Regioselective Transesterifications of Cyclohexanone Derivatives Containing β-Keto and Malonic Ester Moieties

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The cyclohexanone derivatives **1–6** containing β-ketoester and α-disubstituted malonic ester moieties in the same molecule were found to undergo regioselective transesterifications with benzyl alcohol giving exclusively β-keto benzyl esters. On the contrary, the acyclic derivatives **9, 10** containing β-ketoester and α-monosubstituted malonic ester groups gave mixtures of transesterified products under the same reaction conditions.

INTRODUCTION

Some previously published work from our laboratory described the synthesis of 4,5,6,7-tetrahydro-3-hydroxy-1H-indazole-5,5-dicarboxylic acid (HIDA),[1] which in the form of disodium salt was found to efficiently reduce the *cis*-diamminedichloroplatinum (*cis*-DDP) induced nephrotoxic effects.[2] In search for novel analogues of HIDA, the cyclohexanone precursors **1–7** containing the β-keto ester and malonic diethyl ester **1, 6** and **7**, cyano ethyl ester **2** or amide ethyl ester **3** moieties within the same structure have been prepared. Further transformations on precursors **1**, **6** or **7** required ester hydrolysis which was found to be accompanied by some extent of malonic acid decarboxylation. To overcome this problem we decided to investigate the transesterifications of such cyclohexane derivatives with benzyl alcohol. This would allow the transformation of formed benzyl ester derivatives to free acids by mild Pd/C catalysed hydrogenolysis in neutral conditions. It is well known that β-keto esters and malonic esters behave differently from simple carboxylic esters in transesterification reactions. Bader *at al*.[3] have
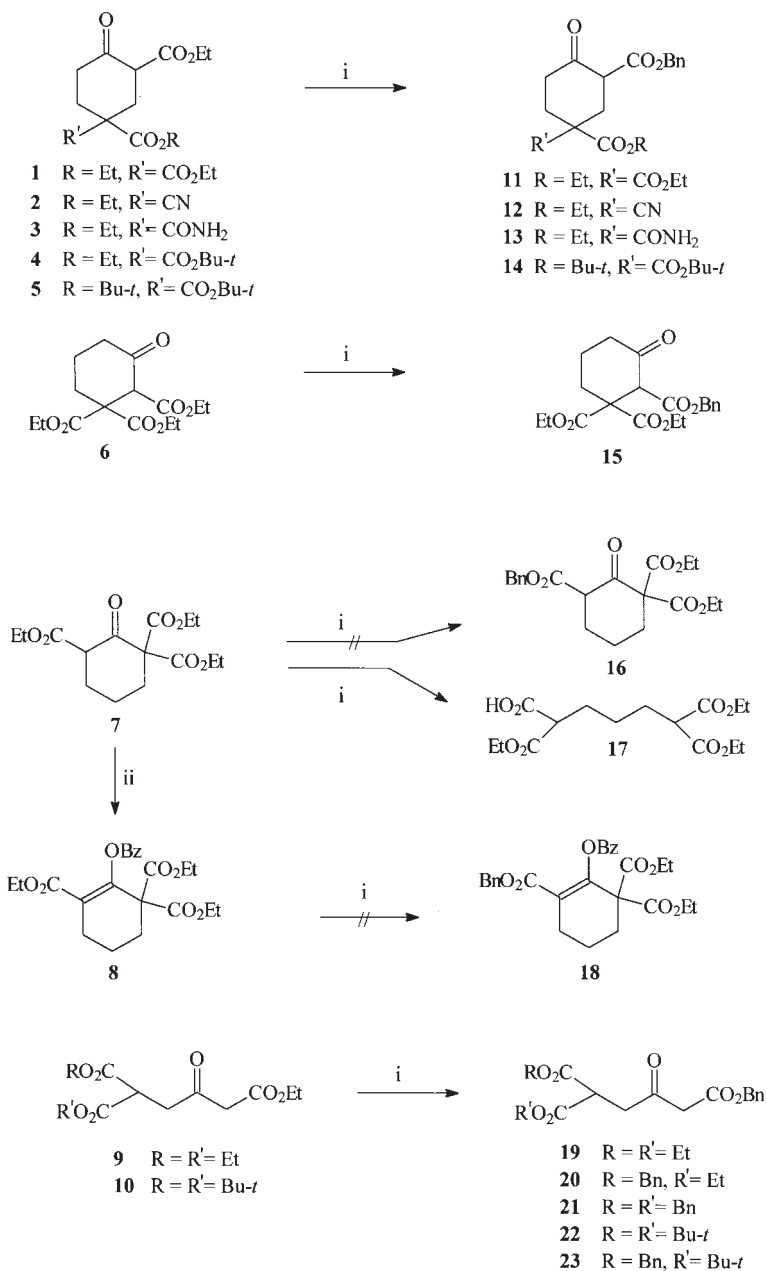
found that β-keto esters could be transesterified in the absence of catalyst. However, the pronounced catalytic effect of DMAP was found in transesterification of acetoacetate with primary and secondary alcohols.[4] Therefore, the precursors **1–7** have been subjected to transesterifications by benzyl alcohol under noncatalytic and catalytic (DMAP,[4] imidazole[5]) conditions in toluene by using molecular sieves.[6] For cyclohexanone derivatives **1–6** we have found that transesterifications under both conditions were highly regioselective, giving β-keto benzyl esters as exclusive products.

