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NITROALLYLATION OF HIGHLY REACTIVE ORGANOLITHIUM COMPOUNDS BY 2-NITRO-3-PIVALOYLOXY-1-PROPENE (NPP)

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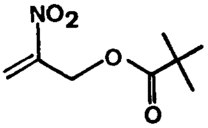
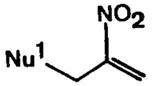
Summary: *The nitroolefin 1 (NPP) efficiently transfers a 2-nitroallyl group even to the most reactive nucleophilic centres of organolithium reagents to give the products of type 2 listed in the table.*

We have recently reported2), that the nitroallyl pivalate 1 (NPP) can be used as a nitroallylating reagent to furnish products of type 2 with nucleophiles Nu^1 derived from rather stable anions such as ketone and ester enolates. The acceptor property of the nitro group can be exploited once again, by adding a second nucleophile Nu^2 to give unsymmetrical nitroalkanes 3. In view of the many functional group transformations of the nitro group, the reagent NPP corresponds to the a^2,a$^{2'}$-synthon 4.



1 (NPP)



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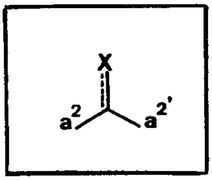

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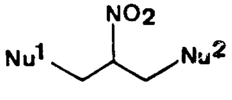

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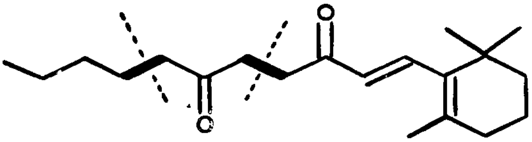
Since the most reactive nucleophiles, such as alkyllithiums, do *not* normally add well to nitroolefins with a terminal double bond3), we were surprised to find in the course of our investigations aimed at determining the scope and the limitations of the new reagent, that NPP nitroallylates *prim.*, *sec.*, and *tert.* alkyl, as well as vinylic, acetylenic, and aromatic lithium and magnesium derivatives. The results are shown in the accompanying table; note that the reaction conditions and the work-up2) are sufficiently mild to prevent multiple bond shifts. To the products of type 2 thus obtained the less reactive nucleophiles can be added, as demonstrated by the synthesis of the 1,4-diketone 5, of the bis(indolyl)-nitropropane 6, and of the γ-lactam 7. The portions of the compounds 5-7 derived from NPP are emphasized in the *formulae*. [The applicability of NPP is increased by its use as a dienophile in *Diels-Alder* reactions, for instance with cyclopentadiene (93%) and butadiene (87%)].



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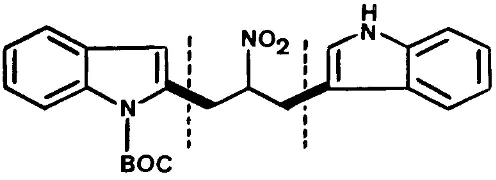
[from 2, Nu^1=C_4H_9, (see table) and β-ionone (75%), with subsequent *Nef*-reaction$^{8)}$ (78%); ^{1}H-NMR(CCl_4): 2 olef. H, δ=6,02 and 7,20 ppm; J_{AB}=16,5 Hz]



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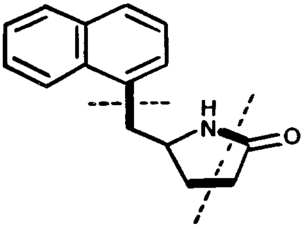
[m.p. 157^{0}C, from 2, Nu^1=1-Boc-2-indolyl (see table) and indole$^{2)}$ (65%)]



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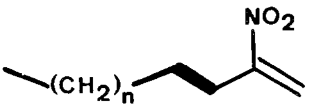
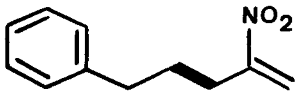
[m.p. 119^{0}C, from 2, Nu^1=1-naphthyl (see table) and ethyl acetate Li-enolate (66%) with subsequent *Raney*-Ni reduction$^{9)}$(82%)

From our experiences with NPP, we conclude that the pivaloyloxy group has a profound effect on the reactivity of the 2-nitropropene moiety: It enhances the acceptor properties of the double bond (by an S_N2'component?), and at the same time it renders the reaction of the nitroolefin with highly reactive nucleophiles more selective in that undesired processes competing with the *Michael*-addition are suppressed. A possible mechanism was proposed earlier$^{2)}$, investigations to elucidate it are underway; a one electron transfer radical mechanism is not likely, since cis-1-heptenyllithium reacts with retention of configuration$^{10)}$ (see table).

