47.46 (C-5a), 62.06 (C-6), 82.88 (C-5), 101.32, 116.16, 127.23, 127.89, 128.38, 129.19, 129.43, 129.62, 130.12, 130.35, 131.74, 135.76, 147.32, 149.33, 150.40 (Ar–C) ppm; MS: $m/z = 409.0$ [M+H$^+$].

(5aR,11bS)-3-(2,5-Dichlorophenyl)-3,5a,6,11b-tetrahydro-1,5,5,10,11b-pentamethyl-5H-chromeno[4′,3′:4,5]-pyrano[2,3-c]pyrazole (**10d**, $C_{24}H_{24}Cl_{12}N_2O_2$)
White powder; yield 638 mg (63 %); m.p.: 169–171 °C; $R_f = 0.43$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}972$, 2,936, 1,591, 1,519, 1,439, 1,227, 1,091, 1,042, 822, 752, 669 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.09$ (s, 3H, CH_3 attached to 3° ring junction carbon), 1.52 (s, 3H, CH_3-5), 1.76 (s, 3H, CH_3-5′), 1.96 (d, $J = 3.6$ Hz, 1H, H_{5a}), 2.34 (s, 3H, CH_3-10), 2.75 (s, 3H, CH_3 of pyrazolone), 4.44 (td, $J = 12.4$, 1.2 Hz, 1H, H_6), 4.67 (ddd, $J = 12.4$, 4.2, 1.6 Hz, 1H, $H_{6'}$), 6.61–7.66 (m, 6H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.85$ (CH_3 of pyrazolone), 20.64 (CH_3-10), 22.87 (CH_3 attached to 3° ring junction carbon), 28.65 (CH_3-5), 32.54 (CH_3-5′), 33.86 (C-11b), 47.34 (C-5a), 62.81 (C-6), 83.01 (C-5), 101.32, 116.16, 127.23, 127.89, 128.38, 129.19, 129.43, 129.62, 130.12, 130.35, 131.74, 135.76, 147.32, 149.33, 150.40 (Ar–C) ppm; MS: $m/z = 443.1$ [M+H$^+$].

(5aR,11bS)-3,5a,6,11b-Tetrahydro-1,5,5,10,11b-pentamethyl-3-(4-methylphenyl)-5H-chromeno[4′,3′:4,5]-pyrano[2,3-c]pyrazole (**10e**, $C_{25}H_{28}N_2O_2$)
White powder; yield 622 mg (70 %); m.p.: 250–252 °C; $R_f = 0.49$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu}$= 2,983, 2,922, 1,593, 1,517, 1,442, 1,230, 1,085, 1,043, 817, 764, 667 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.09$ (s, 3H, CH_3 attached to 3° ring junction carbon), 1.62 (s, 3H, CH_3-5), 1.76 (s, 3H, CH_3-5′), 1.96 (d, $J = 4.0$ Hz, 1H, H_{5a}), 2.28 (s, 3H, CH_3-10), 2.38 (s, 3H, CH_3 of phenyl), 2.72 (s, 3H, CH_3 of pyrazolone), 4.39 (td, $J = 12.4$, 1.6 Hz, 1H, H_6), 4.69 (ddd, $J = 12.8$, 4.4, 1.6 Hz, 1H, $H_{6'}$), 6.64–7.64 (m, 7H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.85$ (CH_3 of pyrazolone), 20.84 (CH_3 of phenyl), 20.95 (CH_3-10), 22.74 (CH_3 attached to 3° ring junction carbon), 29.16 (CH_3-5), 32.15 (CH_3-5′), 33.67 (C-11b), 47.26 (C-5a), 61.91 (C-6), 82.63 (C-5), 101.15, 116.03, 120.71, 127.91, 128.27, 128.96, 129.37, 130.04, 135.12, 136.31, 146.44, 148.01, 150.42 (Ar–C) ppm; MS: $m/z = 389.1$ [M+H$^+$].

