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Passerini Multi-Component Reaction of Indane-1,2,3-trione, Isocyanides and 2-Furancarboxylic Acid

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The Passerini reaction of indane-1,2,3-trione, isocyanides and 2-furancarboxylic acid proceed at room temperature and the related α-acyloxycarboxamides is synthesized in quantitative yield. The reactions are one-pot, single spot and the products were obtained without any purification.

Key Words: α-Acyloxycarboxamides, Indane-1,2,3-trione, Isocyanide, Multicomponent reaction, Passerini reaction, 2-Furancarboxylic acid.

INTRODUCTION

Multicomponent reactions, though fashionable these days, have in fact a long history. Indeed, many important reactions such as the Strecker amino acid synthesis[1], Hantsch dihydropyridine synthesis[2], the Biginelli dihydropyrimidine synthesis[3], Mannich reaction[4] and the isocyanide-based Passerini reactions[5] and Ugi four-component reactions[6], among others, are all multicomponent in nature. A multicomponent reaction (MCR) comprises reactions with more than two starting materials participating in the reaction and at the same time, the atoms of these adducts contribute the majority of the novel skeleton of the product. In spite of the significant contribution of MCRs to the state of the art of modern organic chemistry and their potential use in complex organic syntheses, little attention was paid to the development of novel MCRs in the second half of the 20th century. However, with the introduction of molecular biology and high-throughput biological screening, the demand on the number and the quality of compounds for drug discovery has increased enormously. By virtue of their inherent convergence and high productivity, together with their exploratory and complexity-generating power, MCRs have naturally become a rapidly evolving field of research and have attracted the attention of both academic and industrial scientists[7].

Among the known multicomponent reactions to date, the most valuable reactions are those based on isocyanides. Isocyanide-based multicomponent reactions (abbreviated to IMCRs by Ugi and Dömling) by virtue of their synthetic potential, their inherent atom efficiency, convergent nature, ease of implementation and the generation of molecular diversity, have attracted much attention because of the advantages that they offer to the field of combinatorial chemistry[8]. IMCRs are parti-cularly interesting because they are more versatile and diverse than the remaining MCRs. The chemistry of the isocyanides began in 1859 when Lieke had prepared allyl isocyanide as the first isocyanide[9]. Isocyanide based multicomponent reactions have been around for 90 years, with the first described in 1921 and named after its founder, Passerini[5]. In 1921, Passerini pioneered the use of isocyanides and successfully developed a three-component synthesis of α-acyloxycarboxamide by reaction of a carboxylic acid, an aldehyde and an isocyanide. Today most IMCR chemistry relates to the classical reactions of Passerini and Ugi. Indeed, the large number of different scaffolds now available mostly builds on these two IMCRs and their combination with other types of reactions[10-14]. Passerini reactions involve an oxo component, an isocyanide and a nucleophile. Ugi reactions are defined as the reaction of a Schiff base or an enamine with a nucleophile and an isocyanide, followed by a (mumm) rearrangement reaction. The Passerini reactions are beginning to find utility in the drug discovery process and total syntheses of biologically relevant natural products[15]. In connection with our recent interest to multicomponent reactions[16-29], we report the Passerini multicomponent reaction between, indane-1,2,3-trione (**1**), isocyanides (**2**) and 2-furan carboxylic acid (**3**) in this article.

EXPERIMENTAL

Starting materials and solvents were obtained from Merck (Germany) and Fluka (Switzerland) and were used without

further purification. Melting points were measured on an electrothermal 9100 apparatus and are uncorrected. IR spectra were measured on a Jasco FT-IR 6300 spectrometer. ^{1}H and ^{13}C NMR spectra were measured ($CDCl_3$ solution) with a Bruker DRX-250 AVANCE spectrometer at 250.0 and 62.5 MHz, respectively. Mass spectra were recorded on a Finnigan-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. Elemental analyses were performed using a Heraeus CHN-O-rapid analyzer. The results agreed favourably with the calculated values.

General procedure: To a magnetically stirred solution of indane-1,2,3-trione (**1**) (0.2 mmol) and 2-furancarboxylic acid (**3**) (0.2 mmol) in dry CH_2Cl_2 (5 mL) was added dropwise a solution of isocyanides (**2**) (0.2 mmol) in CH_2Cl_2 (2 mL) at room temperature over 10 min. The mixture was stirred for 1 to 2 h for **4a-c** and 72 h for **4d** at room temperature. The solvent was removed under reduced pressure and pure products (**4a-d**) were obtained. The characterization data of the compounds are given below.

