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A CONVENIENT PHOTOSYNTHESIS OF HETEROCYCLIC QUINONES BY A ONE-POT REACTION

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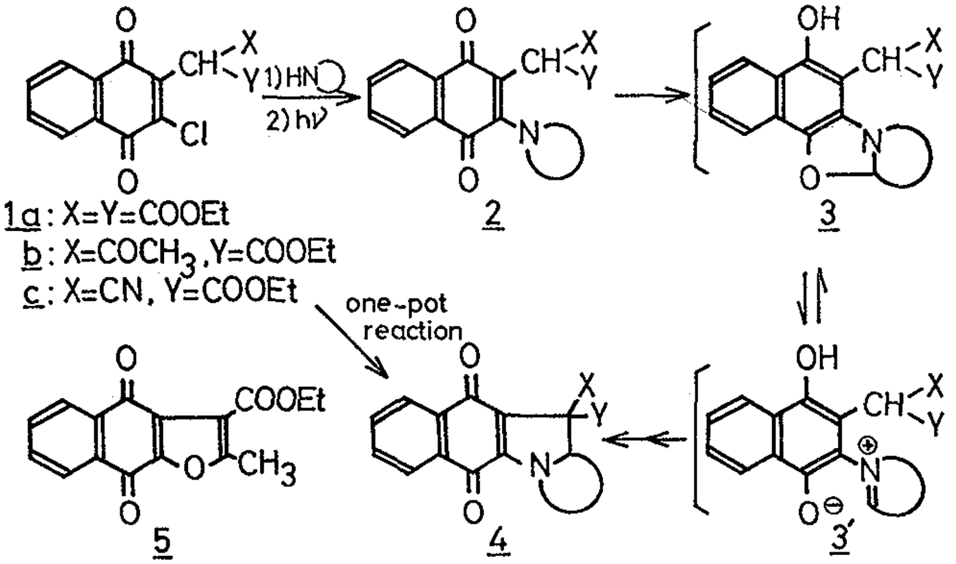
The photochemical reaction of 2-chloro-3-acetylethoxycarbonylmethyl-1,4-naphthoquinone (1b) with various secondary amines (pyrrolidine, piperidine, morpholine, and hexamethyleneimine) provided a convenient, one-pot, preparative route to the heterocyclic quinones (4b) as a mixture of stereoisomers due to the different substituents. A similar photoreaction of 2-chloro-3-ethoxycarbonylcyanomethyl-1,4-naphthoquinone (1c) with amines gave selectively one diastereomer of the series (4c).

The stereochemical studies on these photoproducts were investigated by using the europium-shifted spectra.

1,4-Benzoquinones bearing certain secondary amino-substituents have been shown to photoisomerize readily in sunlight to the benzoxazoline and benzoxazole derivatives[1]. More recently, we have reported an example of a novel type of photoinduced intramolecular cyclization in various solvents using the cyclic amino-1,4-naphthoquinones (2a) possessing an active methylene group at the 2-position to form the indoloquinones (4a)[2]. Also, these consecutive reactions (amino substitution, photolysis, and ring conversion) might be carried out in high yields in a one-pot sequence without isolation of intermediates[3].

In this paper we wish to describe some other examples of this novel type of the photosynthesis of the heterocyclic quinones by a one-pot reaction. The overall process can be represented as shown in Scheme I.

A solution of aminoquinones (2b) prepared from the reaction of 2-chloro-3-

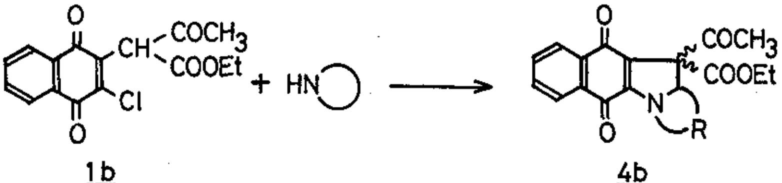


Scheme I

acetylethoxycarbonylmethyl-1,4-naphthoquinone (1b)[4] with various secondary amines (pyrrolidine, piperidine, morpholine, and hexamethyleneimine) in ethanol was irradiated with a high pressure mercury lamp through Pyrex glass under a stream of nitrogen for 1~2 h. After allowing each of the irradiated solutions of (2b) to stand for more than 24 h at room temperature followed by evaporation of the solvent, each of the two stereoisomers of the ring-closed quinones (4b) due to the different substituents ($COCH_3$, COOEt) were isolated by preparative thin layer chromatography. The phthaloylfuran (5)[4], mp 163°, was also obtained as a minor product. A similar photoreaction using 2-chloro-3-ethoxycarbonylcyanomethyl-1,4-naphthoquinone (1c)[4] gave selectively one stereoisomer of (4c), except when using hexamethyleneimine, as a major product.

