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ALKYLATION OF ALKYL NITROACETATES UNDER PTC CONDITIONS[1]

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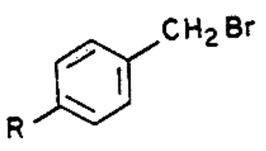
Abstract : Alkyl nitroacetates were alkylated to give C-alkylated products in good yields under PTC conditions.

Alkyl nitroacetates constitute a class of attractive synthones for a variety of organic molecules[2]. The factors influencing their alkylation/acylation reactions have not yet been studied. In the recent past, there have been some attempts towards the alkylation of alkyl nitroacetates by classical methods[3-8], which led to C-alkylated nitroacetates in low yields (9-25%). PTC and related techniques allow much experimental simplification and improved yields in a variety of alkylation reactions[9] as compared to classical methods. In the present communication, we particularly describe the alkylation of alkyl nitroacetates under PTC conditions.

We have found that alkylation of methyl nitroacetate 2 by benzyl bromide 1A using TEBA as a catalyst and powdered sodium hydroxide as a base in polar and non-polar aprotic solvents resulted in a complex reaction mixture. After the



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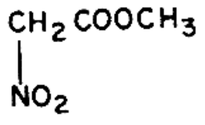

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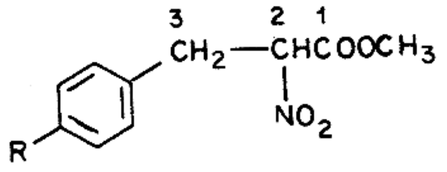

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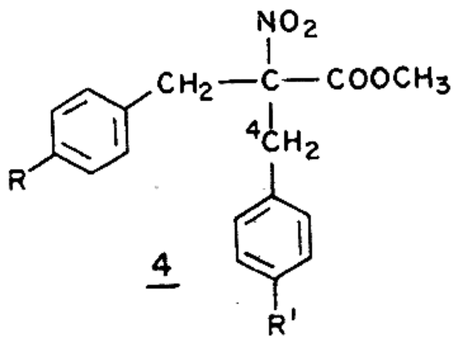

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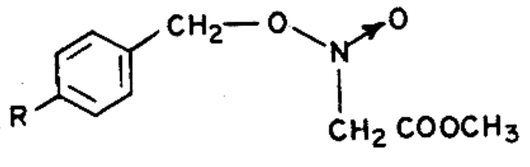

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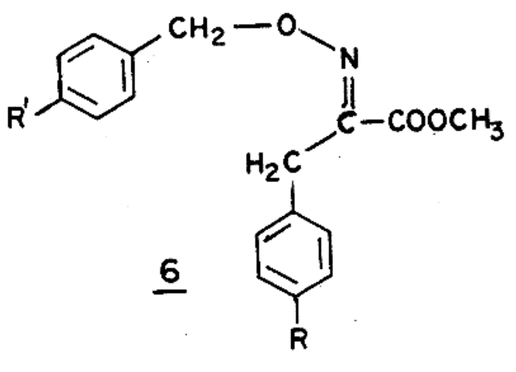

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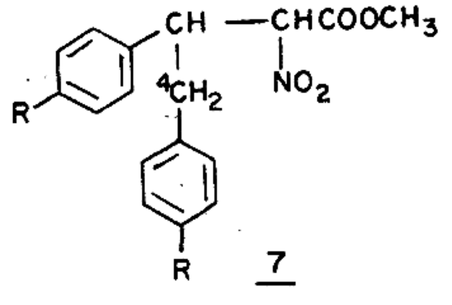

