A NOVEL SYNTHESIS OF QUINAZOLINEQUINONE AND CARBAZOLEQUINONE THROUGH ANIONIC CYCLOADDITION: ITS APPLICATION TO A SYNTHESIS OF MURRAYAQUINONE A

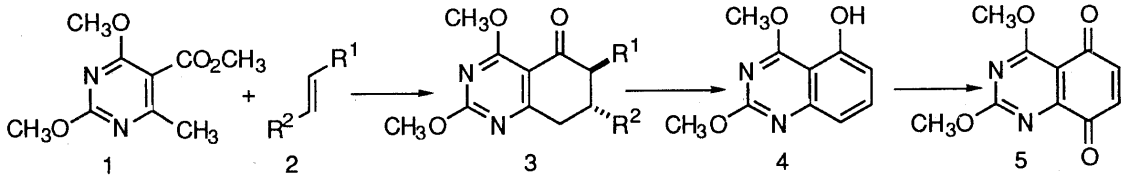
Akimori WADA, Syuichi HIRAI, and Miyoji HANAOKA*

Faculty of Pharmaceutical Sciences, Kanazawa University, Takara-machi, Kanazawa 920, Japan

A novel synthesis of the quinazolinequinone (**5**) and the carbazolequinone (**9**) is described. Anionic cycloaddition of the heterocyclic esters (**1** and **6**) with phenyl β-trimethylsilylvinyl sulfone (**2c**) afforded the cycloadducts (**3** and **7**), which were converted to the quinones (**5** and **9**) *via* the phenols (**4** and **8**). This method was applied to a covenient synthesis of murrayaquinone A (**10**).

KEYWORDS anionic cycloaddition; quinazolinequinone; carbazolequinone; murrayaquinone A; phenyl β-trimethylsilylvinyl sulfone; [bis(trifluoroacetoxy)iodo]-benzene

Many syntheses of heterocyclic quinones have been intensively investigated because of their potential pharmacological activities including antitumor, antibacterial, and antifungal ones.[1] In connection with our synthetic studies on heterocycles through anionic cycloaddition of methyl 2,4-dimethoxy-6-methyl-5-pyrimidinecarboxylate (**1**) with olefines,[2] acetylenes,[2] aldehydes,[3] and imines,[4] we report herein a novel synthesis of the quinazolinequinone (**5**) as well as the carbazolequinone (**9**) as an extension of anionic cycloaddition and its application to a synthesis of murrayaquinone A (**10**).



