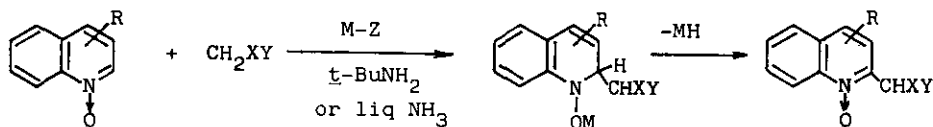


FACILE FORMATION OF 2,2'-DIQUINOLYLMETHANE N,N'-DIOXIDES
AND MONO-N-OXIDES AND RELATED REACTIONS

Genji Iwasaki, Kazuko Wada, Seitaro Saeki and Masatomo Hamana*,¹
Faculty of Pharmaceutical Sciences, Kyushu University
Maidashi 3-1-1, Higashi-ku, Fukuoka 812, Japan

Abstract — Reactions of quinoline N-oxides with derivatives of quinaldine or its N-oxide in the presence of *t*-BuOK in THF at low temperatures afford mono-N-oxides or N,N'-dioxides of 2,2'-diquinolylmethanes, respectively. Some related reactions are also described, which involve reactions of *p*-chloronitrobenzene giving 2-substituted 4-chloronitrobenzenes.

We previously reported that quinoline N-oxides readily undergo nucleophilic substitution by means of hydride elimination to give 2-substituted quinoline N-oxides, upon treatment with active methylenes and strong bases (*t*-BuOK, *n*-BuLi, KNH₂ or NaNH₂) in *t*-BuNH₂ or liq. NH₃ at low temperatures as shown below.²



R: H, 4-Cl, 3-Br

YXCH-: -CH₂COMe, -CH₂COCMe₃, -CH₂COPh, -CH₂COOMe, -CH₂CN, etc.

M-Z: *t*-BuOK, *n*-BuLi, KNH₂, NaNH₂

As an extension of this work, we applied quinaldine and its N-oxide derivatives as active methylenes to quinoline N-oxides under similar conditions, and successfully obtained mono-N-oxides and N,N'-dioxides of 2,2'-diquinolylmethanes.

At first, the reaction of 4-chloroquinoline N-oxide (**1b**) with quinaldine N-oxide (**2a**) was investigated in some detail. When **1b** was added in small portions to a

solution of 2a (2 equiv) and t-BuOK (2.5 equiv) in THF with stirring at -70°C , the reaction mixture immediately turned black. Stirring was continued at the same temperature for 2 h, and the product was purified by chromatography on silica gel with benzene to give 4-chloro-2,2'-diquinolylmethane *N,N'*-dioxide (3b), colorless needles, mp $209\text{--}211^{\circ}\text{C}$ (dec.), in 47.6% yield.³ The same product 3b was also obtained from the reaction of quinoline *N*-oxide (1a) with 4-chloroquinoline *N*-oxide (2b) under the same conditions in 46.5% yield (Chart 1).

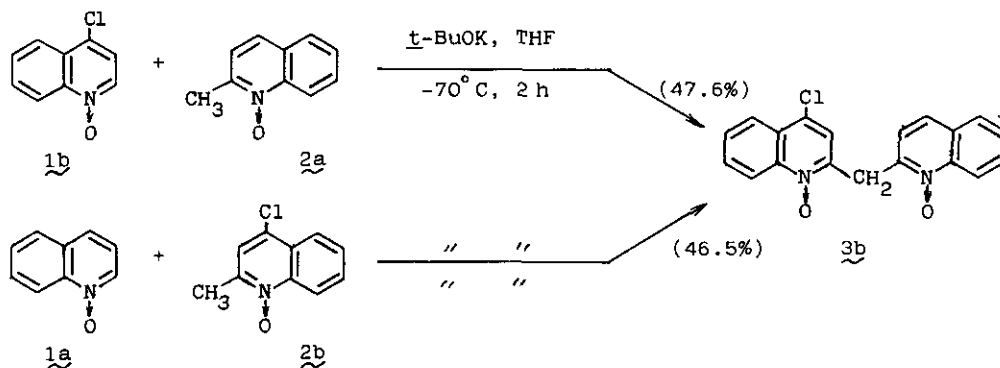


Chart 1

Consecutively, various conditions were examined for the reaction of 1b with 2a, and the results summarized in Table were obtained.

