Reaction of methyl diazoacetate with aldehydes, amines, thiols, alcohols and acids over transition metal-exchanged clays

Prodeep Phukan, Jakkam Madan Mohan and Arumugam Sudalai *

Process Development Division, National Chemical Laboratory, Pune 411 008, India.
E-mail: sudalai@dalton.ncl.res.in

Received (in Cambridge, UK) 23rd June 1993, Accepted 23rd September 1999

Metal-exchanged clays (M = Rh and Cu) catalyze effectively the reaction of methyl diazoacetate with various aldehydes, affording the corresponding β-keto esters in high yields. They have also been effective in the decomposition of methyl diazoacetate to form metallocarbenes which, in turn, successfully insert into X–H (X = N, O, S, CO_2) bonds of a variety of amines, aldehydes, thiols and acids, thereby producing the corresponding esters.

In recent years, use of aluminosilicates, particularly clays, has gained importance for catalysis of various useful organic transformations. These clays are predominantly composed of hydrous phyllosilicates, referred to as clay minerals.[1] They often exhibit high surface acidity and this property has been harnessed to realize useful organic transformations. Many clay mineral crystals carry an excess negative electric charge owing to internal substitution by lower-valent cations and thereby increase internal reactivity in chemical combination and ion exchange. The cation-exchanged clays are found to catalyze various organic transformations and many reports are found in the recent literature.

Carbene-insertion reactions are of current interest as these methods allow us an easy process of C–C and C–X (X = N, O, S) bond formation. Insertion of carbenes into aliphatic C–H and polar X–H bonds have been used increasingly for the synthesis of carbo- and heterocycles.[2] From this point of view, β-keto esters serve as potential synthetic intermediates. Due to the presence of both electrophilic and nucleophilic sites, β-keto esters make their place unique in organic synthesis.[3] We report herein the insertion of the carbene generated from methyl diazoacetate to X–H bonds (X = C, N, S, O) of various compounds such as aldehydes, amines, thiols, acids and alcohols catalyzed by metal-exchanged clays.

Results and discussion

a. Synthesis of β-keto esters

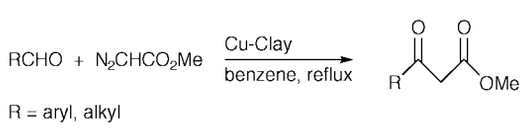
Synthetic routes to β-keto esters essentially involve acylation of acetate anions, carboxylic acid derivatives and malonate anions mostly with acyl halides.[3] However, these methods need low temperatures and use of strong bases such as lithium amides. The direct condensation of methyl diazoacetate with aldehydes has the potential to generate a practical methodology for the synthesis of β-keto esters; nevertheless, studies on such a reaction have been limited.

The earliest example concerns BF_3·diethyl ether-catalyzed transformation of sugar aldehydes to the corresponding β-keto esters, albeit in rather low yields.[4] Holmquist and Roskamp[5] have investigated the $SnCl_2$-catalyzed reaction of aldehydes with ethyl diazoacetate to develop a method for β-keto esters. However, this method was suitable only for aliphatic aldehydes; aromatic aldehydes led to poor yields of the corresponding β-keto esters. Dhavale *et al.*[6] reported activated alumina-promoted reaction of aldehydes with ethyl diazoacetate leading to β-keto esters. The requirement of activated alumina in large quantities constitutes a limitation in the preparation of β-keto esters on a large scale by this method. Synthesis of β-keto esters by reaction of acetyl chloride with ethyl hydrogen malonate is also reported.[7] Balaji *et al.*[8] recently reported a synthetic method to obtain β-keto esters from aldehydes using H-β-zeolite as a catalyst. Aromatic aldehydes were observed to be less reactive than aliphatic ones, while alkyl and aryl ketones were totally unreactive. We have systematically studied the reaction between aldehydes and methyl diazoacetate over various transition metal exchanged clays as catalysts to afford β-keto esters (Scheme 1).