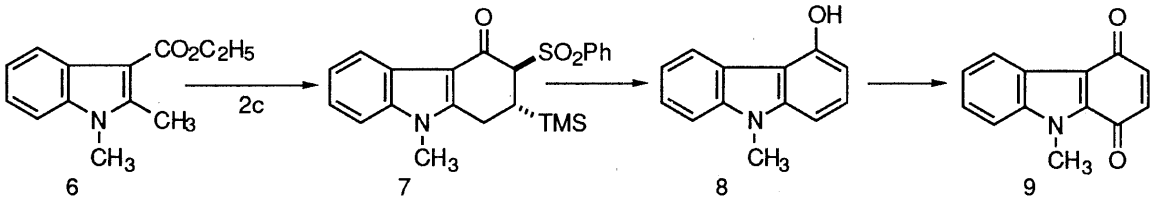
1 2 3 4 5

a: R^1=SOPh, R^2=H ; b: R^1=SO_2Ph, R^2=H ; c: R^1=SO_2Ph, R^2=TMS

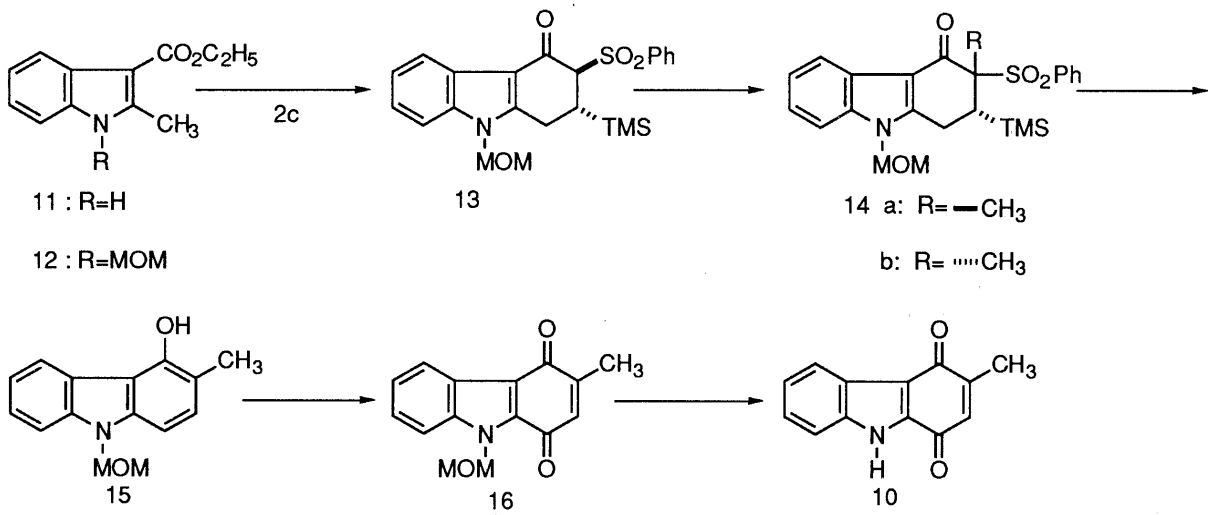
The lithium salt, prepared by deprotonation of **1** with lithium diisopropylamide (LDA), was treated with phenyl vinyl sulfoxide (**2a**) in ether at -70°C to afford the cycloadduct (**3a**) as a mixture of two diastereomers (2:1) due to C_6 and the *S*-oxide in 49% yield. Similar cycloaddition of **1** with a more reactive dipolarophile, phenyl vinyl sulfone (**2b**) in tetrahydrofuran (THF) at -70°C, gave the cycloadduct (**3b**) in 90% yield. On heating in benzene under reflux, **3a** easily gave the phenol (**4**) in 87% yield through

desulfenation, whereas **3b** remained unchanged. In order to improve both cycloaddition and elimination steps, we chose phenyl β-trimethylsilylvinyl sulfone (**2c**)[5] as a dipolarophile. Reaction of **1** with **2c** proceeded smoothly to produce regio- and stereoselectively the adduct (**3c**) as a single isomer in 98% yield. Its *trans* configuration was determined by the appearance of C_6-H at 3.88 ppm as a singlet in its nuclear magnetic resonance (NMR) spectrum because of the dihedral angle(~90°) between C_5-H and C_6-H in the *trans* configuration. Treatment of **3c** with tetrabutylammonium fluoride (TBAF)[6] effected aromatization as expected, to afford the phenol (**4**) in 91% yield. After unsuccessful experiments with several oxidation reagents such as cerium(IV) ammonium nitrate, Fremy's salt, lead tetraacetate, pyridinium chlorochromate, chromium(VI) oxide, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, and oxygen with salcomine, the phenol (**4**) was oxidized with [bis(trifluoroacetoxy)iodo]benzene[7] in acetonitrile and water (2:1) at 0°C to provide the quinazolinequinone (**5**) in 52% yield.

Similarly, anionic cycloaddition of the indole (**6**)[8] with **2c** afforded the adduct (**7**) in 61% yield, which was transformed to the carbazolequinone (**9**) *via* the phenol (**8**).



Next, we applied this method to a synthesis of murrayaquinone A (**10**), [9,10] a representative carbazolequinone alkaloid isolated from *Murraya euchrestifolia* HAYATA.



Condensation of the protected indole (**12**) derived from **11**[11] with **2c** in the presence of LDA in THF gave the cycloadduct (**13**) as a single isomer in 63% yield. Methylation of **13** with methyl iodide in the presence of potassium *t*-butoxide produced two diastereomers (**14a** and **14b**) in 31 and 25% yields, respectively. Their stereochemistry was assigned by the nuclear Overhauser effect experiments. This

mixture was treated with TBAF in THF to afford the phenol (**15**) in 85% yield, which was oxidized with [bis(trifluoroacetoxy)iodo]benzene to provide the carbazolequinone (**16**) in 59% yield. Finally, deprotection of the methoxymethyl group in **16** with hydrochloric acid in methanol afforded murrayaquinone A (**10**), mp 236-239°C (lit.,[10d] 237-239°C), in 93 % yield. The synthetic product was identical with the authentic sample in NMR and IR spectra as well as thin-layer chromatographic behavior.

The present methodology employing anionic cycloaddition as a key step provides a general and convenient route to a synthesis of various heteroquinones from heteroaromatics possessing crotonate moiety in their molecules.

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