RESULTS AND DISCUSSION

The transesterifications of **1–7** as well as those of acyclic β-keto malonic ester derivatives **9**, **10** performed for comparison have been carried out by refluxing of the ester (1.0 mmol) and benzyl alcohol (**a:** 1.2 mmol; **b:** 3.6 mmol or **c:** 9.0 mmol) in toluene (30 ml) for 24 hours. The reactions were performed in the absence (**A**) or in the presence of the catalyst: DMAP (**B**) or imidazole (**C**). The molecular sieves 4 Å have been used to absorb the leaving ethanol. The formed transesterification products were separated by preparative tlc except in the case of **9**, for which the product composition was obtained from the ^{1}H NMR spectrum of the product mixture.

In the case of cyclohexanone derivatives **1–6**, the transesterifications, both in the presence and absence of the catalysts, gave exclusively β-keto benzyl ester products **11–15**, leaving the malonic ethyl ester groups unchanged. The regioselectivity is retained despite the molar excess of benzyl alcohol (entries 2, 3). It should be also noted that the yields of transbenzylated esters are not influenced by the presence of varying amounts of the catalysts (entries 4–7). The recent mechanistic explanation of acyclic β-keto ester (acetoacetate) transesterification postulates the formation of acetylketene intermediate.[7]

The results obtained with cyclic β-keto ester derivatives **1–6**, can be interpreted in accordance with this mechanism. It was shown that the reaction of *tert*-butyl acetoacetate is about 15 times faster compared to corresponding esters with primary alcohols due to facile thermal transformation of *tert*-butyl acetoacetate into acetylketene.[7] In accordance to this, the tlc monitoring of the reaction of *tert*-butyl triester **5** with benzyl alcohol revealed the disappearance of **5** after 1 hour and formation of **14** in 94% yield. In contrast, the transesterifications of **1–4** and **6** take 18–30 hours until the starting ester could not be detected by tlc. The attempted transesterification of the regioisomer **7** resulted with the opening of the cyclohexanone ring, giving 2,6,6-triethoxycarbonylhexanoic acid (**17**) as the major product. The benzoyl enolester **8** was found to be unreactive under transesterification conditions with benzyl alcohol. This result points to the importance of β-keto form for transesterification reaction which is capable to form the re-

1   R = Et, R′= CO₂Et
2   R = Et, R′= CN
3   R = Et, R′= CONH₂
4   R = Et, R′= CO₂Bu-t
5   R = Bu-t, R′= CO₂Bu-t

11 R = Et, R′= CO₂Et
12 R = Et, R′= CN
13 R = Et, R′= CONH₂
14 R = Bu-t, R′= CO₂Bu-t

6

15

7

16

17

8

18

9   R = R′= Et
10   R = R′= Bu-t

19   R = R′= Et
20   R = Bn, R′= Et
21   R = R′= Bn
22   R = R′= Bu-t
23   R = Bn, R′= Bu-t

Reagents: i) BnOH, (with / without imidazole or DMAP as catalyst), 4 Å molecular
sieves, toluene, Δ; ii) BzCl, pyridine

Scheme 1.

active acylketene intermediate at variance to **8** which can not be transformed to such intermediate. In contrast to efficient transesterification of β-keto ester moiety in cyclohexanone derivatives **1–6,** the malonic ester **1, 4** and **5**, or malonic mononitrile **2** or malonic monoamide **3** fragments remain unchanged under all applied transesterification conditions. This could be explained by the absence of α-hydrogen in malonic ester moiety so that a ketene intermediate could not be formed.

