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# SYNTHETIC CHALLENGES IN THE CONSTRUCTION OF 8- TO 10-MEMBERED PYRAZOLE-FUSED RINGS VIA RING-CLOSING METATHESIS

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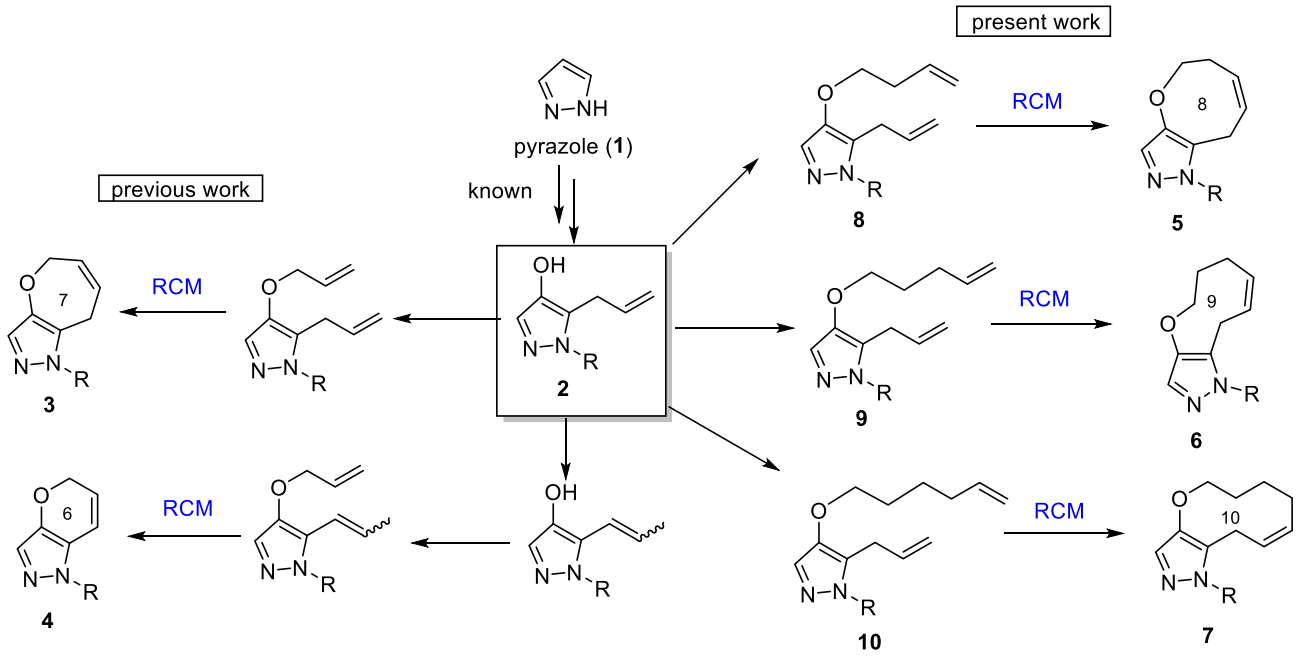
**Abstract** – Novel pyrazole-fused heterobicyclic systems, i.e., trihydrooxocino[3,2-*c*]pyrazoles, tetrahydrooxonino[3,2-*c*]pyrazoles, and pentahydrooxecino[3,2-*c*]pyrazoles, were synthesized starting from 3- or 5-allyl-4-hydroxy-1*H*-pyrazoles via ring-closing metathesis (RCM) as the key step for the construction of the medium-sized rings (8- to 10-membered rings). The RCM reactions at room temperature required longer times and gave lower yields than those in our previous studies on the preparation of normal RCM products with 6- or 7-membered rings. The microwave-assisted RCM generally afforded double-bond migrated products or ring-contracted products along with normal RCM products.

## INTRODUCTION

The synthesis of functionalized pyrazoles or pyrazole-fused heterocycles is crucial for drug discovery since these compounds are expected to exhibit various bioactivities such as antiinflammatory, antibacterial, antitumor, or analgesic properties. Therefore, their synthesis has gained considerable attention.[1–5] We have been studying the C4-functionalization of pyrazoles and have expanded our work to include pyrazole-fused heterocyclic compounds. Recently, we reported the synthesis of dihydrooxepino[3,2-*c*]pyrazoles (**3**) via a combination of the Claisen rearrangement of 4-allyloxy-1*H*-pyrazoles and subsequent functionalization and ring-closing metathesis (RCM) as key steps,[6] and the successful synthesis of dihydropyrano[3,2-*c*]pyrazoles (**4**) with a smaller pyrazole-fused heterocyclic ring.[7] This resulted in the construction of 5-7 or 5-6 pyrazole-containing bicyclic compounds. Thus, our next challenge was the construction of novel pyrazole-fused molecules by expanding the size of

the pyrazole-fused ring by using a similar basic strategy (Scheme 1). This contrasts our previous work.[7] Generally, the construction of medium-sized cyclic compounds is difficult compared to that of 5- or 6-membered rings.[8–11] Therefore, it was an attractive challenge to construct pyrazole-fused 8- to 10-membered heterocycles. Herein we report the synthesis of trihydrooxocino[3,2-*c*]pyrazoles (**5**), tetrahydrooxonino[3,2-*c*]pyrazoles (**6**), and pentahydrooxecino[3,2-*c*]pyrazoles (**7**), which correspond to new 5-8, 5-9, and 5-10 pyrazole-fused heterobicyclic molecules.



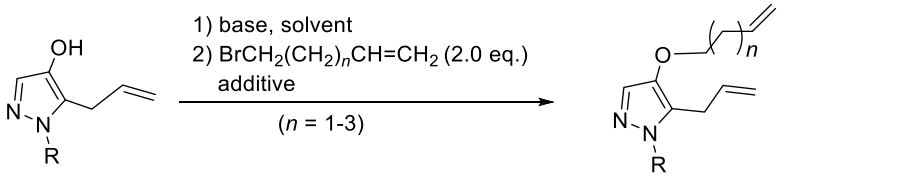

**Scheme 1.** Comparison of the present work with our previous work

## RESULTS AND DISCUSSION

Compounds **2a** and **2b**, which were prepared from commercially available pyrazole (**1**) according to the literature,[11] were treated with alkenyl halides in the presence of NaOH as a base to afford the RCM substrates, i.e., 5-allyl-4-*O*-alkenyl-1*H*-pyrazoles (**8-10**). The results are summarized in Table 1. 5-Allyl-4-hydroxy-1-trityl-1*H*-pyrazole (**2a**) was treated with aqueous NaOH followed by the addition of the appropriate alkenyl halide with catalytic amounts of tetrabutylammonium bromide to give the desired products **8a**, **9a**, and **10a**, as shown in entries 1–3, respectively, but the reaction times were longer compared to those for *O*-allylation in the previous paper. The same reaction on *N*-benzylated substrate **2b** gave the desired products in poor yields (entries 4, 5) without recovery of **2b**. Prolonged reaction times under basic conditions in the presence of significant amounts of water might lead to debenzylation, so alternative conditions were examined. When sodium hydride was applied as a base to **2b** for 4-*O*-butenylation in dry THF, the yield of the desired **8b** was slightly improved to 23% (entry 6).

Reaction using potassium *t*-butoxide (*t*-BuOK) with **2b** in *t*-BuOH under microwave (MW) irradiation at 80 °C afforded **8b** in 37% yield (entry 7). Reaction of **2b** in acetone with a minimum amount of 20% NaOH aq. was then examined (entry 10). The reaction at room temperature (rt) overnight gave a satisfactory yield of **8b** (91%). Compounds **9b** and **10b** were prepared similarly using these conditions (entries 11, 12).

**Table 1.** *O*-Alkenylation of 5-allyl-4-hydroxy-1*H*-pyrazoles (**2**)

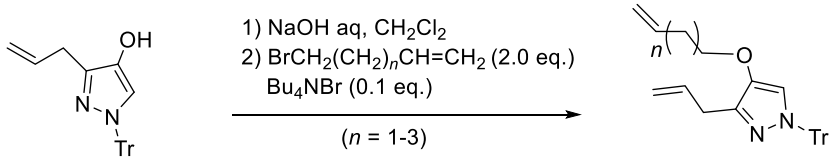



**2a**: R = Tr
**2b**: R = Bn

R = Tr: **8a** (*n* = 1), **9a** (*n* = 2), **10a** (*n* = 3)
R = Bn: **8b** (*n* = 1), **9b** (*n* = 2), **10b** (*n* = 3)

| entry | substrate | alkenyl bromide | solvent | base | additive | temp. (°C) | time | product |
|---|---|---|---|---|---|---|---|---|
| 1 | **2a** | *n* = 1 | $CH_2Cl_2$ | NaOH | $Bu_4NBr$ | rt | overnight | **8a** (59%) |
| 2 | **2a** | *n* = 2 | $CH_2Cl_2$ | NaOH | $Bu_4NBr$ | rt | overnight | **9a** (57%) |
| 3 | **2a** | *n* = 3 | $CH_2Cl_2$ | NaOH | $Bu_4NBr$ | rt | overnight | **10a** (60%) |
| 4 | **2b** | *n* = 1 | $CH_2Cl_2$ | NaOH | $Bu_4NBr$ | rt | overnight | **8b** (3%) |
| 5 | **2b** | *n* = 2 | $CH_2Cl_2$ | NaOH | $Bu_4NBr$ | rt | overnight | **9b** (0%) |
| 6 | **2b** | *n* = 1 | THF | NaH | | rt | 2.5 h | **8b** (23%) |
| 7 | **2b** | *n* = 1 | *t*-BuOH | KO$^t$Bu | | MW: 80 | 30 min | **8b** (37%) |
| 8 | **2b** | *n* = 2 | *t*-BuOH | KO$^t$Bu | | MW: 80 | 30 min | **9b** (39%) |
| 9 | **2b** | *n* = 3 | *t*-BuOH | KO$^t$Bu | | MW: 80 | 30 min | **10b** (47%) |
| 10 | **2b** | *n* = 1 | acetone | NaOH | $Bu_4NBr$ | rt | overnight | **8b** (91%) |
| 11 | **2b** | *n* = 2 | acetone | NaOH | $Bu_4NBr$ | rt | overnight | **9b** (87%) |
| 12 | **2b** | *n* = 3 | acetone | NaOH | $Bu_4NBr$ | rt | overnight | **10b** (78%) |

