Synthesis of Heterodiquinanes by Photoreaction of β-Keto Esters with Oxime Methyl Ethers Derived from 3-Acyl-1,2-dihydrocinnoline-1,2-dicarboximides

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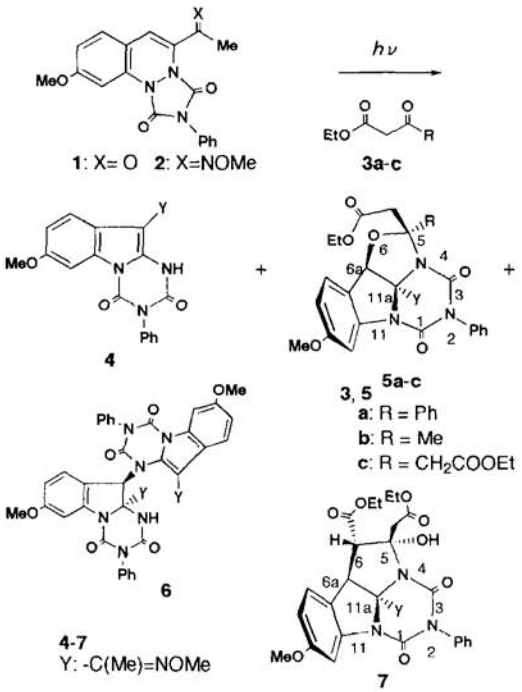
Photoreaction of hydrazodicarboximide with β-keto esters in acetonitrile in the presence and absence of triethylamine afforded intriguing heterodiquinane-based tricycles in moderate yields, together with both rearranged and dimeric products.

Naturally occurring and artificially synthesized polyquinanes composing of fused five-membered carbocyclic framework have received considerable attentions, on account of challenging targets for stereocontrolled syntheses and biological activities exhibited by some members of the family.[1,2] In contrast, stereoselective synthetic methodology of the corresponding heterocyclic polyquinane analogues has little been studied. Recently we have exploited one-pot synthetic methodologies for novel heterocycles, using urazoles (*N*-phenyl-1,2-hydrazo-1,2-dicarboximides) **1** and **2**, which include hetero angular triquinane analogues,[3] hetero propellanes,[4] indoles,[5,6] indolines,[6] and imidazoquinazolinone.[7] As further extension of our studies, we report here the photochemical construction of heterodiquinane-based tricycles from **2**.

Irradiation of urazole (**2**)[6] (0.26 mmol) and ethyl benzoylacetate (**3a**) (13.0 mmol) in acetonitrile (60 mL) containing triethylamine (10.0 mmol) by a 400-W high-pressure mercury lamp through a Pyrex filter for 6 h gave a mixture of two products (**4**, **5a**), which were isolated by column chromatography on silica gel. The structures of the isolated products were determined by ^{1}H and ^{13}C NMR, IR, and MS spectroscopies, and elemental analyses. The photoproduct **4** was already identified as a rearranged product in the photochemical reactions of **2** without nucleophiles.[6] The compound **5a** (isolated yield 66%) had an intricate heterodiquinane framework containing a triazinoindoline and an oxazolidine skeletons (Scheme 1).



Scheme 1.

The ^{1}H NMR spectrum of **5a** showed a methine proton (6a-H) at δ 5.36 and non-equivalent methylene protons at δ 2.83 and 3.89 coupled with each other (J =15.4 Hz) in addition to a *C*-methyl proton, two *O*-methyl protons, and an ethoxyl proton. In the ^{13}C NMR spectrum a doublet (C-6a) and two singlet signals (C-11a and C-5) appeared at δ 83.3, 85.4, and 100.6, respectively. The mass and IR spectra and elemental analysis also supported its structure.[8]

Photoreactions of urazole **2** with **3b-c** under similar conditions also afforded corresponding heterodiquinane analogues **5b-c** in moderate yields,[8] although competitive dimerization for **3b** occurred to give **6** (Table 1). These structures were also confirmed by spectral and previously reported data.[6]

Table 1. Photoreactions of urazole **2** with β-keto esters in the presence of triethylamine

β-Keto ester	Irradiation time/h	Yield / %[a]			
		4	**5**	**6**	**7**
3a	6	14	66(**5a**)	0	0
3b	6	4	42(**5b**)	33	0
3c	10	4	62(**5c**)	0	0
3c[b]	10	3	15(**5c**)	0	39

[a] Isolated yields. [b] In the absence of triethylamine.