Table 1 The reaction of benzaldehyde with methyl diazoacetate over various clay catalysts[a]

Entry	Catalyst	*t*/h	Yield[b]
1	No catalyst	15	0
2	Mont K10	15	0
3	Cu^{II}-Mont K10	5	80
4	Rh^{III}-Mont K10	5	78
5	Mn^{III}-Mont K10	12	20
6	Rh-SiO_2	2	55
7	Rh-Al_2O_3	5	52
8	Rh/C	15	0

[a] Reaction conditions: benzaldehyde (5 mmol), methyl diazoacetate (5.5 mmol), catalyst (10 wt%), benzene (10 mL), 80 °C. [b] Isolated yield after chromatographic purification.



Scheme 1

Initially, a systematic study was undertaken with various metal-exchanged clay catalysts and it was found that both Cu^{II} and Rh^{III} Mont K10 clays showed excellent activity for the condensation of methyl diazoacetate with benzaldehyde (Table 1).

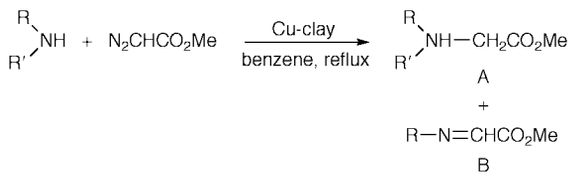
The reaction failed in the case of Mont K10 clay alone as well as with Rh/C as catalyst. We have further subjected various aldehydes for reaction with methyl diazoacetate under the influence of the best catalyst Cu^{II}-Mont K10 clay (Table 2). Both aromatic and aliphatic aldehydes underwent condensation to yield the β-keto esters in good yields. An interesting feature from the β-keto ester products from aromatic aldehydes is that the products comprised both keto and enol components, as indicated by the splitting of a ^{1}H NMR signal at around δ 4.

Table 2 Synthesis of β-keto esters using Cu-Mont K10 as catalyst[a]

Entry	Substrate	Product	*t*/h	Yield (%)[b]
1	Benzaldehyde	Methyl 3-oxo-3-phenylpropionate	5	80
2	4-Methoxybenzaldehyde	Methyl 3-(4-methoxyphenyl)-3-oxopropionate	5	69
3	3,4-Dimethoxybenzaldehyde	Methyl 3-(3,4-dimethoxyphenyl)-3-oxopropionate	5	72
4	4-Chlorobenzaldehyde	Methyl 3-(4-chlorophenyl)-3-oxopropionate	2	70
5	Decanal	Methyl 3-oxododecanoate	2	90
6	Isobutyraldehyde	Methyl 4-methyl-3-oxopentanoate	3	62

[a] Reaction conditions: aldehyde (5 mmol), methyl diazoacetate (5.5 mmol), Cu-Clay (10 wt%), benzene (10 mL), 80 °C. [b] Isolated yield after chromatographic purification.

Table 3 Cu-Mont K10-catalyzed insertion of methyl diazoacetate into an NH bond[a]



				Yield[b] (%)	
Entry	R	R′	*t*/h	A	B
1	Ph	H	3	82	
2	2-Methylphenyl	H	3	50	
3	1-Naphthyl	H	3	93	
4	Cyclohexyl	H	4	82	
5	Ph	Me	3	61	
6	Ph	Et	3	47	20
7	Ph	*n*-Bu	3	68	

[a] Reaction conditions: substrate (5 mmol), methyl diazoacetate (7 mmol), Cu-Clay (10 wt%), benzene (10 mL), 80 °C, 3 h. [b] Isolated yield after chromatographic purification.

Another significant feature of the work is the enhancement in the rate of the reaction observed for Cu-Mont K10 as catalyst, as compared with the earlier work where longer reaction times are generally required for the reaction to achieve good yields.[8] The catalyst, recovered by filtration, was successfully reused in the case of benzaldehyde without affecting the reactivity of the process. In order to check for leaching of ruthenium from the catalyst the filtrate was analyzed for metal content by atomic absorption spectroscopy and no metal leaching was observed.

b. Synthesis of α-amino esters

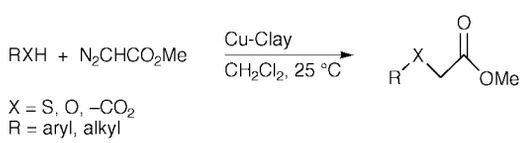
With the advent of rhodium(II) acetate as a superior catalyst, intramolecular metal carbenoid insertions into unactivated C–H bonds have emerged as an effective strategy for C–C bond formation. On the other hand, the study of metal-carbenoid insertions into X–H (X = heteroatom) bonds has been relatively limited; nonetheless, such reactions have led to methods for pharmaceutically important compounds. The Rh-catalyzed carbene-insertion reaction is used as a powerful methodology for the synthesis of various antibiotics such as aza-β-lactams,[9] Thienamycin,[10] 1-oxacephem,[11] *etc*. Thus there is great importance in the development of a new methodology for NH-insertion reactions. We found that Cu-clay is an excellent heterogeneous catalyst for this transformation (Table 3).

