

A Facile Preparation of 4-Quinolinols by the Condensation
of Dilithiobenzoylacetone or $C(\alpha),O$ -Dilithiooximes
with Methyl Anthranilate or 5-Chloroisatoic Anhydride

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Dilithiobenzoylacetone or $C(\alpha),O$ -dilithiooximes were prepared in an excess of lithium diisopropylamide and condensed with methyl anthranilate or 5-chloroisatoic anhydride to give intermediates, which after neutralization were cyclized to 4-quinolinols.

J. Heterocyclic Chem., **16**, 1669 (1979).

Sir:

We are reporting our initial results on the preparation of substituted 4-quinolinols resulting from the condensation of intermediates, dilithiobenzoylacetone or $C(\alpha),O$ -dilithiooximes, with methyl anthranilate or 5-chloroisatoic anhydride followed by cyclization.

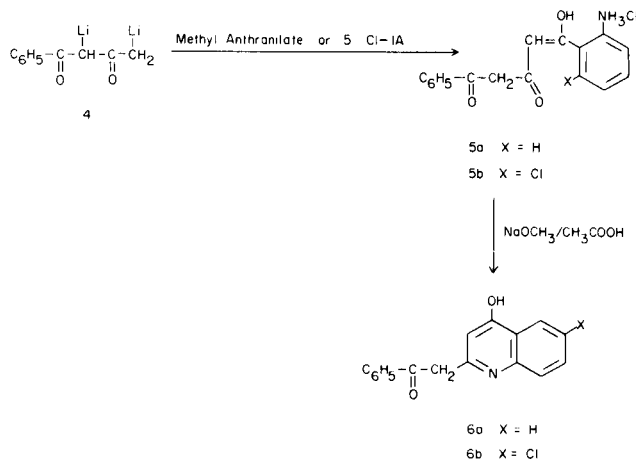
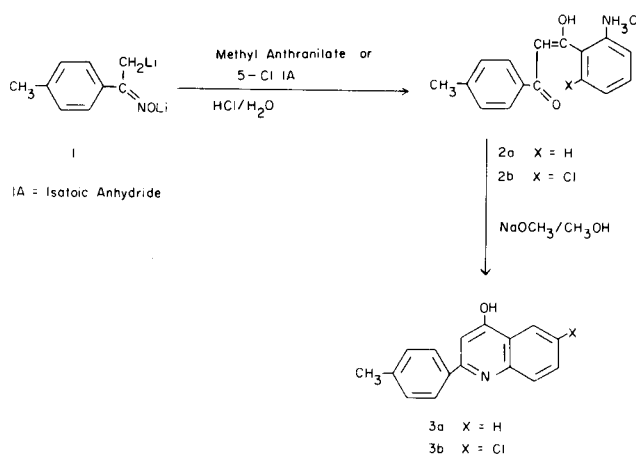
$C(\alpha),O$ -dilithiooxime **1** was prepared by the metalation of *p*-methylacetophenone oxime with an excess of lithium diisopropylamide (**2**); **1** was condensed with methyl anthranilate, acidified with 3*N* hydrochloric acid and hydrolyzed to give keto-hydrochloride **2**, which was isolated in 46% yield, m.p. 204-206° (methanol).

Anal. Calcd. for $C_{16}H_{16}ClNO_2$: C, 66.32; H, 5.57; N, 4.83. Found: C, 66.46; H, 5.56; N, 4.97.

The pmr spectrum of **2** displayed absorptions of δ 2.43 (s, ArCH₃) and 7.16-8.5 ppm (m, ArH and vinyl). Its ir spectrum (nujol) exhibited a strong absorption at 1600 cm^{-1} (C=O). When **2** was suspended in hot methanol and treated with finely divided sodium methoxide, solution occurred, and precipitation of 4-quinolinol **3a** resulted after an equivalent (1:1) amount of base had been added. The yield for the cyclization step was 77%, and the m.p. 278-280° (methanol) agreed with that reported (Lit. m.p. 277-278° (3)). A pmr spectrum (trifluoroacetic acid) of **3a** displayed a methyl resonance at δ 2.50 ppm. Quinolinol **3b** was prepared in a similar manner by the condensation of **1** with 5-chloroisatoic anhydride, followed by cyclization of an analogous keto-hydrochloride, and gave an overall yield (two steps) of 25%, m.p. > 300° (methanol).

Anal. Calcd. for $C_{16}H_{12}ClNO$: C, 71.25; H, 4.48; N, 5.19. Found: C, 71.43; H, 4.48; N, 5.15.

Benzoylacetone was metalated in an excess of lithium diisopropylamide (dione:base - 1:3) to give **4** and condensed with methyl anthranilate or 5-chloroisatoic anhydride followed by acidification with 3*N* hydrochloric acid. The solid material **5ab** isolated appeared to contain hydrochloride, and was suspended in methanol, brought into solution by treatment with sodium methoxide and acidified with acetic acid. The overall yield for 4-quinolinols



linols **6a** and **6b** was 35% and 45% respectively; **6a**, m.p. 237° (methanol).

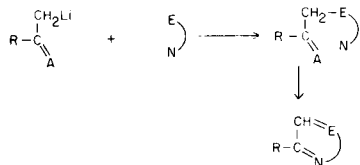
Anal. Calcd. for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.99; N, 5.32. Found: C, 77.30; H, 5.04; N, 5.17.

The pmr spectrum (trifluoroacetic acid): of this material (**6a**) displayed a methylene resonance of δ 4.97 ppm and an ir spectrum (nujol) exhibited a band at 1680 cm^{-1} (C=O); 4-quinolinol **6b**, m.p. 281° (methanol).

Anal. Calcd. for $C_{17}H_{12}ClNO_2$: C, 68.58; H, 4.06; N, 4.70. Found: C, 68.29; H, 4.14; N, 4.72.

Its nmr (trifluoroacetic acid) contained a methylene resonance at δ 5.00 ppm and an ir exhibited a band at 1675 cm^{-1} (CO).

There are numerous documented preparations of 4-quinolinols (4); but the methods described by Fuscon (5) and Hauser (6) are mentioned here because of their overall interest to this investigation. Fuscon condensed ketals with anthranilates and Hauser condensed aniline with β -ketoesters. The experimental procedures, especially the cyclization steps, are more involved and time consuming than the new route described here. The use of easily prepared starting materials, oximes (6) and aroylketones (7) suggests that this route has excellent potential for development. Other extensions of the method are being fully investigated, such as the condensation of **1** and **4** with aminoacids, esters and other molecules containing both nucleophilic and electrophilic centers.



Acknowledgement.

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REFERENCES AND NOTES

- (1) To whom correspondence should be addressed.
- (2) Other dilithiated intermediates prepared from *n*-butyllithium underwent Claisen-type condensations and sacrificed half of these reagents. Lithium diisopropylamide in excess overcomes this difficulty. See: R. S. Foote, C. F. Beam, and C. R. Hauser, *J. Heterocyclic Chem.*, **7**, 589 (1970).
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