The stereochemistry at C-5 of **5a** was determined as *endo*-ethoxycarbonylmethyl and *exo*-phenyl configurations with respect to the *cis*-fused indoline-oxazolidine ring on the basis of ^{1}H NMR. Inspection of the molecular model reveals that *endo*-ethoxyl group is above the phenyl ring of indoline. In fact, the ethoxyl protons resonated at higher field by diamagnetic anisotropy of the phenyl ring. The shift of ethoxyl protons in the *endo*-position to higher field is more clear in compound **5c** bearing the same substituent in the *exo* and the *endo* positions at C-5 (δ 0.94, 3.66 in *endo*-position, and δ 1.30, 4.19 in *exo*-position). Similarly, the anisotropic effect of C-5 *exo*-phenyl group in **5a** makes 6a-H and the C-methyl proton of the iminoethyl group resonate at higher field by 0.18-0.40 ppm than those in **5b-c**. Finally, the structure of **5a** was unambiguously determined by a single cyrstal X-ray analysis (Figure. 1).[9]

Photoreaction of **2** with **3c** in the absence of triethylamine afforded other heterodiquinane **7** containing a triazinoindoline and a pyrrolidine skeletons.[10] The stereochemistry in **7** was

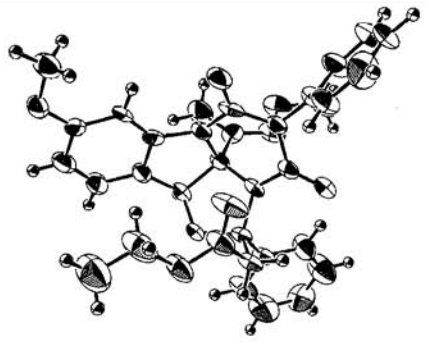
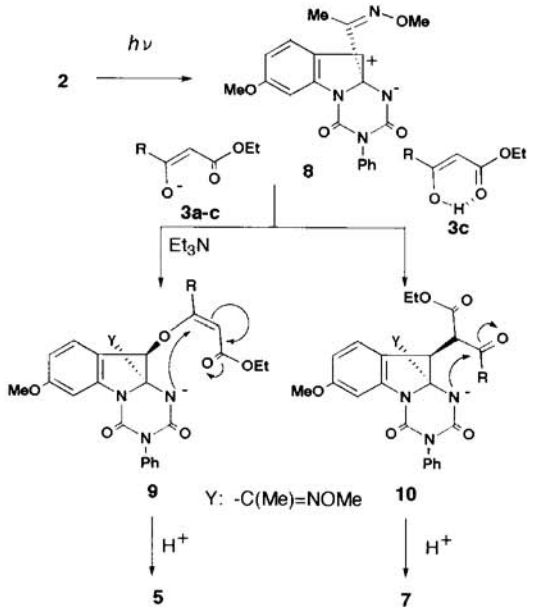


Figure 1. ORTEP drawing of **5a**.



Scheme 2.

determined by a single crystal X-ray analysis.[11]

The following consecutive reaction mechanism will be surmised to account for the formation of the photoproducts (Scheme 2). In the presence of Et_3N an attack of an enol anion of β-keto ester to a polar and imino-stabilized intermediate (1,3-dipole) **8** generated from a photo-induced rearrangement[6] gives an adduct **9**, followed by a stereoselective intramolecular nucleophilic reaction of amide nitrogen and protonation to form compounds **5**. On the other hand, *C*-attack to **8** in the absence of Et_3N will become predominant because of a lowering of *O*-attack due to a strong intramolecular hydrogen-bond in **3c**.[12] However, attempts of the isolation of protonated **9** and **10** failed probably because of rapid intramolecular cyclizations.