Both aromatic and aliphatic amines underwent the insertion reaction, affording good yields of the product. The reaction of secondary amines has an interesting feature. The reaction of *N*-methylaniline under the conditions described above furnished N–H-inserted product in 61% yield. However, reaction of *N*-ethylaniline with methyl diazoacetate furnished a mixture of products, comprising 47% of the *N*-alkylated product **A** and 20% of the imine **B**. The yield of the imine increases with increasing chain length of the alkyl substituent on the nitrogen atom. For example, use of *N*-butylaniline resulted in 34% of the imine as a side-product. The formation of the imines could be rationalized as arising from elimination of the *n*-alkyl side-chain leading to a doubly conjugated system.

c. Synthesis of α-thiol, α-acetoxy and α-oxa esters

Aryl or alkyl thioesters are important compounds for the synthesis of biologically active compounds such as $\Delta^{\alpha,\beta}$-butenolides,[12] α-methylene lactones and cyclic ketones *via* alkylative elimination.[12] Further, polyunsaturated compounds having β-oxa, γ-oxa, β-thia and γ-thia substituents have been found to possess antimalarial and neutrophil-stimulatory activity.[13]

Reaction of thiols and alcohols with diazoacetate has already been studied by using copper compounds such as cupric [copper(II)] chloride,[14] rhodium compounds such as $RhCl_3 \cdot 3H_2O$, $RhCl(PPh_3)_3$,[15] $Rh_2(OAc)_4$[13–20] and ruthenium complexes.[21] It has recently been reported that $Cu(acac)_2$ catalyzes insertion reactions of diazoketones with various acids.[22] We report here the study of Cu- and Rh-exchanged montmorillonite clay as heterogeneous catalysts to achieve insertion reactions of carbenes into X–H (X = S, O, CO_2) bonds (Scheme 2).



Scheme 2

Table 4 shows the results of reaction of various thiols, acids and alcohols with methyl diazoacetate in the presence of Cu- and Rh-clay as catalysts. It can be seen from Table 4 that thiols and acids react at a faster rate than dialcohols. While Cu-clay catalyzes efficiently the insertion of methyl diazoacetate into thiols and acids at 25 °C, insertion into OH of alcohols with Cu-clay as catalyst did not proceed at all at 25 °C. However, Rh-clay has been found to be a good catalyst for O–H insertions of alcohols at 60 °C.

The catalytic pathway for these insertion reactions with methyl diazoacetate can be explained by initial formation of metal-carbenoid species. The carbene first coordinated to the heteroatom to produce an intermediate ylide, which further rearranged to give the inserted product.

Conclusions

Metal-exchanged clays efficiently catalyze the insertion reaction of methyl diazoacetate into the X–H bond of amines, thiols, acids and alcohols. Reactivity of insertion into N–H of amines, S–H of thiols, and O–H of acids is much higher than that of O–H insertion of alcohols. A Cu-Clay catalyst can efficiently promote the insertion reaction in the case of thiols and acids but is not effective for O–H insertion. On the other hand,

Table 4 Reaction of methyl diazoacetate with acids, thiols and alcohols in the presence of M-exchanged clay catalysts

Entry	Substrate	Solvent	Catalyst	Temp. (T/°C)	t/h	Yield (%)[a]
1	Thiophenol	Benzene	Cu-Clay	80	5	84
2	Thiophenol	Dichloromethane	Cu-Clay	25	8	82
3	Butanethiol	Dichloromethane	Cu-Clay	25	10	73
4	Ethyl 2-mercaptoacetate	Dichloromethane	Cu-Clay	25	8	75
5	Crotonic acid	Dichloromethane	Cu-Clay	25	5	95
6	Cinnamic acid	Dichloromethane	Cu-Clay	25	5	96
7	2-Phenylbutyric acid	Dichloromethane	Cu-Clay	25	5	91
8	Ethanol	Dichloromethane	Cu-Clay	25	12	NR
9	Ethanol	Benzene	Cu-Clay	80	12	18
10	Ethanol		Rh-Clay	60	12	63
11	Butan-1-ol		Rh-Clay	60	12	62
12	Benzyl alcohol		Rh-Clay	60	12	67

[a] Isolated yield after chromatographic purification. NR = not recorded.