The structural assignments for (4b) and (4c) were based on their analytical and spectral results which were in good agreement with their formulation. The results are summarized in Table I and II. The NMR and IR spectra of both stereo-

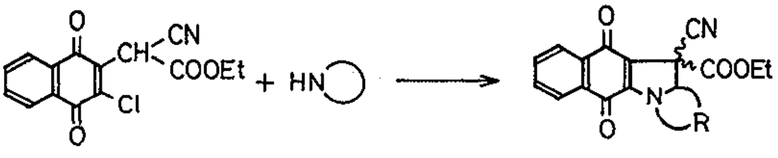
Table I. Photoreaction of 2-Chloro-3-acetylethoxycarbonylmethyl-1,4-naphthoquinone (1b) with Various Cyclic Amines in a One-pot Sequence.



1b 4b

Product (4b) No.	-R-	mp (°C)	Yield (%)	IR(KBr) cm^{-1} ester	acetyl	keto	amide	NMR δ($CDCl_3$) ppm bridgehead CH	$COCH_3$	Mass M^+(m/e)
I-A	$(CH_2)_3$	78	20	1730	1705	1675	1632	4.72	2.40	353
I-B	$(CH_2)_3$	175	20	1736	1696	1672	1618	5.04	2.50	353
II-A	$(CH_2)_4$	139	26	1724	1700	1670	1620	5.08	2.34	367
II-B	$(CH_2)_4$	170	20	1742	1700	1680	1620	5.10	2.52	367
III-A	$(CH_2)_3O$	107	25	1720	1702	1670	1623	4.78	2.18	369
III-B	$(CH_2)_3O$	154	24	1730	1702	1673	1620	4.88	2.52	369
IV-A	$(CH_2)_5$	169	14	1732	1702	1690	1635	4.60	2.38	381
IV-B	$(CH_2)_5$	140	20	1740	1699	1678	1620	4.92	2.50	381

Table II. Photoreaction of 2-Chloro-3-ethoxycarbonylcyanomethyl-1,4-naphthoquinone (1c) with Various Cyclic Amines in a One-pot Sequence.



1c 4c

Product (4c) No.	-R-	mp (°C)	Yield (%)	IR(KBr) cm^{-1} ester	keto	amide	NMR δ($CDCl_3$) ppm bridgehead CH	Mass M^+(m/e)
I-B	$(CH_2)_3$	183	32	1742	1685	1630	4.62	336
II-B	$(CH_2)_4$	210	24	1755	1695	1635	5.06	350
III-B	$(CH_2)_3O$	203	40	1740	1680	1625	4.88	352
IV-A	$(CH_2)_5$	192	9	1728	1676	—	5.14	364
IV-B	$(CH_2)_5$	136	24	1740	1675	1618	4.54	364

isomers of (4b) were similar to each other expect for the following observations. The more polar isomers, (4b-A) series (I, II, III, and IV), showed the ester absorptions at a lower frequency in their IR spectra and the appearance of a bridgehead methine and acetyl methyl proton higher in the field in their NMR spectra in comparison to the less polar isomer (4b-B).

In attempt to elucidate the stereochemistry of these photoproducts, we investigated the LIS[5] spectra of (4b-I-A) and (4b-I-B) as model compounds with $Eu(fod)_3$. We also observed a distinctive difference between europium-coordinated forms of these compounds. The NMR spectra of these isomers were studied in detail using a double irradiation experimental technique. Figure 1 and 2 show plots of the chemical shifts of selected protons in (4b-I-A) and (4b-I-B) as a function of added shift reagent.

The signals centered at δ 5.04 (C_{11a}-H) and 8.00 (C_9-H) ppm in (4b-I-B) showed the greatest shift, suggesting that these indicated the closest protons to the metal ion in the complex. On the other hand, in (4b-I-A), a bridgehead methine proton at 4.72 ppm was affected greatly with the contact shift, but an aromatic proton (C_9-H) was not affected. The observed S values were 2.5 and 1.24 for the C_{11a} and C_9 protons in the former case and 4.1 and 0 in the latter. The comparable difference between the S values for the C_{11a} or C_9 protons in (4b-I-B) and (4b-I-A) would be consistent with having different europium-coordinated forms of these compounds. Namely, the above results indicate that the shift reagent may coordinate predominantly with the acetyl carbonyl oxygen owing to the steric hindrance of the ring D in (4b-I-A), and bidentately with acetyl and amide carbonyl oxygen in (4b-I-B) considering the coordinating ability (acetyl > vinylogous amide > ester carbonyl oxygen). Therefore, the stereochemistry of the acetyl group and C_{11a}-H was assigned as the cis configuration in the (4b-A) series and trans in (4b-B) from the S values.