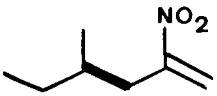
Table: Products of type 2 obtained by addition$^{2)}$ of THF-solutions of lithium or magnesium derivatives to the nitroallylating reagent 1 at temperatures between -70 and -110°C. The yields given are those of flash chromatographically purified materials; recrystallization or Kugelrohr destillation furnished analytically pure samples, all spectroscopic data of which were compatible with the structures shown. The melting points of solid products and the ^{1}H-NMR shifts (δ[ppm]) and coupling constants (multiplicities, J[Hz]) of the β-NO_2-allylic CH_2-groups of liquid products are listed below the *formulae*, together with the precursors employed. - Newly formed bonds are indicated by heavy lines.



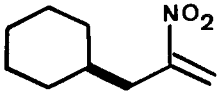
n=2 [δ=2,58, t, J=6;
77% from buLi, 54% from C_4H_9MgCl]
n=6 [δ=2,67, t, J=6,5;
56% from chlorooctane$^{4)}$]



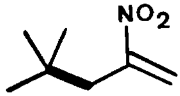
[δ=2,60, q, J=7,5; 68% from
1-chloro-2-phenyl-ethane$^{4)}$]



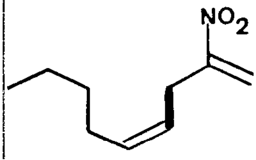
[δ=2,5, qxd, J_{AB}=14,5,
J_{AX}=J_{BX}=6; 56% from *sec.*-buLi]



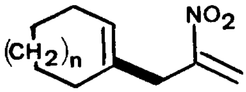
[δ=2,47, d, J=6; 63% from
chlorohexane$^{4)}$]



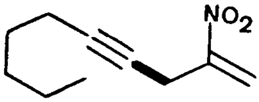
[δ=2,64, s; 21% from
tert.-buLi]



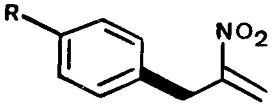
[δ=3,31, d, J=8;
71% from cis-1-iodo-
-1-hexene$^{5)}$]



n=0 [δ=3,21, s; 51% from bromo-
-cyclohexene$^{6)}$]
n=2 [δ=3,52, s, 51% from bromo-
-cyclooctene$^{6)}$]

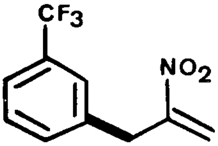


[δ=3,52, m; 53% from
1-heptyne]

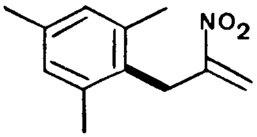


R = H [δ=3,85, s; 77% from bromobenzene$^{6)}$]
R = OCH_3 [δ=3,82, s; 71% from
p-bromo-methoxy-benzene$^{6)}$]
R = F [δ=3,90, s; 74% from
p-bromo-fluoro-benzene$^{6)}$]

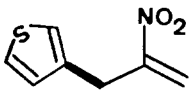
Table continued



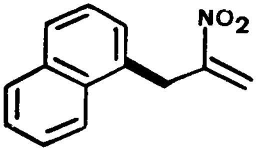
[δ=3,98, s; 78% from m-bromo-trifluoromethyl-benzene[6]]



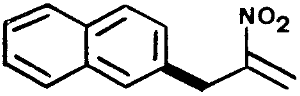
[δ=3,85, s; 78% from bromo-mesitylene[6]]



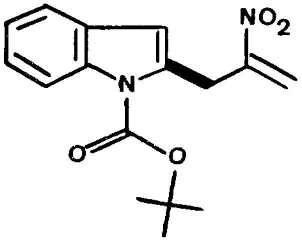
[δ=3,88, s; 69% from 3-bromo-thiophene[6]]



[m.p. 63°C; 88% from 1-bromo-naphthalene[6]]



[m.p. 35°C; 73% from 2-bromo-naphthalene[6]]



[m.p. 59°C; 73% from N-Boc protected indol[7]]

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