Rh-Clay is found to be effective for O–H insertion at 60 °C in the presence of excess of alcohol without any solvent.

Experimental

All solvents are distilled before use. 'Petroleum ether' refers to the fraction with boiling range 60–80 °C. Compounds are purified by flash chromatography over silica gel. IR spectra were recorded on a Perkin-Elmer 137 E spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 200 MHz instrument using TMS as an internal standard. Mass spectra (MS) were recorded on an automated Finnigan MAT 1020C mass spectrometer using an ionization energy of 70 eV. Microanalyses were done on a Carlo EA1108 elemental analyzer.

Preparation of metal-exchanged clays

The metal-exchanged clays were prepared by stirring clay with dilute solutions of $CuCl_2$, $RhCl_3$ and $Mn(NO_3)_2$, respectively. For example, a mixture containing $CuCl_2$ (0.3 g) and montmorillonite clay (25 g) in distilled water (600 mL) was stirred vigorously at room temperature for 24 h. It was centrifuged and the clay was washed repeatedly with distilled water until the discarded filtrate was free from Cl^- ions. Finally, the clay was dried at 110 °C for 12 h. The metal content of the clays was determined by an electron-disperse X-ray microscope (EDX) connected to a JEOL, scanning electron microscope. Surface area was determined by the Brunaver–Emmette–Teller (BET) method. The X-ray diffraction (XRD) and FT IR spectra of these samples show that they are crystalline; however, no significant differences were observed between their structures.

The metal content and the surface area of the clays are given in Table 5.

Reaction of methyl diazoacetate with aldehydes

General procedure. Into a solution of the aldehyde in dry benzene were introduced 1.1 equivalents of methyl diazoacetate and Cu-clay catalyst (10% w/w). The mixture was refluxed until the disappearance of the aldehyde as monitored by TLC and until the cessation of nitrogen evolution (3–4 h). When the reaction mixture had cooled to room temperature the catalyst was filtered off, and washed twice with benzene. The combined benzene extract was distilled and the residue was passed through a column of silica gel eluting with 2% ethyl acetate in petroleum ether. The yields of the products are given in Table 2.

Methyl 3-oxo-3-phenylpropionate. IR ($CHCl_3$; cm^{-1}) 1720, 1690, 1445; ^{1}H NMR (200 MHz; $CDCl_3$) δ 3.80 (s, 3H), 3.90, 4.00 and 5.90 (3, 2H), 7.30–7.50 (m, 5H); ^{13}C NMR (50 MHz; $CDCl_3$) δ 192.25, 168.01, 133.90, 133.30, 129.00, 125.70, 86.90 (enolic), 61.01, 52.14.

Methyl 3-(4-methoxyphenyl)-3-oxopropionate. IR ($CHCl_3$, cm^{-1}) 3300, 1730, 1695, 1590, 1450; ^{1}H NMR (200 MHz; $CDCl_3$) δ 3.8 (s, 3H), 3.95 (s, 3H), 4.0 and 4.05 (2s, 2H), 6.90–7.3 (m, 4H); ^{13}C NMR (50 MHz; $CDCl_3$) δ 191.87, 167.65, 163.90, 132.11, 130.98, 130.55, 114.24, 113.79, 61.13, 55.48, 52.17.

Methyl 3-(3,4-dimethoxyphenyl)-3-oxopropionate. IR ($CHCl_3$; cm^{-1}) 3320, 1730, 1695, 1600, 1510, 1260; ^{1}H NMR (200 MHz; $CDCl_3$) δ 3.75 (s, 3H), 3.85 (s, 3H), 3.90 and 3.95 (2s, 2H), 6.70–6.90 (m, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ 191.63, 167.67, 153.87, 149.21, 129.29, 126.74, 123.53, 110.49, 61.43, 56.18, 55.98, 52.20.