TABLE I

Yields (%) on transesterification of **1–4** and **9**, **10** (1.0 mmol) with benzyl alcohol

		Products, %									
Entry	*React. cond.*	**11**	**12**	**13**	**14**[a]	**(14)**[b]	**19**	**20**	**21**	**22**	**23**	**21**
1	**Aa**	87	92	–	84	–	80			80	3	5
2	**Ab**	86	91	–	–	(96)	70	16		73	8	7
3	**Ac**	89	94	91		–	49	35	4[f]	67	15	8
4	**BbI**	87	94[c]	–	81	(83)	70	20		65	11	6
5	**BcI**	85	–	92[d]		–	46	40	5[f]	39	29	19
6	**CbI**	86	82[c]	–	87	(70)	74	21		26	23	10
7	**CcII**	83	–	91[e]		–	46	40	5f	21	28	19

Reactione conditions: **A:** absence of catalyst; **B:** imidazole: **C**; DMAP; Catalyst: **I**: 0,2 mmol: **II**: 0.6 mmol: benzyl alcohol: **a**. 1.2 mmol; **b**: 3.6 mmol; **c**: 9.0 mmol; [a] from **4**; [b] from **5**; [c] heating for 4 days; [d] heating for 30 h; [f] heating for 2 days).

To check this assumption, the transesterifications of acyclic derivatives **9**, **10** containing the β-keto ester and the α-monosubstituted malonic ester fragments were performed. The results collected in Table I show that the transesterifications are less regioselective compared to cyclohexanone derivatives **1–6**. Depending on the reaction conditions, various amounts of mono-, di- and tribenzylated products resulting from simultaneous alcoholyses at β-keto and malonic ester moieties could be obtained. While for triethyl ester **9** no significant influence of the catalyst present could be observed, the results with di-*tert*-butyl derivative **10** show considerable differences in product distribution in the presence of both imidazole and DMAP. Tribenzylated product **21** could be prepared from **22** in refluxing xylene (**BII**, 18 mmol benzyl alcohol). Under the same conditions, **19** gave the mixture of di- and tribenzylated products, which again, points to higher reactivity of malonic *tert*-butyl esters toward transesterification compared to malonic ethyl esters.

The presented results show that the transesterifications with benzyl alcohol of cyclohexanone derivatives **1–6** containing β-keto ester and α-disu-

bstituted malonic ethyl ester **1** and **6**, *tert*-butyl ester **4**, mononitrile ethyl ester **2** or monoamide ethyl ester **3** moieties in the same molecule could be performed regioselectively at β-keto ester moiety. This method may be of synthetic interest due to possibility of subsequent selective transformations of mixed β-keto benzyl ester and malonic ethyl ester cyclohexanone derivatives due to possible hydrogenolytic cleavage of benzyl esters.

EXPERIMENTAL

Melting points (uncorrected) were determined on a Kofler hot-stage apparatus. ^{1}H and ^{13}C NMR spectra (in CDCl$_3$) were recorded on either a JOEL FX 90Q (90/22.5 MHz) or Varian Gemini 300 (300/75 MHz); IR spectra were recorded in KBr pallets on a Perkin-Elmer 297 spectrometer.