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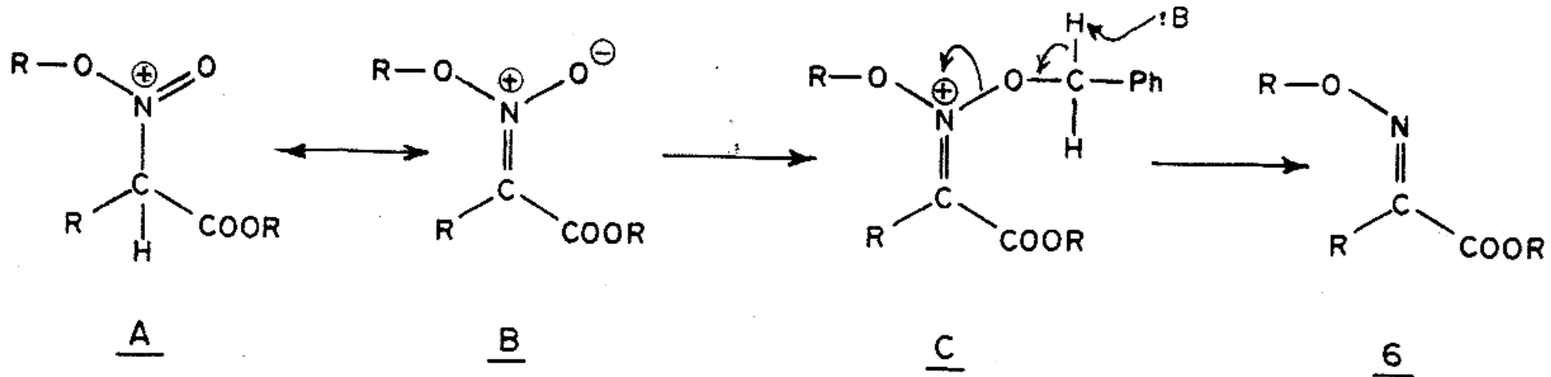
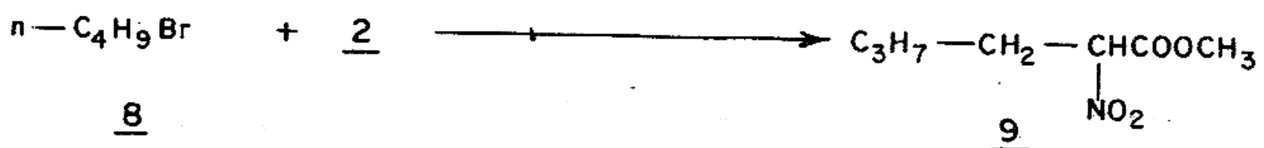
FOR COMPOUNDS ----- 1 & 3 A R=H, B R=Cl, C R=OCH_3, D R=NO_2, E R=R'=NO_2

4 A R=R'=H B R=Cl, R'=H

6 A R=R'=H B R=Cl, R'=H



A B C 6



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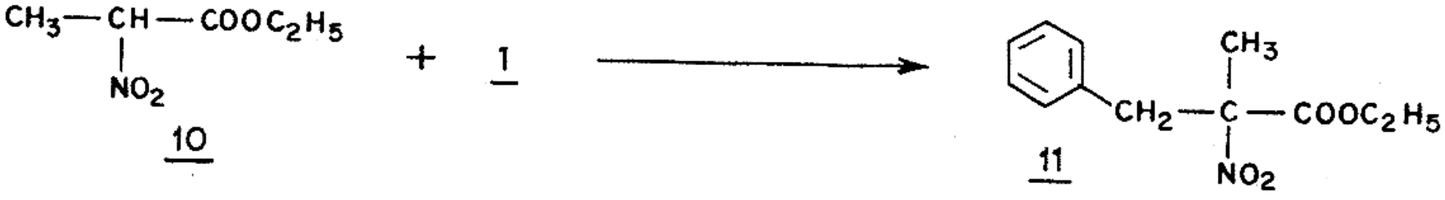

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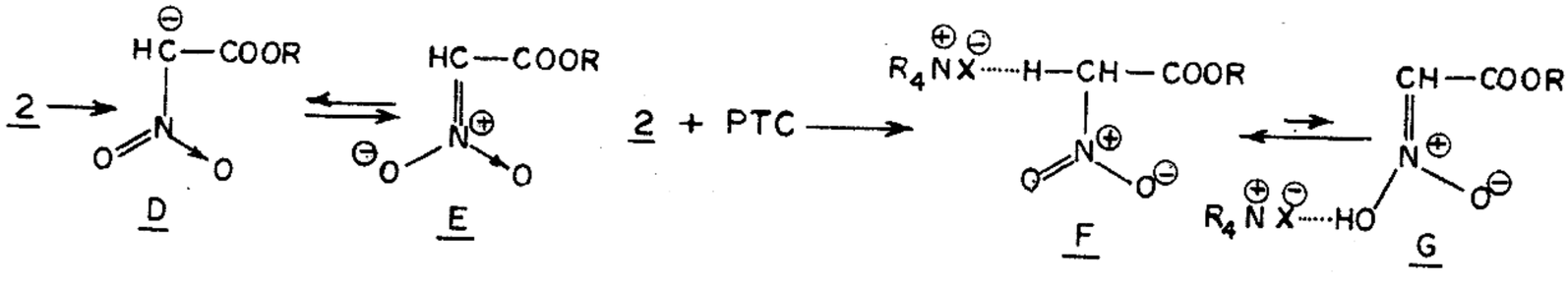

D E F G

use of the combination of various solvents, inorganic bases and PT catalysts[10] we have found that the C-alkylation can be achieved by using TEBA as a PT catalyst, dimethyl formamide as a solvent and potassium bicarbonate as a base. In this reaction, methyl 2-nitro-3-phenyl propanoate 3A (R=H) was the only isolable product by distillation (70% yield). The PMR analysis of the crude reaction mixture, however, indicated the presence of O-alkylated product 5 and C,O-dialkylated product 6A in small quantities (for spectroscopic data see experimental section).