(5aR,11bS)-11b-Ethyl-3,5a,6,11b-tetrahydro-1,5,5-trimethyl-3-phenyl-5H-chromeno[4′,3′:4,5]pyrano-[2,3-c]pyrazole (**11a**, $C_{24}H_{26}N_2O_2$)
White powder; yield 394 mg (46 %); m.p.: 145–147 °C; $R_f = 0.42$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 3{,}065$, 2,933, 1,596, 1,501, 1,487, 1,315, 1,228, 1,086, 1,051, 984, 794, 753, 689 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.81$ (t, $J = 7.6$ Hz, 3H, CH_3 of ethyl), 1.09 (s, 3H, CH_3-5), 1.66 (s, 3H, CH_3-5′), 2.03 (m, 1H, –CH_2CH_3), 2.17 (d, $J = 4.0$ Hz, 1H, H_{5a}), 2.27 (m, 1H, –CH_2CH_3), 2.64 (s, 3H, CH_3 of pyrazolone), 4.40 (d, $J = 12.8$ Hz, 1H, H_6), 4.62 (dd, $J = 12.4$, 4.4 Hz, 1H, $H_{6'}$), 6.74–7.80 (m, 9H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 8.08$ (CH_3 of ethyl), 16.49 (CH_3 of pyrazolone), 23.15 (CH_3-5), 29.41 (CH_3-5′), 34.18 (CH_2 of ethyl), 37.83 (C-11b), 40.68 (C-5a), 61.56 (C-6), 82.56 (C-5),

98.01, 116.11, 120.44, 120.91, 125.32, 127.43, 127.62, 128.83, 130.07, 138.82, 146.66, 149.47, 152.69 (Ar–C) ppm; MS: $m/z = 375.2$ [M+H$^+$].

General procedure for the synthesis of ***12a–12e****,* ***13a–13e****, and* ***14a***

In a round-bottom flask, a mixture of *O*-propargylated acetophenones/propiophenone **4a–4c** (3.0 mmol), 5-pyrazolones **5a–5e** (3.0 mmol), and zinc oxide (0.75 mmol, 25 mol%) in TEAA (0.75 mmol, 25 mol%) was heated at 150 °C until the reaction was completed as monitored by TLC. The crude products thus obtained in good yields were purified further by column chromatography.

(11bS)-3,11b-Dihydro-1,11b-dimethyl-3-phenyl-6H-chromeno[4′,3′:4,5]pyrano[2,3-c]pyrazole
(**12a**, $C_{21}H_{18}N_2O_2$)
White powder; yield 588 mg (62 %); m.p.: 156–158 °C; $R_f = 0.55$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}969$, 2,927, 1,672, 1,595, 1,518, 1,488, 1,451, 1,227, 1,109, 1,039, 844, 753, 683 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.87$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.66 (s, 3H, CH_3 of pyrazolone), 4.65 (d, $J = 12.4$ Hz, 1H, H_6), 5.17 (dd, $J = 12.0$, 1.6 Hz, 1H, $H_{6'}$), 6.56 (d, $J = 1.2$ Hz, 1H, H_5), 6.87–7.73 (m, 9H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.10$ (CH_3 of pyrazolone), 27.67 (CH_3 attached to 3° ring junction carbon), 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 (C=C and Ar–C) ppm; MS: $m/z = 331.1$ [M+H$^+$].

(11bS)-3-(2-Chlorophenyl)-3,11b-dihydro-1,11b-dimethyl-6H-chromeno[4′,3′:4,5]pyrano[2,3-c]pyrazole
(**12b**, $C_{21}H_{17}ClN_2O_2$)
White powder; yield 628 mg (60 %); m.p.: 157–160 °C; $R_f = 0.27$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}966$, 2,926, 1,687, 1,613, 1,524, 1,428, 1,239, 1,113, 1,042, 852, 761, 686 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.84$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.66 (s, 3H, CH_3 of pyrazolone), 4.65 (d, $J = 12.4$ Hz, 1H, H_6), 5.17 (dd, $J = 12.8$, 1.2 Hz, 1H, $H_{6'}$), 6.57 (d, $J = 1.2$ Hz, 1H, H_5), 6.56–7.63 (m, 8H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.33$ (CH_3 of pyrazolone), 27.48 (CH_3 attached to 3° ring junction carbon), 36.44 (C-11b), 64.36 (C-6), 101.09, 114.94, 116.41, 120.51, 127.66, 128.31, 129.38, 129.56, 129.84, 130.57, 131.02, 131.61, 135.23, 147.54, 149.41, 150.55 (C=C and Ar–C) ppm; MS: $m/z = 365.2$ [M+H$^+$].