Preparation of β-keto tricarboxylates. The compounds **1**,[8] **2**,[9a] **3**,[9b] **6**,[9c] **9**[9d] *and* **10**[9d] *have been prepared as were described previously.*

1,1-Di-t-*butyl, 3-ethyl 4-oxocyclohexane-1,1,3-tricarboxylate (**4**)*

Prepared by the Dieckmann condensation[8a] from di-*t*-butyl malonate and ethyl acrylate with *t*-BuOK/*t*-BuOH, 58%; oily product which crystalized upon standing at 0 °C, mp 60–62 °C; IR (film) v_{max}/cm^{-1}: 1745, 1723, 1659, 1651, 1613; ^{1}H NMR (CDCl$_3$) δ/ppm: 12.23 (s, OH$_{enol}$), 4.23 (q, 2H, J=7.1, CH$_{2(OEt)}$), 2.67 (s, 2H, H$_2$(C-2)), 2.34 (t, 2H, *J*=6.6, H$_2$(C-5)), 2.11 (t, 2H *J*=6.6, H$_2$(C-6)), 1.46 (s, 18H, CH$_{3(OBu-t)}$), 1.32 (t, 3H, *J*=7.1, CH$_{3(OEt)}$); ^{13}C NMR (CDCl$_3$) δ/ppm: 172.0, 170.3, 170.0 (CO$_{esters}$ and C-4), 95.2 (C-3), 81.2 (C$_{OBu-t}$), 60.1 (CH$_{2(OEt)}$), 53.7 (C-1), 27.5 (CH$_{3(OBu-t)}$), 27.5, 26.3, 25,8 (C-2, C-5 and C-6), 13.9 (CH$_{3(OEt)}$).

Anal. Calcd. for C$_{19}$H$_{30}$O$_7$ (M_r = 370.43): C 61.60, H 8.16%; found: C 61.40, H 8.14%.

Tri-t-*butyl 4-oxocyclohexane-1,1,3-tricarboxylate (**5**)*

Prepared by the Dieckmann condensation[8a] from di-*t*-butyl malonate and *t*-butyl acrylate with *t*-BuOK/*t*-BuOH, 62%, mp 92–94 °C (light petroleum); IR (KBr) v_{max}/cm^{-1}: 1750, 1736, 1728, 1672, 1626; ^{1}H NMR (CDCl$_3$) δ/ppm: 12.07 (s, OH$_{enol}$), 2.62 (s, 2H, H$_2$(C-2)), 2.32 (t, 2H, *J*=6.6, H$_2$(C-5)), 2.09 (t, 2H, *J*=6.6, H$_2$(C-6)), 1.51, 1.45 (2s, 27H, CH$_{3(OBu-t)}$); ^{13}C NMR (CDCl$_3$) δ/ppm: 171.9, 170.2, 169.7, (CO$_{esters}$ and C-4), 96.2 (C-3), 81.1 (C$_{OBu-t}$), 53.9 (C-1), 37.6, 33.2, 30.8 (C-2, C-5 and C-6), 28.0, 27.5 (CH$_{3(OBu-t)}$).

Anal. Calcd. for C$_{21}$H$_{34}$O$_7$ (M_r = 393.48): C 63.29, H 8.60%; found: C 63.47, H 8.68%.

*Triethyl 2-oxocyclohexane-1,1,3-tricarboxylate (**7**)*

To the solution of diethyl 2-oxocyclohexane-1,3-dicarboxylate (0.954 g, 3.938 mmol) in dry THF (27 mL), 50% NaH (0.189 g, 3.937 mmol) was added at 0 °C. The reaction mixture was stirred for 10 min., 1.6 M BuLi (2.46 mL, 3.936 mmol) was added and the stirring continued for additional 10 min. Ethyl chloroformate (0.375 mL, 3.922 mmol) was added and the mixture stirred for 10 min at 0 °C and 30 min

at room temperature. The reaction was quenched by aq. NH_4Cl and extracted with EtOAc. The organic layer was washed with water, dried (Na_2SO_4) and evaporated. The purification of the croude product by preparative tlc gave 1.051g of **7** (84.9%), oil, R_f 0.23 (Et_2O-light petroleum, 1:3); IR (film) v_{max}/cm^{-1}: 1738, 1622, 1243; ^{1}H NMR ($CDCl_3$) v/ppm: 12.4 (s, OH_{enol}), 4.41–4.17 (m, 6H, $CH_{2(OEt)}$), 3.79 (dd, J=6.4, J=12.7, H_{keto}(C-3)), 2.68–1.5 (m, H_2(C-4), H_2(C-5) and H_2(C-6)), 1.35–1.25 (m, 9H, $CH_{3(OEt)}$); ^{13}C NMR ($CDCl_3$) δ/ppm: 197.7 ($C-2_{keto}$), 171.8, 168.3, 168.0, 166.8, 165.9, 164.4 (CO_{esters} and $C-2_{enol}$), 99.3 ($C-3_{enol}$), 69.2 ($C-1_{keto}$), 61.6, 61.4, 61.2, 60.2, 60.1 ($CH_{2(OEt)}$), 59.9 ($C-1_{enol}$), 55.2 ($C-3_{keto}$), 32.9, 29.0, 19.0 ($C-4_{enol}$, $C-5_{enol}$ and $C-6_{enol}$), 29.7, 21.5, 16.1 ($C-4_{keto}$, $C-5_{keto}$ and $C-6_{keto}$), 13.3, 13.1 and 13.0 ($CH_{3(OEt)}$).

