Continuation of the distillation gave another 1.31 g of 4 containing small amounts of 1 and 3; the pot residue was mostly *N*-4-pentenylisoindolin-1-one (3).

Registry No. 1, 72893-85-7; 2, 72893-86-8; 3, 72905-19-2; 4, 72905-20-5; 4 methiodide, 72905-21-6; 5-bromo-1-pentene, 1119-51-3; *N*-4-pentenylphthalimide, 7736-25-6.

Rearrangement of 2,2,6,6-Tetramethyl-4-piperidone in Phase-Transfer Catalyzed Reactions[1]

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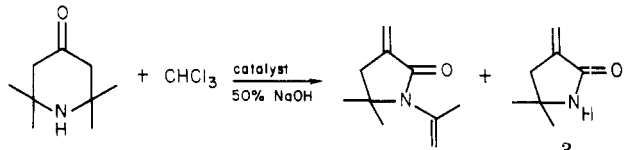
We recently described a novel synthesis of 1,3,3,5,5-pentasubstituted 2-piperazinones[2] from N[1],2,2-trisubstituted 1,2-ethanediamines, ketones, and chloroform by a phase-transfer[3] catalyzed reaction. We proposed that trichloromethide ion is the reactive species while dichlorocarbene involvement is minimal at most.[2] We now report a novel rearrangement of 2,2,6,6-tetramethyl-4-piperidone (1) to *N*-isopropenyl-3,3-methylene-5,5-dimethyl-2-pyrrolidinone (2) and 3,3-methylene-5,5-dimethyl-2-pyrrolidinone (3) which occurs when 1 is reacted with excess chloroform and 50% aqueous NaOH in the presence of a phase-transfer catalyst, where trichloromethide ion rather than dichlorocarbene[4] is still believed to play a dominant role.

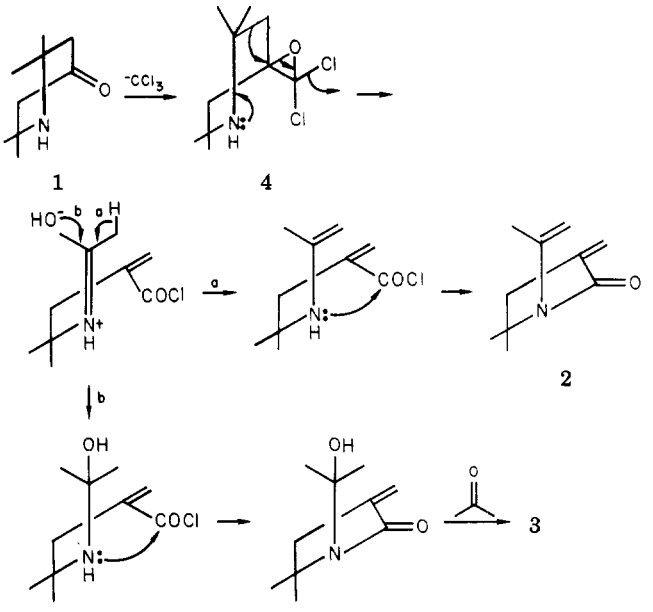


1 2 3

catalyst	ratio[5]	
1, $PhNH_2NEt_3^+Cl^-$	78	22
2, 18-crown-6	90	10
3, 18-crown-6/1.0 piperidine	21	79

The reaction proceeds essentially quantitatively to the products in a few hours at 0–5 °C. When 1 equiv of piperidine is added to the reaction (see reaction 3), the ratio of 2 to 3 changes drastically, although 2 and 3 still make up most of the product (85–90%). This suggests that dichlorocarbene, being an electrophile, is quite unlikely as an intermediate because it would react with the stronger base piperidine[6] much faster than with 1. 2 and 3 are not interchangeable under the reaction conditions, and adding piperidine to reactions 1 and 2 does not cause the conversion of 2 to 3 after their formation. We outline a possible mechanism in Scheme I featuring $^-CCl_3$ as the reactive species which forms the dichlorooxirane 4 with 1.

Scheme I



Experimental Section

^1H NMR spectra were recorded on a Varian A-60 spectrometer. ^{13}C NMR spectra were recorded on a Bruker HX90E spectrometer. $CDCl_3$ was used as solvent and Me_4Si was added as internal standard in all NMR samples. Infrared spectra were obtained on a Perkin-Elmer 467 spectrometer. Mass spectra were recorded on a Varian MAT311A mass spectrometer. Microanalyses were performed by Huffman Lab, Inc., Wheatridge, CO.