In addition, substrate **11**, which is reported as a minor product in the Claisen rearrangement of 4-allyloxy-1*H*-1-tritylpyrazole, was *O*-alkenylated using the conditions mentioned in entries 1–3 of Table 1. As shown in Scheme 2, the desired products **12**–**14** were obtained in lower yields than **8a**–**10a**.



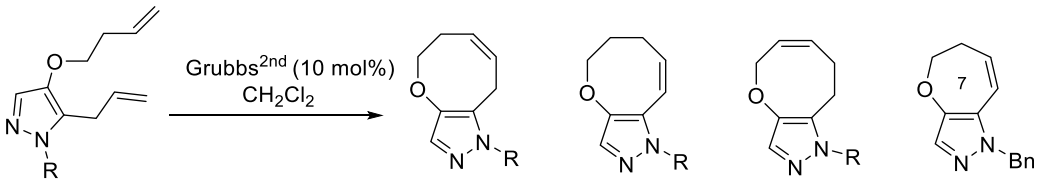

**11**

**12** (*n* = 1, 44%)
**13** (*n* = 2, 38%)
**14** (*n* = 3, 53%)

**Scheme 2.** *O*-Alkenylation of 3-allyl-4-hydroxy-1*H*-pyrazoles (**11**)

With the reaction substrates **8**–**10** and **12**–**14** in hand, RCM was investigated. The same reaction conditions described in our previous paper were applied here; they are reaction at rt and MW-aided reaction at 140 °C for 10 min. Since every substrate required a longer reaction time at rt, the reaction time was fixed as overnight (15 h). The results of the RCM of **8a** and **8b** are summarized in Table 2. Neither the reaction of **8a** nor that of **8b** was complete within the reaction time. The desired RCM products **8a** and **8b** were obtained in 55% and 38% yields, respectively, with recovery of significant amounts of the starting materials (entries 1 and 4). The MW-aided reaction of **8a** gave the desired **5a** in 25% yield, accompanied by the double-bond migrated product **16a** in 26% yield, and the starting material **8a** was completely consumed (entry 2).[12,13] Adding *p*-benzoquinone to the reaction mixture to avoid the double bond migration[14] did not produce satisfactory results, but improved selectivity was realized (entry 3). Changing the substrate to **8b** in the MW reaction gave **15b** as the major product (33%), and the accompanying products were **5b** (10%), **16b** (7%), and the 7-membered ring compound **17b**[6] (4%) (entry 5). The formation of **17b** is explained by the double bond migration in **8b** proceeding before RCM. Addition of *p*-benzoquinone only inhibited the formation of **17b** (entry 6).

**Table 2.** RCM of 5-allyl-4-(3-butenyl)oxy-1*H*-pyrazoles (**8**)

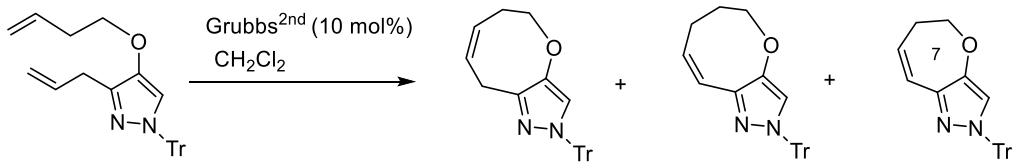



| entry | substrate | temperature | time | product | | | |
|---|---|---|---|---|---|---|---|
| 1[a] | **8a** | rt | overnight | **5a** (55%) | - | - | - |
| 2 | | MW: 140 °C | 10 min | **5a** (25%) | - | **16a** (26%) | |
| 3[b] | | MW: 140 °C | 10 min | **5a** (56%) | - | **16a** (6%) | |
| 4[c] | **8b** | rt | overnight | **5b** (38%) | - | - | - |
| 5 | | MW: 140 °C | 10 min | **5b** (10%) | **15b** (33%) | **16b** (7%) | **17b** (4%) |
| 6[b] | | MW: 140 °C | 10 min | **5b** (0%) | **15b** (37%) | **16b** (0%) | - |

a. **8a** was recovered in 7%. b. 20 mol% of *p*-benzoquinone was used as an additive.
c. **8b** was recovered in 29%.

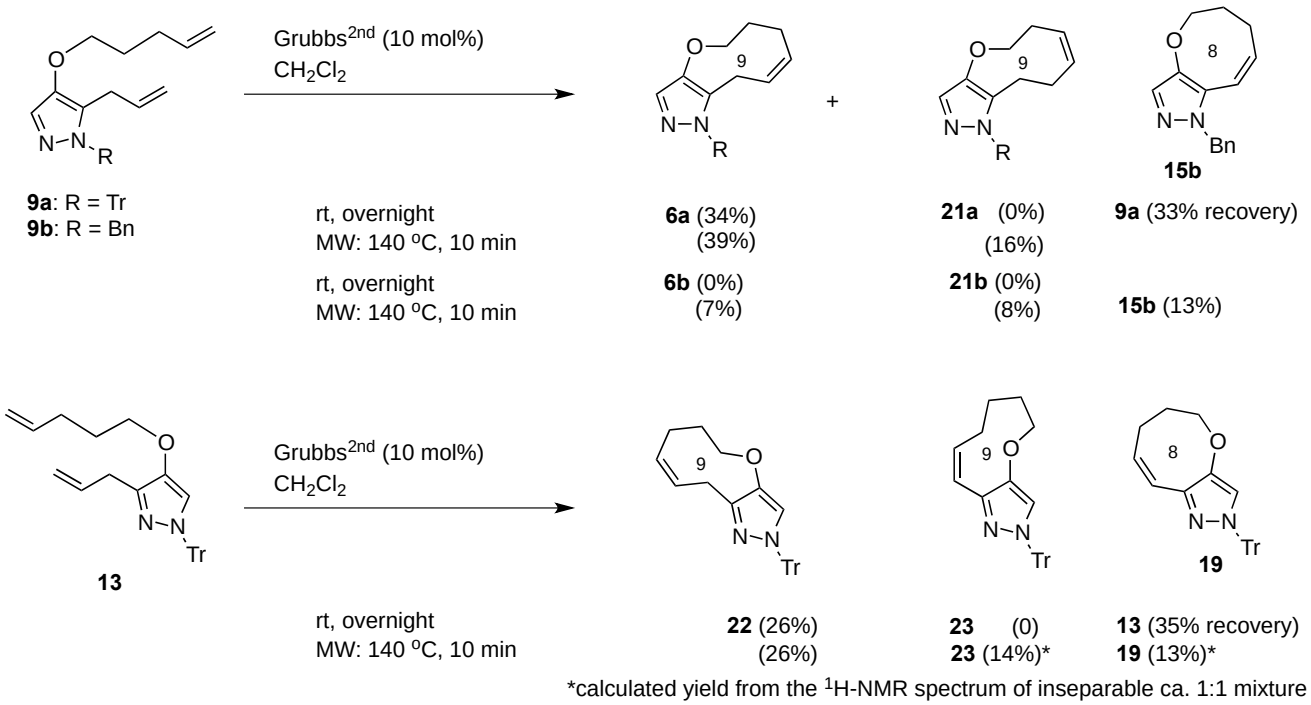
A similar approach was applied to the 3-allylated substrate **12**. However, the desired RCM products **18** or **19** were obtained in low yields (Scheme 3). The MW-aided reaction gave the normal product **18**, the double-bond migrated compound **19**, and the ring-contracted product **20** in similar yields (17%, 15%, and 19%, respectively). The different preference for the double bond migration position between the

MW-aided reaction of **12** and that of **8a** is interesting. The bulky trityl group might inhibit the double bond migration to give **15a** mediated by the ruthenium hydride species formed at higher temperatures (entries 2 and 3 in Table 2), but had no effect on substrate **12** because the reaction site is distant from the trityl group. Addition of *p*-benzoquinone prevented the formation of 7-membered product **20**, as mentioned above.