Anal. Calcd. for $C_{15}H_{22}O_7$ (M_r=314.33): C 57.31, H 7.06%; found: C 57.50, H 7.26%.

Triethyl 4-benzoyloxy-2-cyclohexene-1,1,3-tricarboxylate (8)

Prepared from **7** (0.423 mmol) and benzoyl chloride (0.563 mmol) in pyridine (1 mL).[9c] Yield: 80%, oil; IR (film) v_{max}/cm^{-1}: 1750, 1737, 1650, 1604, 1588 ; ^{1}H NMR ($CDCl_3$) δ/ppm: 8.15–8.00 (m, 2H, H_{arom}), 7.65–7.34 (m, 3H, H_{arom}), 4.186, 4.175, 4.05 (3q, 6H, $3J$=7.0, $CH_{2(OEt)}$), 2.59 (t, 2H, J=6.1, H_2(C-6)), 2.46–2.30 (m, 2H, H_2(C-3)), 1.92–1.63 (m, 2H, H_2(C-5)), 1.14, 1.00 (2t, 9H, $2J$=7.0, $CH_{3(OEt)}$); ^{13}C NMR ($CDCl_3$) δ/ppm: 168.3, 165.2, 162.9 (CO_{esters}), 145.8 (C-2), 133.0, 129.7, 129.4, 128.1 (C_{arom}), 122.7 (C-3), 61.8, 60.4 ($CH_{2(OEt)}$), 60.8 (C-1), 30.5, 25.4, 18.5 (C-4, C-5 and C-6), 13.4 ($CH_{3(OEt)}$).

Anal. Calcd. for $C_{22}H_{26}O_8$ (M_r= 418.43): C 63.15, H 6.26%; found: C 63.21, H 6.51%.

Transesterifications with benzyl alcohol.

General conditions : A solution of β-keto ester (1.0 mmol) and benzyl alcohol (**a:** 1.2 mmol; **b:** 3.6 mmol or **c:** 9.0 mmol) in toluene (30 mL) was heated at reflux for 24 h (or as specified in Table I). The reflux condenser was fitted onto reaction flask over the adapter containing 4 Å molecular sieves to ensure removal of EtOH formed during transesterification reaction. The reactions were performed in the absence (**A**) or in the presence of the catalyst: DMAP (**B**) or imidazole (**C**), **I**: 0.2 mmol or **II**: 0.6 mmol (Table I). The products were purified by preparative tlc.

3-Benzyl 1,1-diethyl 4-oxocyclohexane-1,1,3-tricarboxylate (11)

IR (film) v_{max}/cm^{-1}: 1725, 1658, 1615 br; ^{1}H NMR ($CDCl_3$) δ/ppm: 12.10 (s, 1H, OH_{enol}), 7.35 (s, 5H, H_{arom}), 5.22 (s, 2H, $CH_{2(OBn)}$), 4.18 (q, 4H, J=7.1, $2CH_{2(OEt)}$), 2.84 (s br, 2H, H_2(C-2)), 2.50–2.10 (m, 4H, H_2(C-5) and H_2(C-6)), 1.23 (t, 6H, J=7.1, $2CH_{3(OEt)}$); ^{13}C NMR ($CDCl_3$) δ/ppm: 171.2, 170.5, 170.3 (CO_{esters} and C-4), 135.6, 128.2, 127.8, 127.5 (C_{arom}), 94.7 (C-3), 65.6 ($CH_{2(OBn)}$), 61.2 ($CH_{2(OEt)}$), 52.6 (C-1), 27.5, 26.3, 25.8 (C-2, C-5 and C-6), 13.6 ($CH_{3(OEt)}$)

Anal. Calcd. for $C_{20}H_{24}O_7$ (M_r= 376.39): C 63.82, H 6.43%; found: C 63.80, H 6.38%.

