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α-BROMINATION OF ALDOXIMES. A ROUTE TO FUSED AZETIDINES[1].

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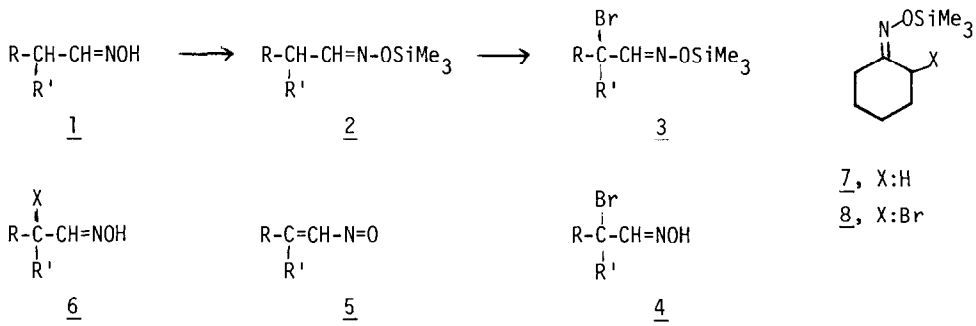
Abstract: Unlike aldehydes and aldoximes, O-silylated aldoximes 2 are smoothly α-brominated with NBS to produce 3, useful intermediates in the conversion to vinylnitroso species or in α-substitution reactions. For instance, 3 + 9→10 provided precursors for nitrile oxide-olefin cycloadditions.

α-Bromooximes are useful intermediates for a variety of synthetic transformations[2], in particular for the formation of vinyl nitroso compounds[3]. The preparation of α-bromoketoximes via bromination of ketones and oxime formation is usually straightforward. On the other hand, α-bromoaldoximes are difficult to obtain partly because alpha bromination of aldehydes is a low yield reaction leading to unstable products[4]. In conjunction with our recent studies[5] on intramolecular nitrile oxide-olefin cyclizations (INOC)[6], we wished to explore nucleophilic displacements on bromoaldoximes 4 as a convenient route to the INOC precursors (see 11 → 12).

We found that direct alpha bromination of aldoximes 1 with a variety of brominating agents was not successful, but we were able to accomplish smooth bromination of the silylated oximes 2. Thus reaction of 2b-e with N-bromosuccinimide (NBS) proceeded in the presence of benzoyl peroxide in refluxing CCl_4 to produce the brominated products 3b-e in high yield (see Table 1). An exception were the acetaldehyde and phenylacetaldehyde derivatives 2a and 2f which gave impure products in poor yield.



A more convenient alternate route proved to be the photochemical bromination of 2 with NBS which proceeded at room temperature and permitted the isolation of 3a and 3f. The latter was found to polymerize on standing, which explains our inability to obtain this product via the thermal method. The sequence 1→2→3 can be carried out without purification of intermediate 2 and the yields in Table 1 reflect the overall sequence. Ketoximes can be transformed into their bromo derivatives in the same manner (see 7 → 8).

Table 1

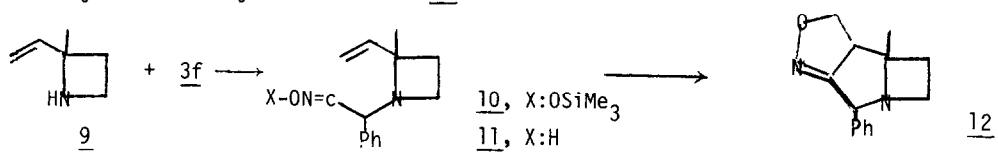
Conversion of Aldoximes 1 to 3 via Bromination of 2[a]

3	a	b	c	d	e	f
R	H	Me	Et	n-Bu	Me	Ph
R'	H	H	H	H	Me	H
yield(%)	30[b]	95	95	90	100	70[c]

(a) 2 were prepared from 1 upon stirring with Me_3Si_{Cl}-ET_3N in CCl_4. After filtration, conversion of 2 to 3 was carried out either by refluxing for 3.5 hr with 1 equiv. of NBS and 0.05 equiv. of benzoyl peroxide or by photochemical irradiation for 2 hr with 1 equiv. of NBS at room temperature in CCl_4. All compounds showed consistent ^1H and ^{13}C-NMR as well as mass spectra. (b) formed by photochemical irradiation for 14 hr. (c) formed by photochemical irradiation for 30 min.

Further transformation of 3 to 4 can be carried out by means of fluoride ions but, since 4 are unstable, this reaction is best performed in the presence of other nucleophiles in which case it leads to products 6. The reaction apparently proceeds via the transient intermediacy of unsaturated nitroso compounds 5, which we detected by the appearance of a blue color. An advantage of our bromination procedure is the isolation of O-silyl-α-bromoaldoximes 3 which react cleanly in nucleophilic substitutions. For instance, treatment of 3b with 1 equiv. of tetrabutylammonium fluoride in the presence of MeOH at room temperature gave the methoxy oxime 6 (R;Me,R':H, X:OMe) in quantitative yield.

Another example of the utility of 3 is provided by the reaction of 9 with 3f to produce at room temperature and in high yield the substitution product 10 which on desilylation gave 11. Treatment of 11 with NaOCl converted it to an unsaturated nitrile oxide which ring closed spontaneously to the tricyclic azetidine 12 [7].



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7. Details about this transformation will be reported elsewhere.

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