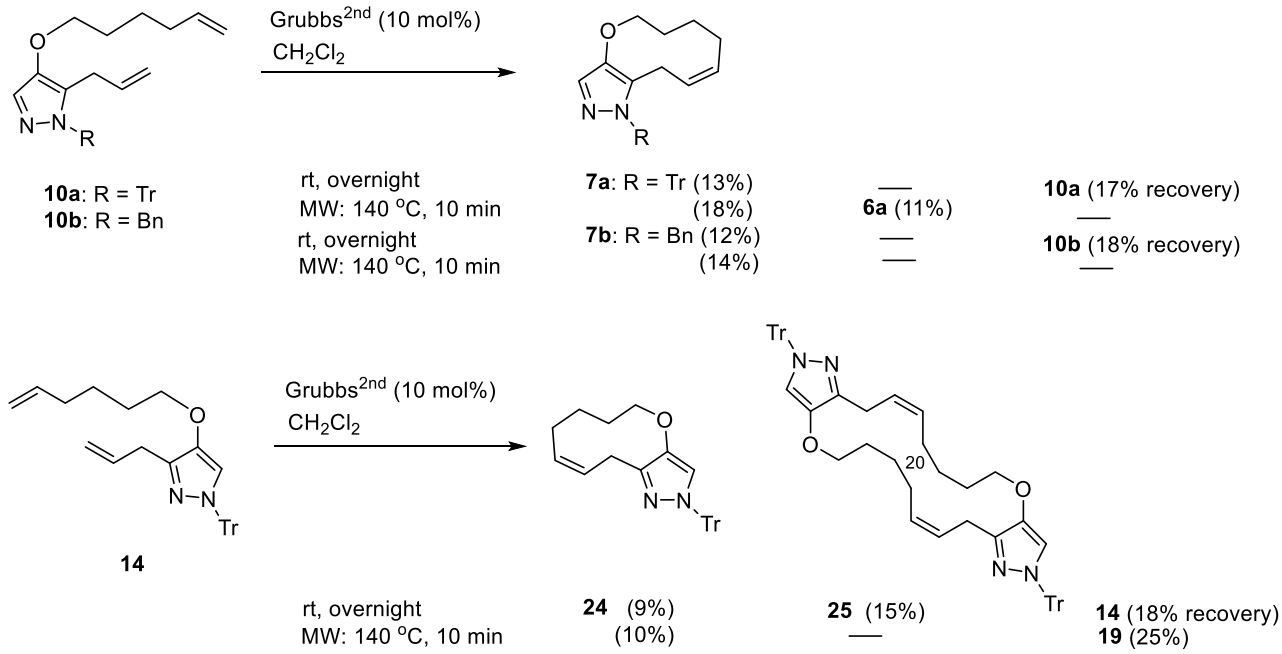

**Scheme 3.** RCM of 3-allyl-4-(3-butenyl)oxy-1*H*-1-tritylpyrazole (**12**)

The construction of a 9- or 10-membered ring fused to pyrazole was quite difficult, with many products being observed in TLC analysis. The results for 9- and 10-membered rings are summarized in Schemes 4 and 5, respectively, and only identified products are included.




**Scheme 4.** RCM of 5- or 3-allyl-4-(4-pentenyl)oxy-1*H*-pyrazoles (**9, 13**)

Reactions of substrates **9a** or **13** at rt overnight gave the desired products **6a** or **22** in 34% or 26% yield, respectively. However, the same reaction using **9b** did not afford the desired product **6b** although the starting material **9b** was consumed.[15] The MW-aided RCM of **9a** afforded **6a** (39%) and **21a** (16%). When the substrate was changed to **9b**, products **6b**, **21b**, and **15b** could be isolated in poor yields from the reaction mixture. Similarly, compounds **22** (26%), **23** (14%), and **19** (13%) were obtained from the MW reaction mixture starting from substrate **13** (Scheme 4).




**Scheme 5.** RCM of 5- or 3-allyl-4-(5-hexenyl)oxy-1*H*-pyrazoles (**10, 14**)

Finally, we examined the synthesis of **7a**, **7b**, and **24** (Scheme 5). In all the experiments, the chemical yields of the desired products **7a**, **7b**, and **24** were only 9%–18%. As mentioned above, many spots were observed in TLC analysis, even in the reactions at rt. For example, the RCM of **10a** at rt showed at least six bands on the preparative TLC plates. Formation of an interesting side product was observed in the reaction of **14** at rt. The side product **25** had a molecular weight of 840, which corresponds to just twice that of the normal RCM product **24**. From the simplicity of the NMR spectra, a symmetrical structure involving a 20-membered ring moiety was proposed for compound **25**. It is thought to be formed by RCM dimerization.[16,17]

## CONCLUSION

Syntheses of trihydrooxocino[3,2-*c*]pyrazoles, tetrahydrooxonino[3,2-*c*]pyrazoles, and pentahydrooxe-cino[3,2-*c*]pyrazoles via RCM were examined. While the desired RCM products were

obtained, their yield at rt was lower than that of the corresponding 7-membered ring product as the newly constructed ring size increased. The corresponding reactions at higher temperature with MW irradiation resulted in various RCM products. Controlling the products is difficult in pyrazoles with more than 9-membered rings. Addition of *p*-benzoquinone only prevented the formation of ring-contracted products.

## EXPERIMENTAL

NMR spectra were recorded at 27 °C on Agilent 300- and 400-MR-DD2 spectrometers in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard. IR spectra were obtained with a JEOL FT/IR-680 Plus spectrometer. HRMS was determined with a JEOL JMS-700 (2) mass spectrometer. Melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. Liquid column chromatography was conducted over silica gel (Nacalai, silica gel 60, mesh 70–230 or 230–400). Analytical TLC was performed on precoated Merck glass plates (silica gel 60 $F_{254}$) and compounds were detected by dipping the plates in an ethanol solution of phosphomolybdic acid, followed by heating. All microwave-aided reactions were carried out with a Biotage Initiator® (Switzerland).

**Synthesis of 3- or 1-protected 5-allyl-4-alkenyloxy-1*H*-pyrazoles** (Table 1, Scheme 2)

*General procedure of O-alkenylation in $CH_2Cl_2$* (Table 1, entry 1): To a solution of **2a** (114.8 mg, 0.31 mmol) in $CH_2Cl_2$ (2 mL) were added 20% NaOH aq. (2 mL), 4-bromo-1-butene (0.092 mL, 0.63 mmol), and $Bu_4NBr$ (3.7 mg, 0.011 mmol) at rt. Then the reaction mixture was stirred overnight, quenched with sat. $NH_4Cl$ aq., and extracted 3 times with $CH_2Cl_2$. The combined organic layer was dried over $MgSO_4$, filtered, and evaporated to give a crude residue, which was purified by column chromatography (eluent: hexane:EtOAc = 10:1) to afford **8a** (77.9 mg, 59%).

*General procedure of MW-aided O-alkenylation* (Table 1, entry 7): To a solution of **2b** (36.3 mg, 0.18 mmol) in *t*-BuOH (4.5 mL) in a MW vial were added 4-bromo-1-butene (0.031 mL, 0.20 mmol) and *t*-BuOK (25.5 mg, 0.23 mmol) at rt. Then the sealed vial was heated under MW irradiation at 100 °C for 30 min. After cooling, the reaction mixture was quenched with sat. $NH_4Cl$ aq. and extracted 3 times with $CH_2Cl_2$. The combined organic layer was dried over $MgSO_4$, filtered, and evaporated to give a crude residue, which was purified by column chromatography (eluent: hexane:EtOAc = 3:1) to afford 5-allyl-1-benzyl-4-(3-butenyl)oxy-1*H*-pyrazole (**8b**) (17.0 mg, 37%)

*General procedure of O-alkenylation in acetone* (Table 1, entry 10): To a solution of **2b** (30.7 mg, 0.15 mmol) in acetone (2 mL) were added 20% NaOH aq. (50 μL, 0.25 mmol), 4-bromo-1-butene (31.2 μL, 0.30 mmol), and $Bu_4NBr$ (0.7 mg, 0.011 mmol) at rt. Then the reaction mixture was stirred overnight, quenched with sat. $NH_4Cl$ aq., and extracted 3 times with $CH_2Cl_2$. The combined organic layer was dried

over $MgSO_4$, filtered, and evaporated to give a crude residue, which was purified by column chromatography (eluent: hexane:EtOAc = 3:1) to afford **8b** (35.4 mg, 91%)

5-Allyl-4-(3-butenyl)oxy-1*H*-1-tritylpyrazole (**8a**): Colorless crystals ($CH_2Cl_2$); mp 75–78 °C; IR (KBr) $\nu_{max}$ 1583 (C=C), 1493 (C=C), 1446 (C=C) $cm^{-1}$; $^1$H-NMR (600 MHz, $CDCl_3$): δ 2.46 (2H, qt, *J* = 6.7, 1.4 Hz, -$CH_2CH_2$CH=), 2.82 (2H, br d, *J* = 6.4 Hz, ArC$H_2$CH=), 3.95 (2H, t, *J* = 6.7 Hz, -OC$H_2CH_2$-), 4.60 (1H, dq, *J* = 17.0, 1.8 Hz, -CH=CH*H*), 4.64 (1H, dq, *J* = 10.3, 1.5 Hz, -CH=CH*H*), 4.98 (1H, ddt, *J* = 16.7, 10.3, 6.5 Hz, -C*H*=$CH_2$), 5.06 (1H, br d, *J* = 16.7Hz, -CH=CH*H*), 5.12 (1H, dq, *J* = 17.0, 1.8 Hz, -CH=CH*H*), 5.86 (1H, ddt, *J* = 17.1, 10.3, 6.6 Hz, -$CH_2$C*H*=$CH_2$), 7.10–7.14 (6H, m, Tr-H), 7.23–7.30 (9 H, m, Tr-H), 7.32 (1H, s, pyrazole-H); $^{13}$C-NMR (150 MHz, $CDCl_3$): δ 29.2, 31.2, 31.7, 34.1, 53.8, 70.9, 78.5, 115.6, 116.8, 127.3, 127.5, 130.0, 132.5, 134.6, 143.0; HREIMS *m/z* calcd for $C_{29}H_{28}N_2O$ ($M^+$) 420.2202, found 420.2198.