(11bS)-3-(3-Chlorophenyl)-3,11b-dihydro-1,11b-dimethyl-6H-chromeno[4′,3′:4,5]pyrano[2,3-c]pyrazole
(**12c**, $C_{21}H_{17}ClN_2O_2$)
White powder; yield 670 mg (64 %); m.p.: 119–121 °C; $R_f = 0.57$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}963$, 2,928, 1,701, 1,611, 1,527, 1,431, 1,246, 1,098, 1,045, 869, 765, 687 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.86$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.67 (s, 3H, CH_3 of pyrazolone), 4.65 (d, $J = 12.4$ Hz, 1H, H_6), 5.18 (dd, $J = 12.2$, 1.2 Hz, 1H, $H_{6'}$), 6.58 (d, $J = 1.2$ Hz, 1H, H_5), 6.87–7.68 (m, 8H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.42$ (CH_3 of pyrazolone), 27.56 (CH_3 attached to 3° ring junction carbon), 36.28 (C-11b), 64.36 (C-6), 101.05, 114.79, 117.27, 120.48, 121.31, 125.78, 127.65, 128.58, 129.37, 129.87, 138.63, 146.23, 148.63, 150.92 (C=C and Ar–C) ppm; MS: $m/z = 365.2$ [M+H$^+$].

(11bS)-3-(2,5-Dichlorophenyl)-3,11b-dihydro-1,11b-dimethyl-6H-chromeno[4′,3′:4,5]pyrano[2,3-c]pyrazole
(**12d**, $C_{21}H_{16}Cl_2N_2O_2$)
White powder; yield 699 mg (61 %); m.p.: 149–151 °C; $R_f = 0.62$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}968$, 2,922, 1,700, 1,596, 1,520, 1,437, 1,232, 1,097, 1,044, 862, 758, 676 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.86$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.65 (s, 3H, CH_3 of pyrazolone), 4.66 (d, $J = 12.4$ Hz, 1H, H_6), 5.19 (dd, $J = 12.2$, 1.2 Hz, 1H, $H_{6'}$), 6.58 (d, $J = 1.2$ Hz, 1H, H_5), 6.67–7.68 (m, 7H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.66$ (CH_3 of pyrazolone), 27.62 (CH_3 attached to 3° ring junction carbon), 36.69 (C-11b), 64.52 (C-6), 100.94, 114.68, 117.52, 121.63, 128.02, 128.79, 129.32, 129.51, 129.67, 128.03, 131.16, 132.45, 134.66, 137.03, 147.66, 149.12, 151.23 (C=C and Ar–C) ppm; MS: $m/z = 399.0$ [M+H$^+$].

(11bS)-3,11b-Dihydro-1,11b-dimethyl-3-(4-methylphenyl)-6H-chromeno[4′,3′:4,5]pyrano[2,3-c]pyrazole
(**12e**, $C_{22}H_{20}N_2O_2$)
White powder; yield 662 mg (67 %); m.p.: 147–149 °C; $R_f = 0.55$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}967$, 2,931, 1,702, 1,614, 1,517, 1,428, 1,229, 1,107, 1,042, 870, 759, 682 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.86$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.36 (s, 3H, CH_3 of phenyl), 2.67 (s, 3H, CH_3 of pyrazolone), 4.65 (d, $J = 12.4$ Hz, 1H, H_6), 5.18 (dd, $J = 12.2$, 1.2 Hz, 1H, $H_{6'}$), 6.58 (d, $J = 1.2$ Hz, 1H, H_5), 6.87–7.68 (m, 8H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.23$ (CH_3 of pyrazolone), 20.76 (CH_3 of phenyl), 27.75 (CH_3 attached to 3° ring junction carbon), 36.13 (C-11b), 64.87 (C-6), 101.55, 114.46, 117.15, 120.76, 121.11, 127.65, 129.24, 129.33, 129.72, 134.32,

