Nitrosative Elimination of Terpenyl Alkanolamines leading to Alkynyl *N*-Nitroso-analogues

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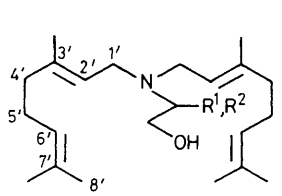
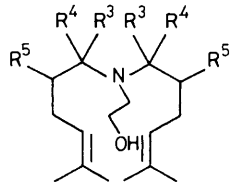
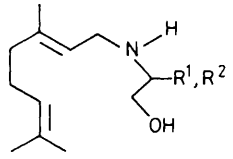
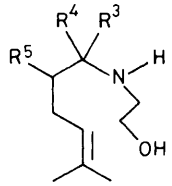
Treatment of selected terpenyl alkanolamines containing isopropylidene moieties with an excess of sodium nitrite in aqueous acetic acid affords the corresponding ethylidyne *N*-nitrosamines.

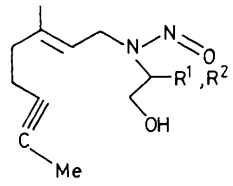
We report the first direct conversion of isopropylidene groups into ethylidyne functionalities involving the title compounds in reactions with nitrous acid under normal nitrosative dealkylation conditions.[1] Earlier studies[2,3] showed that the β,γ-unsaturated ethanolamine (**1a**) underwent mild nitrosative dealkylation at room temperature giving exclusively the *N*-nitroso-derivative of (**3a**), (**3a**-NA), together with a small amount of the 6′,7′-acetylenic nitrosamine (**5a**). Subsequently, when (**1a**) was nitrosated with a large excess of sodium nitrite (amine : nitrite 1 : 15) for an extended period of 4 hours at 60 °C, (**5a**) was obtained in moderate yield as the major product. The monoterpenyl nitrosamine (**3a**-NA) was not detected in the reaction product. In order to preclude the possible involvement of (**1a**) in the elimination process leading

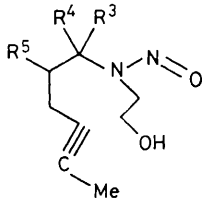

(1a-d)

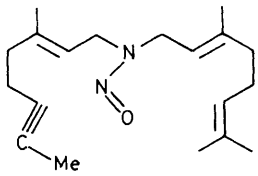

(2e,f)


(3a-d)


(4e,f)


(5a-d)


(6e,f)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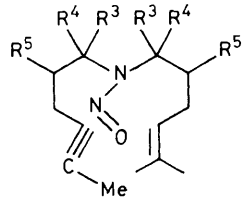
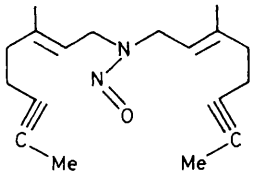

(8e,f)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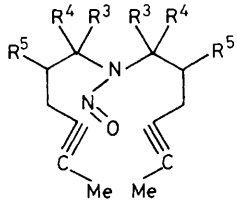
(10e,f)

(a) $R^1 = R^2 = H$
(b) $R^1 = H$, $R^2 = Me$
(c) $R^1 = R^2 = Me$
(d) $R^1 = H$, $R^2 = Et$
(e) $R^3 = Me$, $R^4 = CH{=}CH_2$, $R^5 = H$
(f) $R^3 = R^4 = H$, $R^5 = C(Me){=}CH_2$

to (**5a**), (**3a**-NA) was prepared from the amine (**3a**) and was found to react readily with nitrous acid under the same conditions to yield quantitatively (**5a**). It is evident that (**5a**) was formed *via* a stepwise reaction sequence going from initial *N*-nitrosation to apparent elimination of a CH_4 unit from the isopropylidene moiety in the last step: (**1a**) → (**3a**-NA) → (**5a**). This was further experimentally corroborated by the appearance and disappearance of relevant chromatographic peaks during monitoring of the reaction course.

We extended the scope of the nitrosative elimination reaction to a series of mono- and di-terpenyl alkanolamines including the saturated as well as partially saturated counterparts. As shown in Table 1, without exception ethylidyne nitrosamines were produced in moderate to high yield from the terpenyl alkanolamines [(**1**)—(**4**)] where at least one requisite isopropylidene olefinic bond was present in each of the terpenyl groups. The β,γ- and γ,δ-saturated analogues of the same series were similarly converted into the acetylenic compounds. On the other hand, the saturated analogues in the series failed to yield any products other than those formed by the usual nitrosative dealkylation pathway.[1] Analogously, saturation of all the isopropylidene double bonds in the reactant alkanolamines led only to products devoid of the proposed ethylidyne structures. The product distribution data (Table 1) for the ethylidyne nitrosamines derived from diterpenyl alkanolamines [(**1**), (**2**)] reflect the conformational outcome of the nitrosative dealkylation process.

Table 1. Nitrosation of some terpenyl alkanolamines.

Compound	Reaction temperature /°C	Ethylidyne nitrosamine product (yield, %) Type I	Type II	Type III
(**1a**)	60	(**5a**) (75)	(**7**) (4)	(**9**) (2)
(**1b**)	60	(**5a**) (79)	(**7**) (0)	(**9**) (0)
(**1c**)	60	(**5c**) (80)	(**7**) (0)	(**9**) (0)
(**1d**)	60	(**5d**) (78)	(**7**) (0)	(**9**) (0)
(**2e**)	60	(**6e**) (68)	(**8e**) (11)	(**10e**) (9)
(**2f**)	60	(**6f**) (41)	(**8f**) (39)	(**10f**) (18)
(**3a**)	45	(**5a**) (92)		
(**3b**)	45	(**5b**) (95)		
(**3c**)	45	(**5c**) (90)		
(**3d**)	45	(**5d**) (87)		
(**4e**)	45	(**6e**) (78)		
(**4f**)	45	(**6f**) (73)		
(**1**-DA)	50		(**7**) (66)	(**9**) (24)
(**2e**-DA)	50		(**8e**) (71)	(**10e**) (20)
(**2f**-DA)	50		(**8f**) (63)	(**10f**) (27)
(**1**-DA)	70		(**7**) (31)	(**19**) (58)

Structures of all the ethylidyne nitrosamines isolated were unequivocally established by elemental analyses, high-resolution mass spectrometry, independent syntheses, and spectral analyses (i.r., C≡C, 2210—2220 cm^{-1}; ^{13}C n.m.r., $CH_3C{\equiv}C$, 2.75—3.22, C≡C, 75.4—78.6). In every case studied, the mass spectrum of a pure ethylidyne product in the respective (**5**)—(**8**) and (**9**), (**10**) series exhibited a molecular ion signal at 16 and 32 mass units less than that of the corresponding isopropylidene olefinic reactant. The structures of Type II [(**7**), (**8**)] and Type III [(**9**), (**10**)] compounds were also confirmed by direct preparation from the diterpenyl amines, (**1**-DA) and (**2**-DA), at 50 and 70 °C (Table 1). Catalytic hydrogenation of the β,γ- and γ,δ-saturated analogues of compounds (**5**)—(**10**) afforded alkylamines identical with those obtained from exhaustive catalytic hydrogenation of corresponding compounds in (**5**)—(**10**) series.

While the reaction of certain olefins with various nitrosating agents has been reported previously,[4] the unique alkene–alkyne transformation as described in this study is new and warrants further study on the mechanistic details of this reaction.

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