5-Allyl-4-(4-pentenyl)oxy-1*H*-1-tritylpyrazole (**9a**): Colorless crystals ($CH_2Cl_2$); mp 104–108 °C; IR (KBr) $\nu_{max}$ 1582 (C=C), 1445 (C=C) $cm^{-1}$; $^1$H-NMR (600 MHz, $CDCl_3$): δ 1.80 (2H, br quint, *J* = 6.4 Hz, -$CH_2CH_2CH_2$-), 2.19 (2H, br q, *J* = 7.1 Hz, -$CH_2CH_2$CH=), 2.83 (2H, br d, *J* = 6.5 Hz, ArC$H_2$CH=), 3.91 (2H, t, *J* = 6.4 Hz, -OC$H_2CH_2$-), 4.61 (1H, br dq, *J* = 17.0, 1.5 Hz, -CH=CH*H*), 4.64 (1H, br dq, *J* = 10.3, 1.2 Hz, -CH=CH*H*), 4.95–5.00 (2H, m), 5.03 (1H, br dq, *J* = 17.0, 1.5 Hz, -CH=C*H*H), 5.83 (1H, ddt, *J* = 17.0, 10.2, 6.5 Hz, -$CH_2$C*H*=$CH_2$), 7.11–7.13 (6H, m, Tr-H), 7.23–7.30 (9 H, m, Tr-H), 7.31 (1H, s, pyrazole-H); $^{13}$C-NMR (150 MHz, $CDCl_3$): δ 28.8, 30.1, 31.2, 70.9, 78.5, 115.0, 115.5, 125.1, 127.3, 127.5, 127.9, 130.1, 132.6, 138.0, 143.0, 144.5; HREIMS *m/z* calcd for $C_{30}H_{30}N_2O$ ($M^+$) 434.2358, found 434.2356.

5-Allyl-4-(5-hexenyl)oxy-1*H*-1-tritylpyrazole (**10a**): White amorphous powder ($CH_2Cl_2$–hexane); mp 73–78 °C; IR (KBr) $\nu_{max}$ 1579 (C=C), 1492 (C=C), 1446 (C=C) $cm^{-1}$; $^1$H-NMR (600 MHz, $CDCl_3$) δ 1.52 (2H, br tt, *J* = 7.3, 6.8 Hz, -$CH_2CH_2CH_2$-), 1.72 (2H, br tt, *J* = 6.8, 6.4 Hz, -$CH_2CH_2CH_2$-), 2.10 (2H, br q, *J* = 6.8 Hz, -$CH_2CH_2$CH=), 2.83 (2H, dt, *J* = 6.4, 1.2 Hz, ArC$H_2$CH=$CH_2$), 3.90 (2H, t, *J* = 6.4 Hz, -OC$H_2CH_2$-), 4.60 (1H, br dq, *J* = 17.0, 1.5 Hz, -CH=CH*H*), 4.64 (1H, br dq, *J* = 10.3, 1.5 Hz, -CH=CH*H*), 4.94–5.03 (3H, overlapped), 5.80 (1H, ddt, *J* = 17.0, 10.2, 6.5 Hz, -$CH_2$C*H*=$CH_2$), 7.11–7.13 (6H, m, Tr-H), 7.23–7.30 (9 H, m, Tr-H), 7.31 (1H, s, pyrazole-H); $^{13}$C-NMR (150 MHz, $CDCl_3$) δ 25.2, 29.0, 31.2, 33.4, 71.4, 78.5, 114.6, 115.5, 125.1, 127.3, 127.5, 128.7, 130.1, 132.6, 138.6, 143.0, 144.6; HREIMS *m/z* calcd for $C_{31}H_{32}N_2O$ $[M]^+$ 448.2515, found 448/2513.

3-Allyl-4-(3-butenyl)oxy-1*H*-1-tritylpyrazole (**12**): Oil; IR (film) $\nu_{max}$ 1639 (C=C), 1573 (C=C), 1493 (C=C), 1445 (C=C) $cm^{-1}$; $^1$H-NMR (600 MHz, $CDCl_3$): δ 2.41 (2H, qt, *J* = 6.7, 1.4 Hz, -$CH_2C\mathit{H}_2CH_2$-), 3.36 (2H, ddd, *J* = 6.4, 1.8, 1.5 Hz, Ar$C\mathit{H}_2CH{=}CH_2$), 3.74 (2H, t, *J* = 6.8 Hz, -$OC\mathit{H}_2CH_2$-), 4.99 (1H, dq, *J* = 10.0, 1.5 Hz, -$CH_2CH{=}CH\mathit{H}$), 5.02 (1H, dq, *J* = 17.0, 1.5 Hz, -$CH_2CH{=}CH\mathit{H}$), 5.04 (1H, dq, *J* = 10.4, 2.0 Hz, -$CH_2CH{=}CH\mathit{H}$), 5.05 (1H, dq, *J* = 10.4, 1.8 Hz, -$CH_2CH{=}CH\mathit{H}$), 5.09 (1H, dq, *J* = 17.3, 1.7 Hz, -$CH_2CH{=}CH\mathit{H}$), 5.82 (1H, ddt, *J* = 13.0, 10.2, 6.8 Hz, $CH_2C\mathit{H}{=}CH_2$), 5.98 (1H, ddt, *J* = 17.0, 10.3, 6.2 Hz, -$CH_2C\mathit{H}{=}CH_2$), 6.88 (1H, s, pyrazole-H), 7.15–7.19 (6H, m, Tr-H), 7.26–7.30 (9 H, m, Tr-H); $^{13}$C-NMR (150 MHz, $CDCl_3$): δ 30.0, 33.9, 71.4, 78.1, 115.1, 116.9, 118.2, 127.5, 127.6, 130.1, 134.5, 135.9, 140.1, 141.9, 143.5; HREIMS *m/z* calcd for $C_{29}H_{28}N_2O$ ($M^+$) 420.2202, found 420.2192.

3-Allyl-4-(4-pentenyl)oxy-1*H*-1-tritylpyrazole (**13**): Oil; IR (film) $\nu_{max}$ 1571 (C=C), 1493 (C=C), 1446 (C=C) $cm^{-1}$; $^1$H-NMR (600 MHz, $CDCl_3$): δ 1.75 (2H, br quint, *J* = 6.4 Hz, -$CH_2C\mathit{H}_2CH_2$-), 2.15 (2H, br q, *J* = 7.2 Hz, -$CH_2C\mathit{H}_2CH{=}$), 3.36 (2H, dt, *J* = 6.2, 1.5 Hz, Ar$C\mathit{H}_2CH{=}CH_2$), 3.70 (2H, t, *J* = 6.4 Hz, -$OC\mathit{H}_2CH_2$-), 4.94–5.04 (4H, overlapped), 5.80 (1H, ddt, *J* = 17.0, 10.3, 6.5 Hz, -$CH_2C\mathit{H}{=}CH_2$), 5.97 (1H, ddt, *J* = 17.3, 10.2, 6.2 Hz, -$CH_2C\mathit{H}{=}CH_2$), 6.87 (1H, s, pyrazole-H), 7.15–7.19 (6H, m, Tr-H), 7.26–7.30 (9 H, m, Tr-H); $^{13}$C-NMR (150 MHz, $CDCl_3$): δ 28.6, 29.99, 30.02, 71.4, 78.1, 115.1, 117.9, 127.4, 127.6, 130.1, 135.9, 135.9, 137.9, 140.0, 142.1, 143.5; HREIMS *m/z* calcd for $C_{30}H_{30}N_2O$ ($M^+$) 434.2358, found 434.2356.