In order to study the effects of substitution in aromatic nucleus of 1 on the product pattern, 4-chloro 1B, 4-methoxy 1C and 4-nitro 1D benzyl halides were reacted with 2 under similar conditions. Chloro and methoxy compounds 1B and 1C furnished the anticipated methyl 2-nitro-3-phenyl propanoates 3B and 3C in good yields (70% and 75% respectively). However, 1D gave only dialkylated products i.e. methyl 2-nitro-2-(4-nitro)-benzyl-3-(4-nitro)-phenylpropanoate 4C and methyl 2-nitro-3, 4-bis-(4-nitro)phenylbutanoate 7. It appears that compound 3D which itself was not found in the reaction mixture is the precursor for both 4C and 7. This is logical since carbanions at C_2 and C_3 in compound 3D are more stabilised due to $-NO_2$ group as compared to 3A.. Intermediacy of 3 was confirmed by converting 3A to C,C-dialkylated 4A under drastic conditions. Similarly 3B when reacted with 1A furnished 4B and C,O-dialkylated compound 6B which was similar to 6A obtained from

3A earlier. Structures 6A and 6B were evident from the absence of NO_2 peaks and presence of C=N peak in IR. This was ably supported by mass and PMR spectra. These compounds are probably formed by the elimination of PhCHO from C,O,O-trialkylated species such as C (see chart). In order to establish the generality of the reaction simple alkyl halides such as n-butyl bromide 8 was treated with 2 to give methyl 2-nitropentanoate 9 (yield 72%). Substituted ethyl nitroacetate 10 yielded ethyl 2-nitro-2-methyl-3-phenylpropanoate 11 also in good yields (78%).

The extent of C-versus O-alkylation in the alkyl nitroacetate depends on the position of equilibrium between the two anionic species, (D & E), generated from it and their relative nucleophilicities towards the substrate. To explain the exclusive/preferential C-alkylation reactions, it is reasonable to assume that the reactive methylene and the halide ion from PTC from a hydrogen bonded complex F in which the polarisation towards the carbanion occurs without the generation of full negative charge Implication of this type of intermediate has been reported in the literature [11]. This phenomenon also curbs the equilibration with species (G), encouraging thereby exclusive/preferential C-alkylation product.

It is perhaps, for the first time that the utility of PTC-technique for the preferential exclusive C-alkylation of alkyl nitroacetates has been demonstrated.

EXPERIMENTAL

Methyl nitroacetate 2 was prepared according to the

procedure mentioned in the literature[12]. Compounds 1B, 1C and 1D were obtained from corresponding toluens. Purity of all the compounds was checked by TLC and PMR. Satisfactory elemental analysis was obtained for all new compounds.

Typical procedure for the alkylation of methyl nitroacetate 2

Benzyl bromide (1A, 1.8g) was added to a stirring solution of methyl nitroacetate (2, 1.21g) in dimethyl formamide (10 ml) containing benzyl triethylammonium chloride (TEBA, 0.009g) and anhydrous $KHCO_3$ (0.5g) at room temperature. The reaction mixture was stirred at 60°C for 16 hrs. DMF was removed under vacuum and the mixture was diluted with water and extracted with ether. Drying and evaporation of the solvent furnished on oil which on vacuum distillation (110°-115°C/3mm) yielded pure (TLC) (3A, 1.49g).

In case of 3B and 3C purification was achieved by SiO_2 chromatography using EtoAc : PhH. (1:9) as eluents.

Conversion of 3A to 4A.

Same procedure as described for 1A to 3A is followed except that the base used was K_2CO_3 instead of $KHCO_3$.

From 1.05g 3A 1.21g 4A was obtained. Yield 80%.

Spectroscopic data of the compounds: All chemical shifts are in units from TMS. 3A, H-NMR($CDCl_3$) 5.28 (1H, t, J=8 Hz, C_3-H), 3.7 (3H, s, COOMe); IR (Neat) 1750 (C=O). 1560, 1360(NO_2) cm^{-1}; Mass (m/e) 209 (M^+), 91 ($Ph\text{-}CH_2^+$) base peak).