Table Reaction of 1b with 2a

Solvent	Base	Temp. ($^{\circ}\text{C}$)	Time(h)	Yield of <u>3b</u> (%)
THF	<u>t</u> -BuOK	-70	2.0	47.6
	<u>n</u> -BuLi	-70	2.0	13.8
	LDA ^{a)}	-50	2.5	—
liq NH_3	<u>t</u> -BuOK	-70	2.0	45.9
	KNH_2	-60	1.0	35.2
	NaNH_2	-60	1.0	29.5
	LiNH_2	-60	1.0	5.8
<u>t</u> -BuNH ₂	<u>t</u> -BuOK	-70	2.0	32.1

a) Lithium diisopropylamide

Thus it was found that the ease of the reaction was considerably affected by the nature of both base and solvent. Among the bases so far examined, t-BuOK was

highly effective, and THF and liq. NH_3 were preferable as the reaction medium. It is noteworthy that the combination of LDA and THF did not give $\underline{3b}$ at all, while that of LiNH_2 and liq. NH_3 produced $\underline{3b}$, though in poor yield.

2,2'-Diquinolylmethane N,N'-dioxide ($\underline{3a}$), its 3-bromo- ($\underline{3c}$) and 4-chloro-4'-methyl derivatives ($\underline{3d}$) were similarly obtained under similar conditions as illustrated in Chart 2.

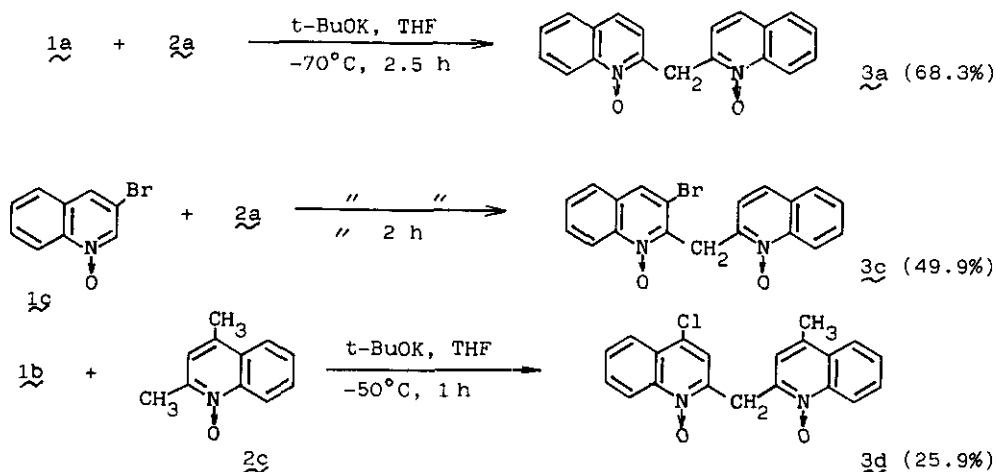


Chart 2

Subsequently, 2,2'-diquinolylmethane mono-N-oxides were obtained from similar reactions with quinaldine or 2,4-dimethylquinoline (Chart 3).

The reactions using 2,4-dimethylquinoline or its N-oxide clearly demonstrate that the 2-methyl group in quinoline ring is much more reactive than the 4-methyl group. However, the reaction of $\underline{1b}$ with lepidine proceeded similarly to give 4-chloro-2,4'-diquinolylmethane N-oxide. Further, 2-picoline N-oxide reacted also smoothly with $\underline{1b}$ to afford 2-pyridyl-2-(4-chloroquinolyl)methane N,N'-dioxide (Chart 3).