3-Allyl-4-(5-hexenyl)oxy-1*H*-1-tritylpyrazole (**14**): Oil; IR (film) $\nu_{max}$ 1571 (C=C), 1493 (C=C), 1446 (C=C) $cm^{-1}$; $^1$H-NMR ($CDCl_3$) δ 1.46–1.52 (2H, m, -$CH_2C\mathit{H}_2CH_2$-), 1.64–1.70 (2H, m, -$CH_2C\mathit{H}_2CH_2$-), 2.07 (2H, br q, *J* = 7.2 Hz, -$CH_2C\mathit{H}_2CH{=}$), 3.36 (2H, dt, *J* = 6.1, 1.5 Hz, Ar$C\mathit{H}_2CH{=}CH_2$), 3.69 (2H, t, *J* = 6.4 Hz, -$OC\mathit{H}_2CH_2$-), 4.94 (1H, ddt, *J* = 10.2, 2.3, 1.2 Hz, -$CH_2CH{=}C\mathit{H}$H), 4.96-5.04 (3H, overlapped), 5.79 (1H, ddt, *J* = 17.3, 10.3, 6.7 Hz, -$CH_2C\mathit{H}{=}CH_2$), 5.97 (1H, ddt, *J* = 17.4, 10.0, 6.2 Hz, -$CH_2C\mathit{H}{=}CH_2$), 6.86 (1H, s, pyrazole-H), 7.15-7.20 (6H, m, Tr-H), 7.25–7.36 (9H, m, Tr-H); $^{13}$C-NMR ($CDCl_3$) δ 25.2, 29.0, 31.2, 33.4, 71.4, 78.4, 114.6, 115.5, 125.1, 127.3, 127.5, 128.7, 130.1, 132.6, 138.6, 143.0, 144.6; HREIMS *m/z* calcd for $C_{31}H_{32}N_2O$ $[M]^+$ 448.2515, found 448/2518.

5-Allyl-1-benzyl-4-(3-butenyl)oxy-1*H*-pyrazole (**8b**): Oil; IR (film) $\nu_{max}$ 1570 (C=C), 1456 (C=C) $cm^{-1}$; $^1$H-NMR (400 MHz, $CDCl_3$): δ 2.45 (2H, qt, *J* = 6.6, 1.3 Hz, -$CH_2C\mathit{H}_2CH{=}$), 3.23 (2H, dt, *J* = 5.9, 1.4 Hz, Ar$C\mathit{H}_2CH{=}$), 3.93 (2H, t, *J* = 6.6 Hz, -$OC\mathit{H}_2CH_2$-), 4.95 (1H, dq, *J* = 17.2, 1.7 Hz, -CH=CH*H*), 5.03 (1H, dq, *J* = 10.0, 1.5 Hz, -CH=CH*H*), 5.05 (1H, br d, *J* = 10.0 Hz, -$C\mathit{H}{=}CH_2$), 5.11 (1H, dq, *J* = 17.2, 1.5 Hz, -CH=CH*H*), 5.19 (2H, s, Ar$C\mathit{H}_2$Ph), 5.74 (1H, ddt, *J* = 17.0, 10.0, 6.0 Hz, -$CH_2C\mathit{H}{=}CH_2$), 5.84 (1H, ddt,

*J* = 17.2, 10.4, 6.6 Hz, -$CH_2C$*H*=$CH_2$), 7.23–7.30 (2 H, d, *J* = 6.7 Hz, Bn-H), 7.22–7.30 (4H, m, Bn-H, pyrazole-H); $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 27.1, 33.9, 53.8, 71.8, 116.3, 117.0, 126.7, 126.8, 127.0, 128.7, 133.8, 134.4, 137.1, 142.5 (two carbon signals are observed as one peak); HREIMS *m/z* calcd for $C_{17}H_{20}N_2O$ ($M^+$) 268.1576, found 268.1577.

5-Allyl-1-benzyl-4-(4-pentenyl)oxy-1*H*-pyrazole (**9b**): Oil; IR (film) $\nu_{max}$ 1639 (C=C), 1584 (C=C), 1496 (C=C), 1455 (C=C) $cm^{-1}$; $^1$H-NMR (400 MHz, $CDCl_3$): δ 1.79 (2H, dt, *J* = 7.0, 6.5 Hz, -$CH_2C$*H*$_2CH_2$-), 2.18 (2H, br q, *J* = 7.0 Hz, -$CH_2C$*H*$_2$CH=), 3.23 (2H, dt, *J* = 6.0, 1. 5 Hz, Ar$C$*H*$_2CH$=$CH_2$), 3.89 (2H, t, *J* = 6.5 Hz, -O$C$*H*$_2CH_2$-), 4.91–5.05 (4H, m, -$CH_2$CH=CH*H*), 5.02 (1H, dq, *J* = 17.0, 1.5 Hz, -$CH_2$CH=CH*H*), 5.19 (2H, s, Ar$C$*H*$_2$Ph), 5.74 (1H, ddt, *J* = 17.1, 10.0, 6.1 Hz, -$CH_2C$*H*=$CH_2$), 5.80 (1H, ddt, *J* = 17.0, 10.2, 6.7 Hz, -$CH_2C$*H*=$CH_2$), 7.15–7.19 (2H, br d, *J* = 7.3 Hz, Ph-H), 7.23–7.30 (3H, m, Ph-H), 7.30 (1H, s, pyrazole-H); $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 27.1, 28.7, 30.0, 53.8, 71.7, 115.1, 116.3, 126.6, 126.70, 126.74, 127.6, 128.7, 133.8, 137.1, 137.9, 142.6; HREIMS *m/z* calcd for $C_{18}H_{22}N_2O$ ($M^+$) 282.1782, found 282.1730.

5-Allyl-1-benzyl-4-(5-hexenyl)oxy-1*H*-pyrazole (**10b**): Oil; IR (film) $\nu_{max}$ 1639 (C=C), 1584 (C=C), 1496 (C=C) $cm^{-1}$; $^1$H-NMR (400 MHz, $CDCl_3$) δ 1.53 (2H, br quint, *J* = 7.4 Hz, -$CH_2C$*H2*$CH_2$-), 1.73 (2H, br quint, *J* = 6.7 Hz, -$CH_2C$*H2*$CH_2$-), 2.10 (2H, br q, *J* = 7.2 Hz, -$CH_2C$*H2*CH=), 3.25 (2H, dt, *J* = 5.9, 1.5 Hz, Ar$C$*H2*CH=$CH_2$), 3.90 (2H, t, *J* = 6.5 Hz, -O$C$*H*$_2CH_2$-), 4.93–5.06 (4H, overlapped), 5.21 (2H, s, Ar$C$*H*$_2$Ph), 5.20–5.86 (2H, m, overlapped, -CH=CH*H*), 7.05 (2H, d, *J* = 6.9 Hz, Ph-H), 7.22–7.32 (3H, m, Ph-H), 7.30 (1H, s, pyrazole-H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ25.5, 27.1, 28.9, 33.4, 53.8, 72.3, 114.7, 116.3, 126.6, 126.7, 127.5, 128.6, 133.8, 137.1, 138.5, 142.7; HREIMS *m/z* calcd for $C_{19}H_{24}N_2O$ $[M]^+$ 296.1889, found 296.1884.

**RCM of 3- or 5-allyl-4-alkenyloxy-1*H*-pyrazoles** (Table 2, Schemes 3–6)

*General procedure of RCM at room temperature* (Table 2, entry 1): To a solution of **8a** (29.7 mg, 0.071 mmol) in $CH_2Cl_2$ (4.5 mL) was added Grubbs' second-generation catalyst (Grubbs$^{2nd}$) (3.5 mg, 0.007 mmol) at rt. After stirring at rt overnight, the reaction mixture was condensed under reduced pressure giving a crude residue, which was purified using silica gel column chromatography (eluent: EtOAc:hexane = 1:5) to afford **5a** (15.3mg mg, 55%) with recovery of **8a** (2.7 mg, 7%).

**General procedure for MW-aided reaction* (Table 2, entry 2): To a solution of **8a** (19.8 mg, 0.047 mmol) in $CH_2Cl_2$ (4 mL) was added Grubbs$^{2nd}$ (4.9 mg, 0.0047 mmol) in a microwave vial. The reaction mixture was heated under microwave irradiation at 140 °C for 10 min. After the reaction mixture had

cooled, the solvent was removed under reduced pressure, affording a crude residue, which was purified by preparative TLC (eluent: EtOAc:hexane = 1:10) to afford **5a** (3.1 mg, 17%), **16a** (2.2 mg, 12%), and **17a** (1.7 mg, 9%).