3-Benzyl, 1-ethyl 1-ciano-4-oxocyclohexane-1,3-dicarboxylate (12)

IR (film) v_{max}/cm^{-1}: 2240, 1745, 1662, 1614; ^{1}H NMR ($CDCl_3$) δ/ppm: 12.24 (s, 1H, OH_{enol}), 7.36 (s, 5H, H_{arom}), 5.24, 5.18 (2d, 2H, $2J$=12.4, $CH_{2(OBn)}$), 4.28 (q, 4H, J=7.0, $CH_{2(OEt)}$), 2.94, 2.78 (2d, 2H, $2J$=16.4, H_2(C-2)), 2.83–2.05 (m, 4H, H_2(C-5) and H_2(C-6)), 1.32 (t, 3H, J=7.0, $CH_{3(OEt)}$); ^{13}C NMR ($CDCl_3$) δ/ppm: 171.0, 170.4, 168.0

(CO_{ester} and C-4), 135.3, 128.5, 128.4, 128.1 (C_{arom}), 118.3 (CN), 66.3 ($CH_{2(OBn)}$), 63.0 ($CH_{2(OEt)}$), 42.2 (C-1), 29.7, 27.8, 25.6 (C-2, C-5 and C-6), 13.6 ($CH_{3(OEt)}$).

Anal. Calcd. for $C_{18}H_{19}NO_5$ (M_r= 329.34): C 65.64, H 5.82, N 4.25%; found: C 65.42, H 5.60, N 4.31%.

3-Benzyl, 1-ethyl 1-carbamoyl-4-oxocyclohexane-1,3-dicarboxylate (*13*)

Mp 88–90 ºC (CH_2Cl_2-light petroleum). IR (film) v_{max}/cm^{-1}: 3460 br, 3350 br, 3195 br, 1726 br, 1692, 1679, 1669, 1607; ^{1}H NMR (CDCl$_3$) δ/ppm: 12.14 (s, 1H, OH$_{enol}$), 7.36 (s, 5H, H$_{arom}$), 6.55, 6.18 (2 br s, 2H, CONH$_2$), 5.22 (2s, 2H, CH$_{2(OBn)}$), 4.20 (q, 2H, J=7.0, CH$_{2(OEt)}$), 3.01, 2.71 (2d, 2H, 2J=16.1, H$_2$(C-2)), 2.76–190 (m, 4H, H$_2$(C-5) and H$_2$(C-6)), 1.23 (t, 3H, J=7.0, CH$_{3(OEt)}$); ^{13}C NMR (CDCl$_3$) δ/ppm: 172.7, 172.1, 171.5, 171.1 (CO$_{esters, amid}$ and C-4), 135.6, 128.5, 128.3, 128.2 (C$_{arom}$), 95.0 (C-3), 65.9 (CH$_{2(OBn)}$), 61.9 (CH$_{2(OEt)}$), 52.9 (C-1), 28.0, 26.5, 26.0 (C-2, C-5 and C-6), 13.6 (CH$_{3(OEt)}$).

Anal. Calcd. for $C_{18}H_{21}NO_6$ (M_r= 347.36): C 62.24, H 6.10, N 4.03%; found: C 62.28, H 6.29, N 4.14%.

3-Benzyl, 1,1-di-t-butyl 4-oxocyclohexane-1,1,3-tricarboxylate (*14*)

IR (film) v_{max}/cm^{-1}: 1742, 1724, 1653, 1620; ^{1}H NMR (CDCl$_3$) δ/ppm: 12.07 (s, OH$_{enol}$), 7.27 (s, 5H, H$_{arom}$), 5.10 (s, 2H, CH$_{2(OBn)}$), 2.20 (s, 2H, H$_2$(C-2)), 1.95 (t, 2H, J=6.6, H$_2$(C-5)), 1.95 (t, 2H, J=6.6, H$_2$(C-6)), 1.36 (s, 18H, CH$_{3(OBu--t)}$); ^{13}C NMR (CDCl$_3$) δ/ppm: 171.7, 170.9, 170.0 (CO$_{esters}$), 135.9, 128.4, 128.0, 127.8 (C$_{arom}$), 95.1 (C-3), 81.3 (C$_{OBu-t}$), 65.7 (CH$_{2(OBn)}$), 37.6, 33.3, 30.8 (C-2, C-5 and C-6), 27.5 (CH$_{3(OBu-t)}$).