While a few methods are known for the preparation of 2,2'-diquinolylmethane and its analogs,⁴ there has been no report on the synthesis of their N-oxide or N,N'-dioxide. The N-oxidation of 2,2'-diquinolylmethane is quite unpractical for this purpose because its methylene group is highly susceptible to oxidation.^{4,5}

Therefore, the above mentioned reaction is evidently a very promising method for the preparation of 2,2'-diquinolylmethane N-oxide, N,N'-dioxide and their analogs. In addition, this route is also useful and convenient for the preparation of 2,2'-diquinolylmethane, its analogs and their derivatives, since deoxygenation of aro-

matic N-oxide can be easily performed by a number of means.

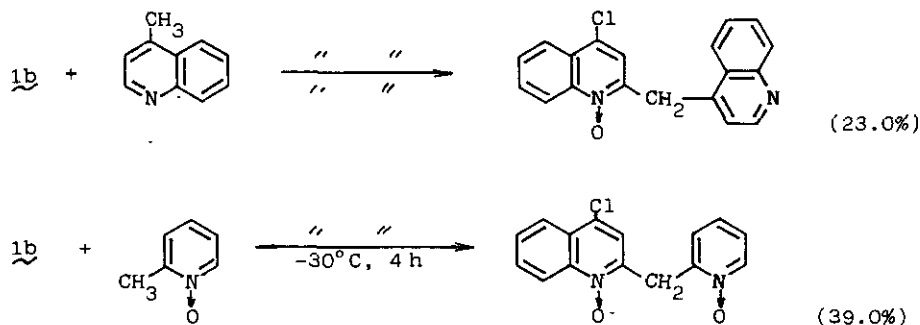
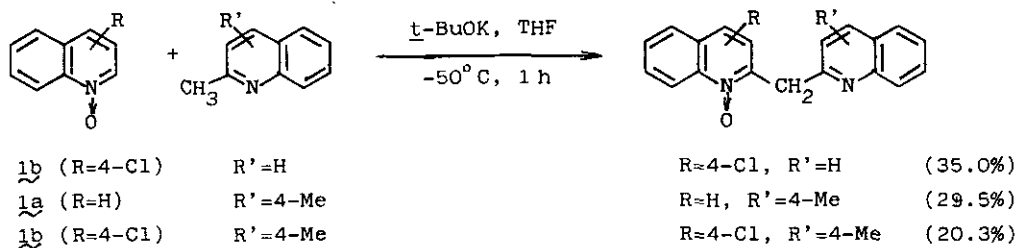


Chart 3

It was previously described that *p*-chloronitrobenzene is also able to undergo the nucleophilic substitution mentioned at the beginning, giving 2-substituted 4-chloronitrobenzenes.² This fact prompted us to investigate the reactivity of *p*-chloronitrobenzene toward the reaction concerned here, and some attempted reactions were found to give the corresponding 2-substituted 4-chloronitrobenzenes as was expected (Chart 4).

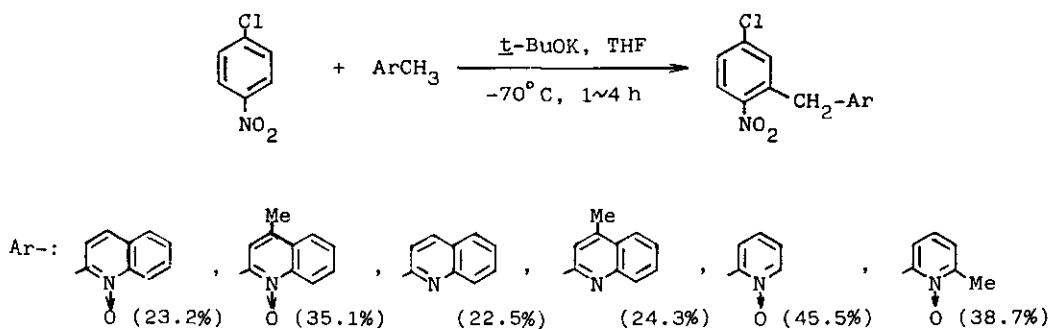


Chart 4

ACKNOWLEDGMENT

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REFERENCES AND NOTES

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