135.55, 137.13, 146.22, 148.48, 151.51 (C=C and Ar–C) ppm; MS: $m/z = 345.2$ [M+H$^+$].

(11bS)-3,11b-Dihydro-1,10,11b-trimethyl-3-phenyl-6H-chromeno[4′,3′:4,5]pyrano[2,3-c]pyrazole (**13a**, $C_{22}H_{20}N_2O_2$)

White powder; yield 621 mg (68 %); m.p.: 169–172 °C; $R_f = 0.57$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}961$, 2,924, 1,689, 1,596, 1,519, 1,421, 1,232, 1,113, 1,041, 859, 764, 678 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.87$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.28 (s, 3H, CH_3-10), 2.64 (s, 3H, CH_3 of pyrazolone), 4.64 (d, $J = 12.2$ Hz, 1H, H_6), 5.16 (dd, $J = 12.4$, 1.6 Hz, 1H, $H_{6'}$), 6.59 (d, $J = 1.2$ Hz, 1H, H_5), 6.77–7.73 (m, 8H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.31$ (CH_3 of pyrazolone), 20.72 (CH_3-10), 27.26 (CH_3 attached to 3° ring junction carbon), 36.29 (C-11b), 65.10 (C-6), 102.15, 114.59, 116.96, 120.71, 125.82, 128.15, 128.76, 129.09, 129.92, 139.23, 146.61, 149.14, 151.67 (C=C and Ar–C) ppm; MS: $m/z = 345.1$ [M+H$^+$].

(11bS)-3-(2-Chlorophenyl)-3,11b-dihydro-1,10,11b-trimethyl-6H-chromeno[4′,3′:4,5]pyrano[2,3-c]-pyrazole (**13b**, $C_{22}H_{19}ClN_2O_2$)

White powder; yield 574 mg (57 %); m.p.: 174–176 °C; $R_f = 0.31$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}968$, 2,922, 1,692, 1,612, 1,521, 1,458, 1,240, 1,098, 1,042, 867, 756, 669 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.85$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.29 (s, 3H, CH_3-10), 2.64 (s, 3H, CH_3 of pyrazolone), 4.64 (d, $J = 12.0$ Hz, 1H, H_6), 5.16 (dd, $J = 12.8$, 1.2 Hz, 1H, $H_{6'}$), 6.60 (d, $J = 1.2$ Hz, 1H, H_5), 6.75–7.70 (m, 6H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 15.93$ (CH_3 of pyrazolone), 22.17 (CH_3-10), 27.36 (CH_3 attached to 3° ring junction carbon), 36.77 (C-11b), 66.49 (C-6), 102.10, 114.82, 116.71, 127.53, 127.96, 128.43, 129.09, 129.48, 129.76, 130.23, 130.52, 131.71, 135.38, 147.33, 149.34, 151.17 (C=C and Ar–C) ppm; MS: $m/z = 379.1$ [M+H$^+$].