(*Z*)-5,6,9-Trihydro-1-tritylooxocino[3,2-*c*]pyrazole (**5a**): white powder; mp 155–160 °C; IR (KBr) $\nu_{max}$ 1573 (C=C), 1492 (C=C), 1444 (C=C) $cm^{-1}$; $^1$H-NMR (600 MHz, $CDCl_3$): δ 2.31 (2H, br dd, *J* = 12.9, 5.5 Hz, -OCH$_2$C*H*$_2$CH=), 2.67 (2H, dd, *J* = 6.2, 0.9 Hz, ArC*H*$_2$CH=), 3.83 (1H, dd, *J* = 5.6, 5.3 Hz, -OC*H*$_2$CH$_2$-), 4.06 (1H, dt, *J* = 10.8, 6.2 Hz, -CH=C*H*CH$_2$Ar), 5.44 (1H, m, -CH$_2$C*H*=CH-), 7.12–7.15 (6H, m, Tr-H), 7.25–7.31 (9 H, m, Tr-H), 7.33 (1H, s, pyrazole-H); $^{13}$C-NMR (150 MHz, $CDCl_3$): δ 26.7, 27.7, 70.8, 78.7, 126.9, 127.4, 127.6, 127.7, 130.1, 130.4, 135.4, 141.7, 142.8; HREIMS *m/z* calcd for $C_{27}H_{24}N_2O$ ($M^+$) 392.1889, found 392.1885.

(*Z*)-1-Benzyl-5,6,9-trihydrooxocino[3,2-*c*]pyrazole (**5b**): Oil; IR (film) $\nu_{max}$ 1558 (C=C), 1496 (C=C), 1456 (C=C) $cm^{-1}$; $^1$H-NMR (400 MHz, $CDCl_3$): δ 2.31 (2H, dt, *J* = 6.8, 5.9 Hz, -OCH$_2$C*H*$_2$CH=), 3.23 (2H, d, *J* = 5.7 Hz, ArC*H*$_2$CH=), 3.84 (1H, t, *J* = 5.9 Hz, -OC*H*$_2$CH$_2$-), 5.22 (2H, s, ArC*H*$_2$Ph), 5.66–5.74 (1H, m, -CH=C*H*CH$_2$Ar), 5.78 (1H, dt, *J* = 9.7, 5.4 Hz, -CH$_2$C*H*=CH-), 7.03 (2H, br d, *J* = 6.9 Hz, Ph-H), 7.24–7.33 (3H, m, Ph-H), 7.30 (1H, s, pyrazole-H); $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 23.8, 27.1, 54.2, 70.0, 125.3, 126.5, 127.7, 128.7, 128.8, 132.1, 132.3, 136.8, 139.2; HREIMS *m/z* calcd for $C_{15}H_{16}N_2O$ ($M^+$) 240.1263, found 240.1261.

(*Z*)-1-Benzyl-5,6,7-trihydrooxocino[3,2-*c*]pyrazole (**15b**): Oil; IR (film) $\nu_{max}$ 1557 (C=C), 1455 (C=C) $cm^{-1}$; $^1$H-NMR (400 MHz, $CDCl_3$): δ 1.73 (2H, tt, *J* = 8.0, 5.5 Hz, -CH$_2$C*H*$_2$CH$_2$-), 2.43 (2H, br q, *J* = 7.9 Hz, -CH$_2$C*H*$_2$CH=), 4.22 (2H, t, *J* = 5.5 Hz, -OC*H*$_2$CH$_2$-), 5.18 (2H, s, ArC*H*$_2$Ph), 5.71 (1H, dt, *J* = 11.0, 8.0 Hz, -CH$_2$C*H*=CH-), 6.23 (1H, d, *J* = 11.0 Hz, ArC*H*=CH-), 7.06 (2H, br d, *J* = 7.4 Hz, Ph-H), 7.15 (1H, s, pyrazole-H), 7.23–7.31 (3H, m, Ph-H); $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 24.5, 25.6, 53.9, 69.3, 118.8, 124.6, 126.6, 127.5, 128.6, 130.8, 137.2, 144.4; HREIMS *m/z* calcd for $C_{15}H_{16}N_2O$ ($M^+$) 240.1263, found 240.1259.

(*Z*)-5,8,9-Trihydro-1-tritylooxocino[3,2-*c*]pyrazole (**16a**): white amorphous; mp 104–108 °C; IR (KBr) $\nu_{max}$ 1573 (C=C), 1492 (C=C), 1444 (C=C) $cm^{-1}$; $^1$H-NMR (600 MHz, $CDCl_3$): δ 1.78 (2H, t, *J* = 6.7 Hz, ArC*H*$_2$CH$_2$-), 2.46 (2H, dt, *J* = 7.6, 7.0 Hz, -CH$_2$C*H*$_2$CH=), 4.58 (1H, dd, *J* = 2.7, 2.3 Hz, -OC*H*$_2$CH$_2$-), 5.43 (1H, dt, *J* = 11.5, 2.9 Hz, -CH$_2$C*H*=CH-), 5.59 (1H, m, -OCH$_2$CH=C*H* CH$_2$-), 7.08–7.12 (6H, m, Tr-H), 7.26–7.30 (9H, m, Tr-H), 7.40 (1H, s, pyrazole-H); $^{13}$C-NMR (150 MHz, $CDCl_3$): δ 23.4, 27.3,

74.2, 78.8, 126.9, 127.3, 127.4, 127.7, 127.9, 130.5, 135.3, 142.6, 142.8; HREIMS *m/z* calcd for $C_{27}H_{24}N_2O$ ($M^+$) 392.1889, found 392.1889.

(*Z*)-1-Benzyl-5,8,9-trihydrooxocino[3,2-*c*]pyrazole (**16b**): Oil; IR (film) $\nu_{max}$ 1639 (C=C), 1584 (C=C) $cm^{-1}$; $^1$H-NMR (400 MHz, $CDCl_3$): δ 2.61 (2H, dd, *J* = 6.8, 5.7 Hz, ArC*H*$_2$CH$_2$-), 2.73–2.78 (2H, m, -CH$_2$C*H*$_2$CH=), 4.56 (2H, br s, -OC*H*$_2$CH$_2$-), 5.18 (2H, s, ArC*H*$_2$Ph), 5.38 (1H, dt, *J* = 11.6, 2.9 Hz, -CH$_2$C*H*=CH-), 5.66–5.75 (1H, m, -OCH$_2$CH=C*H*CH$_2$-), 7.00 (2H, br d, *J* = 7.3 Hz, Ph-H), 7.22–7.33 (3H, m, Ph-H), 7.34 (1H, s, pyrazole-H); $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 22.4, 25.1, 54.0, 74.6, 126.7, 127.6, 127.7, 128.69, 128.72, 131.6, 132.6, 136.8, 141.8; HREIMS *m/z* calcd for $C_{15}H_{16}N_2O$ ($M^+$) 240.1263, found 240.1261.

(*Z*)-5,6,9-Trihydro-2*H*-2-trityloxocino[3,2-*c*]pyrazole (**18**): Oil; IR (film) $\nu_{max}$ 1581 (C=C), 1492 (C=C), 1445 (C=C) $cm^{-1}$; $^1$H-NMR (600 MHz, $CDCl_3$): δ 2.24 (2H, td, *J* = 5.6, 5.3 Hz, -CH$_2$C*H*$_2$CH=), 3.47 (2H, br d, *J* = 6.1 Hz, ArC*H*$_2$CH=), 3.88 (1H, t, *J* = 5.6 Hz, -OC*H*$_2$CH$_2$-), 5.68 (1H, dt, *J* = 10.8, 5.3 Hz, -CH$_2$C*H*=CH-), 5.95 (1H, dt, *J* = 10.8, 6.1 Hz, -CH$_2$C*H*=CH-),7.01 (1H, s, pyrazole-H), 7.13–7.16 (6H, m, Tr-H), 7.25–7.34 (9 H, m, Tr-H); $^{13}$C-NMR (125 MHz, $CDCl_3$): δ 26.4, 27.9, 71.7 81.9, 124.5, 127.0, 127.3, 127.6, 127.8, 127.9, 129.7, 130.1, 130.2, 143.3, 145.2; HREIMS *m/z* calcd for $C_{27}H_{24}N_2O$ ($M^+$) 392.1888, found 392.1883.

(*Z*)-5,6,7-Trihydro-2-trityloxocino[3,2-*c*]pyrazole (**19**): pale brown powder; mp 115–117 °C; IR (film) $\nu_{max}$ 1558 (C=C), 1494 (C=C), 1447 (C=C) $cm^{-1}$; $^1$H-NMR (600 MHz, $CDCl_3$): δ 1.74–1.79 (2H, m, -CH$_2$C*H*$_2$CH$_2$-), 2.44–2.48 (2H, m, -CH$_2$C*H*$_2$CH=), 4.22 (1H, t, *J* = 5.9 Hz, -OC*H*$_2$CH$_2$-), 5.73 (1H, dt, *J* = 11.2, 8.0 Hz, -CH$_2$C*H*=CH-), 6.54 (1H, d, *J* = 11.2 Hz, ArC*H*=CH-), 6.91 (1H, d, *J* = 0.6 Hz, pyrazole-H), 7.13–7.18 (6H, m, Tr-H), 7.27–7.31 (9 H, m, Tr-H); $^{13}$C-NMR (125 MHz, $CDCl_3$): δ 23.8, 26.8, 69.9, 78.5, 121.1, 125.2, 127.6, 127.9, 128.4, 130.2, 137.7, 142.9, 143.1 HREIMS *m/z* calcd for $C_{27}H_{24}N_2O$ ($M^+$) 392.1888, found 392.1885.