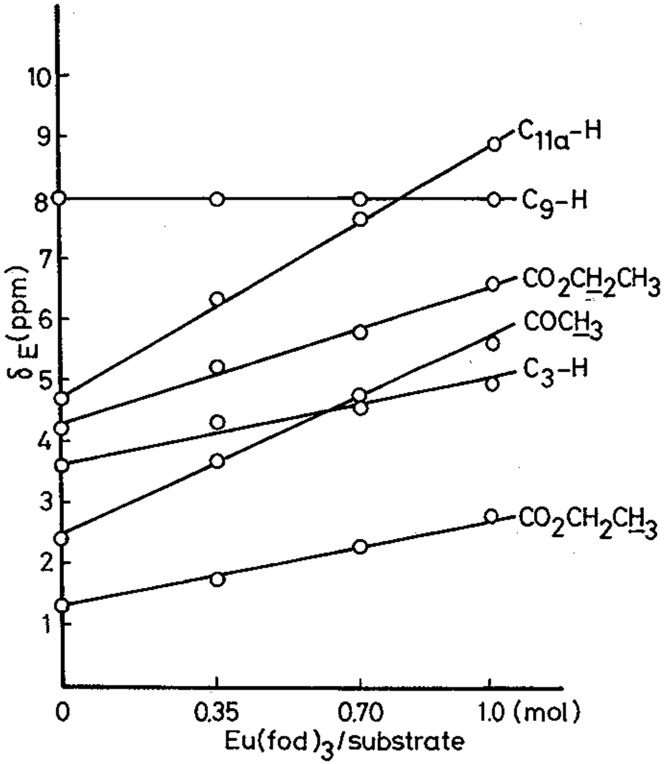


Fig. 1. The Relationship between Chemical Shifts and the Molar Ratio of Eu(fod)$_3$/(4b-I-A)

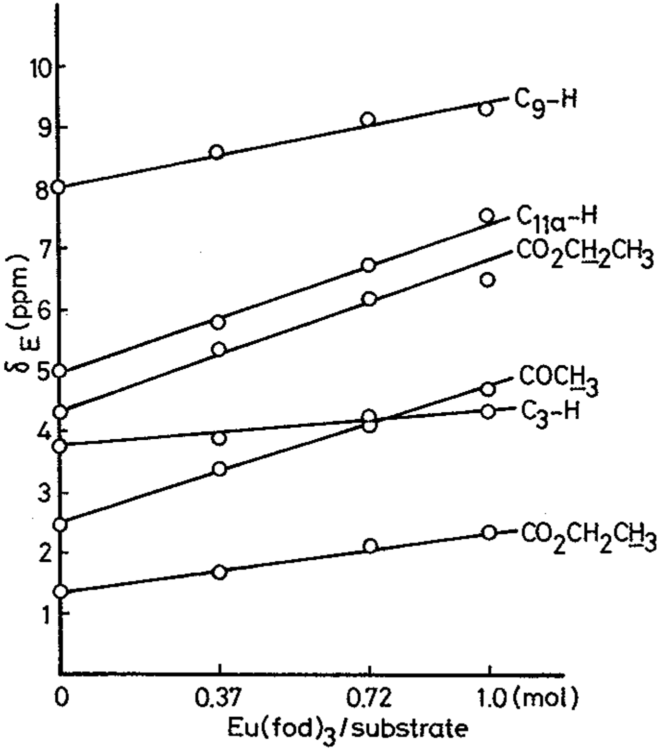
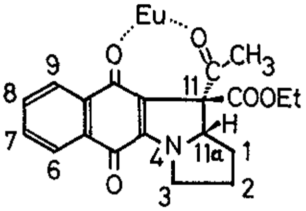
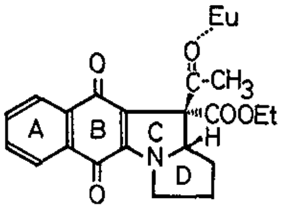


Fig. 2. The Relationship between Chemical Shifts and the Molar Ratio of Eu(fod)$_3$/(4b-I-B)



4b-I-B



4b-I-A

The stereochemistry of the ethoxycarbonyl group and C_{11a}-H in (4c-I~IV) might be assigned as the trans configuration, except the case of (4c-IV-A), by the similarity with the europium-shifted spectra of (4b-I-B) and (4c-I) and comparing the ester carbonyl absorptions in the IR spectra of (4b) and (4c). It is noteworthy that this photocyclization of (2c) containing the smaller ring appears to be stereoselective giving only one diastereomer.

The stereochemical studies on a series of change in the europium-shifted spectra influenced by the ring size are in progress.

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References and Notes

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5 For the meaning of abbreviations, see the glossary in "Nuclear Magnetic Resonance Shift Reagent", R.E. Sievers, Ed., Academic Press, New York, 1973.

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