(11bS)-3-(3-Chlorophenyl)-3,11b-dihydro-1,10,11b-trimethyl-6H-chromeno[4′,3′:4,5]pyrano[2,3-c]-pyrazole (**13c**, $C_{22}H_{19}ClN_2O_2$)

White powder; yield 543 mg (64 %); m.p.: 147–150 °C; $R_f = 0.64$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}964$, 2,926, 1,691, 1,608, 1,516, 1,443, 1,240, 1,111, 1,037, 859, 757, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.89$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.31 (s, 3H, CH_3-10), 2.66 (s, 3H, CH_3 of pyrazolone), 4.67 (d, $J = 12.4$ Hz, 1H, H_6), 5.17 (dd, $J = 12.0$, 1.2 Hz, 1H, $H_{6'}$), 6.60 (d, $J = 1.2$ Hz, 1H, H_5), 6.80–7.71 (m, 7H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.18$ (CH_3 of pyrazolone), 21.02 (CH_3-10), 27.13 (CH_3 attached to 3° ring junction carbon), 36.01 (C-11b), 65.31 (C-6), 101.54, 114.62, 116.51, 127.46, 128.18, 128.39, 129.08, 129.49, 129.74, 130.18, 130.35, 131.48, 134.57, 135.71, 147.61, 149.41, 150.58 (C=C and Ar–C) ppm; MS: $m/z = 379.1$ [M+H$^+$].

(11bS)-3-(2,5-Dichlorophenyl)-3,11b-dihydro-1,10,11b-trimethyl-6H-chromeno[4′,3′:4,5]pyrano[2,3-c]pyrazole (**13d**, $C_{22}H_{18}Cl_2N_2O_2$)

White powder; yield 615 mg (56 %); m.p.: 133–135 °C; $R_f = 0.49$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}964$, 2,930, 1,701, 1,611, 1,518, 1,466, 1,233, 1,102, 1,043, 867, 756, 671 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.87$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.31 (s, 3H, CH_3-10), 2.66 (s, 3H, CH_3 of pyrazolone), 4.65 (d, $J = 12.2$ Hz, 1H, H_6), 5.16 (dd, $J = 12.0$, 1.2 Hz, 1H, $H_{6'}$), 6.61 (d, $J = 1.2$ Hz, 1H, H_5), 6.78–7.71 (m, 6H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.61$ (CH_3 of pyrazolone), 21.44 (CH_3-10), 27.49 (CH_3 attached to 3° ring junction carbon), 37.13 (C-11b), 66.51 (C-6), 101.15, 114.74, 117.91, 127.52, 127.62, 127.92, 129.46, 129.76, 130.21, 130.59, 131.43, 132.68, 134.80, 136.56, 147.83, 149.33, 151.42 (C=C and Ar–C) ppm; MS: $m/z = 413.0$ [M+H$^+$].

(11bS)-3,11b-Dihydro-1,10,11b-trimethyl-3-(4-methylphenyl)-6H-chromeno[4′,3′:4,5]pyrano[2,3-c]pyrazole (**13e**, $C_{23}H_{22}N_2O_2$)

White powder; yield 657 mg (69 %); m.p.: 193–196 °C; $R_f = 0.59$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}967$, 2,923, 1,681, 1,614, 1,522, 1,498, 1,239, 1,110, 1,047, 822, 776, 663 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.86$ (s, 3H, CH_3 attached to 3° ring junction carbon), 2.26 (s, 3H, CH_3-10), 2.34 (s, 3H, CH_3 of phenyl), 2.65 (s, 3H, CH_3 of pyrazolone), 4.64 (d, $J = 12.2$ Hz, 1H, H_6), 5.18 (dd, $J = 12.0$, 1.6 Hz, 1H, $H_{6'}$), 6.62 (d, $J = 1.2$ Hz, 1H, H_5), 6.75–7.72 (m, 7H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.51$ (CH_3 of pyrazolone), 20.69 (CH_3-10), 20.91 (CH_3 of phenyl), 27.30 (CH_3 attached to 3° ring junction carbon), 36.45 (C-11b), 65.17 (C-6), 101.12, 116.86, 120.89, 127.95, 128.23, 128.82, 129.36, 130.47, 135.75, 136.41, 146.71, 148.76, 150.38 (C=C and Ar–C) ppm; MS: $m/z = 359.2$ [M+H$^+$].