2-[(Cyclohexylamino)carbonyl]-1,3-dioxo-2,3-dihydro-1*H*-inden-2-yl 2-furoate (4a): White powder, yield 94 %, m.p. 164.0-165.2 ºC, IR cm^{-1} 3387 (NH), 2933, 2856, 1726, 1667, 1523, 1307; ^{1}H NMR (250 MHz, $CDCl_3$) 1.28-1.95 (m, 10H, 5CH_2 of cyclohexyl), 3.73 (m, 1H, N-CH), 6.66 (d, J = 6.75 Hz, 1H, NH), 6.57-6.59 and 7.24-8.07 (m, 7H, arom CH); ^{13}C NMR (62.5 MHz, $CDCl_3$) 24.60, 25.34, 32.56 (CH_2 of cyclohexyl), 48.98 (NCH), 83.71 (C-O), 112.67, 121.29, 124.09, 136.10, 141.59, 141.84, 147.83 (aromatic carbons), 155.10 (CO of ester), 161.24 (CO of amide), 191.26 (CO of ketone); MS: m/e (%) 381 (M^+, 6 %), 283 ([M- RNH]$^+$, 2), 269 (3), 187 (7), 104 (4), 95 ([C_4H_3OCO]$^+$, 100), 83 ([C_6H_{11}]$^+$, 6), 67 (3), 55 (8), 41 (6); anal. calcd for $C_{21}H_{19}NO_6$ (381.38): C, 66.13; H, 5.02; N, 3.67. found: C, 66.02; H, 5.08; N, 3.60.

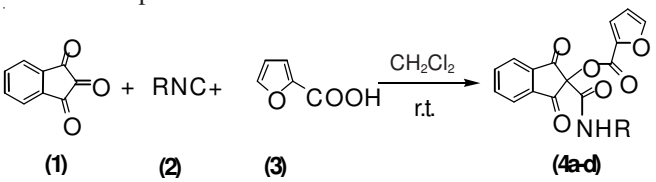
2-[(tert-butylamino)carbonyl]-1,3-dioxo-2,3-dihydro-1*H*-inden-2-yl 2- furoate 4b: White powder, yield 95 %, m.p. 174.5-176.0 ºC (dec), IR cm^{-1} 3391 (NH), 3127, 2977, 1724, 1676, 1530, 1310; ^{1}H NMR (250 MHz, $CDCl_3$,) 1.39 (s, 9H, *t*-Bu), 6.63 (s, 1H, NH), 6.57-6.59 and 7.26-8.07 (m, 7H, arom CH); ^{13}C NMR (62.5 MHz, $CDCl_3$) 28.49 (C*Me*$_3$), 52.61 (N-C); 83.66 (C-O), 112.66, 121.24, 124.07, 136.07, 141.72, 141.84, 147.82 (aromatic carbons), 154.98 (CO of ester), 161.33 (CO of amide), 191.49 (CO of ketone); MS: m/e (%) 355 (M^+, 3 %), 283 ([M- RNH]$^+$, 5), 187 (3), 104 (108), 95 ([C_4H_3OCO]$^+$, 100), 91 (12), 76 (6), 57 ([*t*-Bu]$^+$, 20), 43 (3), 41 (8); anal. calcd for $C_{19}H_{17}NO_6$ (355.34): C, 64.22; H, 4.82; N, 3.94. found: C, 64.13; H, 4.72; N, 3.99.