Anal. Calcd. for $C_{24}H_{32}O_7$ (M_r= 432.50): C 66.65, H 7.46%; found: C 66.43, H 7.44%.

2-Benzyl, 1,2-diethyl 3-oxocyclohexane-1,1,2-tricarboxylate (*15*)

Yield: 82% (**Aa**). IR (film) v/cm^{-1}: 1735, 1647, 1612; ^{1}H NMR (CDCl$_3$) δ/ppm: 12.91 (s br,OH$_{enol}$), 7.33 (s, 5H, H$_{arom}$), 3.97, 3.93 (2q, 4H, 2J=7.1, CH$_{2(OEt)}$), 2.38 (t, 2h, J=6.5, H$_2$(C-2)), 2.30–2.20 (m, 2H, H$_2$(C-6)), 1.75–1.63 (m, 2H, H$_2$(C-5)), 1.08 (t, 6H, J=7.1, CH$_{3(OEt)}$); ^{13}C NMR (CDCl$_3$) δ/ppm: 174.8, 171.9, 171.3 169.6, 168.6, 167.3(CO$_{esters(keto,enol)}$ and C-3$_{enol}$), 135.2, 128.5, 128.4, 128.2 (C$_{arom}$), 67.3 (CH$_{2(OBn)-keto}$), 66.3 (CH$_{2(OBn)-enol}$), 62.1, 61.8 (CH$_{2(OEt)-keto}$), 62.3 (CH$_{2(OEt)-enol}$), 60.0 (C-2$_{keto}$), 58.9 (C-1$_{keto}$), 55.6 (C-1$_{enol}$), 38.5, 27.2, 20.5 (C-4$_{keto}$, C-5$_{keto}$ and C-6$_{keto}$), 32.0, 28.9, 18.4 (C-4$_{enol}$, C-5$_{enol}$ and C-6$_{enol}$), 13.9, 13.6 (CH$_{3(OEt)}$).

Anal. Calcd. for $C_{20}H_{24}O_7$ (M_r = 376.39): C 63.82, H 6.43%; found: C 63.97, H 6.16%.

6-Benzyl, 1-ethyl 2-ethoxycarbonyl-4-oxohexane-1,6-dioate (*19*)

IR (film) v_{max}/cm^{-1}: 1725 br; ^{1}H NMR (CDCl$_3$) δ/ppm: 7.34 (s, 5H, H$_{arom}$), 5.16 (s, 2H, CH$_{2(OBn)}$), 4.18 (q, 4H, J=7.0, 2CH$_{2(OEt)}$), 3.87 (t, 1H, J=7.0, H(C-2)), 3.55 (s, 2H, H$_2$(C-5)), 3.15 (d, 2H, J=7.0, H$_2$(C-3)), 1.25 (t, 6H, J=7.0, 2CH$_{3(OEt)}$); ^{13}C NMR (CDCl$_3$) δ/ppm: 198.8 (C-4), 168.0, 166.0 (CO$_{esters}$), 135.1, 128.2, 127.9 (C$_{arom}$), 66.8 (CH$_{2(OBn)}$), 61.8 (CH$_{2(OEt)}$), 48.6 (C-5), 46.7 (C-2), 41.0 (C-3), 13.6 (CH$_{3(OEt)}$).

Anal.Calcd. for $C_{18}H_{22}O_7$ (M_r = 350.36): C 61.70, H 6.33%; found: C 61.63, H 6.20%.