(11bS)-11b-Ethyl-3,11b-dihydro-1-methyl-3-phenyl-6H-chromeno[4′,3′:4,5]pyrano[2,3-c]pyrazole (**14a**, $C_{22}H_{20}N_2O_2$)

White powder; yield 293 mg (32 %); m.p.: 134–136 °C; $R_f = 0.44$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu}$= 2,973, 2,934, 1,683, 1,591, 1,573, 1,492, 1,448, 1,234, 1,113, 1,042, 856, 761, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.90$ (t, $J = 7.6$ Hz, 3H, CH_3 of ethyl), 2.14 (m, 1H, –CH_2CH_3), 2.39 (m, 1H, –CH_2CH_3), 2.67 (s, 3H, CH_3 of pyrazolone), 4.64 (d, $J = 12.0$ Hz, 1H, H_6), 5.19 (dd, $J = 12.8$, 2.0 Hz, 1H, $H_{6'}$), 6.58 (d, $J = 1.2$ Hz, 1H,

H_5), 6.91–7.72 (m, 9H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 8.42$ (CH_3 of ethyl), 16.72 (CH_3 of pyrazolone), 32.31 (CH_2 of ethyl), 36.57 (C-11b), 64.94 (C-6), 100.26, 115.46, 117.71, 120.82, 121.53, 125.25, 126.18, 128.27, 129.35, 133.39, 133.94, 138.14, 145.62, 146.56, 152.64 (C=C and Ar–C) ppm; MS: $m/z = 345.2$ [M+H$^+$].

(E)-4-[1-[2-(Allyloxy)phenyl]ethylidene]-2,4-dihydro-5-methyl-1-phenyl-3H-pyrazol-3-one (Knoevenagel intermediate 1, $C_{21}H_{20}N_2O_2$)

Yellow oil; $R_f = 0.60$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}967, 2{,}926, 1{,}689, 1{,}629, 1{,}500, 1{,}232, 1{,}119, 1{,}048, 818, 755, 690$ cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.61$ (s, 3H, CH_3), 2.84 (s, 3H, CH_3 of pyrazolone), 4.60 (d, $J = 4.0$ Hz, 2H, CH_2), 5.28 (dd, $J = 10.4$, 1.2 Hz, 1H, methylene), 5.37 (dd, $J = 17.2$, 1.6 Hz, 1H, methylene), 5.99 (m, 1H, CH), 6.98–7.99 (m, 9H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.62$ (CH_3 of pyrazolone), 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 (Ar–C), 163.76 (C=N), 163.90 (C=O) ppm; MS: $m/z = 333.1$ [M+H$^+$].

(E)-2,4-Dihydro-5-methyl-4-[1-[2-(3-methylbut-2-enyloxy)phenyl]ethylidene]-1-phenyl-3H-pyrazol-3-one (Knoevenagel intermediate 2, $C_{23}H_{24}N_2O_2$)

Yellow oil; $R_f = 0.62$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}972, 2{,}927, 1{,}692, 1{,}609, 1{,}528, 1{,}496, 1{,}231, 1{,}107, 1{,}041, 823, 757, 688$ cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.62$ (s, 3H, CH_3 of acetyl), 1.68 (s, 3H, CH_3 of prenyl), 1.74 (s, 3H, CH_3 of prenyl), 2.85 (s, 3H, CH_3 of pyrazolone), 4.60 (d, $J = 5.6$ Hz, 2H, CH_2), 5.62 (t, $J = 6.7$ Hz, 1H, CH=), 7.00–7.96 (m, 9H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 17.11$ (CH_3 of pyrazolone), 23.08 (CH_3 of acetyl), 27.23 (CH_3 of prenyl), 31.30 (CH_3 of prenyl), 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 (Ar–C), 164.14 (C=N), 165.63 (C=O) ppm; MS: $m/z = 361.2$ [M+H$^+$].