(*Z*)-5,6,7,10-Tetrahydro-1*H*-1-trityloxonino[3,2-*c*]pyrazole (**6a**): Colorless crystals ($CH_2Cl_2$); mp 146–150 °C; IR (film) $\nu_{max}$ 1560 (C=C), 1492 (C=C), 1446 (C=C) $cm^{-1}$; $^1$H-NMR (600 MHz, $CDCl_3$): δ 1.67–1.74 (2H, m, -CH$_2$C*H*$_2$CH$_2$-), 2.36–2.44 (2H, m, =CHC*H*$_2$CH$_2$-), 2.96 (2H, d, *J* = 5.3 Hz, ArCH$_2$CH=), 3.83–3.88 (2H, m, -CH$_2$C*H*$_2$O-), 4.01 (1H, dt, *J* = 10.8, 8.2 Hz, ArCH$_2$C*H*=CH-), 5.16 (1H, dt, *J* = 10.8, 8.6 Hz, -CH$_2$CH$_2$C*H*=CH-), 7.12–7.15 (6H, m, Tr-H), 7.25–7.33 (9H, m, Tr-H), 7.33 (1H, s,

pyrazole-H); $^{13}$C-NMR (150 MHz, $CDCl_3$): δ 22.3, 24.0, 28.7, 74.9, 78.4, 126.3, 127.3, 127.6, 129.4, 130.1, 130.3, 134.8, 143.1, 145.4; HREIMS *m/z* calcd for $C_{28}H_{26}N_2O$ ($M^+$) 406.2045, found 406.2046.

(*Z*)-1-Benzyl-5,6,7,10-tetrahydro-1*H*-oxonino[3,2-*c*]pyrazole (**6b**): Oil; IR (film) $\nu_{max}$ 1568 (C=C), 1456 (C=C) $cm^{-1}$; $^1$H-NMR (600 MHz, $CDCl_3$): δ 1.76 (2H, tt, *J* = 6.3, 5.6 Hz, -$CH_2CH_2CH_2$-), 2.53 (2H, dt, *J* = 7.5, 6.3 Hz, =$CHCH_2CH_2$-), 3.31 (2H, d, *J* = 8.3 Hz, $ArCH_2CH$=), 3.90 (2H, br t, *J* = 5.3, Hz, -$CH_2CH_2O$-), 5.28 (2H, s, $ArCH_2Ph$), 5.28 (1H, dt, *J* = 10.0, 8.2 Hz, $ArCH_2CH$=CH-), 5.45 (1H, dt, *J* = 10.0, 7.5 Hz, -$CH_2CH_2CH$=CH-), 7.08 (2H, br d, *J* = 7.3 Hz, Ph-H), 7.28 (1H, s, pyrazole-H), 7.25–7.34 (3H, m, Ph-H); $^{13}$C-NMR (150 MHz, $CDCl_3$): δ 21.1, 22.3, 28.9, 53.4, 54.2, 75.3, 126.2, 126.6, 127.7, 128.8, 130.7, 131.5, 132.5, 137.4, 144.0; HREIMS *m/z* calcd for $C_{16}H_{18}N_2O$ ($M^+$) 254.1419, found 254.1419.

(*Z*)-5,6,9,10-Tetrahydro-1*H*-1-trityloxonino[3,2-*c*]pyrazole (**21a**): Oil; IR (film) $\nu_{max}$ 1573 (C=C), 1493 (C=C), 1446 (C=C) $cm^{-1}$; $^1$H-NMR (600 MHz, $CDCl_3$): δ 1.86–1.93 (2H, m, =$CHCH_2CH_2O$-), 2.08 (2H, br t, *J* = 5.9 Hz, $ArCH_2CH_2$-), 2.17–2.22 (2H, m, =$CHCH_2CH_2Ar$), 4.01 (2H, br t, *J* = 4.9 Hz, -$CH_2CH_2O$-), 5.23 (1H, dt, *J* = 10.6, 8.6 Hz, -$CH_2CH$=$CHCH_2$-), 5.54 (1H, dt, *J* = 10.6, 8.2 Hz, -$OCH_2CH_2CH$=CH-), 7.11–7.15 (6H, m, Tr-H), 7.24–7.30 (9H, m, Tr-H), 7.35 (1H, s, pyrazole-H); $^{13}$C-NMR (150 MHz, $CDCl_3$): δ 23.5, 26.8, 27.6, 75.3, 78.4, 126.4, 127.3, 127.5, 127.6, 129.9, 130.1, 130.2, 132.1, 142.9; HREIMS *m/z* calcd for $C_{28}H_{26}N_2O$ ($M^+$) 406.2045, found 406.2043.

(*Z*)-2-Benzyl-5,6,9,10-tetrahydro-1*H*-oxonino[3,2-c]pyrazole (**21b**): Oil; IR (film) $\nu_{max}$ 1573 (C=C), 1496 (C=C), 1454 (C=C) $cm^{-1}$; $^1$H-NMR (600 MHz, $CDCl_3$): δ 2.20–2.52 (2H, m, -$CH_2CH_2CH$=), 2.34–2.38 (2H, m, -$CH_2CH_2CH$=), 2.60 (2H, dd, *J* = 8.2, 5.0 Hz, $ArCH_2CH_2$-), 4.00 (2H, dt, *J* = 5.9, 4.1 Hz, -$OCH_2CH_2$-), 5.23 (2H, s, $ArCH_2Ph$), 5.45 (1H, br dt, *J* = 10.9, 8.2 Hz, -CH=$CHCH_2$-), 5.58 (1H, br dt, *J* = 10.9, 8.3 Hz, -CH=$CHCH_2$-), 7.02–7.04 (2H, m, Ph-H), 7.23–7.32 (3H, m, Tr-H), 7.31 (1H, s, pyrazole-H); $^{13}$C-NMR (150 MHz, $CDCl_3$): δ 24.1, 27.7, 29.7, 54.1, 75.5, 126.55, 126.64, 127.4, 127.6, 128.7, 128.8, 131.1, 131.7, 137.3; HEIRMS *m/z* calcd for $C_{16}H_{18}N_2O$ ($M^+$) 254.1419, found 254.1414.

(*Z*)-5,6,7,10-Tetrahydro-2*H*-2-trityloxonino[3,2-*c*]pyrazole (**22**): white powder; mp 115–120 °C; IR (film) $\nu_{max}$ 1558 (C=C), 1489 (C=C), 1456 (C=C) $cm^{-1}$; $^1$H-NMR (600 MHz, $CDCl_3$): δ 1.73 (2H, br quint, *J* = 5.9 Hz, -$CH_2CH_2CH_2$-), 2.55–2.61 (2H, m, -$CH_2CH_2CH$=), 3.42 (2H, d, *J* = 8.5 Hz, $ArCH_2CH$=), 3.88 (2H, t, *J* = 5.8 Hz, -$OCH_2CH_2$-), 5.48 (1H, br q, *J* = 8.5 Hz, -CH=$CHCH_2$), 5.81 (1H, br q, *J* = 8.5 Hz, -CH=$CHCH_2$), 7.02 (1H, s, pyrazole-H), 7.13–7.16 (6H, m, Tr-H), 7.27–7.32 (9H, m,

Tr-H); $^{13}$C-NMR (150 MHz, $CDCl_3$): δ 23.4, 24.2, 26.2, 28.4, 77.7, 78.4, 124.6, 127.28, 127.32, 127.4, 127.6, 128.0, 130.3, 130.4, 143.0; HREIMS *m/z* calcd for $C_{28}H_{26}N_2O$ ($M^+$) 406.2045, found 406.2041.

(*Z*)-5,6,7,8-Tetrahydro-2*H*-1-trityloxonino[3,2-*c*]pyrazole (**23**): the data noted were obtained from a mixture with **19**; $^1$H-NMR (600 MHz, $CDCl_3$): δ 1.67–1.71 (2H, m, -$CH_2CH_2CH_2$-), 1.72–1.78 (2H, m, -$CH_2CH_2CH_2$-), 2.72 (2H, dt, *J* = 8.5, 6.1 Hz, -$CH_2CH_2$CH=), 4.01 (2H, t, *J* = 5.3 Hz, -O$CH_2CH_2$-), 5.66 (1H, dt, *J* = 12.0, 8.8 Hz, -CH=C*H*$CH_2$-), 6.49 (1H, d, *J* = 12.0 Hz, ArC*H*=CH-), 7.06 (1H, br s, pyrazole-H), 7.14–7.17 (6H, m, Tr-H), 7.27–7.31 (9H, m, Tr-H); $^{13}$C-NMR (150 MHz, $CDCl_3$): δ 23.4, 24.2, 26.2, 28.4, 77.7, 78.4, 124.6, 127.28, 127.32, 127.4, 127.6, 128.0, 130.3, 130.4, 143.0; HREIMS *m/z* calcd for $C_{28}H_{26}N_2O$ ($M^+$) 406.2045, found 406.2043.