Methyl 3-(4-chlorophenyl)-3-oxopropionate. IR ($CHCl_3$; cm^{-1}) 1740, 1710, 1590, 810; ^{1}H NMR (200 MHz; $CDCl_3$) δ 3.90 (s, 3H), 3.80, 4.10 and 5.80 (3s, 2H), 6.80 (d, J 8.2 Hz, 2H), 7.20 (d, J 8.2 Hz, 2H).

Methyl 3-oxododecanoate. IR ($CHCl_3$; cm^{-1}) 1725, 1695, 1450; ^{1}H NMR (200 MHz; $CDCl_3$) δ 0.85–1.00 (m, 10H), 1.10–1.30 (m, 9H), 3.50 (s, 2H), 3.70 (s, 3H).

Methyl 4-methyl-3-oxopentanoate. IR ($CHCl_3$; cm^{-1}) 1735, 1700, 1470; ^{1}H NMR (200 MHz; $CDCl_3$) δ 0.95 (d, J 7.7 Hz, 6H), 2.0 (m, 1H), 3.70 (s, 2H) 3.90 (s, 3H).

Table 5 Metal content and surface areas of various clays

Entry	Catalyst	Surface area/m^2 g^{-1}	Metal content (wt%)
1	Cu^{II}-Mont K10	238.9	0.39
2	Rh^{III}-Mont K10	238.0	0.39
3	Mn^{III}-Mont K10	255.0	0.45

Reaction of methyl diazoacetate with amines

General procedure. A solution of aniline in dry benzene was treated with 1.2 molar equivalents of methyl diazoacetate, and the catalyst Cu-clay (10% by weight of the substrate) was introduced. The mixture was refluxed and the progress of the reaction was monitored by TLC. When the starting material almost disappeared (3–4 h), the reaction mixture was cooled to room temperature and the catalyst was filtered off. Evaporation of the solvent and passage of the residue through a column of SiO_2 yielded the product in a pure form. Yields of products are given in Table 3.

Methyl N-phenylglycinate. IR (neat; cm^{-1}) 3350, 1710, 1600, 1500, 1420, 1200, 1000, 750, 680, 500; ^{1}H NMR (200 MHz; $CDCl_3$) δ 3.80 (s, 3H), 3.95 (s, 2H), 4.25 (br s, 1H), 6.60 (d, J 8.3 Hz, 2H), 6.80 (t, J 8.3 Hz, 1H), 7.20 (t, J 7.3 Hz, 2H); MS (m/z, % rel. intensity) 165 (M^+, 20), 106 (100), 93 (10), 77 (30), 65 (10), 59 (10), 51 (20).

Methyl N-(2-methylphenyl)glycinate. Bp 152 °C/15 mmHg (bath temp.); IR (neat; cm^{-1}) 3050, 2900, 1740, 1600, 1500, 1430, 1200; ^{1}H NMR (200 MHz; $CDCl_3$) δ 2.25 (s, 3H), 3.85 (s, 3H), 4.0 (s, 2H), 4.20 (br s, 1H), 6.55 (d, J 7.2 Hz, 1H), 6.75 (t, J 8.1 Hz, 1H), 7.15 (t, J 8.1 Hz, 2H); MS (m/z, % rel. intensity)

179 (M^+, 20), 120 (100), 106 (40), 91 (35), 86 (20), 84 (30), 77 (20), 65 (20), 59 (35), 51 (15) (Found: C, 67.24; H, 7.28; N, 7.76. Calc. for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82%).

Methyl N-(1-naphthyl)glycinate. Mp 72–74 °C; IR (neat; cm^{-1}) 3100, 2920, 1720, 1240; ^1H NMR (200 MHz; $CDCl_3$) δ 3.80 (s, 3H), 4.0 (s, 2H), 6.40 (br s, 1H), 7.23 (br s, 3H), 7.45 (m, 2H), 7.80 (m, 2H) (Found: C, 72.49; H, 6.06; N, 6.56. Calc. for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51%).

Methyl N-hexylglycinate. Bp 75 °C/15 mmHg (bath temp.); IR (neat; cm^{-1}) 3000, 2850, 1730, 1440; ^1H NMR (200 MHz; $CDCl_3$) δ 0.90–1.35 (m, 5H), 1.50–1.80 (m, 6H), 2.40 (m, 1H), 3.40 (s, 2H), 3.65 (s, 3H); MS (*m*/*z*, % rel. intensity) 171 (M^+, 10), 128 (70), 112 (100), 83 (15), 68 (65), 56 (75).