3B; H-NMR ($CDCl_3$) 5.25 (1H, t, J=8 Hz, C_2-H), 3.4 (2H, d, J=8 Hz, C_3-H), 3.8 (3H, s, COOMe); IR(Neat) 1760 (C=O), 1570, 1370 (NO_2) cm^{-1} ; Mass (m/e) 243 (M^+), 125 (Cl-

$C_6H_4\text{-}CH_2^+$, base peak), 196 ($M\text{-}HNO_2$).

3C; H-NMR ($CDCl_3$) 5.25 (1H, t, J=8 Hz, C_2-H), 3.33 (2H, d, J=8 Hz, C_3-H), 3.76 (3H, s, COOMe), 3.8 (3H, s, Ar-OMe); IR (neat) 1750 (C=O), 1560, 1360 (NO_2) cm^{-1}; Mass (m/e) 239 (M^+), 121 ($Meo\text{-}C_6H_4\text{-}CH_2^+$, base peak), 107 ($MeO\text{-}C_6H_4^+$).

4A; H-NMR ($CDCl_3$) 3.44 (4H, s, C_3 and C_4-H), 3.62 (3H, s, COOMe); IR (Neat) 1760 (C=O), 1550, 1370(NO_2) cm^{-1}; Mass (m/e) 299 (M^+), 91 ($C_6H_5\text{-}CH_2^+$, base peak).

4B; H-NMR ($CDCl_3$) 3.48 (2H, s, C_3-H), 3.68 (3H, s, COOMe), 3.42(2H,s,C_4-H); IR(Neat) 1750 (C=O),1550, 1360(NO_2)cm^{-1}; Mass (m/e) 333(M^+), 91($C_6H_5\text{-}CH_2^+$, base peak), 125($Cl\text{-}C_6H_4\text{-}CH_2^+$)

4C; H-NMR($CDCl_3$) 3.8 (4H,s,C_3 and C_4-H), 4.05(3H,s,COOMe); IR(Nujol) 1735(C=O), 1520, 1360 (NO_2)cm^{-1}

5; H-NMR($CDCl_3$), 4.00 (2H, s, C_2-H), 3.8 (3H, s, COOMe), 4.5(2H, s, OCH_2).

6A; H-NMR ($CDCl_3$) 3.93 (2H, s, C_3-H), 3.81 (3H, s, COOMe), 5.25 (2H, s, O-CH_2); IR (neat), 1730 (C=O), 1600 (C=N) cm^1 ; Mass (m/e) 283 (M^+), 91 ($C_6H_5CH_2^+$, base peak), 224 (M-COOMe).

6B; H-NMR($CDCl_3$), 3.88 (2H, s, C_3H), 3.81 (3H, s, COOMe), 5.31(2H, s, O-CH_2); IR (neat) 1730 (C=O), 1600 (C=N) cm^{-1}; Mass (m/e) 317 (M^+), 91 ($C_6H_5\text{-}CH_2^+$, base peak), 125 ($Cl\text{-}C_6H_4\text{-}CH_2^+$).

7; H-NMR($CDCl_3$), 5.37 (1H, d, J=10 Hz, C_2-H), 5.44 (1H, m, C_3-H) shown by decoupling, 3.87 (3H, s, COOMe), 3.66 (2H, d, J=10 Hz, C_4-H); IR(neat) 1760 (C=O), 1530, 1350 (NO_2) cm^{-1}.

9; H-NMR ($CDCl_3$) 5.1 (1H, q, C_2-H), 2.2 (2H, m, C_3-H), 3.8 (3H, s, COOMe), 0.8 to 1.6 (7H, m, aliphatic); IR(neat) 1770 (C=O), 1570, 1380 (NO_2) cm^{-1}; Mass (m/e) 175 (M^+). 11; H-NMR ($CDCl_3$) 1.68 (3H, s, C_2-Me), 3.5 (2H, q, C_3-H), 1.26 (3H, t, J=6 Hz) and 4.28 (2H, q, J=6 Hz) for COOEt; Mass (m/e) 237 (M^+), 91 (C_6H_5-CH_2^+, base peak).

REFERENCES AND FOOTNOTES

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10 Solvents used -THF, CH_2Cl_2, PhH and DMF. Bases used- anhydrous K_2CO_3, NaOH, $Ca(OH)_2$, Na_2CO_3, Na-k-tartarate, dipotassium tartarate and $KHCO_3$. Catalysts used- TEBA, NBu_4Cl N-n-Pr_4Cl.

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