(*Z*)-1,5,6,7,8,11-Hexahydro-1-trityloxecino[3,2-*c*]pyrazole (**7a**): Oil; IR (film) $\nu_{max}$ 1562 (C=C), 1492 (C=C), 1447 (C=C) $cm^{-1}$; H-NMR (600 MHz, $CDCl_3$): δ 1.36–1.40 (2H, m, -$CH_2CH_2CH_2$-), 1.58 (2H, br quint, *J* = 5.9 Hz, -$CH_2CH_2CH_2$-), 2.36–2.43 (2H, m, -$CH_2CH_2$CH=), 2.89 (2H, d, *J* = 8.2 Hz, Ar$CH_2$CH=), 3.51 (1H, br q, *J* = 8.2 Hz, -CH=C*H*$CH_2$-), 4.12 (1H, br dd, *J* = 4.7, 4.7 Hz, -O$CH_2CH_2$-), 4.88 (1H, br q, *J* = 8.2 Hz, -CH=C*H*$CH_2$-), 7.11–7.15 (6H, m, Tr-H), 7.25–7.31 (9 H, m, Tr-H), 7.33 (1H, s, pyrazole-H); $^{13}$C-NMR (150 MHz, $CDCl_3$): δ 23.4, 24.2, 26.2, 28.4, 77.7, 78.4, 124.6, 127.3, 127.6, 128.0, 130.4, 131.2, 134.0, 142.6, 143.0; HREIMS *m/z* calcd for $C_{29}H_{28}N_2O$ ($M^+$) 420.2202, found 420.2205.

(*Z*)-1-Benzyl-1,5,6,7,8,11-hexahydrooxecino[3,2-*c*]pyrazole (**7b**): Oil; IR (film) $\nu_{max}$ 1574 (C=C), 1494 (C=C), 1454 (C=C) $cm^{-1}$; H-NMR (600 MHz, $CDCl_3$): δ 1.36–1.40 (2H, m, -$CH_2CH_2CH_2$-), 1.66 (2H, br quint, *J* = 5.8 Hz, -$CH_2CH_2CH_2$-), 2.36–2.43 (2H, dt, *J* = 6.7, 5.6 Hz, -$CH_2CH_2$CH=), 3.23 (2H, br d, *J* = 7.4 Hz, Ar$CH_2$CH=), 4.14 (1H, br dd, *J* = 4.7, 4.7 Hz, -O$CH_2CH_2$-), 4.20–4.27 (2H, br q, *J* = 8.2 Hz, 2 × -CH=C*H*$CH_2$-, overlapped), 5.27 (2H, s, Ar$CH_2$Ph), 7.10 (2H, br d, *J* = 7.3 Hz, Ph-H), 7.25–7.33 (3H, m, Ph-H), 7.30 (1H, s, pyrazole-H); $^{13}$C-NMR (150 MHz, $CDCl_3$): δ 20.7, 23.7, 26.3, 28.7, 53.9, 78.0, 124.7, 126.7, 127.7, 128.7, 129.7, 132.5, 132.6, 137.4, 140.2; HREIMS *m/z* calcd for $C_{17}H_{20}N_2O$ ($M^+$) 268.1576, found 268.1578.

(*Z*)-5,6,7,8,11-Pentahydro-2-trityloxecino[3,2-*c*]pyrazole (**24**): Oil; IR (film) $\nu_{max}$ 1560 (C=C), 1491 (C=C), 1448 (C=C) $cm^{-1}$; $^1$H-NMR (600 MHz, $CDCl_3$): δ 1.42–1.67 (2H, m, -$CH_2CH_2CH_2$-), 1.65–1.70 (2H, m, -$CH_2CH_2CH_2$-), 2.56–2.60 (2H, m, -$CH_2CH_2$CH=), 3.31 (2H, d, *J* = 8.2 Hz, Ar$CH_2$CH=), 4.00 (1H, dd, *J* = 5.0, 4.7 Hz, -O$CH_2CH_2$-), 5.27 (1H, br q, *J* = 8.2 Hz, -CH=C*H*$CH_2$-), 5.27 (1H, br q, *J* = 8.2

Hz, -CH=C*H*$CH_2$-), 6.98 (1H, s, pyrazole-H), 7.13–7.19 (6H, m, Tr-H), 7.25–7.31 (9H, m, Tr-H); $^{13}$C-NMR (150 MHz, $CDCl_3$): δ 23.4, 23.9, 26.2, 28.6, 78.2, 79.0, 122.4, 127.5, 127.6, 127.9, 128.1, 130.05, 130.12, 130.5, 139.9, 143.5, 144.9 ; HREIMS *m/z* calcd for $C_{29}H_{28}N_2O$ ($M^+$) 420.4201, found 420.2198.

(9*Z*,20*Z*)-2,5,6,7,8,11,13,16,17,18,19,22-Dodecahydro-2,13-dityrityl[1,11]dioxacycloicosino[3,2-*c*:13,12-*c*']dipyrazole (**25**): amorphous powder; IR (KBr) $\nu_{max}$ 1573 (C=C), 1493 (C=C), 1446 (C=C) $cm^{-1}$; $^1$H-NMR (600 MHz, $CDCl_3$): δ 1.47–1.51 (4H, m, 2 × -$CH_2$-), 1.62–1.68 (4H, m, 2 × -$CH_2$-), 1.98–2.01 (4H, m, 2 × -$CH_2$-), 3.29 (4H, d, *J* = 5.0 Hz, 2 × ArC*H*$_2$CH=), 3.65–3.68 (4H, m, 2 × -OC*H*$_2$$CH_2$-), 5.35–5.44 (2H, m, 2 × -$CH_2$C*H*=CH-), 5.48–5.56 (2H, m, 2 × Ar$CH_2$C*H*=CH-), 8.83 (2H, s, 2 × pyrazole-H), 7.16–7.19 (12H, m, Tr-H), 7.16–7.19 (18 H, m, Tr-H); $^{13}$C-NMR (150 MHz, $CDCl_3$): δ 26.3 ($CH_2$), 29.2 ($CH_2$), 29.2 ($CH_2$), 32.4 ($CH_2$), 71.4 ($CH_2$), 77.9 (Cq), 117.2 (CH), 127.4 (CH), 127.6 (CH), 127.9 (CH), 130.1 (CH), 130.8 (CH), 140.5 (Cq), 142.5 (Cq), 143.6 (Cq); HREIMS *m/z* calcd for $C_{58}H_{56}N_4O_2$ ($M^+$) 840.4404, found 840.4412.

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## REFERENCES AND NOTES

1. K. Karrouchi, S. Radi, Y. Ramil, J. Taoufik, Y. N. Mabkhot, F. A. Al-aizari, and M. Ansar, *Molecules*, 2018, **23**, 134.
2. B. S. S. Rajput, S. N. Patel, Sureshbhai, and S. B. Chaudhari, *World J. Pharm. Res*., 2014, **3**, 1151.
3. J. J. Li, 'Pyrazoles, pyrazolones, and indazoles' In *Heterocyclic Chemistry in Drug Discovery*, ed. by J. J. Li, Wiley-VCH, Weinheim, 2013, pp. 198–229.
4. A. Schmidt and A. Dreger, *Curr. Org. Chem.*, 2011, **15**, 1423.
5. M. Li and B.-X. Zhao, *Eur. J. Med. Chem.*, 2014, **85**, 311.
6. Y. Usami, A. Kohno, H. Yoneyama, and S. Harusawa, *Molecules*, 2018, **23**, 592.
7. Y. Usami, K. Sumimoto, A. Kishima, Y. Tatsui, H. Yoneyama, and S. Harusawa, *Molecules*, 2019, **24**, 296.

8. N. Blanchard and J. Eustache, in *Metathesis in Natural Product Synthesis*, ed. by J. Cossy, S. Arseniyadis, and C. Meyer, Wiley-VCH, Weinheim, 2010, pp. 1–43.
9. M. Sasaki and M. Inoue, *J. Synth. Org. Chem. Jpn.*, 2001, **59**, 193.
10. R. W. Carling, J. S. Clark, and A. B. Holmes, *J. Chem. Soc., Perkin Trans. 1*, 1992, 83.
11. H. Ichikawa, R. Watanabe, Y. Fujino, and Y. Usami, *Tetrahedron Lett.*, 2011, **52**, 4448.
12. H. Wakamatsu, M. Nishida, N. Adachi, and M. Mori, *J. Org. Chem.*, 2000, **63**, 3966.
13. B. Schmidt, *Eur. J. Org. Chem.*, 2003, 816.
14. S. H. Hong, D. P. Sanders, C. W. Lee, and R. H. Grubbs, *J. Am. Chem. Soc.*, 2005, **127**, 17160.
15. The HRMS of the major fraction in the reaction showed a peak for *m/z*: 508.2837 corresponding to $C_{32}H_{36}N_4O_2$, which corresponds to exactly double the molecular weight of the desired **6b** (calculated *m/z* $M^+$ ($C_{16}H_{18}N_2O$): 254.1419). But the structure could not be assigned however, because of the broadness of the peaks in the $^1$H- and $^{13}$C-NMR spectra.
16. J. Tae and Y.-K. Yang, *Org Lett.*, 2003, **5**, 741.
17. A. B. Smith III, S. A. Kozmin, C. M. Adams, and D. V. Paone, *J. Am. Chem. Soc.*, 2000, **122**, 4984.