(E)-2,4-Dihydro-5-methyl-1-phenyl-4-[1-[2-(prop-2-ynyloxy)phenyl]ethylidene]-3H-pyrazol-3-one (Knoevenagel intermediate 3, $C_{21}H_{18}N_2O_2$)

Yellow oil; $R_f = 0.58$ (ethyl acetate/*n*-hexane 1.5:8.5); IR (KBr): $\bar{\nu} = 2{,}966, 2{,}932, 2{,}158, 1{,}695, 1{,}612, 1{,}513, 1{,}494, 1{,}236, 1{,}113, 1{,}038, 815, 754, 691$ cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.62$ (s, 3H, CH_3 of acetyl), 2.68 (s, 3H, CH_3), 2.43 (s, 1H, CH), 4.90 (s, 2H, CH_2), 7.08–7.98 (m, 9H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 17.11$ (CH_3 of pyrazolone), 23.08 (CH_3 of acetyl), 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 (Ar–C), 164.02 (C=N), 165.42 (C=O) ppm; MS: $m/z = 331.0$ [M+H$^+$].

X-ray crystallography

CCDC-840896 and CCDC-893722 contain the supplementary crystallographic data for this article. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.

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References

1. Kawakami K, Yasuda M, Ishii K, Kokusenya Y, Sato T (1999) Chem Pharm Bull 47:919
2. Tarantin AV, Glushkov VA, Suponitskii KYu, Kudryashov AA, Maiorova OA, Tolstikov AG (2010) Russ J Org Chem 46:1479
3. Simon C, Lieby-Muller F, Peyronel J-F, Constantieux T, Rodriguez J (2003) Synlett 2301
4. Matsuzawa S, Suzuki T, Suzuki M, Matsuda A, Kawamura T, Mizuno Y, Kikuchi K (1994) FEBS Lett 356:272
5. Dinkova-Kostova AT, Talalay P, Sharkey J, Zhang Y, Holtzclaw WD, Wang XJ, David E, Schiavoni KH, Finlayson S, Mierke DF, Honda T (2010) J Biol Chem 285:33747
6. Cordova J, Leon LG, Leon F, San Andres L, Luis JG, Padron JM (2006) Eur J Med Chem 41:1327
7. Chao K, Hua K, Hsu H, Su Y, Chang S (2005) Planta Med 71:300
8. Furukawa A, Arita T, Fukuzaki T, Satsh S, Mori M, Honda T, Mastsui Y, Wakabayashi K, Hayashi S, Avaki K, Ohsumi J (2012) Bioorg Med Chem Lett 22:1348
9. Subba Reddy BV, Divya B, Swain M, Rao TP, Yadav JS, Vishnu Vardhan MVPS (2012) Bioorg Med Chem Lett 22:1995
10. Zhang G, Ma N, Jiang B, Shi F, Tu SJ (2010) Synthesis 3993
11. Hanus LO (2009) Med Res Rev 29:213
12. Adebajo AC, Ayoola OF, Iwalewa EO, Akindahunsi AA, Omisore NOA, Adewunmi CO, Adenowo TK (2006) Phytomedicine 13:246
13. Biellmann J-F (2003) Chem Rev 103:2019
14. Tietze LF, Beifuss U, Lökös M, Rischer M, Göhrt A, Sheldrick GM (1990) Angew Chem Int Ed 29:527
15. Tietze LF, Wölfling J, Schneider G (1991) Chem Ber 124:591
16. Tietze LF, Bärtels C (1991) Liebigs Ann Chem 155
17. Mukherjee S, Yang JW, Hoffmann S, List B (2007) Chem Rev 107:5471
18. Chapman CJ, Frost CG (2007) Synthesis 1
19. Tietze LF, Modi A (2000) Med Res Rev 20:304
20. Pellissier H (2006) Tetrahedron 62:2143
21. Tietze LF, Brasche G, Gericke KM (2006) Domino reactions in organic synthesis. Wiley-VCH, Weinheim
22. Nicolaou KC, Montagnon T, Snyder SA (2003) Chem Commun 551
23. Ho T-L (1992) Tandem organic reactions. Wiley, New York