Methyl N-methyl-N-phenylglycinate. Bp 152 °C/7 mmHg (bath temp.); IR (neat; cm^{-1}) 1720, 1590, 1250; ^1H NMR (200 MHz; $CDCl_3$) 3.0 (s, 3H), 3.65 (s, 3H), 4.0 (s, 2H), 6.6 (m, 3H), 6.9 (m, 2H); MS (*m*/*z*, % rel. intensity) 179 (M^+, 30), 128 (40), 120 (100), 106 (40), 91 (20), 77 (40), 64 (10) (Found: C, 66.99; H, 7.40; N, 7.79. Calc. for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82%).

Methyl N-ethyl-N-phenylglycinate. IR ($CHCl_3$; cm^{-1}) 1710, 1600, 1250; ^1H NMR (200 MHz; $CDCl_3$) δ 1.20 (t, *J* 8.0 Hz, 3H), 3.37 (q, *J* 4.1 Hz, 2H), 3.60 (s, 3H), 4.00 (s, 2H), 6.52 (m, 3H), 7.0 (m, 2H); MS (*m*/*z*, % rel. intensity) 193 (M^+, 25), 178 (5), 163 (10), 134 (100), 120 (5), 105 (30), 91 (5), 77 (10) (Found: C, 67.47; H, 7.80; N, 7.29. Calc. for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25%).

Methyl (phenylimino)acetate. IR ($CHCl_3$; cm^{-1}) 2875, 1615, 1560, 1480, 1210; ^1H NMR (200 MHz; $CDCl_3$) δ 3.85 (s, 3H), 6.7 (m, 3H), 7.1 (m, 2H), 8.15 (s, 1H).

Methyl N-butyl-N-phenylglycinate. Bp 176 °C/3 mmHg (bath temp.); IR (neat; cm^{-1}) 1710, 1600; ^1H NMR (200 MHz; $CDCl_3$) δ 1.00 (t, *J* 7.4 Hz, 3H), 1.40 (q, *J* 4.1 Hz, 2H), 1.65 (m, 2H), 3.40 (t, *J* 6.0 Hz, 2H), 3.60 (s, 3H), 3.85 (s), 3.90 (s) and 4.20 (s) (together 2H), 6.70 (t, *J* 7.1 Hz, 3H), 7.25 (t, *J* 8.1 Hz, 2H); MS (*m*/*z*, % rel. intensity) 221 (M^+, 50), 193 (10), 178 (50), 163 (18), 162 (100), 150 (20), 134 (10), 120 (90), 106 (45), 91 (10), 77 (15) (Found: C, 70.46; H, 8.60; N, 6.40. Calc. for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33%).

General procedure for reaction of methyl diazoacetate with thiols, acids and alcohols

To a mixture of thiophenol (0.5 g, 4.5 mmol) and 25 mg (5 wt%) of Cu-Clay in 5 mL of dichloromethane was added dropwise methyl diazoacetate (0.86 g, 6.8 mmol) at room temperature and the mixture was stirred until the reaction was complete (TLC). The catalyst was filtered off and the dichloromethane was evaporated. The crude product was chromatographed with 'petroleum ether' as eluent to give 0.7 g of methyl 2-(phenylthio)acetate as colorless oil. In the case of alcohols, methyl diazoacetate (0.86 g, 6.8 mmol) and 25 mg of Cu-clay were heated at 60 °C. The reaction mixture was filtered, excess alcohol removed and the crude product was chromatographed with 'petroleum ether' as eluent. Yields of products are given in Table 4.

Methyl 2-(phenylthio)acetate. IR (neat; cm^{-1}) 1720, 1570, 1420, 1260, 1150, 995; ^1H NMR (200 MHz; $CDCl_3$) δ 3.7 (s, 2H), 3.8 (s, 3H), 7.25–7.5 (m, 5H); MS (*m*/*z*, % rel. intensity) 182 (M^+, 67), 151 (2), 123 (100), 109 (49), 77 (31).