*1,6-Dibenzyl 2-benzyloxycarbonyl-4-oxohexane-1,6-dioate (**21**)*

IR (film) ν_{max}/cm^{-1}: 1730 br; ^{1}H NMR (CDCl$_3$) δ/ppm: 7.31–7.25 (m, 15H, H$_{arom}$), 5.13, 5.11 (2s, 6H, CH$_{2(OBn)}$), 4.00 (t, 1H, J=7.1, H(C-2)), 3.50 (s, 2H, H$_2$(C-5)), 3.17 (d, 2H, J=7.1, H$_2$(C-3)); ^{13}C NMR (CDCl$_3$) δ/ppm: 199.2 (C-4), 168.1, 166.4 (CO$_{esters}$), 135.1, 135.0, 128.5, 128.4, 128.3, 128.2, 128.0 (C$_{arom}$), 67.3, 67.0 (CH$_{2(OBn)}$), 48.6 (C-5), 46.2 (C-2), 41.0 (C-3).

Anal. Calcd. for C$_{28}$H$_{26}$O$_7$ (M_r = 474.49): C 70.87, H 5.52%; found: C 70.78, H 5.78%.

*1,2-Di-t-butyl 6-benzyloxycarbonyl-4-oxohexane-1,6-dioate (**22**)*

IR (film) ν_{max}/cm^{-1}: 1740 br; ^{1}H NMR (CDCl$_3$) δ/ppm: 7.35 (s, 5H, H$_{arom}$), 5.17 (s, 2H, CH$_{2(OBn)}$), 3.70 (t, 1H, J=7.1, H(C-2)), 3.56 (s, 2H, H$_2$(C-5)), 3.05 (d, 2H, J=7.1, H$_2$(C-3)), 1.45 (s, 19H, CH$_{3(OBu-t)}$); ^{13}C NMR (CDCl$_3$) δ/ppm: 199.6 (C-4), 167.8, 166.6 (CO$_{esters}$), 135.2, 128.5, 128.3, 128.25 (C$_{arom}$), 81.8 (C$_{(OBu-t)}$), 67.0 (CH$_{2(OBn)}$), 48.9 (C-5), 48.8 (C-2), 41.2 (C-3), 27.6 (CH$_{3(OBu-t)}$).

Anal. Calcd. for C$_{22}$H$_{30}$O$_7$ (M_r = 406.46): C 65.01, H 7.44%; found: C 65.04, H 7.57%.

*1,6-Dibenzyl 2-t-butyloxycarbonil-4-oxohexane-1,6-dioate (**23**)*

IR (film) ν_{max}/cm^{-1}: 1735 br, 1725 br; ^{1}H NMR (CDCl$_3$) δ/ppm: 7.32 (s, 10H, H$_{arom}$), 5.17, 5.10 (2d, 2H, 2J=12.2, CH$_{2(OBn)-1}$), 5.14 (s, 2H, CH$_{2(OBn)-6}$), 3.84 (t, 1H, J=7.2, H(C-2)), 3.51 (s, 2H, H$_2$(C-5)), 3.11 (d, 2H, J=7.2, H$_2$(C-3)), 1.36 (s, 9H, CH$_{3(OBu-t)}$); ^{13}C NMR (CDCl$_3$) δ/ppm: 199.3 (C-4), 168.5, 167.1, 166.4 (CO$_{esters}$), 135.16, 135.07, 128.31, 128.37, 128.14, 128.06 (C$_{arom}$), 82.1 (C$_{(OBu-t)}$), 66.8, 66.9 (CH$_{2(OBn)}$), 48.7 (C-5), 47.6 (C-2), 41.0 (C-3), 27.3 (CH$_{3(OBu-t)}$).

Anal. Calcd. for C$_{25}$H$_{28}$O$_7$ (M_r = 440.47): C 68.17, H 6.41%; found: C 68.41, H 6.51%.

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SAŽETAK

Regioselektivne transesterifikacije cikloheksanon derivata s β-keto i malonil ester podjedinicama

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Utvrđeno je da se cikloheksanon derivati **1**–**6**, koji sadrže β-keto ester i disupstituirane malonil ester podjedinice u istoj molekuli, regioselektivno transesterificiraju s benzil alkoholom dajući isključivo β-keto benzil estere. Suprotno tome, aciklički derivati **9**, **10** koji sadrže β-keto ester i monosupstituirane malonil esterske grupe daju pod istim reakcijskim uvjetima smjesu transesterificiranih produkata.