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References and Notes

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8 Spectral [^{1}H NMR (90 MHz, $CDCl_3$), ^{13}C NMR (22.5 MHz, $CDCl_3$), IR (KBr), MS *m/z* (%)] data for **5**. Satisfactory analytical data were obtained for new compounds. **5a**; mp 163-164℃; ^{1}H NMR δ 0.91 (3H, t, Me), 1.49 (3H, s, Me), 2.83 and 3.89 (2H, d, CH_2, J= 15.4 Hz), 3.83 (6H, s, OMe), 3.93 (2H, q, CH_2), 5.36 (1H, s, 6a-H), 6.67 (1H, dd, 8-H), 7.19-7.91 (12H, m, Ph); ^{13}C NMR δ 10.3 (q), 13.8 (q), 41.6 (t), 55.6 (q), 60.7 (t), 62.5 (q), 83.3 (d), 85.4 (s), 100.1 (d), 100.6 (s), 111.2 (d), 117.7 (s), 125.9 (d), 126.6 (d), 128.3 (d), 128.6 (d), 128.8 (d), 129.4 (d), 135.1 (s), 141.4 (s), 144.4 (s), 148.9 (s), 149.4 (s), 152.3 (s), 162.6 (s), 167.9 (s); IR 1730, 1691 cm^{-1}; MS 570 (M$^+$, 22). **5b**; mp 154-155℃; ^{1}H NMR δ 0.90 (3H, t, Me), 1.71 (3H, s, Me), 1.87 (3H, s, Me), 2.74 and 3.67 (2H, d, CH_2, J= 15.4 Hz), 3.63 (2H, q, CH_2), 3.80 (3H, s, OMe), 3.97 (3H, s, OMe), 5.54 (1H, s, 6a-H), 6.66 (1H, dd, 8-H), 7.17-7.54 (7H, m, Ph); ^{13}C NMR δ 10.6 (q), 13.8 (q), 27.5 (q), 40.1 (t), 55.6 (q), 60.7 (t), 63.0 (q), 84.5 (d), 84.8 (s), 99.0 (s), 100.1 (d), 111.6 (d), 118.6 (s), 126.1 (d), 128.4 (d), 128.7 (d), 129.5 (d), 134.9 (s), 144.8 (s), 149.5 (s), 150.4 (s), 151.2 (s), 162.5 (s), 168.4 (s); IR 1739, 1699 cm^{-1}; MS 508 (M$^+$, 70). **5c**; mp 145-146℃; ^{1}H NMR δ 0.94 (3H, t, Me), 1.30 (3H, t, Me), 1.89 (3H, s, Me), 3.06 (2H, s, CH_2), 3.11 and 3.62 (2H, d, CH_2, J= 16.5 Hz), 3.66 (2H, q, CH_2), 3.75 (3H, s, OMe), 3.96 (3H, s, OMe), 4.19 (2H, q, CH_2), 5.71 (1H, s, 6a-H), 6.67 (1H, dd, 8-H), 7.17-7.54 (7H, m, Ph); ^{13}C NMR δ 10.8 (q), 13.8 (q), 14.2 (q), 38.0 (t), 45.3 (t), 55.7 (q), 60.6 (t), 60.9 (t), 62.7 (q), 84.5 (s), 84.7 (d), 98.2 (s), 100.1 (d), 111.6 (d), 118.3 (s), 126.7 (d), 128.4 (d), 128.8 (d), 129.2 (d), 134.9 (d), 144.9 (s), 149.4 (s), 150.5 (s), 151.1 (s), 162.6 (s), 168.1 (s), 168.3 (s); IR 1740, 1697 cm^{-1}; MS 580 (M$^+$, 7).
9 Crystal data for **5a**: $C_{31}H_{30}N_4O_7$, monoclinic, space group $P2_1/c$, a= 9.627 (6), b = 20.901 (8), c = 14.775 (5) Å, β = 104.61 (4)°, V = 2877 (2) Å^3, Z=4, Dx= 1.317 gcm^{-3}.
10 **7**; mp 166-167℃; ^{1}H NMR δ 1.17 (3H, t, Me), 1.36(3H, t, Me), 1.94 (3H, s, Me), 3.26 and 3.79 (2H, d, CH_2, J=15.4 Hz), 3.35 (1H, d, 6-H, J=9.0 Hz), 3.83 (3H, s, OMe), 3.94 (3H, s, OMe), 4.08 (2H, q, CH_2), 4.31 (2H, q, CH_2), 4.49 (1H, d, 6a-H, J=9.0 Hz), 5.03 (1H, s, OH), 6.61 (1H, dd, 8-H), 7.06-7.54 (7H, m, Ph); ^{13}C NMR δ 10.5 (q), 14.0 (q), 14.3 (q), 38.6 (t), 49.9 (d), 55.6 (q), 60.5 (d), 60.9 (t), 61.9 (t), 62.6 (q), 85.3 (s), 91.5 (s), 100.4 (d), 111.2 (d), 121.8 (d), 125.1 (d), 128.4 (d), 128.8 (d), 129.2 (d), 134.7 (s), 142.1 (s), 148.4 (s), 149.7 (s), 154.1 (s), 160.9 (s), 167.9 (s), 170.2 (s); IR 3430, 1738, 1692 cm^{-1}; MS 580 (M$^+$, 5).
11 Crystal data for **7**: $C_{29}H_{32}N_4O_9$, triclinic, space group P_1, a = 12.171 (5), b = 12.372(5), c = 10.431 (2) Å, α = 92.21(2)°, β = 109.75 (2)°, γ = 89.19 (3)°, V = 1477.2 (9) Å^3, Z=2, Dx= 1.305 gcm^{-3}.
12 A possibility of 1,3-dipolar cycloaddition between **8** and an enol in formation of **7** as one of referees has suggested, seems negligible because a photoreaction of **2** with diethyl fumarate or diethyl maleate did not afford the corresponding photoadduct.