Methyl 2-(*n*-butylthio)acetate. IR (neat; cm^{-1}) 3000, 1720, 1425, 1270, 1130, 1005; ^{1} H NMR (200 MHz; $CDCl_3$) δ 0.9 (t, *J* 6.0 Hz, 3H), 1.4 (m, 2H), 1.55 (m, 2H), 2.6 (t, *J* 6.0 Hz, 2H), 3.2 (s, 2H), 3.75 (s, 3H); MS (*m*/*z*, % rel. intensity) 162 (M^+, 21), 132 (6), 103 (30), 89 (59), 74 (91), 61 (64), 55 (100).

Methyl 2-(ethoxycarbonylmethylthio)acetate. IR (neat; cm^{-1}) 1720, 1705, 1635, 1330, 1290, 1120, 1050; ^1H NMR (200 MHz; $CDCl_3$) δ 0.9 (t, *J* 7.0 Hz, 3H), 2.9 (s, 2H), 2.95 (s, 2H), 3.3 (s, 3H), 3.8 (q, *J* 7.0 Hz, 2H) (Found: C, 43.41; H, 6.22; S, 16.58. Calc. for $C_7H_{12}O_4S$: C, 43.74; H, 6.29; S, 16.67%).

Methyl 3-oxohex-4-enoate. IR ($CHCl_3$; cm^{-1}) 2990, 1710, 1440, 1270, 1140; ^1H NMR (200 MHz; $CDCl_3$) δ 2.13 (d, *J* 0.4 Hz, 3H) 3.8 (s, 3H), 4.75 (s, 2H), 5.95 (d, *J* 14.6 Hz, 1H), 7.1 (m, 1H) (Found: C, 53.19; H, 6.43. Calc. for $C_7H_{10}O_4$: C, 53.16; H, 6.37%).

Methyl 3-oxo-5-phenylpent-4-enoate. IR ($CHCl_3$; cm^{-1}) 2990, 1700, 1610, 1420, 1295, 1150; ^1H NMR (200 MHz; $CDCl_3$) δ 3.8 (s, 3H), 4.8 (s, 2H), 6.55 (d, *J* 16.2 Hz, 1H), 7.40 (m, 3H), 7.55 (m, 2H), 7.8 (d, *J* 16.2 Hz, 1H); MS (*m*/*z*, % rel. intensity) 220 (M^+, 2), 189 (3), 131 (5), 113 (100), 91 (82), 77 (13). (Found: C, 65.25; H, 5.46. Calc. for $C_{12}H_{12}O_4$: C, 65.45; H, 5.49%).

Methyl 3-oxo-4-phenylhexanoate. IR (neat; cm^{-1}) 2920, 1730, 1480, 1370, 1140; ^1H NMR (200 MHz; $CDCl_3$) δ 0.95 (t, *J* 7.3 Hz, 3H), 1.85 (m, 1H), 2.2 (m, 1H), 3.6 (t, *J* 7.3 Hz, 1H), 3.7 (s, 3H), 4.6 (d, *J* 15.8 Hz, 2H), 7.3 (m, 5H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 11.62, 26.42, 51.62, 52.70, 60.39, 126.94, 127.73, 128.20, 138.24, 167.74, 172.96; MS (*m*/*z*, % rel. intensity) 236 (M^+, 6), 205 (2), 146 (29), 119 (56), 104 (5), 91 (100), 85 (6), 77 (9), 65 (5), 57 (16) (Found: C, 66.13; H, 6.79. Calc. for $C_{13}H_{16}O_4$: C, 66.08; H, 6.82%).

Methyl ethoxyacetate. IR (neat; cm^{-1}) 2980, 1720, 1220, 1140, 1030; ^1H NMR (200 MHz; $CDCl_3$) δ 1.05 (t, *J* 5.4 Hz, 3H), 3.8 (s, 3H), 4.05 (q, *J* 5.4 Hz, 2H), 4.65 (s, 2H).

Methyl butoxyacetate. IR (neat; cm^{-1}) 2980, 1720, 1395, 1240, 1130, 1005; ^1H NMR (200 MHz; $CDCl_3$) δ 0.9 (t, *J* 5.4 Hz, 3H), 1.45 (m, 2H), 1.6 (m, 2H), 3.85 (s, 3H), 4.0 (t, *J* 6 Hz, 2H), 4.65 (s, 2H).