24. Tietze LF, Rackelmann N (2005) In: Zhu J, Bienayme H (eds) Multicomponent reactions. Wiley-VCH, Weinheim, p 121
25. Tietze LF, Beifuss U (1993) Angew Chem Int Ed 32:131
26. Tietze LF, Rackelmann N (2004) Pure Appl Chem 76:1967
27. Tietze LF, Kettschau G, Gewart JA, Schuffenhauer A (1998) Curr Org Chem 2:19
28. Sridharan V, Menéndez JC (2010) Chem Rev 110:3805
29. Ramachary DB, Ramakumar K, Narayana VV (2007) J Org Chem 72:1458
30. Ramachary DB, Kishor M (2007) J Org Chem 72:5056
31. Toure BB, Hall DG (2009) Chem Rev 109:4439
32. Kumar A, Maurya RA (2007) Tetrahedron 63:1946
33. Sabitha G, Fatima N, Reddy EV, Yadav JS (2005) Adv Synth Catal 347:1353
34. Ramachary DB, Anebouselvy K, Chowdari NS, Barbas CF (2004) J Org Chem 69:5838
35. Hong B-C, Wu M-F, Tseng H-C, Huang G-F, Su C-F, Liao J-H (2007) J Org Chem 72:8459
36. Clarke PA, Martin WHC (2002) Org Lett 4:4527
37. Tietze LF, Bohnke N, Dietz S (2009) Org Lett 11:2948
38. Appendino G, Cravotto G, Toma L, Annunziata R, Palmisano G (1994) J Org Chem 59:5556
39. Tietze LF (1996) Chem Rev 96:115
40. Jiménez-Alonso S, Orellana HC, Estévez-Braun A, Ravelo AG, Pérez-Sacau E, Machín F (2008) J Med Chem 51:6761
41. Pellissier H (2009) Tetrahedron 65:2839
42. Jayashankaran J, Durga R, Manian RS, Raghunathan R (2006) Tetrahedron Lett 47:2265
43. Tietze LF, Brand S, Pfeiffer T, Antel J, Harms K, Sheldrick GM (1987) J Am Chem Soc 109:921
44. Tietze LF, Brumby T, Pretor M, Remberg G (1988) J Org Chem 53:810
45. Baruah B, Bhuyan PJ (2009) Tetrahedron 65:7099
46. Parmar NJ, Teraiya SB, Patel RA, Talpada NP (2011) Tetrahedron Lett 52:2853
47. Parmar NJ, Patel RA, Teraiya SB, Sharma D, Gupta VK (2012) RSC Adv 2:3069
48. Parmar NJ, Teraiya SB, Barad HA, Sharma D, Gupta VK (2013) Synth Commun. doi:10.1080/00397911.2011.652755
49. Lozama A, Cunningham CW, Caspers MJ, Douglas JT, Dersch CM, Rothman RB, Prisinzano TE (2011) J Nat Prod 74:718
50. Ross RA, Brockie HC, Stevenson LA, Murphy VL, Templeton F, Makriyannis A, Pertwee RG (1999) Br J Pharmacol 126:665
51. Poulin J, Grisé-Bard CM, Barriault L (2009) Chem Soc Rev 38:3092
52. Shanmugasundaram M, Manikandan S, Raghunathan R (2002) Tetrahedron 58:997
53. Tietze LF, Pfeiffer T, Schuffenhauer A (1998) Eur J Org Chem 2733
54. Kiamehr M, Moghaddam FM (2009) Tetrahedron Lett 50:6723
55. Khoshkholgh MJ, Balalaie S, Bijanzadeh HR, Rominger H, Gross JH (2008) Tetrahedron Lett 49:6965
56. Sheldrick GM (1997) SHELX97. University of Göttingen, Germany
57. Farrugia LJ (1997) J Appl Cryst 30:565
58. Farrugia LJ (1999) J Appl Cryst 32:837
59. Nardelli MJ (1995) J Appl Cryst 28:659
60. Verma AK, Attri P, Chopra V, Tiwari RK, Chandra R (2008) Monatsh Chem 139:1041