***N*-Isopropenyl-3,3-methylene-5,5-dimethyl-2-pyrrolidinone (2).** 2,2,6,6-Tetramethyl-4-piperidone hydrate[7] (5.20 g, 30 mmol), chloroform (11.94 g, 100 mmol), and 18-crown-6 (0.40 g, 1.5 mmol) were placed in a 100-mL 3-neck flask immersed in a refrigerated circulating bath. The temperature was kept below 5 °C while 50% aqueous NaOH (24 g, 300 mmol) was added dropwise in 25 min. The solution was stirred at 5 °C for 7 h after the addition and then water was added until all solids dissolved. The two layers were separated and the aqueous layer was extracted with two 25-mL portions of $CHCl_3$. The combined organic layers were washed with one 10-mL portion of H_2O, dried, and concentrated under vacuum, 15 mL of hexane was added, the mixture was stirred, and the small amount of solid which formed was filtered off. The filtrate was concentrated and distilled to give 3.5 g (71%) of a clear oil at 63–7 °C (0.2 mm): IR (neat) 1680, 1655, 1640 cm^{-1}; ^1H NMR δ 1.35 (s, 6 H), 2.01 (d, 3 H), 2.70 (t, 2 H), 4.89 (s, 1 H), 5.20 (q, 1 H), 5.32 (dt, 1 H), 6.00 (dt, 1 H); ^{13}C NMR δ 22.04 (q), 28.15 (q), 29.48 (t), 42.12 (s), 114.60 (t), 115.51 (t), 139.47 (s), 140.18 (s), 166.35 (s); mass spectrum, *m/e* 165 (M^+). Anal. Calcd for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48. Found: C, 71.35; H, 8.93; N, 8.42.

3,3-Methylene-5,5-dimethyl-2-pyrrolidone (3). The procedure was as above except that 2.55 g (30 mmol) of piperidine was mixed with the reactants before the addition of 50% NaOH. The obtained crude product was stirred with 15 mL of hexanes to yield 1.95 g (52%) of a slightly yellowish solid after filtration. Recrystallization from heptane–toluene afforded colorless crystals: mp 139–142 °C; IR (KBr) 3180, 1680, 1645 cm^{-1}; ^1H NMR δ 1.32 (s, 6 H), 2.61 (t, 2 H), 5.33 (m, 1 H), 5.97, (t, 1 H); ^{13}C NMR δ 29.67 (q), 41.83 (t), 53.92 (s), 115.64 (t), 141.09 (s), 169.89 (s); mass spectrum, *m/e* 125 (M^+). Anal. Calcd for $C_7H_{11}NO$: C, 67.17;

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(4) An independent observation for the isolation of 2 from 1 under similar conditions was published: Lind, H.; Winkler, T. *Tetrahedron Lett.* **1980**, 119.
(5) Determined by GC by their relative peak heights. A 6 ft × $^3/_{16}$ in. 10% OV-17 on Chromosorb W column was used.
(6) No appreciable amount of *N*-formylpiperidine which would otherwise be formed from piperidine and dichlorocarbene can be detected. Cf. (a) Graefe, J.; Frohlich, I.; Muhtstadt, M. *Z. Chem.* **1974**, *14*, 34. (b) Makosza, M.; Kacprowice, A. *Rocz. Chem.* **1975**, *49*, 1627.
(7) Eastman Kodak; a simple distillation will remove most of the color.

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H, 8.86; N, 11.19. Found: C, 66.89; H, 8.75; N, 11.12.

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Registry No. 1, 826-36-8; 2, 73018-15-2; 3, 73018-16-3; chloroform, 67-66-3; $PhCH_2NEt_3^+Cl^-$, 56-37-1; 18-crown-6, 17455-13-9.

Facile Synthesis of 8-Substituted Quinolines

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8-Substituted quinolines are useful molecular frameworks for studying the interaction of various metals with organic functional groups. Information on the aldehyde decarbonylation reaction,[1] hydroacylation,[2] and metal insertion into carbon–hydrogen bonds[3] has been obtained by using this class of compounds. We wanted a general method for placing groups such as vinyl, propenyl, and aldehyde, which engage in transition-metal-mediated reactions at the 8-postion of quinolines, for our studies on the interaction of metals with carbon–hydrogen, carbon–carbon, and carbon–heteroatom bonds. The classical Skraup synthesis[4] is limited to substituents which can survive strongly acidic reaction conditions. A more flexible synthesis of 8-substituted quinolines appeared to proceed by generation of 8-lithioquinoline via metal–halogen exchange and elaboration of the lithium reagent (or its derived cuprate).[5]