Methyl benzyloxyacetate. IR (neat; cm^{-1}) 3000, 1720, 1595, 1240, 1110, 1040, 980; ^1H NMR (200 MHz; $CDCl_3$) δ 3.8 (s, 3H) 4.65 (s, 4H), 7.35 (m, 5H).

Acknowledgements

P. P. thanks CSIR (New Delhi) for a research fellowship. J. M. M. is thankful to the Director, NCL, for permission to carry out work at NCL.

References

1 P. Laszlo, (*a*) *Pure Appl. Chem.*, 1990, **62**, 2027; (*b*) *Science*, 1987, **235**, 1473; (*c*) A. Corma, *Chem. Rev.*, 1997, **97**, 2373.
2 (*a*) D. F. Taber, *Comprehensive Organic Synthesis*, ed. G. Pattenden, Pergamon Press, Oxford, 1991, 1045; (*b*) D. F. Taber and S.-E. Stiriba, *Chem. Eur. J.*, 1998, **4**, 990.
3 S. Benetti and R. Romagnoli, *Chem. Rev.*, 1995, **95**, 1065.
4 V. H. Fernandez, L. F. J. Herrera and G. C. Perez, *Carbohydr. Res.*, 1983, **124**, 333.
5 C. R. Holmquist and E. J. Roskamp, *J. Org. Chem.*, 1989, **54**, 3258.
6 D. D. Dhavale, P. N. Patil and R. S. Mali, *J. Chem. Res.* (*S*), 1994, 152.
7 W. Wierenga and H. I. Skulnick, *J. Org. Chem.*, 1979, **44**, 310.
8 (*a*) S. G. Sudrik, B. S. Balaji, A. P. Singh, R. B. Mitra and H. R. Sonawane, *Synlett*, 1996, 369; (*b*) B. S. Balaji and B. M. Chanda, *Tetrahedron*, 1998, **54**, 13237.
9 C. J. Moody, C. J. Pearson and P. Teyssie, *Tetrahedron Lett.*, 1985, **26**, 3171.
10 R. W. Ratcliffe, T. N. Salzmann and B. G. Christensen, *Tetrahedron Lett.*, 1980, **21**, 31.
11 S. Yamamoto, K. Itani, H. Takahashi, T. Tsuji and W. Nagata, *Tetrahedron Lett.*, 1984, **25**, 4545.
12 K. Iwai, M. Kawai, H. Kosugi and H. Vda, *Chem. Lett.*, 1974, 385.
13 A. Ferrante, A. Poulos, C. J. Easton, M. J. Pitt, T. A. Robertson and D. A. Rathjen, Int. Pat. WO96/11908 (*Chem. Abstr.*, 1996, **125**, 58194).
14 A. Saegusa, Y. Ito, S. Kobayashi, K. Hirota and T. Shimizu, *J. Org. Chem.*, 1968, **33**, 544.

15 (*a*) B. M. Trost, W. P. Conway, P. E. Strege and T. J. Dietsche, *J. Am. Chem. Soc.*, 1974, **96**, 7165; (*b*) B. M. Trost and K. K. Leung, *Tetrahedron Lett.*, 1975, 4197.
16 A. P. Marchand and N. M. Brockway, *Chem. Rev.*, 1974, **74**, 431.
17 E. Muller and A. Freytag, *J. Prakt. Chem.*, 1931, **146**, 56.
18 (*a*) R. Paulissen, H. Reimlinger, E. Hayez, A. J. Hubert and P. Teyssie, *Tetrahedron Lett.*, 1973, 2233; (*b*) A. F. Noels, A. Demonceau, N. Petiniot, A. J. Hubert and P. Teyssie, *Tetrahedron*, 1982, **38**, 2733.
19 R. Paulissen, E. Hayez, A. J. Hubert and P. Teyssie, *Tetrahedron Lett.*, 1974, 607.
20 M. J. Pitt, C. J. Easton, C. J. Moody, A. Ferrante, A. Poulos and D. A. Rathjen, *Synthesis*, 1977, 1240.
21 F. Simal, A. Demonceau and A. F. Noels, *Tetrahedron Lett.*, 1999, **40**, 63.
22 T. Shinada, T. Kawakami, H. Sakai, I. Takada and Y. Ohfune, *Tetrahedron Lett.*, 1998, **39**, 3757.

Paper 9/05028K