1,3-Dioxo-2-{[(1,1,3,3-tetramethylbutyl)amino]-carbonyl}-2,3-dihydro-1*H*-inden-2-yl 2-furoate 4c: White powder, yield 97 %, m.p. 163.7-165.5 ºC, IR cm^{-1} 3405 (NH), 2951, 1726, 1677, 1524, 1469, 1308, 1253; ^{1}H NMR (250 MHz, $CDCl_3$) 1.08 (s, 9H, C*Me*$_3$), 1.45 (s, 6H, C*Me*$_2$), 1.72 (s, 2H, CH_2), 6.75 (s, 1H, NH), 6.58-6.60 and 7.26-8.07 (m, 7H, arom CH); ^{13}C NMR (62.5 MHz, $CDCl_3$) 28.67 (2*Me*), 31.51 (C*Me*$_3$), 31.70 (*C*Me$_3$), 52.37 (CH_2), 56.57 (N-C), 83.80 (C-O), 112.67, 121.13, 124.04, 136.00, 141.72, 141.93, 147.66 (aromatic carbons), 155.03 (CO of ester), 160.93 (CO of amide), 191.41 (CO of ketone); MS: m/e (%) 412 (M^+ +1, 2 %), 341 (7), 340 (31), 299 (4), 284 (12), 283 ([M- RNH]$^+$, 62), 104 (8), 95 ([C_4H_3OCO]$^+$, 100), 76 (5), 57 ([*t*-Bu]$^+$, 28), 41 (8); anal. calcd for $C_{23}H_{25}NO_6$ (411.45): C, 67.14; H, 6.12; N, 3.40. found: C, 67.01, H, 6,19, N, 3.48.

2-[({[(4-methylphenyl)sulfonyl]methyl}amino)-carbonyl]-1,3-dioxo-2,3-dihydro-1*H*-inden-2-yl 2-furoate (4d): White powder, yield 92 %, m.p. 209.6-210.7 ºC (dec), IR cm^{-1} 3423 (NH), 3143, 2950, 1725, 1692, 1511, 1469, 1323; ^{1}H NMR (250 MHz, $CDCl_3$) 2.43 (s, 3H, CH_3), 4.69 (d, J = 6.75 Hz, 2H, NCH_2), 6.55 (br, 1H, NH), 6.58-8.07 (m, 11H, arom CH); ^{13}C NMR (62.5 MHz, $CDCl_3$) 21.71 (CH_3), 59.83 (NCH_2), 83.41 (C-O), 112.80, 121.86, 124.19, 128.95, 130.20, 132.84, 136.31, 141.11, 141.36, 145.54, 148.27 (aromatic carbons), 154.90 (CO of ester), 162.05 (CO of amide), 189.66 (CO of ketone); MS: m/e (%) 447 (26), 162 (15), 132 (16), 112 (27), 104 (42), 91 ([$C_6H_4CH_3$]$^+$, 55), 76 (42), 58 (100), 50 (28), 41 (17); anal. calcd. for $C_{23}H_{17}NO_8S$ (467.45): C, 59.10; H, 3.67; N, 3.00. found: C, 59.17; H, 3.73; N, 2.91.

RESULTS AND DISCUSSION

The indane-trione (**1**), isocyanides (**2**) and 2-furancarboxylic acid (**3**) in dichloromethane react together in a 1:1:1 ratio at room temperature to produce α-acyloxycarboxamides (**4a-d**) (**Scheme-I**). The reaction proceeds smoothly and cleanly under mild conditions and no side reactions were observed. The structures of the products were deduced from their IR, ^{1}H NMR, ^{13}C NMR and elemental analyses. The mass spectra of these compounds displayed molecular ion peaks at the appropriate m/z values. For example the ^{1}H NMR spectrum of **4a** exhibited distinct signals arising from cyclohexyl (δ_H = 1.28-1.95 ppm), NCH (3.73 ppm), NH (6.66 ppm) and aromatic CH (6.57-6.59 and 7.24-8.07). The ^{13}C NMR spectrum of **4a** showed 15 distinct resonances arising from CH_2 of cyclohexyl (24.60, 25.34, 32.56 ppm), NCH (48.98 ppm), C-O (83.71 ppm), aromatic carbons (112.67, 121.29, 124.09, 136.10, 141.59, 141.84, 147.83 ppm), CO of ester (155.10 ppm), CO of amide (161.24 ppm), CO of ketone (191.26 ppm). The IR spectrum showed an NH absorption at 3387 cm^{-1}.



Scheme-I: Passerini multicomponent reaction of indane-1,2,3-trione (Table-1)

TABLE-1
Synthesis of α-acyloxycarboxamides (**4a-d**) (see **Scheme-I**)

Products	R	Yield/(%)
4a	Cyclohexyl	94
4b	*t*-Bu	95
4c	1,1,3,3-tetramethylbutyl	97
4d	Tosylmethyl	92

Conclusion

It is suggested that the reported method offers a mild, simple, efficient and one-pot synthetic method for the preparation of sterically congested 2,2-disubstituted indane-1,3-dione derivatives from Passerini multicomponent reaction of

indane-1,2,3-trione. The reactions are single spot and the products were obtained in quantitative yield and without any purification. Its ease of work-up, high yields and mild reaction conditions make it a useful addition to modern synthetic methodologies. Other aspects of this process are under investigation.