The ease with which the quinoline ring is attacked by nucleophiles[6] limits the conditions under which metal–halogen exchange can occur. In an earlier study, Pearson and co-workers had reported that substituted 8-bromoquinolines underwent lithium–bromine exchange at −70 °C with *n*-butyllithium in THF, using 2 equiv of lithium reagent.[7] They proposed that 2 equiv of lithium reagent was needed due to the coordination of the lithium cation to the quinolinyl nitrogen and the resulting deactivation. This report was surprising in view of the ability of tertiary amines such as TMEDA to promote metalation of hydrocarbons (although we are not aware of any reports on the effect of TMEDA upon metal–halogen exchange).[8]

Our results on the metalation of 8-bromoquinoline are summarized in Table I. Any deactivating effect of the quinolinyl nitrogen is small, since we find excess *n*-butyllithium gives only slightly better yields of 8-methylquinoline. A superior procedure involved the use of *sec*-butyllithium as the metalation reagent. Due to its greater reactivity, excess *sec*-butyllithium was deleterious since products arising from addition to the imine double bond were formed. The use of *tert*-butyllithium gave approximately equal amounts of addition and exchange products. The superiority of *sec*-butyllithium for lithium–bromine exchange has also recently been observed with vinyl bromides.[9] As in Pearson's work, we found 8-chloroquinoline gave only ring addition products.

Table I. Formation of 8-Lithioquinoline

8-BrQuin + RLi → + CH_3I → 8-MeQuin

T, °C	solvent	R	t,[a] min	% 8-MeQuin
−100	THF	*sec*-butyl	60	49
−78	THF	*sec*-butyl	60	73
−78	THF	*sec*-butyl	5	87
−78	ether	*sec*-butyl	60	46
−78	THF	*tert*-butyl	10	*b*
−78	THF	*sec*-butyl[c]	5	56
−78	THF	*sec*-butyl[d]	5	50
−78	THF	*n*-butyl	15	58
−78	THF	*n*-butyl[c]	15	66

[a] Time between addition of the lithium reagent to the cold solution of 8-bromoquinoline and addition of methyl iodide. [b] The reaction contained products from addition to the ring as well as from metal–halogen exchange. [c] Two equivalents of lithium reagent was used. [d] Addition of 8-bromoquinoline as a THF solution to the lithium reagent.

Table II. Synthesis of 8-Substituted Quinolines

electrophile	yield,[a] %	R[d]
$DCON(CD_3)_2$	43	CDO
$HCON(CH_3)_2$	42[b]	CHO
CH_3CHO	64	$CH_3CH(OH)$
$H_2C{=}CHCH_2Br$[c]	65	$CH_2CH{=}CH_2$
PPh_2Cl	32	PPh_2
CH_3I	87[b]	CH_3
$Sn(CH_3)_3Cl$	55	$Sn(CH_3)_3$
ethylene oxide[c]	71[b]	CH_2CH_2OH

[a] Isolated yields of chromatographically homogeneous products. All new products gave satisfactory analytical and spectral data. [b] Determined by NMR integration, with acetophenone as a standard. [c] Prepared via the cuprate reagent. [d] R is the 8-substituent on quinoline.

The products derived from 8-quinolinyllithium and various electrophiles are summarized in Table II. 8-Allylquinoline and 8-(2-hydroxyethyl)quinoline could only be prepared in reasonable yields by means of the cuprate in diethyl ether. Interference from the metalation byproduct, *sec*-butyl bromide, was not a problem with any of the electrophiles studied. However, 8-lithioquinoline can be prepared in the absence of alkyl halide by the analogous metalation of 8-(trimethylstannyl)quinoline. 8-Vinylquinoline was best prepared by dehydration of 8-(1-hydroxyethyl)quinoline with Burgess' salt [ethyl(carboxysulfamoyl)triethylammonium hydroxide inner salt].[10]

Experimental Section

8-(1-Hydroxyethyl)quinoline. To a magnetically stirred solution of 3.0 g (14.4 mmol) of 8-bromoquinoline[11] in 50 mL of dry THF at −78 °C under argon was added dropwise 12 mL of a 1.2 M commercial solution (Aldrich) of *sec*-butyllithium in hexane. After 5 min 1.28 g (29 mmol) of acetaldehyde was added

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(11) Prepared via a Skraup synthesis from 2-bromoaniline, glycerine, sulfuric acid, and iodine; purified by neutralization of the reaction mixture, extraction with methylene chloride, bulb-to-bulb distillation, and preparative medium-pressure liquid chromatography. Further purification, if necessary, was accomplished by recrystallization of the 8-bromoquinolinium hexafluorophosphate from water.

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