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REFERENCES

1. A. Strecker, *Liebigs Ann. Chem.*, **75**, 27 (1850).
2. A. Hantzsch, *Ber.*, **14**, 1637 (1881).
3. P. Biginelli, *Gazz. Chim. Ital.*, **23**, 360 (1893).
4. C. Mannich and W. Krosche, *Arch. Pharm.*, **250**, 647 (1912).
5. (a) M. Passerini and L. Simone, *Gazz. Chim. Ital.*, **51**, 126 (1921). (b) M. Passerini, *Gazz. Chim. Ital.*, **51**, 181 (1921).
6. I. Ugi, R. Meyr, U. Fetzer and C. Steinbrückner, *Angew. Chem.*, **71**, 386 (1959).
7. J. Zhu and H. Bienaymé, Multicomponent Reactions, Wiley-VCH, Weinheim (2005).
8. (a) I. Ugi, B. Werner and A. Dömling, *Molecules*, **8**, 53 (2003). (b) I. Ugi, *Pure Appl. Chem.*, **73**, 187 (2001).
9. W. Lieke, *Justus Liebigs Ann. Chem.*, **112**, 316 (1859).
10. L. Banfi, G. Guanti, R. Riva, A. Basso and E. Calcagno, *Tetrahedron Lett.*, **43**, 4067 (2002).
11. A.R. Karimi, A.R. Khorrami, Z. Alimohammadi, A.A. Mohammadi and M.R. Mohammadizadeh, *Monatsh. Chem.*, **137**, 1079 (2006).
12. A.G. Neo, J. Delgado, C. Polo, S. Marcaccini and C.F. Marcos, *Tetrahedron Lett.*, **46**, 23 (2005).
13. S. Achatzb and A. Dömling, *Bioorg. Med. Chem. Lett.*, **16**, 6360 (2006).
14. P. Cristau, J.P. Vors and J. Zhu, *Tetrahedron Lett.*, **44**, 5575 (2003).
15. C. Hulme and V. Gore, *Curr. Med. Chem.*, **10**, 51 (2003).
16. A. Souldozi, K. Slepokura, T. Lis and A. Ramazani, *Z. Naturforsch.*, **62b**, 835 (2007).
17. A. Souldozi and A. Ramazani, *Tetrahedron Lett.*, **48**, 1549 (2007).
18. A. Souldozi, A. Ramazani, N. Bouslimani and R. Welter, *Tetrahedron Lett.*, **48**, 2617 (2007).
19. E. Ahmadi, A. Ramazani and M.N. Haghighi, *Tetrahedron Lett.*, **48**, 6954 (2007).
20. A.R. Kazemizadeh and A. Ramazani, *Arkivoc*, 159 (2008).
21. A.R. Kazemizadeh and A. Ramazani, *J. Braz. Chem. Soc.*, **20**, 309 (2009).
22. A. Ramazani, A.R. Kazemizadeh, E. Ahmadi, N. Noshiranzadeh and A. Souldozi, *Curr. Org. Chem.*, **12**, 59 (2008).
23. A. Ramazani, E. Ahmadi, A.R. Kazemizadeh, L. Dolatyari, N. Noshiranzadeh, I. Eskandari and A. Souldozi, *Phosphorus, Sulphur, Silicon Rel. Elem.*, **180**, 2419 (2005).
24. S.M. Shoaei, A.R. Kazemizadeh and A. Ramazani, *Chin. J. Struct. Chem.*, **30**, 568 (2011).
25. A. Ramazani, Y. Ahmadi and R. Tarasi, *Heteroatom Chem.*, **22**, 79 (2011).
26. A. Ramazani, N. Shajari, A. Mahyari and Y. Ahmadi, *Mol. Divers.*, **15**, 521 (2011).
27. A. Ramazani, A. Mahyari, H. Lashgari, K. Slepokura and T. Lis, *Helv. Chim. Acta*, **94**, 611 (2011).
28. A. Ramazani, M. Rohani, A. Rezaei, N. Shajari and A. Souldozi, *Helv. Chim. Acta*, **94**, 282 (2011).
29. A. Ramazani and A. Mahyari, *Helv. Chim. Acta*, **93**, 2203 (2010).